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American
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Association

PSYCHIATRIC NEWS

Inside

PERIODICALS:
TIME-SENSITIVE MATERIALS

Viewers Across the U.S. To Get 'Healthy Minds'

A unique collaboration between the American Psychiatric Foundation, APA's Office of Communications and Public Affairs, and public television leads to the national distribution of a television series on mental health.

BY MARK MORAN

A popular New York public television show on psychiatric topics is going national, with the help of the American Psychiatric Foundation.

"Healthy Minds" is a public television series produced by WLIW in New York, the nation's third largest public television station. And now, with the help of a $50,000 grant from the foundation, 16 of the shows will be distributed nationally to every public television station in the country.

Psychiatrists and foundation officials said that the show is the result of a remarkable synergy of interests shared by the foundation, APA's Office of Communications and Public Affairs, New York's public television production staff, and the public television audience. They also noted that "Healthy Minds" can be a major vehicle for educating the public about psychiatry and psychiatric illness and for promoting the projects of the foundation.

"My hope for the show is to encourage people who may have a psychiatric condition to seek help and not to suffer in silence," said the show's host, psychiatrist Jeffrey Borenstein, M.D. "I end each show by saying, 'With help, there is hope.'

"The other major goal is to reduce stigma by having a combination of experts in the field explaining, for instance, that schizophrenia is a brain disorder and what that means, and also showing real people living with these conditions," he told *Psychiatric News*. "I think the goal of educating the public fits in well with the mission of the foundation and also with the mission of public television. It's the right mix for collaboration."

Borenstein is CEO and medical director of Holliswood Hospital in New York, a deputy representative of the Queens County Psychiatric Society to the APA Assembly, and a member of the APA Committee on Public Affairs.

Credit: Aaron Levin

Jeffrey Borenstein, M.D., is host of "Healthy Minds," a public television program that is being distributed nationally through a grant from the American Psychiatric Foundation.

Richard Harding, M.D., president of the foundation, echoed those comments.

"The American Psychiatric Foundation is proud to be the charitable arm of APA and is deeply committed to our mission to be a public educator on selected mental health issues," Harding said in a statement. "We seek to serve people where they live, work, or learn with educational programs that are national in scope, but local in application. Our partnership, with PBS's affiliate WLIW-21 and the 'Healthy Minds' programs, offers the potential, on a national scale, to increase viewers' awareness of psychiatric conditions. Most importantly, it presents the opportunity to educate the public about mental health issues and to convey the message that help is available and treatment does work."

"Healthy Minds" was born three years ago when Borenstein approached the public television station in New York about producing a half-hour show on psychiatric topics. It quickly proved to be popular with viewers and critics alike, winning four Telly Awards in 2007. (According to the Telly Awards Web site, the awards "honor the very best local, regional, and cable television commercials and programs, as well as the finest video and film productions, and work created for the Web.")

And this year, the show won a Folio Award from the Fair Media Council.

So when Paul Burke, the founda-

please see ***Healthy Minds*** *on page 38*

Short, Intensive ADHD Treatments Are Not Long-Term Panacea

Although intensive medication management with or without behavioral intervention helps with symptoms and impairments, children with ADHD have a hard time catching up with their non-ADHD peers as they leave intensive treatment and become teenagers.

BY JUN YAN

Short-term, intensive treatments for children with attention-deficit/hyperactivity disorder (ADHD), whether medication management or behavioral interventions or the combination, may have immediate clinical benefits, but the benefits disappear over time as patients return to usual care in the community, new data from a long-term study show.

The Collaborative Multisite Multimodal Treatment Study of Children With ADHD, known as the MTA study, began in the 1990s and enrolled 579 children aged 7 to 9 diagnosed with combined-type ADHD. During the initial treatment phase, the study participants were randomized to one of four treatments for 14 months: medication management (primarily with methylphenidate), behavioral interventions, a combination of methylphenidate and behavioral interventions, and usual community care in which the majority of patients received medications from their physicians. After the 14 months of these

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Cardiac Risks Hold Up Approval Of Two Antipsychotics

FDA advisors remain skeptical about the safety of two antipsychotics for which regulatory approval is being sought and are especially troubled by potentially fatal cardiac risks.

BY JUN YAN

Despite positive efficacy data from placebo-controlled trials, experts on a Food and Drug Administration (FDA) psychopharmacology advisory committee have reservations about potentially dangerous adverse effects of two antipsychotic medications under regulatory review for approval.

The FDA held meetings in April to seek the committee's advice on whether sertindole, a second-generation antipsychotic (SGA), should be approved for the treatment of schizophrenia and prevention of suicide in schizophrenia patients, and whether quetiapine XR extended-release tablets should be approved for treating major depressive disorder (MDD) as a monotherapy and as an adjunctive therapy to an antidepressant and for treating generalized anxiety disorder (GAD) as a monotherapy.

Efficacy Demonstrated

At an April 7 meeting, the advisory committee voted unanimously that the efficacy of sertindole in treating schizophrenia was adequately demonstrated in the clinical trials. Lundbeck, the Danish company that developed sertindole, was also seeking approval for the indication that the drug reduces the risk of suicide attempts. This application was based on a randomized, open-label, controlled clinical trial in which sertindole was compared with risperidone. The committee, however, was not sufficiently convinced by the suicide data and voted 12-1 against approving the claim.

While sertindole is not marketed in the United States, it is not a new molecule. In the 1990s, it was approved for marketing by regulators in the United Kingdom and Europe and received approvable letters from the FDA. However, after signals of potentially life-threatening cardiac risks, including prolonged QT interval and arrhythmia, began to emerge in sertindole users, European regulators suspended the drug's marketing in 1999, and the new drug application in the United States was withdrawn.

The drug has mixed affinity for dopamine D_2, 5-HT_{2A}, 5-HT_6, and alpha$_1$ receptors, but does not bind to histamine H_1 receptors and does not have anticholinergic activity. Thus, it has demonstrated antipsychotic efficacy and is associated with lower risks of sedation and weight gain and is less likely to affect cognition than are some antipsychotics.

To address regulators' concerns about the drug's effect on the heart, Lundbeck conducted retrospective epidemiological studies and a prospective, randomized, unblinded trial, known as the Sertindole Cohort Prospective (SCoP) trial, in which sertindole was directly compared with risperidone. The results convinced European regulators to lift the ban, and the drug reentered the market in 2005. The drug is also available in Asia and Latin America. The FDA, however, remains worried about the drug's cardiac risks.

The SCoP trial enrolled nearly 10,000 patients. After taking either sertindole (n=4,930) or risperidone (n=4,928) for one year, there were 64 deaths in the sertindole group and 61 deaths in the risperidone group. This difference in all-cause mortality was not statistically significant.

However, the FDA reviewers told the advisory committee that cardiac-related deaths occurred in 31 sertindole-treated patients, compared with 12 risperidone-treated patients, based on the agency's analyses of data and case descriptions submitted by Lundbeck. This difference was statistically significant (p=0.0022), with a hazard ratio of 2.841 in the sertindole group. In addition, sudden cardiac deaths, defined as "a death that occurred within 24 hours of onset of symptoms and with no other obvious noncardiac cause" and judged by independent reviewers, occurred in 13 sertindole-treated patients and three risperidone-treated patients. The sertindole group had a nearly fivefold increased risk (hazard ratio 4.988, p=0.0121).

Sertindole has long been linked to prolonged QT interval, which is a risk factor for arrhythmia and sudden cardiac death. Clinical trial data showed that 10.6 percent of sertindole-treated patients experienced an increase of greater than 60 milliseconds, and 1.9 percent had an increase of more than 500 milliseconds in their QTc intervals.

Cardiac Events Hard to Predict

In addition, Lundbeck acknowledged that the occurrence of QT interval prolongation and cardiac events in sertindole users appeared to be difficult to predict, although FDA analysis suggested that the risk may be related to sertindole plasma concentration.

Primarily influenced by the cardiac risk,

please see ***Cardiac Risks*** *on page 43*

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On Having Been the President of APA

BY NADA STOTLAND, M.D., M.P.H.


Credit: David Hathcox

I knew for over a year that I was going to become the president of APA at 5 p.m. on a given Thursday in May 2008, but I was surprised by the impact of that moment. Probably finishing my term at 5 p.m. on a Thursday in May this year will be just as powerful. There are many things the APA president can't do: make APA policy, ensure that media statements about psychiatry are positive and accurate, please all the members of APA. The Board of Trustees has the legal responsibility for APA. The medical director/chief executive officer hires and administers the staff to carry out those decisions.

But the president of APA sets the agenda for the Board. The president should ensure that Board members have the information and discussion they need to make good decisions. The APA president receives and responds to hundreds of comments, requests, complaints, and suggestions from APA members and from outside friends and enemies of APA. The president speaks for APA with other organizations, with the media, and at hearings of Congress, the FDA, and other arms of government. As an APA member, I had been candid about my opinions. As the president of APA, I am not entitled to express personal opinions; I am bound by APA policy, and my statements are APA statements. There are also urgent situations that require carefully crafted strategy in the absence of specific APA policy. The attitudes and statements of the APA president carry weight with the APA staff, the membership, and the outside world. The president needs to make the right decisions and the right statements, promptly, for 365 days.

The APA president is received with great respect by colleagues all over the world. I have enjoyed representing you at the meetings of the Royal College of Psychiatrists in London; the Indian Psychiatric Association in Agra; and the World Psychiatric Association in Paris, Shanghai, Prague, and Florence and meeting you at local, state, and regional APA meetings from Seattle to New York and Texas to Minnesota.

I came into my presidential year determined to address our relationships with the pharmaceutical industry, reorganize our large and complex governance structure, increase efforts to serve the underserved, carry on our tradition of leadership on the social issues that impact mental health, highlight preventive psychiatry, strengthen our relationships with mental health advocacy groups and mental health and medical professionals, and not to be intimidated by our enemies. I wanted to use every opportunity to impress upon our government and the public the validity of our diagnoses and the effectiveness of our treatments. I wanted to make our members from every ethnic group, from every medical school, and from every subspecialty know how much we respect their contributions. I wanted APA to participate in health care reform and to prepare us for the psychiatry of five and 10 years from now. With the support of the members and our excellent staff, I was able to get many of these efforts in motion and complete some of them.

There were unexpected demands. Despite our leadership in addressing conflicts of interest and our careful preparations for the development of *DSM-V,* we suffered attacks on both in the past year. We responded with facts. We sent a 50-page report to Sen. Charles Grassley (R-Iowa) and the *New York Times*. I believe we are the first specialty society to put up a Web site offering our members and the public detailed information about the development of our diagnostic system and requesting feedback. Our decision to discontinue industry-supported symposia and meals at our meetings was reported in all the major media and was overwhelmingly well received by members, as was our decision to right-size our governance. Public opinion about psychiatry and psychiatrists is increasingly more informed and more positive.

I have been on call 24/7 for 365 days. It will be a relief not to feel responsible for APA, but it will also be a loss. I have loved traveling the country and the world for APA, and I have felt proud to defend our field and our Association. I have cherished the opportunity to listen and speak to you. It has been an extraordinary privilege to represent the members of APA, who have dedicated their knowledge, compassion, and wisdom to the relief of human suffering. Thank you. ■

NIDA Launches Screening Tools

The National Institute on Drug Abuse (NIDA) has unveiled its first comprehensive Physicians' Outreach Initiative, NIDAMED, which gives medical professionals tools and resources to screen their patients for tobacco, alcohol, illicit, and nonmedical prescription drug use. The resources include an online screening tool, a companion quick-reference guide, and a comprehensive resource guide for clinicians. The initiative stresses the importance of the doctor-patient relationship in identifying unhealthy behaviors before they evolve into life threatening conditions.

NIDAMED was launched in conjunction with NIDA's recently updated *Principles of Drug Abuse Treatment: A Research Based Guide*. This publication summarizes the 13 evidence-based principles of effective treatment, answers common questions, and describes types of treatment, providing examples of scientifically based and tested treatment components.

More information on all NIDAMED products and the guide is posted at <www.drugabuse.gov/nidamed>. ■

Economic Crisis Taking Toll On Americans' Mental Health

Fear of being laid off, distress over losing one's job, forgoing psychotropic medications because of cost—these are several examples of the mental health fallout from the current economic crisis.

BY JOAN AREHART-TREICHEL

Credit: AP Photo/Jim Cole

Thousands of unemployed residents in Manchester, N.H., wait for buses to take them to a job fair in April. It is a sign of how the current economic crisis is affecting the financial security of many Americans.

During a mid-week night recently, restaurants in the Dupont Circle area of Washington, D.C., were packed with young professionals. One would never have guessed from this lively, jovial crowd that America was experiencing a major economic crisis, perhaps the most seismic since the Great Depression.

But it was.

And still is.

And it's taking its toll not just on the pocketbooks of a number of Americans, but also on their mental health as well, psychiatrists in various areas of the United States report. In brief, not all Americans are as lighthearted as the young professionals observed that day in the nation's capital.

Probably the most common emotion that many Americans feel these days is anxiety, Hunter McQuistion, M.D., reported in an interview. McQuistion is director of outpatient and community psychiatry at St. Luke's and Roosevelt Hospitals in New York City and president of the American Association of Community Psychiatrists. And "with everybody sitting on the edge of their seats, it is [often] being manifested clinically," he said.

For example, one of his patients works in the financial industry and is going from week to week waiting for a pink slip. Another patient works as a paralegal for a law firm. The firm has already laid off dozens of lawyers, so he dreads that he will be next. McQuistion suspects that his patient's apprehension may be behind the abdominal discomfort he's been experiencing.

Rosalind Griffin, M.D., a Farmington Hills, Mich., psychiatrist, has observed something interesting in her practice in recent months, she said—an upswing in people seeking mental status evaluations for plastic surgery. This upswing mirrors people's fear of losing their jobs and their hope that a little "nip and tuck" will help them look younger and keep their jobs, she believes.

"The most stressed individuals from the economic downturn in my practice have been small-business owners," observed Charles Berlin, M.D., a private practitioner in Pittsburgh. "These individuals have been extremely worried about the survival of their businesses. At stake for them has been the very real issue of their economic livelihood, as well as much worry about their employees and their employees' families who depend on their business's health."

"Yes, absolutely, people are worried," Barbara Fitzgerald, M.D., an associate professor emeritus of psychiatry at the University of Louisville and past president of the Kentucky Psychiatric Medical Association, said. "They wonder, 'Am I going to have a job?' Or, if they are on disability, which many of our patients are, they wonder, 'Are the [government's] resources going to continue to be available to support me?' Especially in their health care, I would say."

Those Shrinking Investments

There is also widespread trepidation about shrinking investments, especially among people who are retired or near retirement, Berlin noted. "I started hearing frequently about these concerns [from my patients] several months ago. Most individuals expressed distress, but felt that there was little they could do about it, so mostly put it out of their mind. A number stopped opening investment statements."

Young Americans are skittish too, as Leigh White, M.D., who works in a student psychiatry service at Michigan State University and is president-elect of the Michigan Psychiatric Society, pointed out. "You probably know that the car industry in Michigan is in big trouble, and that the unemployment rate in Michigan is very high, quite a bit higher than the national average. . . .A lot of the students I am seeing now [are extremely stressed] because their parents are losing their jobs. . . .There are questions about whether they can continue in college."

The number of students visiting her service has also increased by a third or so since last year, White said. "This is very similar to what is happening nationally. Part of that may be good news in that some of the stigma about seeking mental health care is lifting. There are certainly a lot of public-service campaigns going on now, including APA's, which are trying to get college students to seek mental health care. But part of the increase in visits to our service may be due to students' anxieties about their particular economic situation."

Psychological Impact of Job Loss

Yet the angst that many Americans are experiencing because of the economic crisis may pale in comparison to the psychological devastation that many others are experiencing when they lose their jobs because of it.

Michael Engel, D.O., a psychiatrist in private practice in Traverse City, Mich., has a number of patients who have been especially hard hit by the economic crisis because of the near collapse of the automobile industry in his state. Some of those who have been laid off and have been unable to find other work are terrified that they are going to lose their homes to foreclosure or that they will have to declare bankruptcy, he said. Others have psychologically deteriorated to the point that they qualify for Social Security disability payments. "In some of these patients, a kind of hopelessness—you know, 'Is the sky falling?' or 'Will there be a tomorrow?'—weaves into their world," he observed. "In psychiatry, hopelessness is a very malignant symptom."

Indeed, depression and hopelessness stemming from loss of job, home, or income may play a part or be the trigger behind cases of suicide reported prominently in the news, Daniel Dahl, M.D., said. In addition to being an associate professor of psychiatry and psychiatry residency training director at the University of Alabama, he is presi-

Psychiatrists Impacted Too

Although psychiatrists are generally suffering much less from the economic crisis than many of their patients, it is nonetheless affecting them both psychologically and financially.

Some of the evidence that this is the case comes from a survey that APA conducted of its members in April about the impact of the current economic crisis on their patients, themselves, and their practices. Eight hundred-and-five members responded.

Said one: "I thought as a doctor I'd never have to worry about money. Wrong! Half of my retirement funds are gone. I have worked very intensely my whole career and was looking forward to a great retirement fairly soon."

Said a second: "I am losing money on seeing patients in the office. If it were not for a clinical trials practice and some speaking engagements, I would have gone bankrupt a while ago. . . . In addition, I have given up the thought of retirement."

A third reported: "My patients are more stressed, sicker, and crankier. That increases my stress and also my receptionists' stress."

And a fourth noted: "I am still extremely busy—working harder for less income. Yet I feel lucky to be working nonetheless. If this continues, however, there will be a point of diminishing returns in which my practice will fail."

Interviews that *Psychiatric News* conducted with members likewise illustrate how the economic crisis is impacting some of them.

"I see so many students. . . working long hours as well as carrying heavy academic loads," Leigh White, M.D., who works in a student psychiatry service at Michigan State University, told *Psychiatric News*. She finds their struggle disheartening, she said. Sometimes she is tempted to tell them, "Don't work so hard," but then she recalls, "They need their job to afford college, to afford medication, and to see me. It is sort of a Catch-22 situation."

"As an individual I am not, of course, any more immune to the recent economic forces than my patients are," Charles Berlin, M.D., a Pittsburgh psychiatrist in private practice, said during an interview. "I worry about my declining investments as I approach retirement as much as my patients worry about their own finances. That's given rise for me to need to pay particular attention to my own countertransference feelings when this topic comes up in the office."

"We have had a number of psychiatrists [leave the state], so it has significantly elevated my workload," Michael Engel, D.O., a psychiatrist in private practice in Traverse City, Mich., lamented. Also, "when patients fear that they are going to experience foreclosure or bankruptcy, that makes my life as a psychiatrist more stressful because I have more things to do to help them manage."

"I have been working half time for the state of California and have been furloughed for 10 percent of it," Robert Burchuk, M.D., of Woodland Hills, Calif., reported. Burchuk is also president-elect of the Southern California Psychiatric Society.

"We are on an inner-city urban campus, so we see a fair number of patients who don't have insurance or who have Medicaid," Daniel Dahl, M.D., an associate professor of psychiatry and psychiatry residency training director at the University of Alabama, said. "What would impact us would be substantial cuts in Medicaid. They would drastically affect the financial resources of our department. We hope we don't see those cuts, but there is that potential."

"Our state legislature has just made massive cuts in mental health funding," Howard Weeks, M.D., medical director of youth services at the University of Utah Neuropsychiatric Institute, commented. "That is going to have a very severe impact over the next year or two. . . for our outpatient services. . . as well as for reimbursement for providers."

Psychiatrists Are Helping Their Patients Get Care

In early April, APA surveyed its members about the impact of the current economic crisis on their patients and practices. A total of 805 members responded.

Although only 18 percent of respondents reported that the economic crisis was having a substantial impact on the mental health of their patients, 70 percent said that because of the crisis their patients were having to choose between psychiatric care and other basic needs.

Fifty-nine percent of respondents also said that they were taking steps to help such financially strapped patients get needed care (see chart). One method was reducing fees. Another was structuring flexible payment schedules. Still a third was referring them to alternative, less expensive sources of care. Interviews that *Psychiatric News* conducted with members illustrate some of the steps that they are taking in this regard.

"A lot of my job now is trying to help patients pay for things," said Leigh White, M.D., who works in a student psychiatry service at Michigan State University. "I try to stretch their visits to help them reduce costs."

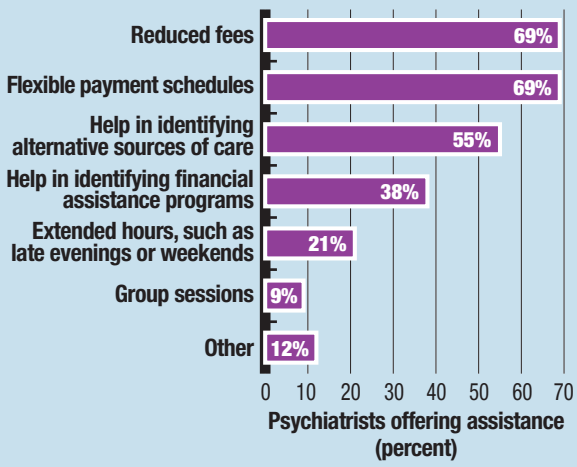
"I have had consultations that I have had to refer out because people have been concerned about how much money [a psychiatrist visit] is going to cost," reported Hunter McQuistion, M.D., director of outpatient and community psychiatry at St. Luke's and Roosevelt Hospitals in New York City.

"I encourage patients not to quit treatment, not to take a hiatus, so that they won't backslide or relapse," said Rosalind Griffin, M.D., a psychiatrist in private practice in Farmington Hills, Mich. "I tell them that I am willing to let them pay as they are able to. . . .[I also try to convince them that] talking about their inability to pay, their guilt, and their shame about being in debt is more therapeutic than staying away from therapy in order to not increase their debt. . . . They need their ego strength to get through this really critical period."

"I had one patient with bipolar disorder who was on an atypical antipsychotic," Daniel Dahl, M.D., an associate professor of psychiatry at the University of Alabama, said. "He had trouble affording his medication and stopped taking it. So we put him in the hospital, where he could afford it."

APA Members Take Steps To Ensure Access to Care

A survey of 805 APA members found that 59% are offering some kind of assistance to encourage members of the community to seek professional mental health services.



Source: APA membership survey, 2009

dent of the Alabama chapter of the American Foundation for Suicide Prevention.

Ironically, the economic crisis that has wrought such havoc with people's psyches is also jeopardizing their access to care (see article on page 22).

"There are more people struggling to keep their psychiatric appointments because of cost," said Howard Weeks, M.D., medical director of youth services at the University of Utah Neuropsychiatric Institute. "They are having more trouble filling prescriptions because of costs."

Dahl described a similar scenario: "Some patients are not coming in for visits because they cannot afford the copay. Others are not buying their medications for the same reason."

As many Americans have lost their jobs, they have also lost their health insurance, and as they have lost their health insurance, a number have turned to the public sector for help, Michele Reid, M.D., said. Reid is medical director of Michigan's largest community mental health program—the Detroit-Wayne County Community Mental Health Agency—and the representative of the Committee of Black Psychiatrists to the APA Board of Trustees. "Normally in times of economic downturn, more people qualify for Medicaid," she explained, "but an ongoing concern is that as we have more and more Medicaid beneficiaries choosing our services, we may be less able to serve people who are totally uninsured. . . ."

That concern is not limited to Michigan. "I was just in California doing a consultation with the medical directors of the county mental health programs," David Pollack, M.D., a professor of public policy at Oregon Health and Science University, told *Psychiatric News*. "They were describing how fairly stark the cuts in services for their patients have been. I'm sure that the same is true, maybe to a lesser degree, for many other states. For example, in some counties, all the case management and counseling services for patients with severe mental illness have been cut, so that they are receiving only psychotropic medications. In at least one county it is the other way around—they are getting case management but no psychotropic medications. . . . And in many places, services for people who are totally uninsured are being slashed or eliminated altogether."

Still other Americans who have lost their jobs and thus their health insurance are not even trying to seek refuge in the public safety net. And those who do may still have to cope with unintended, sometimes tragic, consequences. Take, for example, 57-year-old "Jim." After he lost his construction job, he could no longer afford health insurance, and once he

please see ***Economy*** *on page 12*

New Resource Educates Latinos About MH Issues

The bilingual *Mental Health: A Guide for Latinos and Their Families* comes with a companion DVD program. The two are being unveiled in San Francisco at APA's 2009 annual meeting.

BY STEPHANIE WHYCHE

It was about a year and a half ago that a producer of culturally sensitive consumer health education materials contacted APA's Annelle Primm, M.D., for help in developing a mental health education tool for Latino individuals.

Primm, director of APA's Office of Minority and National Affairs (OMNA), put the producer in contact with Andres Pumariega, M.D., chair of APA's Committee of Hispanic Psychiatrists.

"The rest is history," said Pumariega, speaking of the creation of a 59-page consumer health guide and 30-minute companion DVD designed for Latinos. The bilingual package is titled *Mental Health: A Guide for Latinos and Their Families—Salud Mental: Una Guia para Latinos y sus Familias.*

The guide and DVD were created to educate Latinos about mental illness in their own language and cultural context with the goal of reducing the stigma of mental illness, Pumariega told *Psychiatric News*. The guide and DVD will be distributed, free of charge, to Latino communities and others who seek it via APA and Latino service organizations.

Credit: Jose Ortega

This colorful illustration, created by the renowned Equador-born artist Jose Ortega, appears in *Mental Health: A Guide for Latinos and Their Families*.

Pumariega said he believes the guide and DVD package is the first of its kind in terms of national reach "directed toward the general public of a particular racial/ethnic/cultural group around mental illness." He said it is "also unique in that it combines printed and video psychoeducational material, both presented in a culturally appropriate context." Indeed, the guide bridges cultural and scientific understanding of mental illness and its treatment by addressing the unique cultural beliefs and attitudes about mental illness in Latino communities (see box).

Illustrating the cover and the inside pages of the guide are the whimsically abstract and colorful images of Ecuador-born artist Jose Ortega, now of Toronto and New York. It was the guide's designer, Cinda Debbink, of Design Partners in Kensington, Md., who reached out to the well-known artist. Ortega in turn provided the artistic images at a cost significantly below market value, said Carol Brandenburg, project manager/executive producer with Conrad Productions—"as a way to give back to the community."

The idea for the public service endeavor was the brainchild of Conrad and Associates LLC of Potomac, Md. Conrad and Associates reached out to APA to provide the psychiatric content and collaborated with the National Hispanic Medical Association and the League of United Latin American Citizens. Conrad then sought funding support for production of the video and guidebook and received it from Janssen, a division of Ortho-McNeil-Janssen Pharmaceuticals Inc.

APA's official seal on the cover of the guide "symbolizes APA's commitment to addressing the special mental health needs and disparities of our diverse populations in America" said Pumariega. Specifically,

Know Your Definitions

Mental health and illness are expressed in countless languages and intertwined with tradition, ritual, social mores, and culture.

It is noted in *Mental Health: A Guide for Latinos and Their Families* (see article above) that "some traditional Latino cultures view and describe mental illnesses in different ways from most doctors in the U.S." As a result, "[m]ore and more doctors are learning about different cultural views on mental illness."

Here excerpted from the guide are two examples of common words in the Latino culture used to describe different emotional ills:

Nervios (nerves) refers to a general sense of vulnerability and stress brought on by difficult events. Symptoms include headaches and "brain aches' irritability," stomach pains, sleep problems, nervousness, easy tearfulness, and *mareos* (dizziness or spells of lightheadedness). This is a very broad syndrome. It may be mild and temporary or very serious and long-lasting.

Sulston means "fright" or "soul loss." It is also known as *esparto, Pismo, tripe Ida, perdida del alma,* or *chibih*. It is an illness due to a frightening event that causes the soul to leave the body, resulting in unhappiness and sickness. Typical symptoms include changes in appetite, troubled sleep and dreams, headache and stomach aches, sadness, and lack of motivation.

American Journal of Psychiatry Wins Unique Honor

APA's flagship publication—the oldest, continuously printed medical specialty journal in the United States—is listed among the 100 most influential scientific publications of the past 100 years by the Special Libraries Association.

BY STEPHANIE WHYCHE

When it comes to imparting cutting-edge, peer-reviewed psychiatric research—and doing it in a clear and engaging manner—*The American Journal of Psychiatry (AJP)* keeps proving it stands above the rest of the pack.

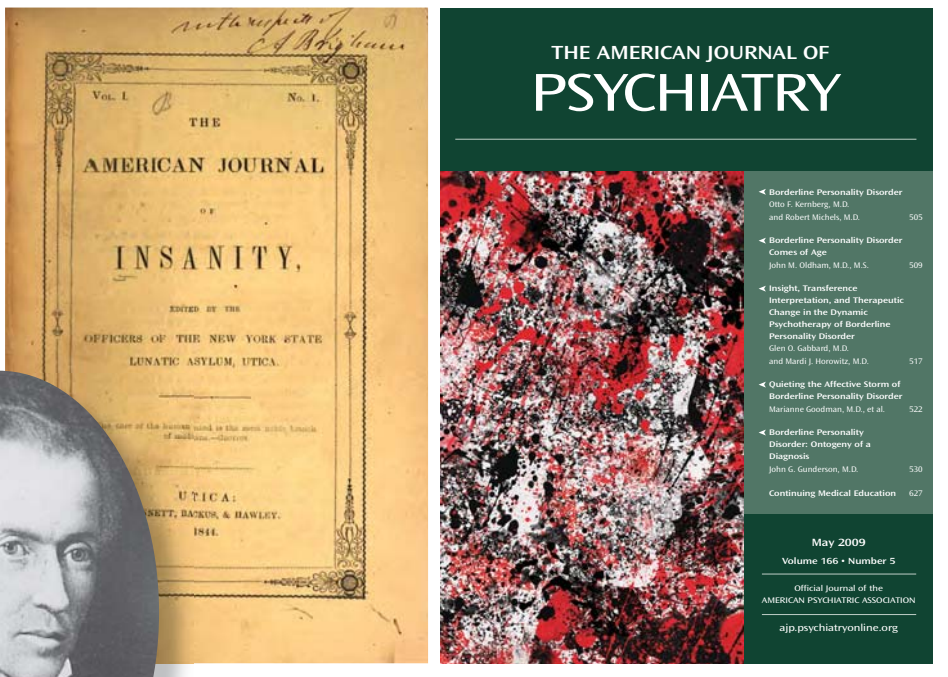
Published in 1844 under the title *The American Journal of Insanity*, *AJP* is the oldest continuously published medical specialty journal in the country, according to its editorial director, Michael Roy. Over time it has become the most cited publication in its field of psychiatry, Roy said.

Now comes news that the venerable journal has been cited with 99 other publications as one of the most influential scientific journals to be published over the past century.

According to a recent poll of 686 members of record of the Special Libraries Association's (SLA) Division of BioMedical and Life Sciences, *AJP* received more votes than any of the six other psychiatric medical journals reviewed by the division's members.

"The laurels and weight of 100 years are on our shoulders," the journal's editor in chief, Robert Freedman, M.D., told *Psychiatric News*.

The Special Libraries Association's Division of BioMedical and Life Sciences (DBIO) decided to conduct the poll as part of the library association's 100th anniversary. Division members who took the poll were asked to name the 100 most influential journals in biology and medicine over the last 100 years. The polling instrument was constructed by an international "panel of experienced DBIO members who worked at institutions with particularly notable biomedical and life sciences journal collections and clientele," according to a DBIO report of the process posted on the SLA Web site.



Amariah Brigham, M.D. (left), an APA founder, published the first psychiatric journal in the summer of 1844—*The American Journal of Insanity*. That journal, a 100-page quarterly, was the predecessor of *AJP*, which is published monthly. *AJP* was recognized as the most influential psychiatric publication by an international scientific library association.

and no less important, he added, is the fact that APA's Committee of Hispanic Psychiatrists and OMNA had the major involvement in the development of this project. That included the committeewide development, vetting, and editing of the guide's narrative content (including the Spanish translation) and the script featured in the DVD. The DVD features Pumariega along with Ana Campo, M.D., past chair of APA's Committee of Hispanic Psychiatrists.

"The committee thoroughly reviewed the rough cuts of the video and the rough drafts of the guide to ensure scientific accuracy and cultural appropriateness," Pumariega said. "It involved very active exchanges about these issues with the producer, and the product reflects the careful thought that went into its development and implementation, right down to the visuals and music."

The committee also developed a dissemination plan in which copies of the guide and DVD will be distributed to APA members, district branches, national medical and Latino organizations, and community clinics and organizations serving Latinos.

"We hope," Pumariega noted, "that the guide will open doors of understanding about mental illness and help reduce the stigma of mental illness among Latinos—not only consumers and family members, but Latino health professionals and the public at large.

"The largest disparity that we Latinos face around mental health is lack of access to early treatment, often waiting for treatable conditions to grow into acute crises. We want to facilitate Latinos to self-identify mental health needs, seek effective treatment early, and advocate for evidence-based, culturally competent treatment for themselves and their families."

APA's premiere of the DVD program is scheduled for APA's annual meeting in San Francisco on May 19 at 4:30 p.m. at the Marriott San Francisco Hotel, Golden Gate Hall, Salon C1, Level B2. ■

molecular and cellular biology, and natural history.

"When one considers the vast number of journals out there—even with an entity limiting the number of possible options from which to choose—it would be considered an honor just to make that list of available options," Roy told *Psychiatric News*. "There are over 35,000 journals listed in PubMed and the molecular biology databases of the National Center for Biotechnology Information. This is why the top 100 is a big deal."

On June 16 the Special Libraries Association will name the top 10 most influential journals—across all categories—from the top 100 already named. Then, from the top 10 journals, the library association will bestow the ultimate honor: naming the single most influential "Journal of the Centennial."

Both announcements will be made that day at the Special Libraries Association's Centennial Conference in Washington, D.C., at an awards ceremony featuring a roll call of all 100 winners and their publishers.

A list of the top 100 most influential scientific journals is posted at <http://units.sla.org/division/dbio/publications/resources/dbio100.html>. Information about the polling methodology and participants is posted at <http://units.sla.org/division/dbio/publications/resources/DBIO100.pdf?>. ■

Most With Mental Illness Meet Voting Competency Criteria

The instrument used to assess voting capacity in this cohort may be useful in cases in which an individual's voting capacity is called into question.

BY MARK MORAN

People with serious mental illness appear to be capable of voting in elections and understanding the value and importance of their vote, according to a small study using a measurement tool that can be used when a person's capacity to vote is called into question.

That was the finding from an assessment of capacity to vote of 52 community-dwelling people with serious mental illness, using the Competency Assessment Tool for Voting (CAT-V). This instrument operationalizes the criteria for capacity to vote established in a 2001 federal court decision. That standard, known now as "the *Doe* standard," is based on a person's ability to understand the nature and effect of voting.

The study appeared in the May *Psychiatric Services*.

"Overwhelmingly, a group of community-dwelling outpatients with serious and chronic mental illness did very well when it came to their capacity to understand the nature and effect of voting and to make a choice about candidates in an election, which is the legal standard on which the study was based," said study author and past APA President Paul Appelbaum, M.D.

The CAT-V was developed by Appelbaum and colleagues Richard Bonnie, J.D., and Jason Karlawish, M.D., for a 2005 study of the capacity to vote of people with Alzheimer's that appeared in the November 2005 *American Journal of Psychiatry*.

The criteria used in the CAT-V are based on those established in a 2001 federal district court decision in Maine, *Doe v. Rowe*, which struck down a provision in Maine's constitution that denied voting to people under guardianship because of mental disabilities. In that decision, the Maine court ruled that persons are considered incompetent to vote only if they "lack the capacity to understand the nature and effect of voting such that they cannot make an individual choice."

Determining Capacity to Vote

Below is an excerpt from the Competency Assessment Tool for Voting (CAT-V) used to assess a person's capacity to vote. This section of the instrument specifically assesses comparative reasoning, ability to generate consequences, and appreciation of the effect of a choice on one's life. Following the excerpt is a guide for scoring.

Interviewer: "Let me ask you to imagine the following about the two candidates who are running. Candidate A thinks the state should be doing more to provide health insurance to people who don't have it and should be spending more money on schools. He is willing to raise taxes to get the money to do these things. Candidate B says the government should not provide health insurance but should make it easier for employers to offer it. He believes that the schools have enough money already but need tighter controls to make sure they use it properly. He is against raising taxes. Based on what I just told you, which candidate do you think you are more likely to vote for: A or B?"

Note to interviewer: If interviewee cannot choose a candidate or is vacillating, ask "If you had to make a choice based on the information you have before you, who would you pick?"

Score of 2: Clearly indicates choice.
Score of 1: Choice is ambiguous or vacillating. For example: "I think I might go for the guy who doesn't like taxes, but I'm not sure because schools are important too." Or "Candidate A, no candidate B, no Candidate A. . . . I can't decide."
Score of 0: No choice is stated. For example: "I don't know. I can never make up my mind."

In the study using the CAT-V, respondents were asked to imagine it is election day for the office of governor in their state and about the nature and effect of voting. They were then asked three questions related to the *Doe* standard, assessing ability to understand the nature of voting, ability to understand the effect of voting, and ability to make a choice.

There were three additional items assessing comparative reasoning, ability to generate consequences, and appreciation of the effect of a choice on one's life. Participants were read descriptions of two candidates and asked to choose one, and to compare the candidates and how choosing one would affect their lives; they were also asked why they would or would not want to vote in the next election for governor (see box for excerpt from the CAT-V).

Each question in the CAT-V is scored on a 3-point scale, with a score of 2 indicating adequate performance, a score of 1 indicating marginal performance, and a score of 0 indicating clearly inadequate performance.

The 52 participants took an average of 7.8 minutes to complete the entire interview. Ninety-two percent (47) scored either a 5 or 6—out of a total 6 possible points—on the three *Doe*-standard questions.

They performed equally well on the assessment of comparative reasoning, but had more difficulty describing the impact of their choices on their own lives, with 77 percent scoring the high score of 2 on the question assessing ability to generate consequences. Moreover, the results did not correlate with cognitive function, intelligence, or severity of symptoms.

"Many decisional tasks correlate with cognitive function, intelligence, and severity of symptoms," Appelbaum explained. "That this wasn't the case in this study suggests that at least within the range of impairments found in a seriously mentally ill outpatient sample, the tasks associated with voting are simple enough that most people are likely to be competent to vote. Had we found a correlation, that might have identified a subset of patients—for instance, those who are more symptomatic or have more cognitive problems—about whom there might be greater concern.

"The bottom line is that standards for competence to vote are not—and should not be—demanding, and hence within the usual range of impairments found in a population with serious mental illnesses, incompetence to vote will be rare," he said.

Appelbaum explained that most states have constitutional or statutory provisions defining who can and cannot vote, and many of these are archaic, denying voting rights to "idiots" or "insane persons." These provisions are largely neglected, but the issue has risen to the surface from time to time in certain high-profile cases, as when officials in Rhode Island tried to restrict the voting rights of two people who had been ruled not guilty of a crime by reason of insanity.

In Missouri a constitutional provision restricting voting by persons under guardianship for mental disabilities was upheld in court because it was interpreted as requiring individualized assessments of capacity to vote.

Appelbaum added that challenges to an individual's right to vote may be more common in local elections, whose outcomes are often close.

He cautioned that the CAT-V, or any similar instrument, should not be used as a routine screening tool, but may be useful in individual cases in which a person's right to vote is being challenged.

"We have to be leery of efforts to use this instrument for wide-scale screening of people with mental illness," he told *Psychiatric News*. "The Americans With Disabilities Act, among other laws, and probably the Constitution protect the rights of people with mental illness from being treated differently from the rest of the population. We don't screen the general population for their capacity to vote, so in general we shouldn't be screening people with mental illness.

"The real utility of an instrument like this is when there are some substantive grounds on which to worry about or challenge a person's capacity to vote," he said. "When an individual decision needs to be made, that's where this might be useful."

"The Capacity to Vote of Persons With Serious Mental Illness" is posted at <http://ps.psychiatryonline.org> under the May issue. ■

Primary Care Doctors Report MH Referral Options Scarce

The rate of difficulty in obtaining outpatient care for psychiatric conditions among primary care patients was more than twice the rate found with three other common types of referrals.

BY RICH DALY

Two-thirds of 6,600 primary care physicians surveyed in 60 U.S. communities said they are unable to obtain outpatient mental health care for their patients, according to a report by researchers from the Center for Studying Health System Change (HSC) published in April's *Health Affairs*.

The researchers discovered that the mental health treatment difficulties occurred far more frequently than referrals to other types of health care services. They also found that mental health manpower and inadequate insurance coverage play a big role in the problem.

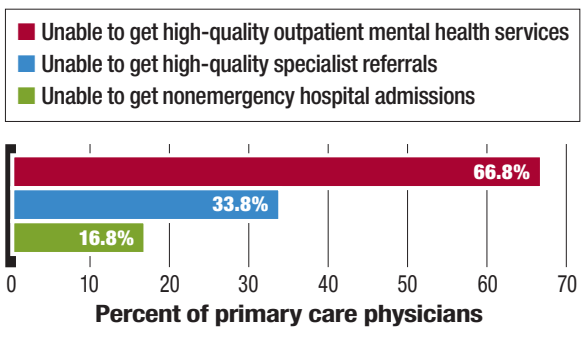
"From the perspective of primary care physicians, the study's findings suggest that lack of access to mental health services is a serious problem—much more serious than for other commonly used medical services," said Peter Cunningham, Ph.D., a senior fellow at the HSC and an author of the study, in a written statement.

Based on the survey, conducted in 2004 and 2005, Cunningham and his colleagues found that mental health referrals proved more elusive for the primary care physicians surveyed than other kinds of medical care referrals, including specialty non-mental health care. Specifically, the rate of difficulty in obtaining needed outpatient mental health care for patients was more than twice the rate reported for any of three other common referrals: other specialists, imaging services, and nonemergency hospital admissions. For example, almost 67 percent of the primary care physicians reported that they couldn't get mental health services for some of their patients, compared with 34 percent who reported other non-mental health specialist referral obstacles, 30 percent who

please see ***Referral*** *on page 22*

MH Outpatient Treatment Hardest to Get for Patients

Primary care physicians identified outpatient psychiatric care as the referral treatment they were most likely to have difficulty finding for their patients. A shortage of clinicians and insurance plan restrictions were among the leading sources of obstacles to specialized care.



Source: Community Tracking Study Physician Survey, 2004 to 2005, Robert Wood Johnson Foundation, 2009

Treat today with NAMENDA

Proven efficacy and tolerability

- Improves function, delays onset of behavioral symptoms, and provides benefits in cognition[1-3]
- Proven safety and tolerability with low risk of gastrointestinal side effects may lead to therapy persistence[4,5]
- Reduces caregiving time, cost, and caregiver distress[3,6,7]
- Effective first-line and in combination with an acetylcholinesterase inhibitor[1,2]

Broad patient access–covered on 98% of Medicare Part D formularies[4]

Namenda® memantine HCl

Extending memory and function

NAMENDA® (memantine HCl) is indicated for the treatment of moderate to severe Alzheimer's disease.

NAMENDA is contraindicated in patients with known hypersensitivity to memantine HCl or any excipients used in the formulation. The most common adverse events reported with NAMENDA vs placebo (≥5% and higher than placebo) were dizziness, confusion, headache, and constipation. In patients with severe renal impairment, the dosage should be reduced.

References: 1. Reisberg B, Doody R, Stöffler A, Schmitt F, Ferris S, Möbius HJ, for the Memantine Study Group. Memantine in moderate-to-severe Alzheimer's disease. *N Engl J Med.* 2003;348:1333-1341. **2.** Tariot PN, Farlow MR, Grossberg GT, Graham SM, McDonald S, Gergel I, for the Memantine Study Group. Memantine treatment in patients with moderate to severe Alzheimer disease already receiving donepezil: a randomized controlled trial. *JAMA.* 2004;291:317-324. **3.** Cummings JL, Schneider E, Tariot PN, Graham SM, for the Memantine MEM-MD-02 Study Group. Behavioral effects of memantine in Alzheimer disease patients receiving donepezil treatment. *Neurology.* 2006;67:57-63. **4.** Data on file. Forest Laboratories, Inc. **5.** NAMENDA® (memantine HCl) Prescribing Information. Forest Pharmaceuticals, Inc., St Louis, Mo. **6.** Wimo A, Winblad B, Stöffler A, Wirth Y, Möbius HJ. Resource utilisation and cost analysis of memantine in patients with moderate to severe Alzheimer's disease. *Pharmacoeconomics.* 2003;21:327-340. **7.** Winblad B, Poritis N. Memantine in severe dementia: results of the ³M-BEST Study (Benefit and efficacy in severely demented patients during treatment with memantine). *Int J Geriatr Psychiatry.* 1999;14:135-146.

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Please see brief summary of Prescribing Information on the adjacent page.

62-1014307R R2 03/09

Namenda
memantine HCl ®

Tablets/Oral Solution
Rx Only

Brief Summary of Prescribing Information.

For complete details, please see full Prescribing Information for Namenda.

INDICATIONS AND USAGE
Namenda (memantine hydrochloride) is indicated for the treatment of moderate to severe dementia of the Alzheimer's type.

CONTRAINDICATIONS
Namenda (memantine hydrochloride) is contraindicated in patients with known hypersensitivity to memantine hydrochloride or to any excipients used in the formulation.

PRECAUTIONS
Information for Patients and Caregivers: Caregivers should be instructed in the recommended administration (twice per day for doses above 5 mg) and dose escalation (minimum interval of one week between dose increases).

Neurological Conditions
Seizures: Namenda has not been systematically evaluated in patients with a seizure disorder. In clinical trials of Namenda, seizures occurred in 0.2% of patients treated with Namenda and 0.5% of patients treated with placebo.

Genitourinary Conditions
Conditions that raise urine pH may decrease the urinary elimination of memantine resulting in increased plasma levels of memantine.

Special Populations
Hepatic Impairment
Namenda undergoes partial hepatic metabolism, with about 48% of administered dose excreted in urine as unchanged drug or as the sum of parent drug and the N-glucuronide conjugate (74%). No dosage adjustment is needed in patients with mild or moderate hepatic impairment. Namenda should be administered with caution to patients with severe hepatic impairment.

Renal Impairment
No dosage adjustment is needed in patients with mild or moderate renal impairment. A dosage reduction is recommended in patients with severe renal impairment (see CLINICAL PHARMACOLOGY and DOSAGE AND ADMINISTRATION in Full Prescribing Information).

Drug-Drug Interactions
N-methyl-D-aspartate (NMDA) antagonists: The combined use of Namenda with other NMDA antagonists (amantadine, ketamine, and dextromethorphan) has not been systematically evaluated and such use should be approached with caution.

Effects of Namenda on substrates of microsomal enzymes: In vitro studies conducted with marker substrates of CYP450 enzymes (CYP1A2, -2A6, -2C9, -2D6, -2E1, -3A4) showed minimal inhibition of these enzymes by memantine. In addition, *in vitro* studies indicate that at concentrations exceeding those associated with efficacy, memantine does not induce the cytochrome P450 isoenzymes CYP1A2, CYP2C9, CYP2E1, and CYP3A4/5. No pharmacokinetic interactions with drugs metabolized by these enzymes are expected.

Effects of inhibitors and/or substrates of microsomal enzymes on Namenda: Memantine is predominantly renally eliminated, and drugs that are substrates and/or inhibitors of the CYP450 system are not expected to alter the metabolism of memantine.

Acetylcholinesterase (AChE) inhibitors: Coadministration of Namenda with the AChE inhibitor donepezil HCl did not affect the pharmacokinetics of either compound. In a 24-week controlled clinical study in patients with moderate to severe Alzheimer's disease, the adverse event profile observed with a combination of memantine and donepezil was similar to that of donepezil alone.

Drugs eliminated via renal mechanisms: Because memantine is eliminated in part by tubular secretion, coadministration of drugs that use the same renal cationic system including hydrochlorothiazide (HCTZ), triamterene (TA), metformin, cimetidine, ranitidine, quinidine, and nicotine, could potentially result in altered plasma levels of both agents. However, coadministration of Namenda and HCTZ/TA did not affect the bioavailability of either memantine or TA, and the bioavailability of HCTZ decreased by 20%. In addition, coadministration of memantine with the antihyperglycemic drug Glucovance® (glyburide and metformin HCl) did not affect the pharmacokinetics of memantine, metformin, and glyburide. Furthermore, memantine did not modify the serum glucose lowering effect of Glucovance®.

Drugs that make the urine alkaline: The clearance of memantine was reduced by about 80% under alkaline urine conditions at pH 8. Therefore, alterations of urine pH towards the alkaline condition may lead to an accumulation of the drug with a possible increase in adverse effects. Urine pH is altered by diet, drugs (e.g. carbonic anhydrase inhibitors, sodium bicarbonate), and clinical state of the patient (e.g. renal tubular acidosis or severe infections of the urinary tract). Hence, memantine should be used with caution under these conditions.

Carcinogenesis, Mutagenesis and Impairment of Fertility
There was no evidence of carcinogenicity in a 113-week oral study in mice at doses up to 40 mg/kg/day (10 times the maximum recommended human dose [MRHD] on a mg/m² basis). There was also no evidence of carcinogenicity in rats orally dosed at up to 40 mg/kg/day for 71 weeks followed by 20 mg/kg/day (20 and 10 times the MRHD on a mg/m² basis, respectively) through 128 weeks.

Memantine produced no evidence of genotoxic potential when evaluated in the *in vitro S. typhimurium* or *E. coli* reverse mutation assay, an *in vitro* chromosomal aberration test in human lymphocytes, an *in vivo* cytogenetics assay for chromosome damage in rats, and the *in vivo* mouse micronucleus assay. The results were equivocal in an *in vitro* gene mutation assay using Chinese hamster V79 cells.

No impairment of fertility or reproductive performance was seen in rats administered up to 18 mg/kg/day (9 times the MRHD on a mg/m² basis) orally from 14 days prior to mating through gestation and lactation in females, or for 60 days prior to mating in males.

Pregnancy
Pregnancy Category B: Memantine given orally to pregnant rats and pregnant rabbits during the period of organogenesis was not teratogenic up to the highest doses tested (18 mg/kg/day in rats and 30 mg/kg/day in rabbits, which are 9 and 30 times, respectively, the maximum recommended human dose [MRHD] on a mg/m² basis).

Slight maternal toxicity, decreased pup weights and an increased incidence of non-ossified cervical vertebrae were seen at an oral dose of 18 mg/kg/day in a study in which rats were given oral memantine beginning pre-mating and continuing through the postpartum period. Slight maternal toxicity and decreased pup weights were also seen at this dose in a study in which rats were treated from day 15 of gestation through the post-partum period. The no-effect dose for these effects was 6 mg/kg, which is 3 times the MRHD on a mg/m² basis.

There are no adequate and well-controlled studies of memantine in pregnant women. Memantine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers
It is not known whether memantine is excreted in human breast milk. Because many drugs are excreted in human milk, caution should be exercised when memantine is administered to a nursing mother.

Pediatric Use
There are no adequate and well-controlled trials documenting the safety and efficacy of memantine in any illness occurring in children.

ADVERSE REACTIONS
The experience described in this section derives from studies in patients with Alzheimer's disease and vascular dementia.

Adverse Events Leading to Discontinuation: In placebo-controlled trials in which dementia patients received doses of Namenda up to 20 mg/day, the likelihood of discontinuation because of an adverse event was the same in the Namenda group as in the placebo group. No individual adverse event was associated with the discontinuation of treatment in 1% or more of Namenda-treated patients and at a rate greater than placebo.

Adverse Events Reported in Controlled Trials: The reported adverse events in Namenda (memantine hydrochloride) trials reflect experience gained under closely monitored conditions in a highly selected patient population. In actual practice or in other clinical trials, these frequency estimates may not apply, as the conditions of use, reporting behavior and the types of patients treated may differ. Table 1 lists treatment-emergent signs and symptoms that were reported in at least 2% of patients in placebo-controlled dementia trials and for which the rate of occurrence was greater for patients treated with Namenda than for those treated with placebo. No adverse event occurred at a frequency of at least 5% and twice the placebo rate.

Table 1: Adverse Events Reported in Controlled Clinical Trials in at Least 2% of Patients Receiving Namenda and at a Higher Frequency than Placebo-treated Patients

Body System Adverse Event	Placebo (N = 922) %	Namenda (N = 940) %
Body as a Whole		
Fatigue	1	2
Pain	1	3
Cardiovascular System		
Hypertension	2	4
Central and Peripheral Nervous System		
Dizziness	5	7
Headache	3	6
Gastrointestinal System		
Constipation	3	5
Vomiting	2	3
Musculoskeletal System		
Back pain	2	3
Psychiatric Disorders		
Confusion	5	6
Somnolence	2	3
Hallucination	2	3
Respiratory System		
Coughing	3	4
Dyspnea	1	2

Other adverse events occurring with an incidence of at least 2% in Namenda-treated patients but at a greater or equal rate on placebo were agitation, fall, inflicted injury, urinary incontinence, diarrhea, bronchitis, insomnia, urinary tract infection, influenza-like symptoms, abnormal gait, depression, upper respiratory tract infection, anxiety, peripheral edema, nausea, anorexia, and arthralgia.

The overall profile of adverse events and the incidence rates for individual adverse events in the subpopulation of patients with moderate to severe Alzheimer's disease were not different from the profile and incidence rates described above for the overall dementia population.

Vital Sign Changes: Namenda and placebo groups were compared with respect to (1) mean change from baseline in vital signs (pulse, systolic blood pressure, diastolic blood pressure and weight) and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. There were no clinically important changes in vital signs in patients treated with Namenda. A comparison of supine and standing vital sign measures for Namenda and placebo in elderly normal subjects indicated that Namenda treatment is not associated with orthostatic changes.

Laboratory Changes: Namenda and placebo groups were compared with respect to (1) mean change from baseline in various serum chemistry, hematology, and urinalysis variables and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed no clinically important changes in laboratory test parameters associated with Namenda treatment.

ECG Changes: Namenda and placebo groups were compared with respect to (1) mean change from baseline in various ECG parameters and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed no clinically important changes in ECG parameters associated with Namenda treatment.

Other Adverse Events Observed During Clinical Trials
Namenda has been administered to approximately 1350 patients with dementia, of whom more than 1200 received the maximum recommended dose of 20 mg/day. Patients received Namenda treatment for periods of up to 884 days, with 862 patients receiving at least 24 weeks of treatment and 387 patients receiving 48 weeks or more of treatment.

Treatment emergent signs and symptoms that occurred during 8 controlled clinical trials and 4 open-label trials were recorded as adverse events by the clinical investigators using terminology of their own choosing. To provide an overall estimate of the proportion of individuals having similar types of events, the events were grouped into a smaller number of standardized categories using WHO terminology, and event frequencies were calculated across all studies.

All adverse events occurring in at least two patients are included, except for those already listed in Table 1, WHO terms too general to be informative, minor symptoms or events unlikely to be drug-caused, e.g., because they are common in the study population. Events are classified by body system and listed using the following definitions: frequent adverse events - those occurring in at least 1/100 patients; infrequent adverse events - those occurring in 1/100 to 1/1000 patients. These adverse events are not necessarily related to Namenda treatment and in most cases were observed at a similar frequency in placebo-treated patients in the controlled studies.

Body as a Whole: *Frequent:* syncope. *Infrequent:* hypothermia, allergic reaction.

Cardiovascular System: *Frequent:* cardiac failure. *Infrequent:* angina pectoris, bradycardia, myocardial infarction, thrombophlebitis, atrial fibrillation, hypotension, cardiac arrest, postural hypotension, pulmonary embolism, pulmonary edema.

Central and Peripheral Nervous System: *Frequent:* transient ischemic attack, cerebrovascular accident, vertigo, ataxia, hypokinesia. *Infrequent:* paresthesia, convulsions, extrapyramidal disorder, hypertonia, tremor, aphasia, hypoesthesia, abnormal coordination, hemiplegia, hyperkinesia, involuntary muscle contractions, stupor, cerebral hemorrhage, neuralgia, ptosis, neuropathy.

Gastrointestinal System: *Infrequent:* gastroenteritis, diverticulitis, gastrointestinal hemorrhage, melena, esophageal ulceration.

Hemic and Lymphatic Disorders: *Frequent:* anemia. *Infrequent:* leukopenia.

Metabolic and Nutritional Disorders: *Frequent:* increased alkaline phosphatase, decreased weight. *Infrequent:* dehydration, hyponatremia, aggravated diabetes mellitus.

Psychiatric Disorders: *Frequent:* aggressive reaction. *Infrequent:* delusion, personality disorder, emotional lability, nervousness, sleep disorder, libido increased, psychosis, amnesia, apathy, paranoic reaction, thinking abnormal, crying abnormal, appetite increased, paronia, delirium, depersonalization, necrosis, suicide attempt.

Respiratory System: *Frequent:* pneumonia. *Infrequent:* apnea, asthma, hemoptysis.

Skin and Appendages: *Frequent:* rash. *Infrequent:* skin ulceration, pruritus, cellulitis, eczema, dermatitis, erythematous rash, alopecia, urticaria.

Special Senses: *Frequent:* cataract, conjunctivitis. *Infrequent:* macula lutea degeneration, decreased visual acuity, decreased hearing, tinnitus, blepharitis, blurred vision, corneal opacity, glaucoma, conjunctival hemorrhage, eye pain, retinal hemorrhage, xerophthalmia, diplopia, abnormal lacrimation, myopia, retina detachment.

Urinary System: *Frequent:* frequent micturition. *Infrequent:* dysuria, hematuria, urinary retention.

Events Reported Subsequent to the Marketing of Namenda, both US and Ex-US
Although no causal relationship to memantine treatment has been found, the following adverse events have been reported to be temporally associated with memantine treatment and are not described elsewhere in labeling: aspiration pneumonia, asthenia, atrioventricular block, bone fracture, carpal tunnel syndrome, cerebral infarction, chest pain, cholelithiasis, claudication, colitis, deep venous thrombosis, depressed level of consciousness (including loss of consciousness and rare reports of coma), dyskinesia, dysphagia, encephalopathy, gastritis, gastroesophageal reflux, grand mal convulsions, intracranial hemorrhage, hepatitis (including increased ALT and AST and hepatic failure), hyperglycemia, hyperlipidemia, hypoglycemia, ileus, increased INR, impotence, lethargy, malaise, myoclonus, neuroleptic malignant syndrome, acute pancreatitis, Parkinsonism, acute renal failure (including increased creatinine and renal insufficiency), prolonged QT interval, restlessness, sepsis, Stevens-Johnson syndrome, suicidal ideation, sudden death, supraventricular tachycardia, tachycardia, tardive dyskinesia, thrombocytopenia, and hallucinations (both visual and auditory).

ANIMAL TOXICOLOGY
Memantine induced neuronal lesions (vacuolation and necrosis) in the multipolar and pyramidal cells in cortical layers III and IV of the posterior cingulate and retrosplenial neocortices in rats similar to those which are known to occur in rodents administered other NMDA receptor antagonists. Lesions were seen after a single dose of memantine, in a study in which rats were given daily oral doses of memantine for 14 days, the no-effect dose for neuronal necrosis was 6 times the maximum recommended human dose on a mg/m² basis. The potential for induction of central neuronal vacuolation and necrosis by NMDA receptor antagonists in humans is unknown.

DRUG ABUSE AND DEPENDENCE
Controlled Substance Class: Memantine HCl is not a controlled substance.

Physical and Psychological Dependence: Memantine HCl is a low to moderate affinity uncompetitive NMDA antagonist that did not produce any evidence of drug-seeking behavior or withdrawal symptoms upon discontinuation in 2,504 patients who participated in clinical trials at therapeutic doses. Post marketing data, outside the U.S., retrospectively collected, has provided no evidence of drug abuse or dependence.

OVERDOSAGE
Signs and symptoms associated with memantine overdosage in clinical trials and from worldwide marketing experience include agitation, confusion, ECG changes, loss of consciousness, psychosis, restlessness, slowed movement, somnolence, stupor, unsteady gait, visual hallucinations, vertigo, vomiting, and weakness. The largest known ingestion of memantine worldwide was 2.0 grams in a patient who took memantine in conjunction with unspecified antidiabetic medications. The patient experienced coma, diplopia, and agitation, but subsequently recovered.

Because strategies for the management of overdose are continually evolving, it is advisable to contact a poison control center to determine the latest recommendations for the management of an overdose of any drug. As in any cases of overdose, general supportive measures should be utilized, and treatment should be symptomatic. Elimination of memantine can be enhanced by acidification of urine.

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Rev. 04/07

Patients Benefit From Merged Traditions

In Saskatchewan and New Mexico, two psychiatrists have found ways to live and work in two cultures.

BY AARON LEVIN

"I lived in two parallel worlds," said Lewis Mehl-Madrona M.D., Ph.D., a psychiatrist and an associate professor of family medicine and psychiatry at the University of Saskatchewan.

Those worlds were not just of place and time, but of history and culture, as Mehl-Madrona and other American-Indian psychiatrists know.

Crossing back and forth from one culture to another is hardly uncommon for anyone, like immigrants and members of minority groups, who, by choice or necessity, have spent parts of their lives as participants in more than one society.

For Mehl-Madrona, one world (his right brain) was indigenous and ceremonial, a tie to his American-Indian ethnicity, said Mehl-Madrona, who is of Cherokee and Lakota ancestry, in an interview. It remained in his mind even as his rational left brain kept him on the job in emergency medicine for 27 years. In the ER, things were cut and dried, he said; there was no question of what to do next.

That conflict was reflected in his ambivalence about a choice of specialty. He considered psychiatry after graduating from Stanford Medical School in 1975, but his relationship to the field had an approach-avoidance quality. His psychiatry residency stretched over 20 years at three institutions, interspersed with a family medicine residency, the years in the ER, and a Ph.D. in psychology in 1980.

Over time, though, he managed to integrate the two halves of his mind and his career. His experience in two cultures has helped him no matter who his patient may be.

"Too many times, medical people—including psychiatrists—say: 'We know it all. Listen to us. It'll be fine,' " he said. "That leads to resentment. The patient feels unimportant and stubborn, and [is] ultimately noncompliant."

Indigenous communities ask one thing of mental health workers, he said: "Listen. Allow us to be separate but different."

Newcomers should not assume they know everything. Find an older mentor within the community to help learn about the community, its healing practices, and its values, urged Mehl-Madrona.

Credit: Aaron Levin

Mary Hasbah Roessel, M.D., embodies overlapping cultures. She is a staff psychiatrist at the Santa Fe Indian Health Services Hospital and Clinic in Santa Fe, N.M., and the granddaughter of a traditional Navajo healer.

"If you watch how elders work, you'll see it's entirely through stories," he said. "People like that approach."

After all, many forms of psychotherapy, from psychoanalysis to cognitive-behavioral therapy, depend on narratives, so they are not so far from native traditions, he said.

Nor are native traditions far removed from a biopsychosocial model. As a former ER doctor, he was puzzled by the old analytic model of avoidance of the body.

"It was not easy for me," he said. "Now, it's easy to use drugs, but if you don't intervene in other ways, the patient will be back in two months. Social intervention is critical. If not, society overpowers the drugs."

Mary Roessel, M.D., has also spent a life and a career moving back and forth across similar boundaries. Her interest in psychiatry was planted early. She grew up on Navajo reservations in Arizona, the daughter of two teachers. Her mother was Navajo, her father was not. Her parents met Karl Menninger at a conference, and he later visited the family on the reservation. Menninger wrote about the connection between Navajo healing and psychiatry and even declared that the Navajos were the first psychiatrists, said Roessel. He encouraged her interests in science, as well.

please see ***Traditons*** *on page 43*

Housing Homeless Alcohol Abusers Brings Substantial Cost Savings

Give someone with alcoholism a shelter bed, and he'll sleep for a night; give him an apartment, and hospital costs will go down.

BY AARON LEVIN

Placing homeless people with severe alcohol-use problems into free housing without requiring abstinence or treatment reduced costs, medical use, and contacts with the criminal justice system, according to University of Washington researchers.

Such Housing First programs "can reduce the public burden associated with overuse of crisis services and reduce alcohol consumption," wrote Mary Latimer, Ph.D., and colleagues in the April 1 *Journal of the American Medical Association*. Other research has shown Housing First programs to be successful in getting homeless mentally ill people off the streets while reducing some costs.

Chronic public inebriates—sometimes referred to as "frequent flyers" by police and emergency medical system crews—disproportionately use publicly funded health- and justice-system resources. Conventional interventions, like shelters, treatment programs, and abstinence-based housing, have poor records in breaking those patterns.

The Seattle researchers developed a list of 388 individuals who incurred the highest costs in 2004 for use of alcohol-related hospital emergency services, the local sobering center, and the King County jail. A total of 134 participants were eventually recruited for the study from November 2005 to March 2007. There were 119 people in the interventional housed group and 39 in a wait-list control group. Their average age was 48, and they had first become homeless at an average age of 31. Nearly all (94 percent) were male, and 30 percent had attended college at some time. Many had serious medical problems such as hepatitis (40 percent) and tuberculosis (18 percent). They each had been treated an average of 16 times for alcohol abuse.

The trial was not randomized for ethical reasons. Also, because participants were approached in rank order of services used and consequent costs in the year prior to the study, the treatment group had incurred larger expenses than did the control group.

The treatment group was housed at a Housing First facility where participants were offered meals and on-site health services. They had no treatment requirements, but case managers did engage residents about substance-use issues. Costs for housing and services averaged $1,120 a month.

The researchers collected administrative data at six months and one year from area medical, social services, and correctional departments, as well as Medicaid.

The individuals who received housing had incurred more than $8 million in costs in the year preceding the trial, but only about $4 million in the first year of intervention. Monthly charges dropped for both housed and wait-list cohorts, but the average had dropped for the housed group at six months and still further at 12 months (see table). Treatment differences were produced mainly by fewer nights in shelters and reduced use of the sobering center.

All measures of service use (except days in detoxification) dropped more with longer time in housing. Cost reductions occurred in charges to Medicaid, Harborview Medical Center, and emergency medical systems.

At one year, average daily alcohol use dropped from an average of 15.7 drinks a day to 10.6 a day.

The study demonstrates the value of stable housing, which is seen as a greater need than alcohol treatment by homeless persons with alcohol problems, said the authors. The lower burden on shelters, hospitals, and jails could mean greater access to care for other people who need it and more attention by police and emergency services to more significant matters of public safety, they suggested.

The study was funded by grants from the Substance Abuse Policy Research Program of the Robert Wood Johnson Foundation, National Institute on Alcohol Abuse and Alcoholism, and National Institutes of Health and received support from Seattle's Downtown Emergency Service Center, which runs the housing program site.

An abstract of "Health Care and Public Service Use and Costs Before and After Provision of Housing for Chronically Homeless Persons With Severe Alcohol Problems" is posted at <http://jama.ama-assn.org/cgi/content/abstract/301/13/1349>. ■

Housing First Cuts Costs, Service Use

Both costs and use of medical, criminal justice, and social services by homeless persons with severe alcohol problems declined when they were placed in housing but permitted to continue drinking.

	1 year prior to housing		6 months after intervention		12 months after intervention
	Housed	Wait-List	Housed	Wait-List	Housed
Contacts/Incidents (median)					
Jail days	0.5	0.6	0.0	0.4	0.0
Jail bookings	0.2	0.2	0.0	0.2	0.0
Shelter nights	0.5	0.4	0.0	0.1	0.0
Medical ctr	0.9	0.7	0.7	0.3	0.3
EMS	0.4	0.4	0.5	0.3	0.2
Detox ctr	0.0	0.1	0.0	0.0	0.0
Sobering ctr	6.1	4.0	0.0	2.1	0.0
Costs (in dollars, per person)					
Medicaid	612	345	204	107	122
Medical ctr	139	743	0	0	0
EMS	505	553	512	438	219
Total	4066	3318	1492	1932	958

Source: Mary Latimer, Ph.D.,et al., *JAMA*, April 1, 2009

government news

Senator Wants Mentally Ill Youth To Get Care, Not Prison Term

That prisons are increasingly housing mentally ill individuals spurs a federal legislative effort to address mental illness among juvenile offenders.

BY RICH DALY

Recently proposed legislation aims to extend and expand a federal program that diverts children with mental illness from the juvenile justice system, which has seen a massive influx of such young offenders in recent years.

The Juvenile Justice and Delinquency Prevention Reauthorization Act of 2009 (S 678), sponsored by Sen. Patrick Leahy (D-Vt.), would authorize increased funding for training juvenile justice personnel to recognize and refer for treatment youth offenders with signs of mental illness. The measure also would provide grants, for the first time, to fund prevention programs to keep children with psychiatric illness from entering the criminal justice system.

"A prevention component that targets children and youth at risk is long overdue," said William Arroyo, M.D., co-chair of the Juvenile Justice Committee for the American Academy of Child and Adolescent Psychiatry (AACAP). "It not only aborts a trajectory of suffering and antisocial behavior, but it avoids enormous costs incurred by public systems when youth enter the juvenile justice system. Research supports this strategy."

The measure would authorize $2.1 billion in juvenile justice grants to states over five years and require any state receiving such funding to develop plans to provide alternatives—when needed—to detention for youth offenders, including diversion to treatment for mental health and substance abuse disorders. Also required would be state plans to reduce the number of children who are housed in jails and awaiting placement in residential treatment programs. States would be expected to engage family members in the design and implementation of prevention and treatment services when a child is released.

States would have to supply a detailed accounting of how they are ensuring that juvenile suspects are offered mental health and substance abuse screening, assessment, referral, and treatment within the state's juvenile justice system. Those efforts must include use of evidence-based mental health and substance abuse screening and further assessments if an initial screening demonstrates a need for further assessment.

"It has become abundantly clear that mental health and drug treatment are fundamental to making real progress toward keeping juvenile offenders from reoffending," said Leahy in a statement on the Senate floor. "This bill takes new and important steps to prioritize and fund mental health and drug treatment."

According to Leahy, the bill's mental illness and substance abuse treatment provisions are needed because a growing body of research has found that jails are becoming the nation's largest facilities for people with mental illness. Mental disorders are up to three times more common among children in the justice system than in the general population, and 80 percent of people in the juvenile justice system have substance abuse problems, he said.

The legislation is supported by AACAP due to its emphasis on detection and treatment of mental illness and addictions as a way to help end the downward spiral of children with untreated health problems that drop them—sometimes repeatedly—into the nation's prisons.

> **"A prevention component that targets children and youth at risk is long overdue."**

Juvenile inmates "have higher rates of mental health diagnoses including learning disabilities and substance abuse compared with their peers," said Louis Kraus, M.D., co-chair of AACAP's Juvenile Justice Committee. "Early education and intervention programs that target at-risk children and adolescents and work with them before, during, and after the adjudication process will reduce recidivism."

The legislation to reauthorize the juvenile justice grant program is expected to advance because it has some bipartisan support and its sponsor is chair of the committee with primary oversight of this issue. But a repeat of Republican opposition that developed last year could derail it. In 2008 Republicans objected to an earlier version of the bill because it lacked measures to tighten management of the 30-year-old juvenile justice grant program, and it did not address previously identified instances of unauthorized spending by states of the juvenile grants.

Leahy's staff told *Psychiatric News* that the latest version of the bill is fairly similar to last year's measure.

The text of the Juvenile Justice and Delinquency Prevention Reauthorization Act of 2009 can be accessed at <www.thomas.loc.gov> by searching on the bill number, S 678. ■

Share Your Musical Talent

The Medical Musical Group Symphony Orchestra and Chorale is seeking participants. For 2009, the group is planning twin "Healing for the Nations" concerts in Washington, D.C., and London. The concerts will be held November 4 and 11 and will raise funds for malaria eradication. The trip, which includes a visit to Wales, offers elegant amenities, sightseeing, and fellowship at an affordable price. More information is available by phone at (202) 797-0700, e-mail at vanmmg@hotmail.com, or online at <www.medicalmusical.org>.

BIPOLAR DISORDER

THROUGHOUT THE LIFE CYCLE:

TREATMENTS AND TREATMENT EXPERIENCE

TUESDAY, MAY 19, 2009
6:30AM Breakfast and Sign-in
7:00AM-9:00AM Educational Activity

SAN FRANCISCO MARRIOTT
B2 Level, Salon 7 and 8
San Francisco, California

WHO SHOULD PARTICIPATE

This activity is designed for clinical psychiatrists and other healthcare professionals interested in the diagnosis and treatment of bipolar disorder throughout the life cycle.

OVERVIEW

Understanding treatment considerations across different populations, including the risks and benefits of specific medications and metabolic factors during various phases in the life cycle, can assist clinicians in individualizing treatment based on sound evidence. To impart knowledge and practice-based skills to psychiatrists attending this symposium, noteworthy research and guidance will be outlined. Attention will also be directed to correct unjustified assumptions about bipolar disorder treatment in the populations discussed.

LEARNING OBJECTIVES

Upon completion of the activity, participants should be able to

1. Compare the risk of continuation or discontinuation of treatment among pregnant women with bipolar disorder.
2. Review the clinically useful treatment guidelines that can be used in the care of children and adolescents with bipolar disorder.
3. Discuss treatment and treatment experience of geriatric patients receiving medication for bipolar disorder.
4. Describe the prevalence, etiology, and clinical implications of metabolic dysregulation across the life cycle in bipolar disorder.

ACCREDITATION STATEMENT

The American Psychiatric Association (APA) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

CREDIT DESIGNATION STATEMENT

The APA designates this educational activity for a maximum of 2 *AMA PRA Category 1 Credits*™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

FACULTY DISCLOSURE STATEMENT

The American Psychiatric Association requires disclosure by faculty of CME activities of all financial interest(s) or other affiliation(s) with commercial organization(s) that may have a direct or indirect interest in the subject matter of the scientific program. A "financial interest" may include, but is not limited to, being a shareholder in the organization; being on retainer with the organization; or having research or honoraria paid by the organization. An "affiliation" may include holding a position on an advisory committee or some other role or benefit to a supporting organization. The existence of such relationships does not necessarily constitute a conflict of interest, but the prospective audience must be informed of the faculty's affiliation with every commercial entity by means of an acknowledgement in the printed materials. This policy is intended to openly identify any potential conflict(s) so that members of the audience in an educational activity are able to form their own judgments about the presentation.

Attendees must be registered for the APA 2009 Annual Meeting to attend this symposium. Seating is limited and will be based on first-come, first-served. For more information about the meeting, please visit the APA Web site at www.psych.org or contact the APA toll free at 1.888.357.7924 (within the US or Canada) or 703.907.7300.

Sponsored by the American Psychiatric Association

Supported by an educational grant from Pfizer

AGENDA

6:30AM
BREAKFAST AND SIGN-IN

7:00AM
WELCOME AND OVERVIEW
Joseph R. Calabrese, MD
Activity Chairperson
Bipolar Disorders Research Chair,
Professor of Psychiatry,
Case Western Reserve University
School of Medicine
Cleveland, Ohio

7:10AM
UNDERSTANDING THE CHALLENGES OF REPRODUCTIVE MENTAL HEALTH: PREGNANCY AND LACTATION
Adele C. Viguera, MD, MPH
Assistant Professor of Psychiatry,
Harvard Medical School
Research Staff,
Massachusetts General Hospital
Boston, Massachusetts
Research Staff, Cleveland Clinic
Neurological Institute
Cleveland, Ohio

7:30AM
TREATMENT OPTIONS IN CHILDHOOD AND ADOLESCENT BIPOLAR DISORDER
Melissa P. DelBello, MD
Vice Chair of Clinical Research,
Department of Psychiatry
Associate Professor,
Psychiatry, Pediatrics, and Psychology
University of Cincinnati College
of Medicine
Cincinnati, Ohio

7:50AM
TREATMENT AND TREATMENT EXPERIENCE: FROM ADULT TO LATE LIFE
Martha Sajatovic, MD
Professor of Psychiatry,
Director,
Neurological Outcomes Center
University Hospitals Case
Medical Center
Case Western Reserve University
School of Medicine
Cleveland, Ohio

8:10AM
METABOLIC SYNDROME ACROSS THE LIFE CYCLE IN BIPOLAR DISORDER
David E. Kemp, MD
Assistant Professor,
Department of Psychiatry
Director,
Mood & Metabolic Clinic
Case Western Reserve University
School of Medicine
Cleveland, Ohio

8:30AM
QUESTION AND ANSWER SESSION

9:00AM
ADJOURNMENT

DON'T MISS THIS IMPORTANT EDUCATIONAL ACTIVITY!

A Symposium Held During the APA 2009 Annual Meeting

government news

Obama: Service Members Need Lifetime Electronic Record

The goal of an Obama administration initiative is to create a comprehensive system enabling streamlined transfer of medical records that follow individuals throughout their lifetime from the time they enter the military.

BY MARK MORAN

President Obama last month called on the Department of Veterans Affairs and the Department of Defense to create a joint seamless health information network.

Appearing at a press briefing with Secretary of Defense Robert Gates and Secretary of Veterans Affairs (VA) Eric Shinseki, the president urged the creation of a joint virtual lifetime electronic health record. The purpose of the record is to create a seamless transfer of health records that would follow an individual from the moment of entry into the military and throughout his or her lifetime.

"Access to electronic records is essential to modern health care delivery and the paperless administration of benefits," the president said in a statement on the White House Web site. "It provides a framework to ensure that all health care providers have all the information they need to deliver high-quality health care while reducing medical errors. The creation of this joint virtual lifetime record by the two organizations would take the next leap to delivering seamless, high-quality care, and serve as a model for the nation."

The vision is far from a new one, however, and the complexities of creating a seamless transfer of data between the two vast information systems are daunting. But VA psychiatrist Peter Fore, M.D., a member of the APA Committee on Health Information Technology, said that progress is being made.

"I have heard talk about this for years," he told *Psychiatric News*. "The goal of having a seamless transition for veterans moving from the military into the VA system has been around for some time."

The VA currently has one of the most comprehensive and sophisticated systems for electronic medical records. Fore said the goal of the initiative is not necessarily a matter of creating one unified system, but allowing the transfer of information between the two systems.

"It's a work in progress," Fore said. "We currently have access to some of the records. We don't get live data, but we can request static reports that come over from the [Department of Defense]. Some of the data have to be standardized in pieces that can move from one system to the next."

But even matching up identifiers in the two systems to match records of the same patient can be difficult: if the VA system uses a middle initial, for instance, and the Department of Defense system doesn't, the records won't follow the patient. Other obstacles have to do with the architecture of the two computer systems and the development of common data-exchange points.

But Fore said the goal is a worthy one, and while it is likely to take time, progress is being made.

"As a psychiatrist, I would like to know the most complete information about my patient that is available," he said. "If someone had a first episode of schizophrenia while in the military and was treated for it, I would much rather have that information available to me than trying to recreate what happened from the patient's own history."

He added that the goal of the seamless transfer of health information had even been a part of the VA's strategic plan prior to the president's remarks in April. The plan calls for the goal to be accomplished by 2011. "It's already partly working, and I think it is going to be more complete as time goes on." ■

community news

Economy

continued from page 5

could no longer afford health insurance, he could no longer afford to visit a psychiatrist or buy his psychotropic medications. He became severely depressed and suicidal and ended up in a hospital as an unfunded patient. His psychiatrist lamented, "And the worst for him is yet to come—the bill that he is going to receive for his hospitalization."

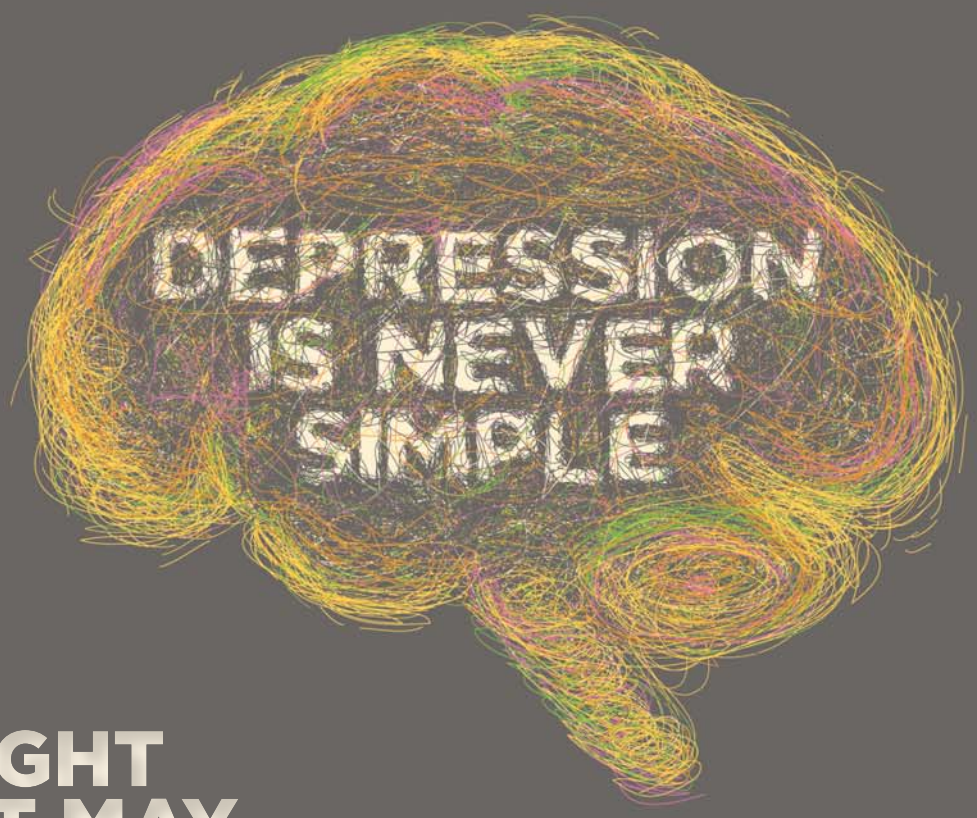
No one knows when the financial gloom will lift. No one knows how many more people will be mentally ailing due to the ailing economy.

"It is my understanding that all of these recessions have a cyclical nature to them," Engel said. "If the economy is better and if job security is better, then obviously you would see patients do a little better in that regard."

"I am fairly optimistic that our economy will start to recover in a year," Weeks opined. "But I think that the average American worker will still be significantly stressed. The downsizing, the layoffs, they are going to have a huge ripple effect on mental health."

"If the economy continues to get worse before it gets better, and if more and more people are out of work, I suspect that we are going to see much more family discord and depression in addition to anxiety and maybe even an increase in the suicide rate over the next couple of years," McQuistion ventured. "We may see an uptick in acute exacerbations of chronic mental illnesses and more utilization of emergency rooms and inpatient services if the social safety net does not remain sufficiently intact. Despite the Obama administration's social commitments and the [recent federal financial] stimulus package, it is important to remember that the American mental health care budget is primarily determined state by state." ■

Venlafaxine Extended Release Tablets, a branded alternative for patients with Major Depressive Disorder (MDD)*



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- A single 225 mg Venlafaxine Extended Release Tablet vs a combination of venlafaxine HCl extended-release capsules may reduce pill burden for patients taking 225 mg for the treatment of MDD
- Patients with MDD should start treatment with 75 mg/day (in some patients, 37.5 mg/day for 4 to 7 days then increased to 75 mg/day); daily dose can be increased by 75 mg/day at intervals of ≥4 days (maximum 225 mg/day)

4 WORDS
1 TABLET
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37.5 mg 75 mg 150 mg 225 mg

For more information, call 1.888.299.1053 or visit www.VERTablets.com

*Venlafaxine Extended Release Tablets are not indicated for the treatment of generalized anxiety disorder or panic disorder.

INDICATIONS AND IMPORTANT SAFETY INFORMATION

WARNING: Suicidality and Antidepressants

See full Prescribing Information for complete boxed warning.

Increased risk of suicidal thinking and behavior has been reported in children, adolescents and young adults taking antidepressants for major depressive disorder (MDD) and other psychiatric disorders. Venlafaxine Extended Release Tablets are not approved for use in pediatric patients.

Venlafaxine Extended Release Tablets (venlafaxine hydrochloride) are indicated for the treatment of Major Depressive Disorder (MDD) and Social Anxiety Disorder (SAD). Efficacy of venlafaxine HCl was shown in both short-term trials and a longer-term trial in MDD, and in short-term SAD trials. Venlafaxine Extended Release Tablets are contraindicated in patients taking monoamine oxidase inhibitors (MAOIs).

All patients should be monitored appropriately and observed closely for clinical worsening and suicidality, especially at the beginning of drug therapy, or at the time of increases or decreases in dose. Such monitoring should include daily observation by families and caregivers for emergence of agitation, irritability, unusual changes in behavior, or emergence of suicidality.

Venlafaxine Extended Release Tablets should not be used in combination with an MAOI, or within at least 14 days of discontinuing treatment with an MAOI. At least 7 days should be allowed after stopping Venlafaxine Extended Release Tablets before starting an MAOI.

The development of a potentially life-threatening serotonin syndrome or Neuroleptic Malignant Syndrome (NMS)-like reactions have been reported with SSRIs and SNRIs (including Venlafaxine Extended Release Tablets) alone, but particularly if used concomitantly with serotonergic drugs (including triptans), MAO inhibitors, or with antipsychotics or other dopamine antagonists. Severe serotonin syndrome can resemble NMS, and patients should be monitored for symptoms of these disorders. If symptoms develop, Venlafaxine Extended Release Tablets and any serotonergic or antidopaminergic agents, including antipsychotics, should be discontinued immediately.

Treatment with venlafaxine hydrochloride is associated with sustained hypertension in some patients. Regular blood pressure monitoring is recommended. Mydriasis has been reported in association with venlafaxine; therefore, patients with raised intraocular pressure or those at risk of acute narrow-angle glaucoma should be monitored.

Dosing must be individualized according to the patient's hepatic and renal function status. Abrupt discontinuation or dose reduction has been associated with discontinuation symptoms (generally self-limiting; serious symptoms possible). A gradual reduction in the dose rather than abrupt cessation is recommended.

After treatment with venlafaxine hydrochloride, insomnia and nervousness, activation of mania/hypomania, symptomatic hyponatremia, seizures, abnormal bleeding (most commonly ecchymosis), clinically relevant increases in serum cholesterol, interstitial lung disease and eosinophilic pneumonia have been reported. Venlafaxine Extended Release Tablets should be used cautiously in patients with a history of seizures. Measurement of serum cholesterol should be considered during long-term treatment. Patients should be cautioned about the risk of bleeding associated with concomitant use of Venlafaxine Extended Release Tablets and NSAIDs, aspirin, or other drugs that affect coagulation.

Venlafaxine Extended Release Tablets should be used during pregnancy and nursing only if clearly needed due to the potential for serious adverse reactions.

Adverse reactions occurring in short-term studies of major depressive disorder* were abnormal ejaculation, gastrointestinal complaints (nausea, dry mouth, anorexia), CNS complaints (dizziness, somnolence, abnormal dreams) and sweating. Adverse reactions occurring in short-term studies of social anxiety disorder* were asthenia, gastrointestinal complaints (anorexia, dry mouth, nausea), CNS complaints (anxiety, insomnia, libido decreased, nervousness, somnolence, dizziness), abnormalities of sexual function (abnormal ejaculation, orgasmic dysfunction, impotence), yawn, sweating, and abnormal vision.

*Occurring in at least 5% of patients receiving venlafaxine extended release capsules and at a rate at least twice that of placebo.

Please see brief summary of full Prescribing Information, including complete boxed warning, on adjacent pages.

TA1136-0409

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Venlafaxine Extended Release Tablets (venlafaxine hydrochloride)

BRIEF SUMMARY. See package insert for full Prescribing Information. For further product information and current package insert, please visit www.VERTablets.com or call our medical communications department toll-free at 1-888-299-1053.

WARNING: SUICIDALITY AND ANTIDEPRESSANT DRUGS
Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of Major Depressive Disorder (MDD) and other psychiatric disorders. Anyone considering the use of Venlafaxine Extended Release Tablets or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 or older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Venlafaxine Extended Release Tablets are not approved for use in pediatric patients. [See *Warnings and Precautions and Patient Counseling Information* in the full Prescribing Information.]

INDICATIONS AND USAGE: Venlafaxine Extended Release Tablets (venlafaxine hydrochloride) are indicated for the treatment of major depressive disorder (MDD) and Social Anxiety Disorder (SAD), also known as Social Phobia, as defined by DSM-IV. Efficacy of venlafaxine in MDD was shown in both short-term trials and a longer-term trial. Efficacy in SAD was established in short-term trials. **CONTRAINDICATIONS:** Concomitant use in patients taking monoamine oxidase inhibitors (MAOIs) [see Warnings and Precautions, Potential for interaction with Monoamine Oxidase inhibitors]. **WARNINGS AND PRECAUTIONS: Clinical Worsening and Suicide Risk:** Patients with MDD, both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Suicide is a known risk of depression and other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. There has been a long-standing concern, however, that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients during the early phases of treatment. Pooled analyses of short-term placebo controlled trials of antidepressant drugs (SSRIs and others) showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in short-term studies in children and adolescents and young adults (ages 18-24) with MDD and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction with antidepressants compared to placebo in adults aged 65 and older. The pooled analyses of placebo-controlled trials in children and adolescents with MDD, obsessive-compulsive disorder, or other psychiatric disorders included a total of 24 short-term trials of 9 antidepressant drugs in over 4400 patients. The pooled analyses of placebo-controlled trials in adults with MDD or other psychiatric disorders included a total of 295 short-term trials (median duration of 2 months) of 11 antidepressant drugs in over 77,000 patients. There was considerable variation in risk of suicidality among drugs, but a tendency toward an increase in the younger patients for almost all drugs studied. There were differences in absolute risk of suicidality across the different indications, with the highest incidence in MDD. The risk differences (drug vs placebo), however, were relatively stable within age strata and across indications. No suicides occurred in any of the pediatric trials. There were suicides in the adult trials, but the number was not sufficient to reach any conclusion about drug effect on suicide. It is unknown whether the suicidality risk extends to longer-term use, i.e., beyond several months. However, there is substantial evidence from placebo-controlled maintenance trials in adults with depression that the use of antidepressants can delay the recurrence of depression. **All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases.** The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for MDD as well as for other indications, both psychiatric and nonpsychiatric. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality. Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse, or who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms. If the decision has been made to discontinue treatment, medication should be tapered, as rapidly as is feasible, but with recognition that abrupt discontinuation can be associated with certain symptoms [*see Dosage and Administration (2.5) and Warnings and Precautions (5.7) in the full prescribing information for a description of the risks of discontinuation of Venlafaxine Extended-Release Tablets*]. **Families and caregivers of patients being treated with antidepressants for MDD or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to health care providers. Such monitoring should include daily observation by families and caregivers.** Prescriptions for Venlafaxine Extended Release Tablets should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose. **Potential for Interaction With Monoamine Oxidase Inhibitors: Adverse reactions, some serious, have been reported in patients who recently discontinued an MAOI and started on venlafaxine hydrochloride, or who recently discontinued venlafaxine hydrochloride prior to initiation of an MAOI. These reactions included tremor, myoclonus, diaphoresis, nausea, vomiting, flushing, dizziness, hyperthermia with features resembling neuroleptic malignant syndrome, seizures, and death. Venlafaxine Extended Release Tablets should not be used in combination with an MAOI, or within at least 14 days of discontinuing treatment with an MAOI. At least 7 days should be allowed after stopping venlafaxine hydrochloride before starting an MAOI.** A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled trials) that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Whether any of the symptoms described above represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder. It should be noted that Venlafaxine Extended Release Tablets are not approved for use in treating bipolar depression. **Serotonin Syndrome or Neuroleptic Malignant Syndrome (NMS)-like Reactions:** The development of potentially life-threatening serotonin syndrome or Neuroleptic Malignant Syndrome (NMS)-like reactions has been reported with SSRIs and SNRIs alone, including Venlafaxine Extended Release Tablets, but particularly with concomitant use of serotonergic drugs (including triptans), with drugs that impair metabolism of serotonin (including MAOIs), with other antipsychotics, or with other dopamine antagonists [see **WARNINGS AND PRECAUTIONS** in full Prescribing Information]. Patients should be monitored for the emergence of serotonin syndrome or NMS-like signs and symptoms including mental status changes, autonomic instability, neuromuscular aberrations, and/or gastrointestinal symptoms *[see Drug Interactions (7.10)]*. Serotonin syndrome, in its most severe form can resemble NMS, which includes hyperthermia, muscle rigidity, autonomic instability with possible rapid fluctuation of vital signs, and mental status changes. The concomitant use of Venlafaxine Extended Release Tablets with MAOIs is contraindicated *[see Contraindications (4) and Warnings and Precautions (5.2)]*. If concomitant treatment of Venlafaxine Extended Release Tablets with a 5-hydroxytryptamine receptor agonist (triptan) is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. The concomitant use of Venlafaxine Extended Release Tablets with serotonin precursors (such as tryptophan supplements) is not recommended *[see Drug Interactions (7.10)]*. Treatment with Venlafaxine Extended Release Tablets and any concomitant serotonergic or antidopaminergic agents, including antipsychotics, should be discontinued immediately if the patient develops any symptoms of serotonin syndrome or NMS, and supportive symptomatic treatment should be initiated. **Sustained Hypertension:** Venlafaxine hydrochloride is associated with sustained dose-related increases in blood pressure (BP) in some patients. Sustained BP increases could have adverse consequences. Postmarketing cases of elevated BP requiring immediate treatment have been reported. Caution should be exercised in treating patients with pre-existing hypertension or other underlying conditions that might be compromised by BP increases. Preexisting hypertension should be controlled before Venlafaxine Extended Release Tablets therapy is initiated. It is recommended that patients receiving Venlafaxine Extended Release Tablets have regular monitoring of BP. For patients experiencing sustained increase in BP, either dose reduction or discontinuation should be considered. **Elevations in Systolic and Diastolic Blood Pressure (SBP, DBP):** In placebo-controlled premarketing studies, there were changes in mean BP. In most indications, a dose-related increase in SBP and DBP was evident. Across all trials, 1.4% of patients receiving extended-release venlaxafine hydrochloride experienced a ≥15 mm Hg increase in supine DBP with BP ≥105 mm Hg, compared to 0.9% of patients in the placebo groups. One percent of patients receiving venlaxafine hydrochloride experienced a ≥20 mm Hg increase in supine SBP with BP ≥180 mm Hg compared to 0.3% of patients in the placebo groups. **Mydriasis:** Mydriasis has been reported in association with venlafaxine hydrochloride; patients with raised intraocular pressure or patients at risk for acute narrow-angle glaucoma should be monitored. **Discontinuation of Treatment with Venlafaxine Extended Release Tablets:** Discontinuation symptoms have been systematically evaluated in patients taking venlafaxine, to include prospective analyses of clinical trials and retrospective surveys of trials in MDD and SAD. Abrupt discontinuation or dose reduction of venlafaxine at various doses has been associated with the appearance of new symptoms, the frequency of which increased with increased dose level and longer duration of treatment. Reported symptoms include agitation, anorexia, anxiety, confusion, impaired coordination and balance, diarrhea, dizziness, dry mouth, dysphoric mood, fasciculation, fatigue, headaches, hypomania, insomnia, nausea, nervousness, nightmares, sensory disturbances (including shock-like electrical sensations), somnolence, sweating, tinnitus, tremor, vertigo, and vomiting. During marketing of venlafaxine hydrochloride extended-release capsules, other SNRIs, and SSRIs, there have been spontaneous reports of adverse reactions occurring upon discontinuation of these drugs, particularly when abrupt, including the following: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesias), anxiety, confusion, headache, lethargy, emotional lability, insomnia, hypomania, tinnitus, and seizures. While these reactions are generally self-limiting, there have been reports of serious discontinuation symptoms. Patients should be monitored for these symptoms when discontinuing treatment. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose but at a more gradual rate [*see Dosage and Administration (2.4) in full prescribing information*]. **Insomnia and Nervousness:** Treatment-emergent insomnia and nervousness were more commonly reported for patients treated with venlafaxine hydrochloride extended-release capsules than with placebo in pooled analyses of short-term MDD and other clinical studies, as shown in *Table 5 in the full prescribing information*. **Changes in Weight:** In some placebo-controlled trials in MDD, 4% of the patients treated with venlafaxine hydrochloride extended-release capsules and 1% of the placebo-treated patients sustained a loss of 7% or more of body weight during up to 6 months of treatment. The safety and efficacy of venlafaxine therapy in combination with weight loss agents have not been established. Co-administration of Venlafaxine Extended Release Tablets and weight loss agents is not recommended. Venlafaxine Extended Release Tablets are not indicated for weight loss alone or in combination with other products. **Changes in Height:** Pediatric Patients: In the six-month, open-label MDD study, children and adolescents had height increases that were less than expected based on data from age- and sex-matched peers. The difference between observed growth rates and expected growth rates was larger for children (<12 years old) than for adolescents (≥12 years old). **Changes in Appetite:** Adult Patients: Treatment-emergent anorexia was more commonly reported for patients treated with venlafaxine hydrochloride extended-release capsules than for placebo-treated patients in the pool of short-term, double-blind, placebo-controlled MDD (8% vs 4%) and SAD (20% vs 2%) studies. Pediatric Patients: In placebo-controlled trials in MDD and another disorder, 10% of patients aged 6-17 treated with venlafaxine hydrochloride extended-release capsules for up to eight weeks and 3% of patients treated with placebo reported treatment-emergent anorexia. **Activation of Mania/Hypomania:** Mania or hypomania occurred during MDD studies in 0.3% of patients treated with extended release venlafaxine compared with 0% of placebo patients. With immediate release venlafaxine, the rate was 0.5% compared with 0% of placebo patients. No reports of mania or hypomania were reported in trials with SAD. As with all drugs effective in the treatment of MDD, Venlafaxine Extended Release Tablets should be used cautiously in patients with a history of mania. **Hyponatremia:** Hyponatremia may occur as a result of treatment with SSRIs and SNRIs, including Venlafaxine Extended Release Tablets. In many cases, this hyponatremia appears to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Cases with serum sodium lower than 110 mmol/L have been reported. Elderly patients may be at greater risk of developing hyponatremia with SSRIs and SNRIs. Also, patients taking diuretics or who are otherwise volume depleted may be at greater risk [*see Use in Specific Populations (8.5) in full prescribing information*]. Discontinuation of Venlafaxine Extended Release Tablets should be considered in patients with symptomatic hyponatremia, and appropriate medical intervention should be instituted. **Seizures:** In all premarketing venlafaxine hydrochloride MDD trials, seizures were reported in 0.3% of venlafaxine hydrochloride-treated patients. Venlafaxine Extended Release Tablets should be used cautiously in patients with a history of seizures and should be discontinued in any patient who develops seizures. **Abnormal Bleeding:** SSRIs and SNRIs, including Venlafaxine Extended Release Tablets, may increase the risk of bleeding events. Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), warfarin, and other anticoagulants may add to this risk. Bleeding events related to SSRIs and SNRIs use have ranged from ecchymoses, hematomas, epistaxis, and petechiae to life-threatening hemorrhages. Patients should be cautioned about the risk of bleeding associated with the concomitant use of Venlafaxine Extended Release Tablets and other drugs that affect coagulation. **Serum Cholesterol Elevation:** Clinically relevant increases in serum cholesterol were recorded in 5.3% of venlafaxine hydrochloride-treated patients and 0.0% of patients receiving placebo for at least 3 months in trials. Measurement of serum cholesterol levels should be considered during long-term treatment. **Interstitial Lung Disease and Eosinophilic Pneumonia:** Interstitial lung disease and eosinophilic pneumonia associated with venlafaxine therapy have been rarely reported. The possibility of these adverse reactions should be considered in venlafaxine-treated patients who present with progressive dyspnea, cough, or chest discomfort. Such patients should undergo prompt medical evaluation, and discontinuation of venlafaxine therapy should be considered. **Use in Patients with Heart Disease:** Premarketing experience with venlafaxine in patients with concomitant systemic illness is limited. Caution is advised in administering Venlafaxine Extended Release Tablets to patients with diseases or conditions that could affect hemodynamic responses. Venlafaxine has not been evaluated or used to any appreciable extent in patients with a recent history of myocardial infarction or unstable heart disease. Patients with these diagnoses were systematically excluded from many clinical studies during venlafaxine's premarketing testing. As increases in heart rate (mean increase of 4 beats per minute in MDD trials and 5 beats per minute in SAD trials) were observed, caution should be exercised in patients whose underlying medical conditions might be compromised by increases in heart rate (e.g., patients with hyperthyroidism, heart failure, or recent myocardial infarction). **ADVERSE REACTIONS: Clinical Studies Experience: Short-Term, Placebo-Controlled Trials:** ***Adverse Events Leading to Discontinuation of Treatment:*** Approximately 11% of the 357 patients who received venlafaxine hydrochloride extended-release capsules in MDD trials discontinued treatment due to an adverse reaction (vs 6% of the 285 placebo-treated patients). Adverse reactions that led to treatment discontinuation in at least 2% of drug-treated patients were nausea, dizziness and somnolence. Approximately 17% of the 277 patients in SAD trials who received venlaxafine hydrochloride extended-release capsules discontinued treatment due to an adverse reaction (vs 5% of the 274 placebo-treated patients). Adverse reactions that led to treatment discontinuation in at least 2% of drug-treated patients were nausea, insomnia, impotence, headache, dizziness and somnolence. **Adverse Events Occurring at an Incidence of 5% or More:** Major Depressive Disorder: Note in particular the following adverse reactions that occurred in at least 5% of the patients receiving venlafaxine hydrochloride extended-release capsules and at a rate at least twice that of the placebo group for all placebo-controlled trials for the MDD indication (see Table 6): Abnormal ejaculation, gastrointestinal complaints (nausea, dry mouth, and anorexia), CNS complaints (dizziness, somnolence, and abnormal dreams), and sweating. In the two U.S. placebo-controlled trials, the following additional reactions occurred in at least 5% of patients treated with venlafaxine hydrochloride extended-release capsules (n = 192) and at a rate at least twice that of the placebo group: Abnormalities of sexual function (impotence in men, anorgasmia in women, and libido decreased), gastrointestinal complaints (constipation and flatulence), CNS complaints (insomnia, nervousness, and tremor), problems of special senses (abnormal vision), cardiovascular effects (hypertension and vasodilatation), and yawning. Social Anxiety Disorder: Note in particular the following adverse reactions that occurred in at least 5% of the patients receiving venlafaxine hydrochloride extended-release capsules and at a rate at least twice that of the placebo group for the 2 placebo-controlled trials for the SAD indication (see Table 7): Asthenia, gastrointestinal complaints (anorexia, constipation, dry mouth, nausea), CNS complaints (dizziness, insomnia, libido decreased, nervousness, somnolence), abnormalities of sexual function (abnormal ejaculation, impotence, libido decreased, orgasmic dysfunction), yawn, sweating, and abnormal vision. **Adverse Events Occurring at an Incidence of 2% or More:** MDD and SAD trials included patients receiving venlafaxine hydrochloride extended-release capsules in doses ranging from 75 mg to 225 mg/day for up to 12 weeks. The prescriber should be aware that the following adverse reactions figures cannot be used to predict the incidence of adverse reactions in the course of usual medical practice. Similarly, the cited frequencies cannot be compared with figures obtained from other clinical investigations involving different treatments, uses, and investigators. The cited figures, however, do provide the prescribing physician with some basis for estimating the relative contribution of drug and nondrug factors to adverse reaction incidence rate in the population studied. [See **TABLE 6** in full Prescribing Information.] **TABLE 6: Treatment Emergent Adverse Reaction Incidence in Short-Term Placebo-Controlled Clinical Trials with Venlafaxine Hydrochloride Extended-Release Capsules in Patients with Major Depressive Disorder.** This table reports adverse events that occurred in 2% or more of patients treated with venlafaxine hydrochloride extended-release capsules where the incidence in patients treated with venlafaxine hydrochloride extended-release capsules (n=357) was greater than the incidence for the respective placebo-treated patients (n=285). For each adverse reaction, the incidence of reactions in the drug-treated patients is listed before the incidence in placebo-treated patients. **Body as a Whole:** Asthenia (8% and 7%). **Cardiovascular System:** Vasodilation (4% and 2%); Hypertension (4% and 1%). **Digestive System:** Nausea (31% and 7%); Constipation (8% and 5%); Anorexia (8% and 4%); Vomiting (4% and 2%); Flatulence (4% and 3%). **Metabolic/Nutritional:** Weight Loss (3% and 0%). **Nervous System:** Dizziness (20% and 9%); Somnolence (17% and 8%) Insomnia (17% and 11%); Dry mouth (12% and 6%); Nervousness (10% and 5%); Abnormal Dreams (7% and 2%); Tremor (5% and 2%); Depression (3% and <1%); Paresthesia (3% and 1%); Libido Decreased (3% and <1%); Agitation (3% and 1%). **Respiratory System:** Pharyngitis (7% and 6%); Yawn (3% and 0%). **Skin:** Sweating (14% and 3%). **Special Senses:** Abnormal vision (4% and <1%). **Urogenital System:** Abnormal ejaculation (16% and <1%); Impotence (4% and <1%); Female anorgasmia (3% and <1%). [See **TABLE 7** in full Prescribing Information]. **TABLE 7: Treatment Emergent Adverse Reaction Incidence in Short-Term Placebo-Controlled Clinical Trials with Venlafaxine Hydrochloride Extended-Release Capsules in Patients with Social Anxiety Disorder.** This table reports adverse events that occurred in 2% or more of patients treated with venlafaxine hydrochloride extended-release capsules where the incidence in patients treated with venlafaxine hydrochloride extended-release capsules (n=277) was greater than the incidence for the respective placebo-treated patients (n=274). For each adverse reaction, the incidence of reactions in the drug-treated patients is listed before the incidence in placebo-treated patients. **Body as a Whole: Headache** (34% and 33%); Asthenia (17% and 8%); Flu Syndrome (6% and 5%); Accidental Injury (5% and 3%); Abdominal Pain (4% and 3%). **Cardiovascular System:** Hypertension (5% and 4%); Vasodilation (3% and 1%); Palpitation (3% and 1%). **Digestive System:** Nausea (29% and 9%); Anorexia (20% and 1%); Constipation (8% and 4%); Diarrhea (6% and 5%); Vomiting (3% and 2%); Eructation (2% and 0%). **Metabolic/Nutritional:** Weight Loss (4% and 0%). **Nervous System:** Insomnia (23% and 7%); Dry mouth (17% and 4%); Dizziness (16% and 8%); Somnolence (16% and 8%); Nervousness (11% and 3%); Libido Decreased (9% and <1%); Anxiety (5% and 3%); Agitation (4% and 1%); Tremor (4% and <1%); Abnormal Dreams (4% and <1%); Paresthesia (3% and <1%); Twitching (2% and 0%). **Respiratory System:** Yawn (5% and <1%); Sinusitis (2% and 1%) **Skin:** Sweating (13% and 2%). **Special Senses:** Abnormal vision (6% and 3%). **Urogenital System:** Abnormal ejaculation (16% and 1%); Impotence (10% and 1%); Female Orgasmic Dysfunction (8% and 0%). **Vital Sign Changes:** Venlafaxine hydrochloride was associated with a mean increase in pulse rate of 4 beats/min in SAD trials. In premarketing trials, the mean change from baseline heart rate for patients treated with extended-release venlafaxine hydrochloride in MDD and SAD trials was 4 beats-per-minute and 5 beats-per-minute, respectively. In a flexible-dose study with doses ranging from 200 mg to 375 mg/day, patients receiving extended-release venlafaxine hydrochloride had a mean increase in heart rate of 8.5 beats-per-minute [see **WARNINGS AND PRECAUTIONS** in full Prescribing Information for effects on heart rate and blood pressure]. **Laboratory Changes:** Clinically relevant increases in serum cholesterol were noted in venlafaxine hydrochloride clinical trials. Increases were duration dependent over the study period and tended to be greater with higher doses. **ECG Changes:** In a flexible-dose MDD study with doses of venlafaxine hydrochloride immediate-release tablets in the range of 200 to 375 mg/day and mean dose greater than 300 mg/day, the mean change in heart rate was 8.5 beats per minute compared with 1.7 beats per minute for placebo. [*See Warnings and Precautions (5.17)*]. **POSTMARKETING EXPERIENCE:** Voluntary reports of other adverse reactions temporally associated with the use of venlafaxine have been received since market introduction. Because these reactions have been reported from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. These reports include the following reactions: agranulocytosis, anaphylaxis, aplastic anemia, catatonia, congenital anomalies, impaired coordination and balance, CPK increased, deep vein thrombophlebitis, delirium, EKG abnormalities such as QT prolongation; cardiac arrhythmias including atrial fibrillation, supraventricular tachycardia, ventricular extrasystoles, and rare reports of ventricular fibrillation and ventricular tachycardia, including torsade de pointes; epidermal necrolysis/Stevens-Johnson syndrome, erythema multiforme, extrapyramidal symptoms (including dyskinesia and tardive dyskinesia), angle-closure glaucoma, hemorrhage (including eye and gastrointestinal bleeding), hepatic reactions (including GGT elevation; abnormalities of unspecified liver function tests; liver damage, necrosis, or failure; and fatty liver), interstitial lung disease, involuntary movements, LDH increased, neutropenia, night sweats, pancreatitis, pancytopenia, panic, prolactin increased, renal failure, rhabdomyolysis, serotonin syndrome, shock-like electrical sensations or tinnitus (in some cases, subsequent to the discontinuation of venlafaxine or tapering of dose), and syndrome of inappropriate antidiuretic hormone secretion (usually in the elderly). **DRUG INTERACTIONS: Alcohol:** The effect of alcohol on plasma levels of Venlafaxine Extended Release Tablets is not known. **Cimetidine:** Use caution when administering venlafaxine hydrochloride with cimetidine to patients with preexisting hypertension or hepatic dysfunction, and the elderly. **Diazepam:** A single dose of diazepam did not appear to affect the PK of either venlafaxine hydrochloride (150 mg/day) or its major active metabolite, 0-desmethylvenlafaxine (ODV). Venlafaxine hydrochloride did not have any effect on the PK of diazepam or its active metabolite, desmethyldiazepam, or affect the psychomotor and psychometric effects induced by diazepam. **Haloperidol:** Venlafaxine hydrochloride (150 mg/day) decreased total oral-dose clearance of haloperidol, resulting in a 70% increase in haloperidol AUC. The haloperidol C_{max} increased 88%, but the haloperidol elimination $t_{1/2}$ was unchanged. **Lithium:** A single dose of lithium (600 mg) did not appear to affect the PK of either venlafaxine hydrochloride (150 mg/day) or ODV. Venlafaxine hydrochloride had no effect on the PK of lithium. **Drugs Highly Bound to Plasma Proteins:** Venlafaxine hydrochloride is not highly bound to plasma proteins; coadministration of Venlafaxine Extended Release Tablets and a highly protein-bound drug should not cause increased free concentrations of the other drug. **Drugs That Inhibit Cytochrome P450 Isoenzymes:** CYP2D6 and CYP3A4 Inhibitors: Venlafaxine hydrochloride is metabolized to ODV by CYP2D6. Drugs inhibiting this isoenzyme have the potential to increase plasma concentrations of venlafaxine hydrochloride and decrease those of ODV. Because venlafaxine hydrochloride and ODV are approximately equiactive and equipotent, no dosage adjustment is required when venlafaxine hydrochloride is coadministered with a CYP2D6 inhibitor. Pharmacokinetic studies with ketoconazole in both poor and extensive metabolizers of CYP2D6 resulted in higher plasma concentrations and AUCs of both venlafaxine hydrochloride and ODV in most subjects following administration of ketoconazole. Concomitant use of CYP3A4 inhibitors and venlafaxine hydrochloride may increase levels of both venlafaxine hydrochloride and ODV. Use caution if therapy includes venlafaxine hydrochloride and any CYP3A4 inhibitor. **Drugs Metabolized by Cytochrome P450 Isoenzymes:** Venlafaxine hydrochloride is a relatively weak inhibitor of CYP2D6 in vitro. Imipramine: Venlafaxine hydrochloride did not affect the PK of imipramine or 2-OH-imipramine. However, desipramine AUC, C_{max}, and C_{min} increased by about 35% in the presence of venlafaxine hydrochloride. The 2-OH-desipramine AUCs increased by 2.5 to 4.5 fold (with venlafaxine hydrochloride doses of up to 75 mg q 12h). The clinical significance of elevated 2-OH-desipramine is unknown. Imipramine did not affect the PK of venlafaxine hydrochloride and ODV. Metoprolol: Venlafaxine hydrochloride (50 mg q 8h for 5 days) appeared to reduce the blood-lowering effect of metoprolol (100 mg q 24h for 5 days) in one study. Caution should be exercised when these drugs are given together. Risperidone: Venlafaxine hydrochloride (150 mg/day) slightly inhibited metabolism of a single 1-mg dose of risperidone, resulting in an about 32% increase in risperidone AUC. Venlafaxine hydrochloride coadministration did not significantly alter the PK profile of the total active moiety (risperidone plus its metabolite 9-hydroxyrisperidone). CYP3A4: Venlafaxine hydrochloride did not inhibit CYP3A4 in vitro or in vivo. Indinavir: In healthy volunteers, venlafaxine hydrochloride (150 mg/day) resulted in a 28% decrease in the AUC of a single dose of a single 800-mg dose of indinavir and a 36% decrease in indinavir C_{max}. Indinavir did not affect the PK of venlafaxine hydrochloride and ODV. CYP1A2: Venlafaxine hydrochloride did not inhibit CYP1A2 in vitro or in vivo. CYP2C9: Venlafaxine hydrochloride did not inhibit CYP2C9 in vitro. In vivo, venlafaxine hydrochloride 75 mg (75 mg q 12h) did not alter the PK of a single 550-mg dose of tolbutamide or the CYP2C9-mediated formation of 4-OH-tolbutamide. CYP2C19: Venlafaxine hydrochloride did not inhibit the metabolism of diazepam, which is partially metabolized by CYP2C19 (see Diazepam above). **MAOIs:** [See CONTRAINDICATIONS and WARNINGS AND PRECAUTIONS in full Prescribing Information.] **Other CNS-Active Drugs:** Caution is advised if there is concomitant use of venlafaxine and other CNS-active drugs. Serotonergic Drugs and Triptans: Based on the mechanism of action of Venlafaxine Extended Release Tablets and the potential for serotonin syndrome, caution is advised when Venlafaxine Extended Release Tablets are coadministered with other drugs that may affect the serotonergic neurotransmitter systems, such as triptans, SSRIs, other SNRIs, linezolid, lithium, tramadol, or St. John's Wort. If concomitant treatment of Venlafaxine Extended Release Tablets with these drugs is warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. Concomitant use of Venlafaxine Extended Release Tablets with tryptophan supplements is not recommended [see **WARNINGS AND PRECAUTIONS** in full Prescribing Information]. There have been rare postmarketing reports of serotonin syndrome with use of an SSRI and a triptan. If concomitant use of Venlafaxine Hydrochloride Extended Release tablets with a triptan is warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases [see **WARNINGS AND PRECAUTIONS** in full Prescribing Information]. **Drugs That Interfere With Hemostasis:** Interference with serotonin reuptake may affect platelet function and result in bleeding. Concurrent use of NSAIDs or aspirin may increase this risk. Increases in prothrombin time (PT), partial thromboplastin time (PTT), or INR have been reported when venlafaxine hydrochloride was given to patients on warfarin therapy. Patients on warfarin should be carefully monitored when Venlafaxine Extended Release Tablets are begun or discontinued. **Electroconvulsive Therapy:** There is no clinical data establishing the benefit of electroconvulsive therapy combined with Venlafaxine Hydrochloride Extended Release Tablets. **Postmarketing Spontaneous Drug Interaction Reports:** There have been reports of elevated clozapine levels temporally associated with adverse reactions, including seizures, following the addition of venlaxafine. There have been reports of increases in PT, PTT, or INR when venlafaxine was given to patients also receiving warfarin. **USE IN SPECIFIC POPULATIONS: Pregnancy: Teratogenic Effects: Pregnancy Category C:** There are no adequate and well-controlled studies of venlafaxine in pregnant women. Venlafaxine Extended Release Tablets should be used during pregnancy only if clearly needed. **Non-Teratogenic Effects:** Neonates exposed to venlafaxine hydrochloride late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Complications can arise immediately upon delivery. Reports include respiratory distress, cyanosis, apnea, seizures, unstable temperature, feeding difficulty, vomiting, hypoglycemia, hypo- and hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. This is consistent with a toxic effect of SSRIs or SNRIs or a drug discontinuation syndrome. In some cases, it is consistent with serotonin syndrome. When treating a pregnant woman with Venlafaxine Extended Release Tablets during the third trimester, carefully consider the potential risks and benefits of treatment. **Labor and Delivery:** The effect of venlafaxine hydrochloride on labor and delivery in humans is unknown. **Nursing Mothers:** Venlafaxine hydrochloride and ODV, its active metabolite, are excreted in human milk. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue Venlafaxine Extended Release Tablets, taking into account the importance of the drug to the mother. **Pediatric Use:** Safety and effectiveness in the pediatric population have not been established [see **BOXED WARNING** and **Warnings and Precautions: Clinical Worsening and Suicide Risk**]. Anyone considering using Venlafaxine Extended Release Tablets in a child or adolescent must balance the potential risks with the clinical need. While no studies have adequately assessed the impact of venlafaxine hydrochloride on growth, development, and maturation of children and adolescents, studies suggest it may adversely affect weight and height [see **WARNINGS AND PRECAUTIONS: General: Changes in Height** and **Changes in Weight** in full Prescribing Information]. Should the decision be made to treat a pediatric patient with Venlafaxine Extended Release Tablets, regular monitoring of weight and height is recommended during treatment, particularly if long term. The safety of venlafaxine hydrochloride in pediatric patients has not been assessed for treatment beyond 6 months. In patients aged 6-17, clinically relevant blood pressure and cholesterol increases were similar to those observed in adult patients. The precautions for adults apply to pediatric patients. **Geriatric Use:** While no overall differences in effectiveness or safety were observed between geriatric and younger patients, greater sensitivity of some older individuals cannot be ruled out. The elderly may be at greater risk for significant hyponatremia. No dose adjustment is recommended based on age alone. **Patients With Hepatic Impairment:** Decreased clearance was noted in patients with cirrhosis. A lower dose may be necessary in these patients; extra caution should be used in these patients. **Patients With Renal Impairment:** In patients with GFR = 10 to 70 mL/min, clearance of venlafaxine hydrochloride and its metabolites were decreased. It is recommended that total daily dose of Venlafaxine Extended Release Tablets be reduced by 25% to 50% in these patients. Individualization of dosage may be desirable in some patients. In hemodialysis patients, it is recommended that total daily dose be reduced by 50%. Venlafaxine Extended Release Tablets should be used with caution in such patients. **DRUG ABUSE AND DEPENDENCE:** Venlafaxine Extended Release Tablets are not a controlled substance. Carefully evaluate patients for history of drug abuse and observe such patients closely for signs of misuse or abuse of venlafaxine hydrochloride. Discontinuation effects have been reported in patients receiving venlafaxine hydrochloride [see **WARNINGS AND PRECAUTIONS;** and **DOSAGE AND ADMINISTRATION** in full Prescribing Information]. **OVERDOSAGE:** In postmarketing experience, overdosage has occurred predominately in combination with alcohol and/or other drugs. The most commonly reported reactions include tachycardia, changes in consciousness, mydriasis, seizures, and vomiting. Electrocardiogram changes (eg, prolongation of QT interval, bundle branch block, QRS prolongation), ventricular tachycardia, bradycardia, hypotension, rhabdomyolysis, vertigo, liver necrosis, serotonin syndrome, and death have been reported. Ensure an adequate airway, oxygenation, and ventilation. Monitor cardiac rhythm and vital signs. General supportive and symptomatic measures are also recommended. Induction of emesis is not recommended. Gastric lavage with a large-bore orogastric tube with appropriate airway protection, if needed, may be indicated if performed soon after ingestion or in symptomatic patients. Activated charcoal should be administered. Due to the large volume of distribution of this drug, forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be of benefit. No specific antidotes for venlafaxine hydrochloride are known. In managing overdosage, consider the possibility of multiple drug involvement. Consider contacting a poison control center for additional information on treatment. Telephone numbers for certified poison control centers are listed in the *Physicians' Desk Reference*® (PDR®). **DOSAGE AND ADMINISTRATION:** Consult full prescribing information for dosing instructions. **Switching Patients to or From an MAOI: At least 14 days should elapse between discontinuation of an MAOI and initiation of therapy with Venlafaxine Extended Release Tablets. At least 7 days should be allowed after stopping Venlafaxine Extended Release Tablets before starting an MAOI** [see **WARNINGS AND PRECAUTIONS** in full Prescribing Information].

To report SUSPECTED ADVERSE REACTIONS, contact Upstate Pharma, LLC Pharmaceutical Corp. at 1-888-299-1053 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

This brief summary is based on Venlafaxine Extended Release Tablets Prescribing Information, January 2009. Osmotica Pharmaceutical Corp.

Marketed by Upstate Pharma, LLC, Rochester, NY 14623 for Osmotica Pharmaceutical, Wilmington, NC 28405.

‘Huge Challenges’ Could Hinder Electronic Record Adoption

Potentially serious obstacles to physicians adopting health information technology systems could affect federal guidelines for determining what systems qualify physicians for refunds through a $17 billion federal incentive program.

BY RICH DALY

The physician charged with implementing a $17 billion federal incentive program that will reimburse physicians for some of the costs of electronic health records recently highlighted problems that a national record system is likely to encounter.

David Blumenthal, M.D., who was appointed as the national coordinator for health information technology (HIT) at the Department of Health and Human Services in March, will oversee the implementation of an unprecedented federal effort to spur nationwide HIT adoption—including use of electronic medical records (EMRs) and e-prescribing—by clinicians and hospitals. In a commentary published April 9 in the *New England Journal of Medicine*, Blumenthal highlighted some of the difficulties facing such a national system.

The former Harvard Medical School professor wrote that “huge challenges” in efforts to establish a national EMR system could include low adoption rates for the technology, potential technical problems, high initial set-up costs, and data-privacy concerns by both clinicians and patients.

The patient-privacy concerns were highlighted by a telephone survey of a nationally representative sample of 1,238 adults by the Kaiser Family Foundation in March; 76 percent of respondents said they believed it would be very or somewhat likely that an unauthorized person would be able to access their medical record.

The privacy concerns and other challenges will need to be addressed by Blumenthal in his key role in implementing the federal program to reimburse physicians up to $44,000 over five years for their costs in installing digital record systems. That role was created by the American Recovery and Reinvestment Act of 2009 (ARRA, PL 111-5), which included $17 billion in grants to encourage the use of EMRs, HIT (which includes the software and hardware needed to operate EMRs), and e-prescribing (*Psychiatric News*, March 20). The law also includes penalties for physicians who have not installed EMR systems by 2015.

Cost estimates for the adoption of HIT systems vary widely. The Agency for Healthcare Research and Quality concluded in 2005 that the average cost to place EMRs in practices overall was about $32,600 per clinician, while smaller practices were likely to incur a somewhat higher cost—about $37,200 per clinician. A March analysis by Avalere, a health care consulting company, concluded that a solo or small-group physician practice implementing an EMR system could spend an estimated $124,000 over five years, or $80,000 more than the maximum federal reimbursement.

Eligibility for federal reimbursements will be limited to those who use “certified” EMR systems, and that certification process and its criteria will be determined by Blumenthal’s office. His role is expected to supersede the work of the Certification Commission for Healthcare Information Technology (CCHIT), which has been working with the health care industry—including physician groups—to develop HIT standards (*Psychiatric News*, January 5, 2007). The economic-stimulus law describes the CCHIT standards as a guide for future federal certification standards—due to be finalized by 2010—but those standards will not be constrained by CCHIT decisions.

Blumenthal wrote that many EMRs certified through the CCHIT process are neither user friendly nor designed to meet the stimulus law’s goal of improving quality and efficiency in the nation’s health care system.

“Tightening the certification process is a critical early challenge” for the national HIT coordinator, he said.

The push toward a nationwide HIT system, which the stimulus law is designed to accelerate, has been driven by the belief that the technology can improve health care efficiency, reduce costs, and boost the quality of care. HIT advocates maintain that an interoperable system for exchanging patient data among physicians’ offices, hospitals, and public agencies will reduce medical errors and provide alerts about dangerous medication interactions.

However, some HIT experts have warned that poorly managed and badly designed systems could increase risks for patients through inadvertent loss of their medical data or poor system interoperability. Problems with EMRs also could arise from clinicians’ trying to install the systems too quickly and without adequate technical support.

Blumenthal’s commentary, “Stimulating the Adoption of Health Information Technology,” is posted at <http://content.nejm.org/cgi/reprint/360/15/1477.pdf>. The Web site of the Office of the National Coordinator for Health Information Technology is <http://healthit.hhs.gov/portal/server.pt>. ■

Resignation

Ryszard Zebrak, M.D., of Spotsylvania, Va., resigned from the American Psychiatric Association and from the Washington Psychiatric Society during the course of an ethics investigation. APA’s “Procedures for Handling Complaints of Unethical Conduct” require that resignations that occur during the course of an ethics investigation be reported in *Psychiatric News*. ■

Anxious Depression: Diagnostic and Treatment Issues

Hilton–San Francisco
Ballroom 4/5/6

Monday, May 18, 2009 • 6:30-7:00 pm Dinner • 7:00-9:00 pm Symposium

Agenda

6:30-7:00 pm	Dinner	
7:00-7:10 pm	Welcome and Introduction	Maurizio Fava, MD (Chair), Massachusetts General Hospital
7:10-7:30 pm	How Do We Define Anxious Depression?	John M. Zajecka, MD, Rush University Medical Center
7:30-7:35 pm	Q&A	
7:35-7:55 pm	Neurobiology of Anxious Depression	Audrey Tyrka, MD, PhD, Brown Medical School
7:55-8:00 pm	Q&A	
8:00-8:20 pm	Pharmacotherapeutic Strategies in the Treatment of Anxious Depression	Maurizio Fava, MD, Massachusetts General Hospital
8:20-8:25 pm	Q&A	
8:25-8:45 pm	Psychotherapeutic Approaches to Anxious Depression	Amy Farabaugh, PhD, Massachusetts General Hospital
8:45-8:50 pm	Q&A	
8:50-9:00 pm	Panel Discussion/Q&A	

Learning Objectives

At the conclusion of this symposium, the participant should be able to:

- Differentiate anxious depression from major depression and appreciate the neurobiological and phenomenological differences between these subtypes.
- Diagnose anxious depression in routine clinical practice.
- Develop treatment plans for patients with anxious depression that recognize the importance of psychotherapy in treatment and the typically less robust response to pharmacotherapy.

Accreditation Statement

The American Psychiatric Association (APA) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Credit Designation

The APA designates this educational activity for a maximum of 2 *AMA PRA Category 1 Credits*™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Registration

Attendees must be registered for the APA Annual Meeting to attend this symposium. Seating is limited and will be based on first-come, first-served. For more information about the meeting, please visit the APA website at www.psych.org or contact the APA toll-free at 1-888-357-7924 (within the U.S. or Canada) or 703-907-7300.

Sponsored by the
American Psychiatric Association

Supported by an educational grant from
H. Lundbeck A/S and Takeda Pharmaceuticals North America, Inc.

Psychiatry Resident Researchers Have Their Eyes on the Prize

Their local baseball team may be long gone, but young psychiatrists in Brooklyn go head to head competing for local research honors.

BY AARON LEVIN

Credit: Aaron Levin

From left are Alan Schatzberg, M.D., Carolina Klein, M.D., Peng Pang, M.D., Marina Smirnov, M.D., Deborah Cross, M.D., Fryderyka Shabry, M.D., and Ramaswamy Viswanathan, M.D., D.Sc. Viswanathan originated the annual all-Brooklyn residents' research competition. Schatzberg, Cross, and Shabry were judges, while Klein, Pang, and Smirnov were contestants.

Competitive psychiatry got a boost in April when three young researchers stepped into the arena and presented their results before throngs (well, dozens) of fellow residents and other members of the Brooklyn Psychiatric Association.

In the town that gave the world the Dodgers, a famous bridge, Nathan's hot dogs, and the transgressive poetry of Walt Whitman, residents from the borough's three psychiatry programs squared off at Brookdale University Hospital Medical Center for the 19th annual contest sponsored by the Brooklyn district branch.

"It's the Super Bowl of Brooklyn," said Ramaswamy Viswanathan, M.D., D.Sc., an associate professor of clinical psychiatry and director of the consultation-liaison service at the State University of New York Downstate Medical Center. He founded the competition in 1991.

Sports were more than a metaphor, as a member of the audience was appointed to ring a bell for the two-minute warning near the end of each 15-minute presentation.

Credit: Aaron Levin

Carolina Klein, M.D., a fourth-year resident at SUNY Downstate Medical Center, took first place in the competition.

Watching the proceedings were partisans from all programs and three judges who had reviewed their share of papers in their careers: Deborah Cross, M.D., president of the New York State Psychiatric Association and director of the adult outpatient psychiatric clinic at Westchester Medical Center in Valhalla, N.Y., and an associate professor of clinical psychiatry at New York Medical College; Fryderyka Shabry, M.D., director of psychiatry at Coney Island Hospital; and Alan Schatzberg, M.D., a professor of psychiatry and behavior sciences at Stanford University and APA's president-elect. Contestants were judged on both the content and style of their presentations.

> **"We gain a skill in doing research instead of just learning the outcomes."**

Peng Pang, M.D., representing Maimonides Medical Center in Brooklyn, got the evening off to a smooth start with a talk on the utility of tai chi chuan in improving the quality of life and reducing depression and anxiety for cancer survivors. Tai chi evolved from Chinese martial arts 700 years ago. It emphasizes controlled, fluid movements and includes both physical and meditative elements.

Her review of prior literature found 13 randomized, controlled studies with 730 subjects on the topic. Most patients had some sort of physical limitations restricting their participation in conventional exercise.

Some studies used sham exercise as a control and found there was no difference physiologically, but sham exercise produced different outcomes compared with tai chi, said Pang. The theoretical basis of any effect was unknown, despite comparisons with physical exercise, reading, and meditation.

A meta-analysis of the studies found positive outcomes for quality of life in cancer patients. However, studies of anxiety and depression were so varied that it was impossible to draw significant conclusions of tai chi's efficacy.

Pang also presented the design of a study intended to answer many of the questions raised by her meta-analysis, including intragroup differences and longer-term follow-up.

Next, Brookdale's own Marina Smirnov, M.D., stepped into the ring, accompanied by raucous cheers from her disproportionately numerous fellow residents in the hall.

Smirnov discussed the role of clinicians' religious and spiritual beliefs in clinical practice.

"Psychiatry and religion provide alternative ways of looking at life," she said. The two have not always played together nicely, reminding the crowd of Freud's view that religion was an obsessional system bordering on mental illness.

While religion and spirituality are often used interchangeably, the former should be seen as organized systems of beliefs and practices, while the latter is more of a subjective, internal appreciation of the divine, she said.

In a survey of fellow Brookdale clinicians, Smirnov found few significant differences in their spiritual beliefs when viewed through the lenses of gender, religious attitudes, and prescribing status. The only significant variable was how much patients talk about these issues.

"Clinicians didn't let their own beliefs influence discussions with patients on religious or spiritual issues," she said. "If patients talk more about these concerns, the clinician became more willing to include them in the discussion."

Regardless of their own religious or spiritual beliefs, clinicians should be sensitive to patients' beliefs, she concluded before leaving the stage to loud cheers from her fans.

After those two presentations, Carolina Klein, M.D., carrying the flag for SUNY Downstate Medical Center, had her work cut out for her. She rocked the audience immediately with a sudden shift in strategy to biological psychiatry.

Klein reported on a study examining the interaction of early life stress and Substance P in bonnet macaques. Substance P is a neuropeptide associated with psychopathology. The monkeys were stressed with variable foraging demands (VFD), in which they always received enough food but sometimes it was hidden within their cages, forcing them to search for it more intensively. Klein and her fellow researchers found that presented with these alternating high and low foraging demands, the macaques tended to cling more to their mothers after weaning but also showed less "huddling," a measure of social interaction. However, there were no significant differences in Substance P levels between VFD and non-VFD cohorts.

Upon closer examination of the VFD group, they found that infant macaques that had clung more closely to their mothers had higher levels of Substance P as adolescents, while those that were more independent as infants had lower Substance P levels as adolescents.

"The lesson is not that Substance P causes elevated dysregulation of neurochemicals, but that it shows the vulnerabilities of the individual."

Klein, too, left the stage to cheers from her visiting fans.

The three judges did some huddling of their own outside the hall as Pang retook the stage for a brief demonstration of the stately art of tai chi.

Cross, Shabry, and Schatzberg returned with a unanimous decision in Klein's favor, a decision that garnered her bragging rights in Brooklyn for the next year and a check for $250. The runners up each received $125 for their efforts.

Klein is not on a research track in residency, but getting involved in research adds scientific rigor to residents' training, she said, as she took congratulations from fellow Downstaters.

"We gain a skill in doing research instead of just learning the outcomes," she said. "I think it also allows us to read the literature more critically."

"All the presentations were excellent, but Klein's won the consensus vote of the judges," commented Schatzberg afterward.

But there was more to the competition than intraborough glory and the winner's check, he added. "It promotes the intellectual and professional development of the residents and it gets them involved with their district branch and APA."

Inspired by the Brooklyn DB contest, a similar contest has been started by the Queens DB, and a written-paper contest has been started by the New York State Psychiatric Association, said Viswanathan.

Schatzberg would like to see a similar program with nationwide scope. In any case, while he was the first APA president-elect to judge the proceedings, he will not be the last. The incoming president-elect, Carol Bernstein, M.D., has agreed to be a judge of next year's contest, and Viswanathan hopes that creates another new tradition. ■

An American Psychiatrist in Cuba

BY JOSE VITO, M.D.

As an APA/SAMHSA fellow, I had the privilege to be invited to present a poster at the 2009 World Psychiatric Association (Zone 3) conference in Havana, Cuba, in February, and since few of my colleagues have been able to travel to Cuba, I want to share some of my impressions.

When I found out that my presentation, "Minority Adolescent Addiction Programs and Advocacy's Role in Enhancement of Services," was accepted, I was excited. Then I quickly realized that as a U.S. citizen, I might be thwarted by U.S. restrictions that have blocked most travel to Cuba since early 1962. I certainly did not want to break the law. I was reassured by Michael Kerman, president of Leading Edge Seminars, the Toronto-based company that acted as registrar for this international conference, that my trip would be allowed once I proved that I was a full-time mental health clinician going to a conference organized by the World Psychiatric Association (WPA). I could do this by presenting my CV to customs officials. I was able to obtain a visa and catch a charter flight from Miami. I brought lots of Band-Aids and medications such as acetaminophen to donate to the outpatient clinic sites I planned to visit.

Once at the conference, it was nice to see familiar faces. I saw Dr. Pedro Ruiz, for example, who is a past APA president and the current WPA president-elect. His speech at the opening ceremony was inspirational, and he noted that he was born in Cuba.

The Cuban Psychiatric Association made arrangements for program presenters to discuss emerging trends in psychotherapy, medications, and social programs in Cuba, the United States, and Canada.

Also, there was an opportunity to go behind the scenes during site visits to community mental health programs. There were, for example, "conversation cafes" where we were able to interact with Cuban mental health professionals. One of the Cuban psychiatrists I met was very interested in ECT and asked me lots of questions, thinking that I must be an expert in this treatment modality. I was kicking myself as I wished I had paid better attention when an ECT lecture was given during my training.

Mental health services in Cuba are free. I was amazed that Cuban mental health professionals typically spend at least two hours with a patient, as opposed to the U.S. system in which visits are almost always far shorter. They do have psychotropic medications, which they receive via donations from other countries, since money is not available to import them. But accessibility to and availability of medications is a problem. The challenge for psychiatrists is deciding who should get the medications and for how long they can prescribe them considering the scarce supply. Imagine treating an out-of-control ADHD or schizophrenia patient when there are few if any medications available to treat their disorder. Since it is difficult to obtain medications, I was told that psychiatrists and mental health professionals focus on educating the public about mental illness prevention. They also use acupuncture, homeopathy, and dance and art therapy to help patients when medications aren't available.

When I think of Cuba, I associate it with the country's famous cigars. I was

surprised to see that Cubans still smoke indoors! It was typical to see people smoking cigars in an enclosed jazz club. Often I had to curb my inclination to tell someone to smoke outside.

Addiction is prevalent in Cuba, particularly alcoholism and cannabis abuse. A small percentage of IV drug users do exist, though syringes are difficult to obtain. I was told that abuse of prescription medications such as pain killers is on the rise and that an "underground black market" in them exists.

I also had the opportunity to visit an HIV/AIDS clinic and realized how desperately Cuba needs antiviral medications.

In addition, since housing is a big problem in Cuba in general, shelters have not been established for victims of domestic violence or adolescent sexual/physical

please see ***ECP Issues*** *on page 36*

Jose Vito, M.D., is an APA/SAMHSA fellow at Albert Einstein College of Medicine.

ADHD

continued from page 1

interventions, all patients went on to community care. The study investigators continued to follow these patients and assessed their outcomes at two, three, six, and eight years after the initial randomization.

Immediately after the 14-month randomized interventions, all four groups had symptom reduction and functional improvement from baseline. Groups receiving intensive medication management, either alone or in combination with behavioral interventions, had significantly larger symptom improvements than the groups receiving behavioral interventions alone or community care.

The combination group had the best outcomes on social skills, parent-child relations, and a few other measures, which were statistically significant compared with other groups, at the end of the 14-month intensive treatments. Both the combination treatment and medication management groups improved significantly more than the behavioral intervention and usual-care groups at the time. However, the advantages of medication management and combination treatment diminished after the interventions stopped, and the differences among the initially randomized groups were no longer significant at the three-year follow-up, or 22 months after the end of the study interventions.

Long-Term Outcomes Converge

At the eight-year follow-up, about three-quarters of the original study participants, now up to age 17, were evaluated. The types of treatment they received eight years before did not significantly predict outcomes, including ADHD symptoms, behavioral and functional assessments, academic performance, and social functioning. The follow-up data were published online in the *Journal of the American Academy of Child and Adolescent Psychiatry* on March 23.

Despite improvements from baseline, all four groups in their adolescence still had more symptoms, such as hyperactivity and impulsivity, and more functional impairments, such as lower academic performance and behavioral problems, than did their peers of the same age and similar characteristics who had never had ADHD.

Medication use in the previous year was not associated with significantly better functioning at the eight-year assessment. About 20 percent of study participants were not medicated at any of the evaluation points during the study, while 17 percent were still taking stimulants at the eight-year follow-up. Among the patients who were medicated during the intervention phase eight years earlier, 62 percent had stopped taking ADHD medications in subsequent years, which may in part account for the loss of treatment benefits seen in the 14-month analyses.

"These findings are not really surprising," said Brooke Molina, Ph.D., an associate professor of psychiatry at the University of Pittsburgh Medical Center, in an interview with *Psychiatric News*. She was the lead author of the eight-year study.

Children Don't Outgrow Symptoms

One of the important messages from the study, she explained, is "the many differences between children with and without ADHD. It used to be believed that these children could outgrow the behavioral and developmental symptoms in their adolescence. The data show that, as a group, they still lag behind [their peers]."

The results do not imply, however, that medications do not work for ADHD patients. "The study demonstrated strong acute effects of the medication treatment in 1999," Molina noted, referring to the results at the end of the 14-month intervention phase.

"The message is not that treatments do not work." Rather, the study showed that a one-year intensive therapy in childhood does not make much difference in the long run compared with less-intensive treatment. "[ADHD] is a chronic disorder that cannot be cured by one-year intensive treatment," she said. In the context of long-term adverse effects of stimulant use, such as growth suppression, "medications are not the panacea for the long-term health of these children. We need to develop more treatment options with long-term effectiveness and palatability with teens."

David Fassler, M.D., a child psychiatrist and clinical professor of psychiatry at the University of Vermont School of Medicine, echoed this interpretation. "The study results should be interpreted with caution," he told *Psychiatric News*. "Treatment conditions were no longer randomized" in most of the follow-up period, he noted, and the dropout rate at eight years should be taken into consideration. Nonetheless, he noted that the findings are generally consistent with clinical experience.

"For many children with ADHD, treatment will vary over time and often include periods on and off medication, as well as working with the child, parents, and, ideally, the school," said Fassler, who is also APA's secretary-treasurer. "Ultimately, treatment is most effective when it's closely monitored and individualized to the needs of the child and family."

In addition, Molina recommended that parents and clinicians regularly reexamine the effects of medication therapy in children with ADHD and carefully consider whether to continue it. "Some children may continue to derive benefits from treatment," she said. "However, it is extremely important that we do not automatically leave patients on medications for years without reevaluation."

The MTA study was funded by the National Institute of Mental Health.

An abstract of "MTA at 8 Years: Prospective Follow-up of Children Treated for Combined-Type ADHD in a Multisite Study" is posted at <journals.lww.com/jaacap/Abstract/publishahead/MTA_at_8_Years__Prospective_Follow_up_of_Children.99835.aspx>. ■

APA 2009 Annual Meeting in San Francisco, CA

Development of New Agents for the Treatment of Schizophrenia

Sunday, May 17, 2009, 12:00-12:30 pm Lunch, 12:30-2:30 pm Symposium, Grand Ballroom, Salon B, Hilton–San Francisco Hotel

Learning Objectives

After participating in this symposium, participants should be able to:

- Recognize unmet needs in the treatment of schizophrenia and the development of new agents aimed at these needs
- Identify barriers to the rapid development and approval of new agents
- Discuss potential drug development targets to improve cognition in patients with schizophrenia

Statement of Need

The field of psychiatry has made significant strides over the last 50 years in developing strategies for managing the symptoms of schizophrenia. As the goal of treatment has shifted from symptomatic reduction toward remission and recovery, a number of unmet needs have emerged. New drug treatments are a key step toward addressing these needs, and a number of agents are in various stages of testing. Drug development is a multifaceted and multistep process with many challenges along the way. Both appropriate symptom targets and pharmacological mechanisms must be identified and characterized, and appropriate methods for studying them must be established. Drugs require testing in laboratory animals, followed by toxicology, safety and efficacy trials in humans. At each stage along the way there is the potential for the agent to be abandoned, modified or retested. Faculty in this interactive, case-based symposium will review unmet needs in the treatment of schizophrenia as well as discuss new symptom domains and mechanisms of action that are likely to be targets for emerging drug development.

Webber MA, Marder SR. Better pharmacotherapy for schizophrenia: what does the future hold? *Curr Psychiatry* 2008;10:352-358.

Terry AV Jr, et al. Cognitive dysfunction in neuropsychiatric disorders: Selected serotonin receptor subtypes as therapeutic targets. *Behav Brain Res* 2008;195:30-38.

Buchanon RW, et al. Recent advances in the development of novel pharmacological agents for the treatment of cognitive impairments in schiozphrenia. *Schizophr Bull* 2007;33:1120-1130.

Gray JA, et al. Molecular targets for treating cognitive dysfunction in schizophrenia. *Schizophr Bull* 2007;33:1100-1119.

Accreditation Statement

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Agenda

12:00-12:30 pm	**Lunch**
12:30-12:40 pm	**Welcome and Introduction** Steven G. Potkin, MD (Chair) University of California, Irvine
12:40-1:00 pm	**Unmet Needs in Schizophrenia** Adrian Preda, MD University of California, Irvine
1:00-1:20 pm	**Drug Development in Psychiatry: Issues and Trends** Amir H. Kalali, MD Quintiles Inc. University of California, San Diego
1:20-1:40 pm	**New Targets for Drug Development** Philip Harvey, PhD Emory University School of Medicine
1:40-2:00 pm	**Late Stage and Recently Approved Antipsychotic Agents** Steven G. Potkin, MD University of California, Irvine
2:00-2:30 pm	**Panel Discussion/Q&A**

Sponsored by the American Psychiatric Association

Supported by an educational grant from Dainippon Sumitomo Pharma Co., Ltd.

DAINIPPON SUMITOMO PHARMA

Chronic Illness More Often Going Untreated

The prevalence of chronic disease among working-age Americans appears to have increased in recent years, leading more to delay needed care when confronted with financial struggles.

BY RICH DALY

More than 28 percent of the 72 million working-age people in the United States with chronic illnesses such as depression lived in households that struggled to pay their medical bills in 2007, according to the results of a national study released last month. And while the uninsured are particularly vulnerable, medical-bill problems are also growing among people with insurance and higher incomes.

The study was done by the Center for Studying Health System Change (HSC), a Washington, D.C., health policy research group.

The number of chronically ill people struggling with health care costs showed a "significant increase" from the 21 percent reporting such problems in the HSC's 2003 survey, according to the report.

Among the approximately 20 million chronically ill working-age adults living in households with medical-bill problems, 25 percent went without needed care. In addition, 50 percent delayed care, and 56 percent did not fill a drug prescription that had been written for them.

"The rising prevalence and increasing financial burden of chronic conditions mean more working-age Americans than ever are forgoing or delaying medical care because of concerns that they cannot afford treatment," said Ha T. Tu, a senior health researcher at the HSC and coauthor of the study.

The 2007 Health Tracking Household Survey findings were based on a nationally representative survey of 4,300 working-age adults. The data were extrapolated for population estimates.

The survey also found that the overall prevalence of chronic conditions increased between 2003 and 2007. About 34 percent of working-age survey respondents in 2003 reported at least one chronic illness, while 39 percent of them, or an estimated 72 million people, had conditions such as diabetes, asthma, or depression in 2007.

Among uninsured people with chronic illnesses, 62 percent, or an estimated 5.7 million people, were in families that were unable to pay medical bills. The survey found that 38 percent of such people decided to forgo needed care, while 65 percent delayed care and 73 percent did not fill a prescription because of cost concerns.

Access to clinicians by working-age people with chronic illness also was identified as a challenge, even among people with insurance. Seventeen percent of such people with private insurance went without needed care, while 43 percent delayed care and 45 percent did not fill a prescription because of cost concerns.

While rates of access problems remained stable—at high levels—for the uninsured with medical debt between 2003 and 2007, unmet-need and delayed-care problems for the privately insured with medical debt increased significantly. The authors attributed the change to a trend among employers and insurers in that time to increase patient cost sharing.

The costs of treating chronic illness appeared to be increasingly borne by the public. In 2007 about 20 percent of working-age people with chronic conditions had public insurance, primarily Medicaid and Medicare, compared with 17 percent in 2003. The period saw commensurate declines in private coverage of people with chronic illness. The result was a "relatively stable" 13 percent rate of uninsurance among working-age people with chronic conditions.

HSC survey findings are posted at <www.hschange.org/CONTENT/1049>. ■

professional news

Referral

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reported they couldn't get diagnostic imaging, and 17 percent who reported they were unable to obtain nonemergency hospital admissions.

Primary care clinicians cited inadequate health coverage, "insurance barriers," and an inability to find a mental health clinician to care for their patients, among the chief reasons their patients could not obtain care for psychiatric conditions.

Among primary care providers, who included general internists, family and general practitioners and pediatricians, the pediatricians were more likely to report problems in getting mental health care for their patients. Pediatricians cited a shortage of providers for children and health plan barriers such as a lack of coverage for mental health services.

The study consistently found a lower number of psychiatrists in areas of the country where there were more problems getting mental health services due to a shortage of providers. Physicians in counties with moderate or large numbers of psychiatrists (defined by the authors as at least eight psychiatrists per 100,000 residents) were about 12 percent less likely to report provider shortages as one reason for the lack of available mental health referral care than were clinicians in counties with fewer psychiatrists.

The authors were surprised that counties with a high number of psychiatrists had a greater probability of patients being denied mental health care because of either "plan barriers" or inadequate or a lack of coverage among patients compared with counties having smaller numbers of psychiatrists. Although areas with large numbers of psychiatrists were likely to have greater mental health care utilization overall, the authors theorized that health insurance plans in those locations may attempt to limit the utilization of psychiatric care through greater restrictions on utilization or less generous benefits.

The study "clearly is an indicator that there are ongoing problems with access to mental health care," said Anita Everett, M.D., chair of APA's Council on Healthcare Systems and Financing.

Still, in many areas with small numbers of psychiatrists, the researchers found that the shortage of such clinicians had a greater impact on the ability to obtain mental health care than did obstacles stemming from a lack of coverage and from insurance-plan barriers.

Problems accessing mental health care that stemmed from a lack of insurance—and underinsurance by policies that provided no or lesser mental health care coverage—were most often cited as factors in patients not receiving needed care. It is not known yet whether access to mental health care was enhanced by the federal mental health insurance parity law enacted in 2008, said the authors. They concluded that state mental health parity laws have had only a modest effect on reducing mental health access disparities when compared with states that do not have insurance parity laws.

"Even with national parity legislation, large gaps in mental health access will likely remain, and the new law will have no effect on the severe access problems of the uninsured as well as problems related to the shortage of mental health care providers," Cunningham and his coauthors wrote.

"Beyond Parity: Primary Care Physicians' Perspectives on Access to Mental Health Care" is posted at <http://hschange.org/CONTENT/1054/?>. ■

Price of Brand-Name Psychiatric Drugs On Steep Upward Course

Brand name antidepressants, antipsychotics, sedatives, and antidementia agents all experienced manufacturer price increases that exceeded general inflation.

BY MARK MORAN

Manufacturer prices for brand-name prescription drugs widely used by Medicare beneficiaries jumped by nearly 9 percent in 2008, according to the 2009 AARP "Rx Watchdog Report."

That increase was the largest annual increase in six years and greatly exceeded the general inflation rate of 3.8 percent.

Major classes of psychiatric brand-name drugs—including antidepressants, antipsychotics, sedatives, and antidementia agents—experienced price increases that exceeded general inflation. Grouped in a class and compared with all other therapeutic drug categories, two dosages of Wellbutrin (300 mg and 150 mg) experienced the greatest increase, rising in price by 21 percent (see chart).

Meanwhile, manufacturer prices of widely used generic drugs continued to decrease in 2008, falling by an average of 10.6 percent. The majority of generics (83 percent) did not change in price in 2008, despite an increase in general inflation.

And some of the generics that did drop in price did so very dramatically. For instance, the manufacturer price for the brand-name antidepressant Zoloft (50 mg and 100 mg tablets) increased by 12.3 percent in 2008, but the price for generic sertraline made by Teva Pharmaceuticals decreased by 45.1 percent, according to the report.

"A person taking three brand-name prescription drugs could see his or her annual costs climb by more than $550 in just one year," AARP Public Policy Director John Rother said in a statement released with the report. "Switching to generic drugs whenever possible is one of the quickest and easiest ways to drastically reduce health care bills."

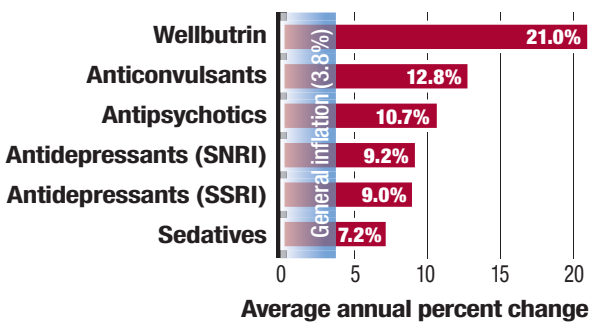
The list of prescription drugs widely used by Medicare beneficiaries is based on the 300 most widely dispensed drug products, the 300 drug products with the highest sales levels, and the 300 drug products with the highest number of days of therapy among the prescriptions provided by United HealthCare-PacificCare. (That company provides Medicare Part D coverage and is also the organization that insures the AARP Medicare Rx Plans.)

Price changes were measured using changes in the wholesale acquisition cost as published by the Medi-Span Price-Chek PC Database.

AARP's "Rx Watchdog Report" is posted at <http://assets.aarp.org/rgcenter/health/2009_07_rxq408.pdf>. ■

Prices of Brand-Name Drugs Rose Faster Than Inflation

Among 300 of the most prescribed name-brand drugs, Wellbutrin at doses of 300 mg and 150 mg—grouped as a therapeutic class and compared with other therapeutic classes—experienced the greatest price increase (21 percent) in 2008. The general 2008 rate of inflation was 3.8 percent.



Source: "Rx Watchdog Report," AARP, April 2009

Valproate Linked To Increased Prenatal Risks

Valproate should not be a first-line treatment for women who are or may become pregnant.

BY JUN YAN

Valproate, an epilepsy drug also used to treat bipolar disorder, is linked to lower IQ scores at age 3 in children exposed to the drug before birth than in children whose mothers took other antiepileptic drugs during pregnancy, a study published in the April 4 *New England Journal of Medicine* showed.

From 1999 to 2004, U.S. and U.K. researchers enrolled 303 pregnant women with epilepsy who were taking lamotrigine, phenytoin, carbamazepine, or valproate in a prospective, observational study known as the Neurodevelopmental Effects of Antiepileptic Drugs study. The researchers conducted follow-up assessments, especially in terms of neurological development, in the children. Women who were not taking any antiepileptic drugs during pregnancy were not included.

The average IQ score of 3-year-old children who had in utero exposure to valproate was 92, which was statistically significantly lower than that of children exposed to lamotrigine (average IQ 101), phenytoin (99), or carbamazepine (98). The comparisons among lamotrigine, phenytoin, and carbamazepine were not statistically different. The authors also found a dose-dependent relationship between valproate and IQ score.

That valproate exposure carries a higher risk of birth defects than other antiepileptics, such as lamotrigine and carbamazepine, is not new knowledge, Torbjorn Tomson, M.D., a professor of clinical neuroscience at the Karolinska Institute in Sweden, pointed out in an editorial. The worthwhile discovery of this study was the differential effects on children's long-term cognitive development associated with various antiepileptics. This was the largest prospective study so far on the effects of antiepileptics on cognitive development.

This study was reported in several media outlets, including the *New York Times* and the Associated Press, with broad headlines such as "I.Q. Harmed by Epilepsy Drug in Utero," without clearly presenting the context that the study was a comparison between valproate and other antiepileptic drugs.

Untreated epilepsy, as well as untreated bipolar disorder, poses a significant risk of harm to pregnant women and their fetuses. For many pregnant patients, stopping medication is not an option. Therefore, accurately describing the different risks among drugs in the same class is critically important for physicians and patients. The authors concluded that valproate should not be used as a first-line treatment for women who are pregnant or may become pregnant. In addition, "discussion of the risks of valproate should be balanced with consideration of the risks of uncontrolled seizures," Tomson recommended.

An abstract of "Cognitive Function at 3 Years of Age After Fetal Exposure to Antiepileptic Drugs" is posted at <content.nejm.org/cgi/content/short/360/16/1597>. ■

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* May vary by state - see policy for details

Moon Phases and Violent Crime: More Than Pie in the Sky?

Most serious crimes committed outdoors seem to occur when the moon is full or waning than when it is not. Is there some mysterious force at work or are there practical reasons?

BY JOAN AREHART-TREICHEL

The derivation of such outdated terms as "lunatic" reflects the centuries-old common belief that the moon (*luna* in Latin) can affect people's psyches and behaviors in deleterious ways.

But can it?

Anecdotal reports suggest so. For example, some clinicians have observed that, at the time of the full moon, hospital emergency rooms are busier than usual and patients in mental hospitals become agitated.

Credit: Sergey Ivanov

Some studies likewise suggest an association between the full moon and pernicious behavior. For instance, a study reported in the July 1972 *American Journal of Psychiatry* found that some 2,000 homicides committed in Dade County, Fla., over a 15-year period peaked at the time of the full moon. The link was statistically significant. The study also found that homicides committed in Cuyahoga County, Ohio, over a 13-year period peaked at the time of the full moon, but this link did not quite reach statistical significance. As for suicides and the full moon, some studies have found a link.

Now Teresa Biermann, M.D., a psychiatrist affiliated with the University Hospital of Erlangen in Germany, and colleagues have taken a fresh look at the ancient belief that the moon can affect people's psyches and behaviors in harmful ways. They attempted to see whether they could find a link between serious violent crimes in their area of Germany (Middle Franconia in Bavaria) and various phases of the moon. The study included 23,000 serious violent crimes committed in this area over seven years (from 1999 to 2005) and recorded by the police department.

The researchers could find no statistically significant link between any of the moon's phases and serious violent crimes in general, they reported in *Comprehensive Psychiatry* online on March 10. However, when they broke the crimes down into those committed outdoors and those committed indoors, they did find a statistically significant link between crimes committed outdoors and a full or waning moon—more crimes were committed at these times.

One possible explanation for this finding is physiological, the researchers proposed in their report. Variations in lunar light have been found to influence melatonin levels in animal brains, which in turn can influence aggressive behavior. Another possible explanation, the researchers wrote, is that criminals can see better on such nights to conduct their nefarious deeds.

Yet another reason there may be a link between the full and waning moon and serious violent crimes, Biermann pointed out to *Psychiatric News*, is that the police nab more criminals when moonlight is strong.

The study had no outside funding.

An abstract of the "Relationship Between Lunar Phases and Serious Crimes of Battery: A Population-Based Study" can be accessed at <www.sciencedirect.com> under "Browse by Title" by clicking on "C," "Comprehensive Psychiatry," "Articles in Press," and then the study title. ■

PAROXETINE HYDROCHLORIDE EXTENDED-RELEASE TABLETS

℞ only

BRIEF SUMMARY: Please see package insert for full prescribing information.

Suicidality and Antidepressant Drugs

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of paroxetine or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Paroxetine is not approved for use in pediatric patients. (See WARNINGS: Clinical Worsening and Suicide Risk, PRECAUTIONS: Information for Patients in full Prescribing Information and PRECAUTIONS: Pediatric Use.)

INDICATIONS AND USAGE: Major Depressive Disorder: Paroxetine hydrochloride extended-release tablets are indicated for the treatment of major depressive disorder.

The efficacy of paroxetine hydrochloride extended-release tablets in the treatment of a major depressive episode was established in two 12 week controlled trials of outpatients whose diagnoses corresponded to the DSM-IV category of major depressive disorder (see CLINICAL PHARMACOLOGY: Clinical Trials in full Prescribing Information).

A major depressive episode (DSM-IV) implies a prominent and relatively persistent (nearly every day for at least 2 weeks) depressed mood or loss of interest or pleasure in nearly all activities, representing a change from previous functioning, and includes the presence of at least 5 of the following 9 symptoms during the same 2 week period: Depressed mood, markedly diminished interest or pleasure in usual activities, significant change in weight and/or appetite, insomnia or hypersomnia, psychomotor agitation or retardation, increased fatigue, feelings of guilt or worthlessness, slowed thinking or impaired concentration, a suicide attempt, or suicidal ideation.

The antidepressant action of paroxetine in hospitalized depressed patients has not been adequately studied.

Paroxetine hydrochloride extended-release tablets have not been systematically evaluated beyond 12 weeks in controlled clinical trials; however, the effectiveness of immediate-release paroxetine hydrochloride in maintaining a response in major depressive disorder for up to one year has been demonstrated in a placebo-controlled trial (see CLINICAL PHARMACOLOGY: Clinical Trials in full Prescribing Information). The physician who elects to use paroxetine hydrochloride extended-release tablets for extended periods should periodically reevaluate the long-term usefulness of the drug for the individual patient.

CONTRAINDICATIONS: Concomitant use in patients taking either monoamine oxidase inhibitors (MAOIs) or thioridazine is contraindicated (see WARNINGS and PRECAUTIONS).

Concomitant use in patients taking pimozide is contraindicated (see PRECAUTIONS).

Paroxetine hydrochloride extended-release tablets are contraindicated in patients with a hypersensitivity to paroxetine or to any of the inactive ingredients in paroxetine hydrochloride extended-release tablets.

WARNINGS: Clinical Worsening and Suicide Risk: Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. There has been a long-standing concern, however, that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients during the early phases of treatment. Pooled analyses of short-term placebo-controlled trials of antidepressant drugs (SSRIs and others) showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18 to 24) with major depressive disorder (MDD) and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction with antidepressants compared to placebo in adults aged 65 and older.

The pooled analyses of placebo-controlled trials in children and adolescents with MDD, obsessive compulsive disorder (OCD), or other psychiatric disorders included a total of 24 short-term trials of 9 antidepressant drugs in over 4,400 patients. The pooled analyses of placebo-controlled trials in adults with MDD or other psychiatric disorders included a total of 295 short-term trials (median duration of 2 months) of 11 antidepressant drugs in over 77,000 patients. There was considerable variation in risk of suicidality among drugs, but a tendency toward an increase in the younger patients for almost all drugs studied. There were differences in absolute risk of suicidality across the different indications, with the highest incidence in MDD. The risk differences (drug vs. placebo), however, were relatively stable within age strata and across indications. These risk differences (drug-placebo difference in the number of cases of suicidality per 1,000 patients treated) are provided in Table 1.

Table 1

Age Range	Drug-Placebo Difference in Number of Cases of Suicidality Per 1,000 Patients Treated
Increases Compared to Placebo	
< 18	14 additional cases
18 to 24	5 additional cases
Decreases Compared to Placebo	
25 to 64	1 fewer case
≥ 65	6 fewer cases

No suicides occurred in any of the pediatric trials. There were suicides in the adult trials, but the number was not sufficient to reach any conclusion about drug effect on suicide.

It is unknown whether the suicidality risk extends to longer-term use, i.e., beyond several months. However, there is substantial evidence from placebo-controlled maintenance trials in adults with depression that the use of antidepressants can delay the recurrence of depression.

All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases.

The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality.

Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse, or who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms.

If the decision has been made to discontinue treatment, medication should be tapered, as rapidly as is feasible, but with recognition that abrupt discontinuation can be associated with certain symptoms (see PRECAUTIONS and DOSAGE AND ADMINISTRATION: Discontinuation of Treatment with Paroxetine Hydrochloride Extended-Release Tablets, for a description of the risks of discontinuation of paroxetine).

Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to healthcare providers. Such monitoring should include daily observation by families and caregivers. Prescriptions for paroxetine should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose.

Screening Patients for Bipolar Disorder: A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled trials) that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Whether any of the symptoms described above represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that paroxetine is not approved for use in treating bipolar depression.

Potential for Interaction With Monoamine Oxidase Inhibitors: In patients receiving another serotonin reuptake inhibitor drug in combination with an MAOI, there have been reports of serious, sometimes fatal, reactions including hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that include extreme agitation progressing to delirium and coma. These reactions have also been reported in patients who have recently discontinued that drug and have been started on an MAOI. Some cases presented with features resembling neuroleptic malignant syndrome. While there are no human data showing such an interaction with paroxetine hydrochloride, limited animal data on the effects of combined use of paroxetine and MAOIs suggest that these drugs may act synergistically to elevate blood pressure and evoke behavioral excitation. Therefore, it is recommended that paroxetine hydrochloride extended-release tablets not be used in combination with an MAOI, or within 14 days of discontinuing treatment with an MAOI. At least 2 weeks should be allowed after stopping paroxetine hydrochloride extended-release tablets before starting an MAOI.

Serotonin Syndrome: The development of a potentially life threatening serotonin syndrome may occur with SNRI sans SSRIs, including paroxetine hydrochloride extended-release tablets, particularly with concomitant use of serotonergic drugs (including triptans) and with drugs which impair metabolism of serotonin (including MAOIs). Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination) and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea).

The concomitant use of paroxetine hydrochloride extended-release tablets with MAOIs intended to treat depression is contraindicated (see CONTRAINDICATIONS and WARNINGS: Potential for Interaction with Monoamine Oxidase Inhibitors). If concomitant use of paroxetine hydrochloride extended-release tablets with a 5-hydroxytryptamine receptor agonist (triptan) is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases (see PRECAUTIONS: Drug Interactions in full Prescribing Information).

The concomitant use of paroxetine hydrochloride extended-release tablets with serotonin precursors (such as tryptophan) is not recommended (see PRECAUTIONS: Drug Interactions in full Prescribing Information). Potential Interaction with Thioridazine: Thioridazine administration alone produces prolongation of the QTc interval, which is associated with serious ventricular arrhythmias, such as Torsade de pointes-type arrhythmias, and sudden death. This effect appears to be dose related.

An *in vivo* study suggests that drugs which inhibit CYP2D6, such as paroxetine, will elevate plasma levels of thioridazine. Therefore, it is recommended that paroxetine not be used in combination with thioridazine (see CONTRAINDICATIONS and PRECAUTIONS).

Usage in Pregnancy: ***Teratogenic Effects:*** Epidemiological studies have shown that infants born to women who had first trimester paroxetine exposure had an increased risk of cardiovascular malformations, primarily ventricular and atrial septal defects (VSDs and ASDs). In general, septal defects range from those that are symptomatic and may require surgery to those that are asymptomatic and may resolve spontaneously. If a patient becomes pregnant while taking paroxetine, she should be advised of the potential harm to the fetus. Unless the benefits of paroxetine to the mother justify continuing treatment, consideration should be given to either discontinuing paroxetine therapy or switching to another antidepressant (see PRECAUTIONS: General: *Discontinuation of Treatment with Paroxetine Hydrochloride Extended-Release Tablets*). For women who intend to become pregnant or are in their first trimester of pregnancy, paroxetine should only be initiated after consideration of the other available treatment options.

A study based on Swedish national registry data evaluated infants of 6,896 women exposed to antidepressants in early pregnancy (5,123 women exposed to SSRIs; including 815 for paroxetine). Infants exposed to paroxetine in early pregnancy had an increased risk of cardiovascular malformations (primarily VSDs and ASDs) compared to the entire registry population (OR 1.8; 95% confidence interval 1.1 to 2.8). The rate of cardiovascular malformations following early pregnancy paroxetine exposure was 2% vs. 1% in the entire registry population. Among the same paroxetine exposed infants, an examination of the data showed no increase in the overall risk for congenital malformations.

A separate retrospective cohort study using U.S. United Healthcare data evaluated 5,956 infants of mothers dispensed paroxetine or other antidepressants during the first trimester (n = 815 for paroxetine). This study showed a trend towards an increased risk for cardiovascular malformations for paroxetine compared to other antidepressants (OR 1.5; 95% confidence interval 0.8 to 2.9). The prevalence of cardiovascular malformations following first trimester dispensing was 1.5% for paroxetine vs. 1% for other antidepressants. Nine out of 12 infants with cardiovascular malformations whose mothers were dispensed paroxetine in the first trimester had VSDs. This study also suggested an increased risk of overall major congenital malformations (inclusive of the cardiovascular defects) for paroxetine compared to other antidepressants (OR 1.8; 95% confidence interval 1.2 to 2.8). The prevalence of all congenital malformations following first trimester exposure was 4% for paroxetine vs. 2% for other antidepressants.

Animal Findings: Reproduction studies were performed at doses up to 50 mg/kg/day in rats and 6 mg/kg/day in rabbits administered during organogenesis. These doses are approximately 8 (rat) and 2 (rabbit) times the MRHD on a mg/m^2 basis. These studies have revealed no evidence of teratogenic effects. However, in rats, there was an increase in pup deaths during the first 4 days of lactation when dosing occurred during the last trimester of gestation and continued throughout lactation. This effect occurred at a dose of 1 mg/kg/day or approximately one-sixth of the MRHD on a mg/m^2 basis. The no effect dose for rat pup mortality was not determined. The cause of these deaths is not known.

Nonteratogenic Effects: Neonates exposed to paroxetine hydrochloride extended-release tablets and other SSRIs or serotonin and norepinephrine reuptake inhibitors (SNRIs), late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Such complications can arise immediately upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. These features are consistent with either a direct toxic effect of SSRIs and SNRIs or, possibly, a drug discontinuation syndrome. It should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome (see WARNINGS: Potential for Interaction with Monoamine Oxidase Inhibitors).

Infants exposed to SSRIs in late pregnancy may have an increased risk for persistent pulmonary hypertension of the newborn (PPHN). PPHN occurs in 1 to 2 per 1,000 live births in the general population and is associated with substantial neonatal morbidity and mortality. In a retrospective case control study of 377 women whose infants were born with PPHN and 836 women whose infants were born healthy, the risk for developing PPHN was approximately 6-fold higher for infants exposed to SSRIs after the 20th week of gestation compared to infants who had not been exposed to antidepressants during pregnancy. There is currently no collaborative evidence regarding the risk for PPHN following exposure to SSRIs in pregnancy; this is the first study that has investigated the potential risk. The study did not include enough cases with exposure to individual SSRIs to determine if all SSRIs posed similar levels of PPHN risk.

There have also been post-marketing reports of premature births in pregnant women exposed to paroxetine or other SSRIs.

When treating a pregnant woman with paroxetine during the third trimester, the physician should carefully consider both the potential risks and benefits of treatment (see DOSAGE AND ADMINISTRATION). Physicians should note that in a prospective longitudinal study of 201 women with a history of major depression who were euthymic at the beginning of pregnancy, women who discontinued antidepressant medication during pregnancy were more likely to experience a relapse of major depression than women who continued antidepressant medication.

PRECAUTIONS: General: ***Activation of Mania/Hypomania:*** During premarketing testing of immediate-release paroxetine hydrochloride, hypomania or mania occurred in approximately 1% of paroxetine-treated unipolar patients compared to 1.1% of active control and 0.3% of placebo-treated unipolar patients. In a subset of patients classified as bipolar, the rate of manic episodes was 2.2% for immediate-release paroxetine and 11.6% for the combined active control groups. Among 1,627 patients with major depressive disorder, panic disorder, social anxiety disorder, or PMDD treated with paroxetine hydrochloride extended-release tablets in controlled clinical studies, there were no reports of mania or hypomania. As with all drugs effective in the treatment of major depressive disorder, paroxetine hydrochloride extended-release tablets should be used cautiously in patients with a history of mania.

Seizures: During premarketing testing of immediate-release paroxetine hydrochloride, seizures occurred in 0.1% of paroxetine-treated patients, a rate similar to that associated with other drugs effective in the treatment of major depressive disorder. Among 1,627 patients who received paroxetine hydrochloride extended-release tablets in controlled clinical trials in major depressive disorder, panic disorder, social anxiety disorder, or PMDD, one patient (0.1%) experienced a seizure. Paroxetine hydrochloride extended- release tablets should be used cautiously in patients with a history of seizures. It should be discontinued in any patient who develops seizures.

Discontinuation of Treatment with Paroxetine Hydrochloride Extended-Release Tablets: Adverse events while discontinuing therapy with paroxetine hydrochloride extended-release tablets were not systematically evaluated in most clinical trials; however, in recent placebo-controlled clinical trials utilizing daily doses of paroxetine hydrochloride extended-release tablets up to 37.5 mg/day, spontaneously reported adverse events while discontinuing therapy with paroxetine hydrochloride extended-release tablets were evaluated. Patients receiving 37.5 mg/day underwent an incremental decrease in the daily dose by 12.5 mg/day to a dose of 25 mg/day for one week before treatment was stopped. For patients receiving 25 mg/day or 12.5 mg/day, treatment was stopped without an incremental decrease in dose. With this regimen in those studies, the following adverse events were reported for paroxetine hydrochloride extended-release tablets, at an incidence of 2% or greater for paroxetine hydrochloride extended-release tablets and were at least twice that reported for placebo: Dizziness, nausea, nervousness, and additional symptoms described by the investigator as associated with tapering or discontinuing paroxetine hydrochloride extended-release tablets (e.g., emotional lability, headache, agitation, electric shock sensations, fatigue, and sleep disturbances). These events were reported as serious in 0.3% of patients who discontinued therapy with paroxetine hydrochloride extended-release tablets.

During marketing of paroxetine hydrochloride extended-release tablets and other SSRIs and SNRIs, there have been spontaneous reports of adverse events occurring upon discontinuation of these drugs, (particularly when abrupt), including the following: Dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesias such as electric shock sensations and tinnitus), anxiety, confusion, headache, lethargy, emotional lability, insomnia, and hypomania. While these events are generally self limiting, there have been reports of serious discontinuation symptoms.

Patients should be monitored for these symptoms when discontinuing treatment with paroxetine hydrochloride extended-release tablets. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose but at a more gradual rate (see DOSAGE AND ADMINISTRATION).

See also PRECAUTIONS: Pediatric Use, for adverse events reported upon discontinuation of treatment with paroxetine in pediatric patients.

Akathisia: The use of paroxetine or other SSRIs has been associated with the development of akathisia, which is characterized by an inner sense of restlessness and psychomotor agitation such as an inability to sit or stand still usually associated with subjective distress. This is most likely to occur within the first few weeks of treatment.

Hyponatremia: Hyponatremia may occur as a result of treatment with SSRIs and SNRIs, including paroxetine. In many cases, this hyponatremia appears to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Cases with serum sodium lower than 110 mmol/L have been reported. Elderly patients may be at greater risk of developing hyponatremia with SSRIs and SNRIs. Also, patients taking diuretics or who are otherwise volume depleted may be at greater risk (see Geriatric Use). Discontinuation of paroxetine should be considered in patients with symptomatic hyponatremia and appropriate medical intervention should be instituted.

Signs and symptoms of hyponatremia include headache, difficulty concentrating, memory impairment, confusion, weakness and unsteadiness, which may lead to falls. Signs and symptoms associated with more severe and/or acute cases have included hallucination, syncope, seizure, coma, respiratory arrest and death.

Abnormal Bleeding: Published case reports have documented the occurrence of bleeding episodes in patients treated with psychotropic drugs that interfere with serotonin reuptake. Subsequent epidemiological studies, both of the case control and cohort design, have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. In two studies, concurrent use of a non-steroidal anti-inflammatory drug (NSAID) or aspirin potentiated the risk of bleeding (see PRECAUTIONS: Drug Interactions in full Prescribing Information). Although these studies focused on upper gastrointestinal bleeding, there is reason to believe that bleeding at other sites may be similarly potentiated. Patients should be cautioned regarding the risk of bleeding associated with the concomitant use of paroxetine with NSAIDs, aspirin, or other drugs that affect coagulation.

Use in Patients with Concomitant Illness: Clinical experience with immediate-release paroxetine hydrochloride in patients with certain concomitant systemic illness is limited. Caution is advisable in using paroxetine hydrochloride extended-release tablets in patients with diseases or conditions that could affect metabolism or hemodynamic responses.

As with other SSRIs, mydriasis has been infrequently reported in premarketing studies with paroxetine hydrochloride. A few cases of acute angle closure glaucoma associated with therapy with immediate-release paroxetine have been reported in the literature. As mydriasis can cause acute angle closure in patients with narrow angle glaucoma, caution should be used when paroxetine hydrochloride extended-release tablets are prescribed for patients with narrow angle glaucoma.

Paroxetine hydrochloride extended-release tablet or the immediate-release formulation has not been evaluated or used to any appreciable extent in patients with a recent history of myocardial infarction or unstable heart disease. Patients with these diagnoses were excluded from clinical studies during premarket testing. Evaluation of electrocardiograms of 682 patients who received immediate-release paroxetine hydrochloride in double-blind, placebo-controlled trials, however, did not indicate that paroxetine is associated with the development of significant ECG abnormalities. Similarly, paroxetine hydrochloride does not cause any clinically important changes in heart rate or blood pressure.

Increased plasma concentrations of paroxetine occur in patients with severe renal impairment (creatinine clearance < 30 mL/min.) or severe hepatic impairment. A lower starting dose should be used in such patients (see DOSAGE AND ADMINISTRATION).

Pregnancy: ***Pregnancy Category D:*** See WARNINGS: Usage in Pregnancy: *Teratogenic Effects:*.

Labor and Delivery: The effect of paroxetine on labor and delivery in humans is unknown.

Nursing Mothers: Like many other drugs, paroxetine is secreted in human milk, and caution should be exercised when paroxetine hydrochloride extended-release tablets are administered to a nursing woman.

Pediatric Use: Safety and effectiveness in the pediatric population have not been established (see BOX WARNING and WARNINGS: Clinical Worsening and Suicide Risk). Three placebo-controlled trials in 752 pediatric patients with MDD have been conducted with paroxetine hydrochloride and the data were not sufficient to support a claim for use in pediatric patients. Anyone considering the use of paroxetine hydrochloride extended-release tablets in a child or adolescent must balance the potential risks with the clinical need.

In placebo-controlled clinical trials conducted with pediatric patients, the following adverse events were reported in at least 2% of pediatric patients treated with immediate-release paroxetine hydrochloride and occurred at a rate at least twice that for pediatric patients receiving placebo: emotional lability (including self harm, suicidal thoughts, attempted suicide, crying, and mood fluctuations), hostility, decreased appetite, tremor, sweating, hyperkinesia, and agitation.

Events reported upon discontinuation of treatment with immediate-release paroxetine hydrochloride in the pediatric clinical trials that included a taper phase regimen, which occurred in at least 2% of patients who received immediate-release paroxetine hydrochloride and which occurred at a rate at least twice that of placebo, were: emotional lability (including suicidal ideation, suicide attempt, mood changes, and tearfulness), nervousness, dizziness, nausea, and abdominal pain (see DOSAGE AND ADMINISTRATION: Discontinuation of Treatment with Paroxetine Hydrochloride Extended-Release Tablets).

Geriatric Use: In worldwide premarketing clinical trials with immediate-release paroxetine hydrochloride, 17% of paroxetine-treated patients (approximately 700) were 65 years or older. Pharmacokinetic studies revealed a decreased clearance in the elderly, and a lower starting dose is recommended; there were, however, no overall differences in the adverse event profile between elderly and younger patients, and effectiveness was similar in younger and older patients (see CLINICAL PHARMACOLOGY in full Prescribing Information and DOSAGE AND ADMINISTRATION).

In a controlled study focusing specifically on elderly patients with major depressive disorder, paroxetine hydrochloride extended-release tablets were demonstrated to be safe and effective in the treatment of elderly patients (> 60 years) with major depressive disorder. (See CLINICAL PHARMACOLOGY: Clinical Trials in full Prescribing Information and ADVERSE REACTIONS: Table 3.)

SSRIs and SNRIs, including paroxetine, have been associated with cases of clinically significant hyponatremia in elderly patients, who may be at great risk for adverse event (see PRECAUTIONS: General: Hyponatremia).

ADVERSE REACTIONS: The information included under the "Adverse Findings Observed in Short-Term, Placebo-Controlled Trials with Paroxetine Hydrochloride Extended-Release Tablets" subsection of ADVERSE REACTIONS is based on data from eleven placebo-controlled clinical trials. Three of these studies were conducted in patients with major depressive disorder, three studies were done in patients with panic disorder and one study was conducted in patients with social anxiety disorder. Two of the studies in major depressive disorder, which enrolled patients in the age range 18 to 65 years, are pooled. Information from a third study of major depressive disorder, which focused on elderly patients (60 to 88 years), is presented separately as is the information from the panic disorder studies. Information on additional adverse events associated with paroxetine hydrochloride extended-release tablet and the immediate-release formulation of paroxetine hydrochloride is included in a separate subsection (see Other Events Observed During the Clinical Development of Paroxetine).

Adverse Findings Observed in Short-Term, Placebo-Controlled Trials With Paroxetine Hydrochloride Extended-Release Tablets: ***Adverse Events Associated With Discontinuation of Treatment:*** *Major Depressive Disorder:* Ten percent (21/212) of patients treated with paroxetine hydrochloride extended-release tablets discontinued treatment due to an adverse event in a pool of two studies of patients with major depressive disorder. The most common events (≥ 1%) associated with discontinuation and considered to be drug-related (i.e., those events associated with dropout at a rate approximately twice or greater for paroxetine hydrochloride extended-release tablets compared to placebo) included the following:

	Paroxetine Hydrochloride Extended-Release Tablets (n = 212)	Placebo (n = 211)
Nausea	3.7%	0.5%
Asthenia	1.9%	0.5%
Dizziness	1.4%	0.0%
Somnolence	1.4%	0.0%

In a placebo-controlled study of elderly patients with major depressive disorder, 13% (13/104) of patients treated with paroxetine hydrochloride extended-release tablets discontinued due to an adverse event. Events meeting the above criteria included the following:

	Paroxetine Hydrochloride Extended-Release Tablets (n = 104)	Placebo (n = 109)
Nausea	2.9%	0.0%
Headache	1.9%	0.9%
Depression	1.9%	0.0%
LFT's abnormal	1.9%	0.0%

Commonly Observed Adverse Events: ***Major Depressive Disorder:*** The most commonly observed adverse events associated with the use of paroxetine hydrochloride extended-release tablets in a pool of two trials (incidence of 5% or greater and incidence for paroxetine hydrochloride extended-release tablets at least twice that for placebo, derived from Table 2) were: Abnormal ejaculation, abnormal vision, constipation, decreased libido, diarrhea, dizziness, female genital disorders, nausea, somnolence, sweating, trauma, tremor, and yawning.

Using the same criteria, the adverse events associated with the use of paroxetine hydrochloride extended-release tablets in a study of elderly patients with major depressive disorder were: Abnormal ejaculation, constipation, decreased appetite, dry mouth, impotence, infection, libido decreased, sweating, and tremor.

Incidence in Controlled Clinical Trials: Table 2 enumerates adverse events that occurred at an incidence of 1% or more among patients treated with paroxetine hydrochloride extended-release tablets, aged 18 to 65, who participated in two short-term (12 week) placebo-controlled trials in major depressive disorder in which patients were dosed in a range of 25 mg to 62.5 mg/day. Table 3 enumerates adverse events reported at an incidence of 5% or greater among elderly patients (ages 60 to 88) treated with paroxetine hydrochloride extended-release tablets who participated in a short-term (12 week) placebo-controlled trial in major depressive disorder in which patients were dosed in a range of 12.5 mg to

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50 mg/day. Table 4 enumerates adverse events reported at an incidence of 1% or greater among patients (19 to 72 years) treated with paroxetine hydrochloride extended-release tablets who participated in short-term (10 week) placebo-controlled trials in panic disorder in which patients were dosed in a range of 12.5 mg to 75 mg/day. Table 5 enumerates adverse events reported at an incidence of 1% or greater among adult patients treated with paroxetine hydrochloride extended-release tablets who participated in a short-term (12 week), double-blind, placebo-controlled trial in social anxiety disorder in which patients were dosed in a range of 12.5 to 37.5 mg/day.

The prescriber should be aware that these figures cannot be used to predict the incidence of side effects in the course of usual medical practice where patient characteristics and other factors differ from those that prevailed in the clinical trials. Similarly, the cited frequencies cannot be compared with figures obtained from other clinical investigations involving different treatments, uses, and investigators. The cited figures, however, do provide the prescribing physician with some basis for estimating the relative contribution of drug and nondrug factors to the side effect incidence rate in the population studied.

Table 2. Treatment Emergent Adverse Events Occurring in ≥ 1% of Patients Treated with Paroxetine Hydrochloride Extended-Release Tablets in a Pool of Two Studies in Major Depressive Disorder[1,2]

	% Reporting Event	
Body System/Adverse Event	**Paroxetine Hydrochloride Extended-Release Tablets (n = 212)**	**Placebo (n = 211)**
Body as a Whole		
Headache	27%	20%
Asthenia	14%	9%
Infection[3]	8%	5%
Abdominal Pain	7%	4%
Back Pain	5%	3%
Trauma[4]	5%	1%
Pain[5]	3%	1%
Allergic Reaction[6]	2%	1%
Cardiovascular System		
Tachycardia	1%	0%
Vasodilatation[7]	2%	0%
Digestive System		
Nausea	22%	10%
Diarrhea	18%	7%
Dry Mouth	15%	8%
Constipation	10%	4%
Flatulence	6%	4%
Decreased Appetite	4%	2%
Vomiting	2%	1%
Nervous System		
Somnolence	22%	8%
Insomnia	17%	9%
Dizziness	14%	4%
Libido Decreased	7%	3%
Tremor	7%	1%
Hypertonia	3%	1%
Paresthesia	3%	1%
Agitation	2%	1%
Confusion	1%	0%
Respiratory System		
Yawn	5%	0%
Rhinitis	4%	1%
Cough Increased	2%	1%
Bronchitis	1%	0%
Skin and Appendages		
Sweating	6%	2%
Photosensitivity	2%	0%
Special Senses		
Abnormal Vision[8]	5%	1%
Taste Perversion	2%	0%
Urogenital System		
Abnormal Ejaculation[9,10]	26%	1%
Female Genital Disorder[9,11]	10%	< 1%
Impotence[9]	5%	3%
Urinary Tract Infection	3%	1%
Menstrual Disorder[9]	2%	< 1%
Vaginitis[3]	2%	0%

1. Adverse events for which the paroxetine hydrochloride extended-release tablets reporting incidence was less than or equal to the placebo incidence are not included. These events are: Abnormal dreams, anxiety, arthralgia, depersonalization, dysmenorrhea, dyspepsia, hyperkinesia, increased appetite, myalgia, nervousness, pharyngitis, purpura, rash, respiratory disorder, sinusitis, urinary frequency, and weight gain.
2. < 1% means greater than zero and less than 1%.
3. Mostly flu.
4. A wide variety of injuries with no obvious pattern.
5. Pain in a variety of locations with no obvious pattern.
6. Most frequently seasonal allergic symptoms.
7. Usually flushing.
8. Mostly blurred vision.
9. Based on the number of males or females.
10. Mostly anorgasmia or delayed ejaculation.
11. Mostly anorgasmia or delayed orgasm.

Table 3. Treatment Emergent Adverse Events Occurring in ≥ 5% of Patients Treated with Paroxetine Hydrochloride Extended-Release Tablets in a Study of Elderly Patients with Major Depressive Disorder[1,2]

	% Reporting Event	
Body System/Adverse Event	**Paroxetine Hydrochloride Extended-Release Tablets (n = 104)**	**Placebo (n = 109)**
Body as a Whole		
Headache	17%	13%
Asthenia	15%	14%
Trauma	8%	5%
Infection	6%	2%
Digestive System		
Dry Mouth	18%	7%
Diarrhea	15%	9%
Constipation	13%	5%
Dyspepsia	13%	10%
Decreased Appetite	12%	5%
Flatulence	8%	7%
Nervous System		
Somnolence	21%	12%
Insomnia	10%	8%
Dizziness	9%	5%
Libido Decreased	8%	< 1%
Tremor	7%	0%
Skin and Appendages		
Sweating	10%	< 1%
Urogenital System		
Abnormal Ejaculation[3,4]	17%	3%
Impotence[3]	9%	3%

1. Adverse events for which the paroxetine hydrochloride extended-release tablets reporting incidence was less than or equal to the placebo incidence are not included. These events are nausea and respiratory disorder.
2. < 1% means greater than zero and less than 1%.
3. Based on the number of males.
4. Mostly anorgasmia or delayed ejaculation.

A comparison of adverse event rates in a fixed dose study comparing immediate-release paroxetine with placebo in the treatment of major depressive disorder revealed a clear dose dependency for some of the more common adverse events associated with the use of immediate-release paroxetine.

Male and Female Sexual Dysfunction with SSRIs: Although changes in sexual desire, sexual performance, and sexual satisfaction often occur as manifestations of a psychiatric disorder, they may also be a consequence of pharmacologic treatment. In particular, some evidence suggests that SSRIs can cause such untoward sexual experiences.

Reliable estimates of the incidence and severity of untoward experiences involving sexual desire, performance, and satisfaction are difficult to obtain; however, in part because patients and physicians may be reluctant to discuss them. Accordingly, estimates of the incidence of untoward sexual experience and performance cited in product labeling, are likely to underestimate their actual incidence.

The percentage of patients reporting symptoms of sexual dysfunction in the pool of two placebo-controlled trials in nonelderly patients with major depressive disorder are as follows:

	Major Depressive Disorder	
	Paroxetine HCl Extended-Release Tablets	**Placebo**
n (males)	**78**	**78**
Decreased Libido	10%	5%
Ejaculatory Disturbance	26%	1%
Impotence	5%	3%
n (females)	**134**	**133**
Decreased Libido	4%	2%
Orgasmic Disturbance	10%	<1%

There are no adequate, controlled studies examining sexual dysfunction with paroxetine treatment.

Paroxetine treatment has been associated with several cases of priapism. In those cases with a known outcome, patients recovered without sequelae.

While it is difficult to know the precise risk of sexual dysfunction associated with the use of SSRIs, physicians should routinely inquire about such possible side effects.

Weight and Vital Sign Changes: Significant weight loss may be an undesirable result of treatment with paroxetine for some patients but, on average, patients in controlled trials with paroxetine hydrochloride extended-release tablet or the immediate-release formulation, had minimal weight loss (about 1 pound). No significant changes in vital signs (systolic and diastolic blood pressure, pulse, and temperature) were observed in patients treated with paroxetine hydrochloride extended-release tablets, or immediate-release paroxetine hydrochloride, in controlled clinical trials.

ECG Changes: In an analysis of ECGs obtained in 682 patients treated with immediate-release paroxetine and 415 patients treated with placebo in controlled clinical trials, no clinically significant changes were seen in the ECGs of either group.

Liver Function Tests: In a pool of two placebo-controlled clinical trials, patients treated with paroxetine hydrochloride extended-release tablets or placebo exhibited abnormal values on liver function tests at comparable rates. In particular, the extended-release paroxetine versus placebo comparisons for alkaline phosphatase, SGOT, SGPT, and bilirubin revealed no differences in the percentage of patients with marked abnormalities.

In a study of elderly patients with major depressive disorder, 3 of 104 patients treated with paroxetine hydrochloride extended-release tablets and none of 109 placebo patients experienced liver transaminase elevations of potential clinical concern.

Two of the patients treated with paroxetine hydrochloride extended-release tablets dropped out of the study due to abnormal liver function tests; the third patient experienced normalization of transaminase levels with continued treatment. Also, in the pool of three studies of patients with panic disorder, 4 of 444 patients treated with paroxetine hydrochloride extended-release tablets and none of 445 placebo patients experienced liver transaminase elevations of potential clinical concern. Elevations in all four patients decreased substantially after discontinuation of paroxetine hydrochloride extended-release tablets. The clinical significance of these findings is unknown.

In placebo-controlled clinical trials with the immediate-release formulation of paroxetine, patients exhibited abnormal values on liver function tests at no greater rate than that seen in placebo-treated patients.

Hallucinations: In pooled clinical trials of immediate-release paroxetine hydrochloride, hallucinations were observed in 22 of 9,089 patients receiving drug and in 4 of 3,187 patients receiving placebo.

Other Events Observed During the Clinical Development of Paroxetine: The following adverse events were reported during the clinical development of paroxetine hydrochloride extended-release tablet and/or the clinical development of the immediate-release formulation of paroxetine.

Adverse events for which frequencies are provided below occurred in clinical trials with the extended-release formulation of paroxetine. During its premarketing assessment in major depressive disorder, panic disorder and social anxiety disorder, multiple doses of paroxetine hydrochloride extended-release tablets were administered to 1,627 patients in phase three double-blind, controlled, outpatient studies. Untoward events associated with this exposure were recorded by clinical investigators using terminology of their own choosing. Consequently, it is not possible to provide a meaningful estimate of the proportion of individuals experiencing adverse events without first grouping similar types of untoward events into a smaller number of standardized event categories.

In the tabulations that follow, reported adverse events were classified using a COSTART based dictionary. The frequencies presented, therefore, represent the proportion of the 1,627 patients exposed to paroxetine hydrochloride extended-release tablets who experienced an event of the type cited on at least one occasion while receiving paroxetine hydrochloride extended-release tablets. All reported events are included except those already listed in Tables one through four and those events where a drug cause was remote. If the COSTART term for an event was so general as to be uninformative, it was deleted or, when possible, replaced with a more informative term. It is important to emphasize that although the events reported occurred during treatment with paroxetine, they were not necessarily caused by it.

Events are further categorized by body system and listed in order of decreasing frequency according to the following definitions: Frequent adverse events are those occurring on one or more occasions in at least 1/100 patients (only those not already listed in the tabulated results from placebo-controlled trials appear in this listing); infrequent adverse events are those occurring in 1/100 to 1/1,000 patients; rare events are those occurring in fewer than 1/1,000 patients.

Adverse events for which frequencies are not provided occurred during the premarketing assessment of immediate-release paroxetine in phase two and three studies of major depressive disorder, obsessive compulsive disorder, panic disorder, social anxiety disorder, generalized anxiety disorder, and posttraumatic stress disorder. The conditions and duration of exposure to immediate-release paroxetine varied greatly and included (in overlapping categories) open and double-blind studies, uncontrolled and controlled studies, inpatient and outpatient studies, and fixed dose and titration studies. Only those events not previously listed for extended-release paroxetine are included. The extent to which these events may be associated with paroxetine hydrochloride extended-release tablets is unknown.

Events are listed alphabetically within the respective body system. Events of major clinical importance are also described in the PRECAUTIONS section.

Body as a Whole: Infrequent were chills, face edema, fever, flu syndrome, malaise; rare were abscess, anaphylactoid reaction, anticholinergic syndrome, hypothermia; also observed were adrenergic syndrome, neck rigidity, sepsis.

Cardiovascular System: Infrequent were angina pectoris, bradycardia, hematoma, hypertension, hypotension, palpitation, postural hypotension, supraventricular tachycardia, syncope; rare were bundle branch block; also observed were arrhythmia nodal, atrial fibrillation, cerebrovascular accident, congestive heart failure, low cardiac output, myocardial infarct, myocardial ischemia, pallor, phlebitis, pulmonary embolus, supraventricular extrasystoles, thrombophlebitis, thrombosis, vascular headache, ventricular extrasystoles.

Digestive System: Infrequent were bruxism, dysphagia, eructation, gastritis, gastroenteritis, gastroesophageal reflux, gingivitis, hemorrhoids, liver function test abnormal, melena, pancreatitis, rectal hemorrhage, toothache, ulcerative stomatitis; rare were colitis, glossitis, gum hyperplasia, hepatosplenomegaly, increased salivation, intestinal obstruction, peptic ulcer, stomach ulcer, throat tightness; also observed were aphthous stomatitis, bloody diarrhea, bulimia, cardiospasm, cholelithiasis, duodenitis, enteritis, esophagitis, fecal impactions, fecal incontinence, gum hemorrhage, hematemesis, hepatitis, ileitis, ileus, jaundice, mouth ulceration, salivary gland enlargement, sialadenitis, stomatitis, tongue discoloration, tongue edema.

Endocrine System: Infrequent were ovarian cyst, testes pain; rare were diabetes mellitus, hyperthyroidism; also observed were goiter, hypothyroidism, thyroiditis.

Hemic and Lymphatic System: Infrequent were anemia, eosinophilia, hypochromic anemia, leukocytosis, leukopenia, lymphadenopathy, purpura; rare were thrombocytopenia; also observed were anisocytosis, basophilia, bleeding time increased, lymphedema, lymphocytosis, lymphopenia, microcytic anemia, monocytosis, normocytic anemia, thrombocythemia.

Metabolic and Nutritional Disorders: Infrequent were generalized edema, hyperglycemia, hypokalemia, peripheral edema, SGOT increased, SGPT increased, thirst; rare were bilirubinemia, dehydration, hyperkalemia, obesity; also observed were alkaline phosphatase increased, BUN increased, creatinine phosphokinase increased, gamma globulins increased, gout, hypercalcemia, hypercholesteremia, hyperphosphatemia, hypocalcemia, hypoglycemia, hyponatremia, ketosis, lactic dehydrogenase increased, nonprotein nitrogen (NPN) increased.

Musculoskeletal System: Infrequent were arthritis, bursitis, tendonitis; rare were myasthenia, myopathy, myositis; also observed were generalized spasm, osteoporosis, tenosynovitis, tetany.

Nervous System: Frequent were depression; infrequent were amnesia, convulsion, depersonalization, dystonia, emotional lability, hallucinations, hyperkinesia, hypesthesia, hypokinesia, incoordination, libido increased, neuralgia, neuropathy, nystagmus, paralysis, vertigo; rare were ataxia, coma, diplopia, dyskinesia, hostility, paranoid reaction, torticollis, withdrawal syndrome; also observed were abnormal gait, akathisia, akinesia, aphasia, choreoathetosis, circumoral paresthesia, delirium, delusions, dysarthria, euphoria, extrapyramidal syndrome, fasciculations, grand mal convulsion, hyperalgesia, irritability, manic reaction, manic-depressive reaction, meningitis, myelitis, peripheral neuritis, psychosis, psychotic depression, reflexes decreased, reflexes increased, stupor, trismus.

Respiratory System: Frequent were pharyngitis; infrequent were asthma, dyspnea, epistaxis, laryngitis, pneumonia; rare were stridor; also observed were dysphonia, emphysema, hemoptysis, hiccups, hyperventilation, lung fibrosis, pulmonary edema, respiratory flu, sputum increased.

Skin and Appendages: Frequent were rash; infrequent were acne, alopecia, dry skin, eczema, pruritus, urticaria; rare were exfoliative dermatitis, furunculosis, pustular rash, seborrhea; also observed were angioedema, ecchymosis, erythema multiforme, erythema nodosum, hirsutism, maculopapular rash, skin discoloration, skin hypertrophy, skin ulcer, sweating decreased, vesiculobullous rash.

Special Senses: Infrequent were conjunctivitis, earache, keratoconjunctivitis, mydriasis, photophobia, retinal hemorrhage, tinnitus; rare were blepharitis, visual field defect; also observed were amblyopia, anisocoria, blurred vision, cataract, conjunctival edema, corneal ulcer, deafness, exophthalmos, glaucoma, hyperacusis, night blindness, parosmia, ptosis, taste loss.

Urogenital System: Frequent were dysmenorrhea*; infrequent were albuminuria, amenorrhea*, breast pain*, cystitis, dysuria, prostatitis*, urinary retention; rare were breast enlargement*, breast neoplasm*, female lactation, hematuria, kidney calculus, metrorrhagia*, nephritis, nocturia, pregnancy and puerperal disorders*, salpingitis, urinary incontinence, uterine fibroids enlarged*; also observed were breast atrophy, ejaculatory disturbance, endometrial disorder, epididymitis, fibrocystic breast, leukorrhea, mastitis, oliguria, polyuria, pyuria, urethritis, urinary casts, urinary urgency, urolith, uterine spasm, vaginal hemorrhage.

*Based on the number of men and women as appropriate.

Post-Marketing Reports: Voluntary reports of adverse events in patients taking immediate-release paroxetine hydrochloride that have been received since market introduction and not listed above that may have no causal relationship with the drug include acute pancreatitis, elevated liver function tests (the most severe cases were deaths due to liver necrosis, and grossly elevated transaminases associated with severe liver dysfunction), Guillain-Barré syndrome, toxic epidermal necrolysis, priapism, syndrome of inappropriate ADH secretion, symptoms suggestive of prolactinemia and galactorrhea, neuroleptic malignant syndrome like events, serotonin syndrome; extrapyramidal symptoms which have included akathisia, bradykinesia, cogwheel rigidity, dystonia, hypertonia, oculogyric crisis which has been associated with concomitant use of pimozide; tremor and trismus; status epilepticus, acute renal failure, pulmonary hypertension, allergic alveolitis, anaphylaxis, eclampsia, laryngismus, optic neuritis, porphyria, ventricular fibrillation, ventricular tachycardia (including Torsade de pointes), thrombocytopenia, hemolytic anemia, events related to impaired hematopoiesis (including aplastic anemia, pancytopenia, bone marrow aplasia, and agranulocytosis), and vasculitic syndromes (such as Henoch-Schönlein purpura). There has been a case report of an elevated phenytoin level after 4 weeks of immediate-release paroxetine and phenytoin coadministration. There has been a case report of severe hypotension when immediate-release paroxetine was added to chronic metoprolol treatment.

DRUG ABUSE AND DEPENDENCE: Controlled Substance Class: Paroxetine hydrochloride is not a controlled substance.

Physical and Psychologic Dependence: Paroxetine hydrochloride extended-release tablets have not been systematically studied in animals or humans for its potential for abuse, tolerance or physical dependence. While the clinical trials did not reveal any tendency for any drug seeking behavior, these observations were not systematic and it is not possible to predict on the basis of this limited experience the extent to which a CNS active drug will be misused, diverted, and/or abused once marketed. Consequently, patients should be evaluated carefully for history of drug abuse, and such patients should be observed closely for signs of misuse or abuse of paroxetine hydrochloride extended-release tablets (e.g., development of tolerance, incrementations of dose, drug seeking behavior).

OVERDOSAGE: Human Experience: Since the introduction of immediate-release paroxetine hydrochloride in the United States, 342 spontaneous cases of deliberate or accidental overdosage during paroxetine treatment have been reported worldwide (circa 1999). These include overdoses with paroxetine alone and in combination with other substances. Of these, 48 cases were fatal and of the fatalities, 17 appeared to involve paroxetine alone. Eight fatal cases that documented the amount of paroxetine ingested were generally confounded by the ingestion of other drugs or alcohol or the presence of significant comorbid conditions. Of 145 nonfatal cases with known outcome, most recovered without sequelae. The largest known ingestion involved 2000 mg of paroxetine (33 times the maximum recommended daily dose) in a patient who recovered.

Commonly reported adverse events associated with paroxetine overdosage include somnolence, coma, nausea, tremor, tachycardia, confusion, vomiting, and dizziness. Other notable signs and symptoms observed with overdoses involving paroxetine (alone or with other substances) include mydriasis, convulsions (including status epilepticus), ventricular dysrhythmias (including Torsade de pointes), hypertension, aggressive reactions, syncope, hypotension, stupor, bradycardia, dystonia, rhabdomyolysis, symptoms of hepatic dysfunction (including hepatic failure, hepatic necrosis, jaundice, hepatitis, and hepatic steatosis), serotonin syndrome, manic reactions, myoclonus, acute renal failure, and urinary retention.

Overdosage Management: Treatment should consist of those general measures employed in the management of overdosage with any drugs effective in the treatment of major depressive disorder.

Ensure an adequate airway, oxygenation, and ventilation. Monitor cardiac rhythm and vital signs. General supportive and symptomatic measures are also recommended. Induction of emesis is not recommended. Gastric lavage with a large-bore orogastric tube with appropriate airway protection, if needed, may be indicated if performed soon after ingestion, or in symptomatic patients.

Activated charcoal should be administered. Due to the large volume of distribution of this drug, forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be of benefit. No specific antidotes for paroxetine are known.

A specific caution involves patients taking or recently having taken paroxetine who might ingest excessive quantities of a tricyclic antidepressant. In such a case, accumulation of the parent tricyclic and an active metabolite may increase the possibility of clinically significant sequelae and extend the time needed for close medical observation (see PRECAUTIONS: Drug Interactions: *Drugs Metabolized by Cytochrome CPY2D6* in full Prescribing Information).

In managing overdosage, consider the possibility of multiple drug involvement. The physician should consider contacting a poison control center for additional information on the treatment of any overdose. Telephone numbers for certified poison control centers are listed in the *Physicians' Desk Reference* (PDR).

DOSAGE AND ADMINISTRATION: Major Depressive Disorder: ***Usual Initial Dosage:*** Paroxetine hydrochloride extended-release tablets should be administered as a single daily dose, usually in the morning, with or without food. The recommended initial dose is 25 mg/day. Patients were dosed in a range of 25 mg to 62.5 mg/day in the clinical trials demonstrating the effectiveness of paroxetine hydrochloride extended-release tablets in the treatment of major depressive disorder. As with all drugs effective in the treatment of major depressive disorder, the full effect may be delayed. Some patients not responding to a 25 mg dose may benefit from dose increases, in 12.5 mg/day increments, up to a maximum of 62.5 mg/day. Dose changes should occur at intervals of at least one week.

Patients should be cautioned that paroxetine hydrochloride extended-release tablets should not be chewed or crushed, and should be swallowed whole.

Maintenance Therapy: There is no body of evidence available to answer the question of how long the patient treated with paroxetine hydrochloride extended-release tablets should remain on it. It is generally agreed that acute episodes of major depressive disorder require several months or longer of sustained pharmacologic therapy. Whether the dose of an antidepressant needed to induce remission is identical to the dose needed to maintain and/or sustain euthymia is unknown.

Systematic evaluation of the efficacy of immediate-release paroxetine hydrochloride has shown that efficacy is maintained for periods of up to one year with doses that averaged about 30 mg, which corresponds to a 37.5 mg dose of paroxetine hydrochloride extended-release tablets, based on relative bioavailability considerations (see CLINICAL PHARMACOLOGY: Pharmacokinetics in full Prescribing Information).

Special Populations: ***Treatment of Pregnant Women During the Third Trimester:*** Neonates exposed to paroxetine hydrochloride extended-release tablets and other SSRIs or SNRIs, late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding (see WARNINGS). When treating pregnant women with paroxetine during the third trimester, the physician should carefully consider the potential risks and benefits of treatment. The physician may consider tapering paroxetine in the third trimester.

Dosage for Elderly or Debilitated Patients, and Patients with Severe Renal or Hepatic Impairment: The recommended initial dose of paroxetine hydrochloride extended-release tablets is 12.5 mg/day for elderly patients, debilitated patients, and/or patients with severe renal or hepatic impairment. Increases may be made if indicated. Dosage should not exceed 50 mg/day.

Switching Patients to or From a Monoamine Oxidase Inhibitor: At least 14 days should elapse between discontinuation of an MAOI and initiation of therapy with paroxetine hydrochloride extended-release tablets. Similarly, at least 14 days should be allowed after stopping paroxetine hydrochloride extended-release tablets before starting an MAOI.

Discontinuation of Treatment with Paroxetine Hydrochloride Extended-Release Tablets: Symptoms associated with discontinuation of immediate-release paroxetine hydrochloride or paroxetine hydrochloride extended-release tablets have been reported (see PRECAUTIONS). Patients should be monitored for these symptoms when discontinuing treatment, regardless of the indication for which paroxetine hydrochloride extended-release tablets are being prescribed. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose but at a more gradual rate.

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Antipsychotics' Adverse Effects Found in Elderly AD Patients

A large government-sponsored clinical trial associates antipsychotic medications with weight gain, girth, and harmful metabolic effects in elderly patients with Alzheimer's disease.

BY JUN YAN

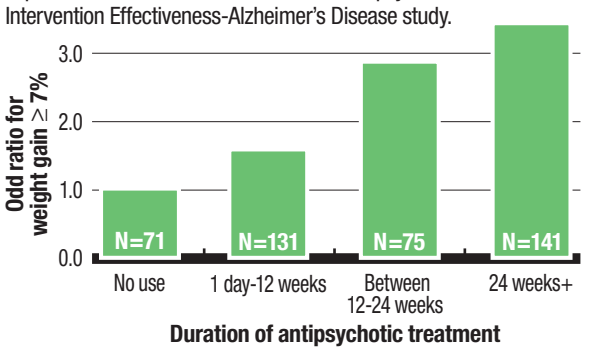
Older adults with dementia experience significant weight gain and worsening cholesterol levels when they are treated with second-generation antipsychotic (SGA) medications in a pattern similar to younger patients taking antipsychotics for schizophrenia or bipolar disorder, according to new analyses of data from the Clinical Antipsychotic Trials of Intervention Effectiveness–Alzheimer's Disease (CATIE-AD).

The CATIE-AD study, a large, randomized, double-blind, placebo-controlled trial funded by the National Institute of Mental Health, was conducted between April 2001 and November 2004 to investigate the effectiveness of SGAs in treating psychosis and agitation in patients with Alzheimer's disease (AD).

Despite modest effectiveness in some of the clinical indicators with active treatments, many patients discontinued antipsychotics because of intolerable adverse effects.

Antipsychotic Drugs Linked To Weight Gain in AD Patients

Elderly patients with Alzheimer's disease (AD) who were randomized to receive second-generation antipsychotics had an increased risk of clinically significant weight gain compared with patients who received placebo. The risk was dependent on the duration of drug exposure. The data are from the Clinical Antipsychotic Trials of Intervention Effectiveness-Alzheimer's Disease study.



Source: Ling Zheng, M.B.B.S., Ph.D., et al., *AJP in Advance*, April 15, 2009

The study investigators had previously reported that the primary outcome, time to discontinuation of the study drug for any reason in 36 weeks of treatment, did not differ significantly among patients treated with olanzapine, quetiapine, risperidone, and placebo (*Psychiatric News*, November 3, 2006).

The current study, by Ling Zheng, M.B.B.S., Ph.D., and colleagues, focused on analyzing the weight and metabolic effects of SGAs in study patients. It was published online in *AJP in Advance* on April 15.

Among the ambulatory Alzheimer's patients who participated in the CATIE-AD

Surprising Trend Characterizes Dementia, Obesity Link

Although obesity at midlife predicts a risk of dementia, being underweight in late life predicts dementia risk.

BY JOAN AREHART-TREICHEL

For a while it seemed pretty simple. Avoid obesity, and you would also reduce your chances of getting cardiovascular disease, some cancers, and dementia. But the obesity-dementia link may be more complicated than that, a new study suggests.

The study was led by Annette Fitzpatrick, Ph.D., a research associate professor in epidemiology at the University of Washington. Results were published in the March *Archives of Neurology*.

The study included some 2,800 older adults, on average age 75 years, without dementia. They reported what their weight had been at age 50. Their height and weight were also measured when they entered the study. The researchers used this information to calculate their body mass index for both midlife and older age.

The subjects were followed on average for five years to see whether any developed dementia. Of 480 who did, 245 had Alzheimer's disease and 213 had vascular dementia or Alzheimer's plus vascular dementia. Finally the researchers examined whether there were any links between the subjects' body mass index at midlife and the risk of developing dementia, taking into account possibly confounding factors such as demographics or cardiovascular risk, or whether there were any links between subjects' body mass index in later age and the risk of developing dementia, taking the same possibly confounding factors into consideration.

Obesity at midlife was associated with an increased risk of dementia, whereas obesity at a later age was associated with a reduced risk of dementia. In contrast, being underweight at midlife was associated with a lower risk of dementia, whereas being underweight at a later age was associated with an increased risk of dementia. The results were similar for both Alzheimer's and vascular dementia, although being underweight at a later

trial, female patients, but not male patients, had statistically significant weight gain and an increase in body mass index (BMI) from baseline. The authors found a significant association between the duration of SGA exposure and weight gain: The longer that patients took SGAs, the more likely they would gain at least 7 percent of their body weight, a conventional standard for clinically significant weight gain. On average, female patients gained 0.14 pounds per week while taking SGAs. In subgroup analyses, the weight and BMI increases reached statistical significance in patients who were randomly assigned to olanzapine or quetiapine.

In addition to weight gain, high-density lipoprotein (HDL) cholesterol level decreased and waist circumference increased significantly in patients on olanzapine compared with those on placebo. Increased waist circumference and decreased HDL cholesterol are both associated with increased risk of cardiovascular diseases. The analyses did not show a significant effect on blood pressure, triglyceride, and glucose levels associated with SGA use.

Unfavorable metabolic effects associated with SGAs, including weight gain, elevated cholesterol and triglyceride levels, and altered glucose regulation/insulin insensitivity, mostly reported in child and adolescent patients taking these medications, have caused much clinical concern and media attention in recent years. The metabolic effects in older adults have been less studied. The average age of patients in the CATIE-AD study was 78 years.

"The important message from the study is that elderly patients with dementia receiving antipsychotics experience some of the same changes of metabolic syndrome that younger patients have," said Lon Schneider, M.D., a professor of psychiatry, neurology, and gerontology at the University of Southern California Keck School of Medicine, in an interview. "Whereas it took a while for the field to

please see ***Antipsychotics*** *on page 38*

age seemed to particularly predict vascular dementia.

Fitzpatrick and her colleagues have no explanation for why midlife obesity seems to be linked with an increased dementia risk and later-age obesity with a reduced dementia risk. But they do tender a possible explanation for why being underweight at a later age seems to be linked with an increased dementia risk: it could be that being underweight is not a risk factor for dementia per se, but rather a sign of encroaching dementia. After all, weight loss is a known symptom of dementia, and some investigators have found that weight loss may predate dementia onset by as much as a decade.

In fact, as Fitzpatrick told *Psychiatric News*, "I've come to the conclusion that. . . the brain is a wonderful thing—we are very good at being able to compensate for many of the mental problems that develop as we age. Diagnosis of dementia may not occur until the process is well under way. The body, however, is not quite so clever. So the physical signs of dementia, including weight loss, may be present first."

The study was funded by the National Institutes of Health.

An abstract of "Midlife and Late-Life Obesity and the Risk of Dementia" is posted at <http://archneur.ama-assn.org/cgi/content/abstract/66/3/336>. ■

Health Officials Criticize Pentagon's TBI Criteria

Lack of a case definition for mild traumatic brain injury hampers diagnosis of U.S. troops exposed to explosive blasts.

BY AARON LEVIN

U.S. military health officials are using an ambiguous and unvalidated method of identifying mild traumatic brain injuries among troops returning from service in Iraq and Afghanistan, according to three Army medical researchers.

The Department of Defense now uses a brief checklist after the troops return from the war zones to screen for medical consequences of deployment. Only one question on the Post Deployment Health Assessment (PDHA) form asks about possible traumatic brain injury (TBI).

The resulting information does not amount to a case definition because it lacks three essential criteria for use months after injury: symptoms, time course, and impairment, wrote Col. Charles Hoge, Col. Carl Castro, and Herb Goldberg in the April 16 *New England Journal of Medicine*. Hoge is director of the Division of Psychiatry and Behavioral Sciences at Walter Reed Army Institute of Research in Silver Spring, Md., and Goldberg is a communications specialist there. Castro is a psychologist and director of the Military Operational Medicine Research Program at Fort Detrick, Md..

Previously, other military health officials have stated that as many as 360,000 (20 percent) returning troops have experienced at least transitory effects of blasts from improvised roadside bombs or other explosives, although half of those cases resolve by the time of return to the United States (*Psychiatric News*, April 3). The remaining cases may require further treatment in primary or specialty care, either in the Department of Defense or the Department of Veterans Affairs (VA) medical systems.

As they return home, service members are asked to recall if they were exposed to a blast and if they were also "dazed or confused" at the time, were unconscious for less than 30 minutes, or had posttraumatic amnesia due to concussion or mild TBI.

"Positive responses to this single, unvalidated question have accounted for two-thirds of all reported cases of concussion/mild TBI," they wrote. The current system may be inflating the number of cases.

"The issue is one of 'caseness,' how to define a person with mild TBI or concussion," explained Castro, in an interview with *Psychiatric News*. "For any symptom-based disorder or injury, a case is based on five factors, each of which has to be independently validated: an event, the reaction to the event, symptoms, impairment, and a time course."

The 360,000 figure is based on only two of those elements, the event and the reaction, neither of which has been validated, said Castro. "So they're saying, 'The soldier has been injured, but he has no injuries.' "

Furthermore, high rates of these symptoms occur in healthy populations, and "postconcussion syndrome" appears after injuries to areas other than the head. Validation of current case definition is poor, he said.

Terminology is fluid, but usually TBI refers to the injury itself, and postconcussive syndrome applies to what follows the injury, said James Couch, M.D., Ph.D., a professor of neurology at the University of Oklahoma Health Sciences Center and a spokesperson for the American Academy of Neurology. Much of the controversy comes from the fact that many symptoms associated with concussion or mild TBI—such as headache, sleep disturbance, irritability, dizziness, balance problems, fatigue, or poor concentration—are not specific to head injury, he said.

"[C]linicians' attribution of such nonspecific symptoms to concussion/mild TBI is subjective," but the present screening process assumes that they are causally related, wrote Hoge and colleagues.

They are also concerned that the present approach encourages negative expectations about recovery, complicated by possible secondary gain, and inappropriate treatment.

"This is an excellent review of the clinically sensitive and policy-relevant consequences of poorly defined diagnostic criteria for mild traumatic brain injury," said Darrel Regier, M.D., M.P.H., director of APA's Office of Research and the American Psychiatric Institute for Research and Education. "There has been reluctance in the Department of Defense to use the diagnosis of postconcussive syndrome simply because of the stigma attached to this being a mental disorder—however transient—rather than a neurological disorder."

Failure to address the consequences of the current concepts of mild TBI could easily lead to expectations of permanent brain damage for those so diagnosed, as happened with soldiers returning from World War I diagnosed with shell shock, said Regier.

Hoge, Goldberg, and Castro have received a mixed response from higher ups to their recommendations.

"Some are supportive, some want more debate and discussion," said Castro. "We want to keep the discussion going until we get the right mixture of policies and procedures in place."

In response to the perspective in the *New England Journal of Medicine*, the Pentagon unit charged with researching TBI acknowledged that there was no clear standard of care for it in the early years of the two current wars, but it has been collecting data to improve screening and clinical practice, said Michael Kilpatrick, M.D., director of strategic communications for the Military Health Service.

"Today DoD [Department of Defense] continues to analyze the data that have been collected to make the best scientific changes to processes to optimally identify, document, and treat mild TBI/concussion," said Kilpatrick in a prepared statement. "The Hoge paper is the expression of an opinion supporting this scientific process."

How DoD and the VA ultimately define mild TBI will have implications not just for diagnosis but for treatment, compensation, and long-term care for returned veterans.

"The research of Hoge and colleagues has guided discussions of the *DSM-V* trauma-related diagnostic criteria and has helped APA improve the Defense Department's proposals to the Centers for Medicare and Medicaid Services and the CDC's [Centers for Disease Control and Prevention's] National Center for Health Statistics to revise the *ICD-9-CM* classification of cognitive and behavioral consequences of concussion and TBI," said Regier.

Castro sees the paper by him and his colleagues as just one element of a continuing debate aimed at getting the best possible solution for TBI issues in veterans.

"Charles Hoge and I want every service member to return home and live a happy and productive life," he said. "If any program, policy, or procedure for which the scientific evidence is not appropriate hinders that, then we need to speak out."

An abstract of "Care of War Veterans With Mild Traumatic Brain Injury—Flawed Perspectives" is posted at <http://content.nejm.org/cgi/content/short/360/16/1588>. ■

Concussion or Mild TBI Is Not Like More Severe Versions

U.S. Army researchers argue that concussion differs from moderate and severe traumatic brain injury, but case definition is poor.

Variable	Mild TBI (Concussion)	Moderate and severe TBI
Clinical definition	Loss of consciousness lasting <30 min., any alteration in consciousness, or posttraumatic amnesia lasting <24 hr.; some definitions include Glasgow Coma Scale score of 13 to 15	Loss of consciousness lasting ≥ 30 min. up to prolonged coma, posttraumatic amnesia lasting ≥ 24 hr. up to permanently, or Glasgow Coma Scale score as low as 3
Focal neurologic signs	Usually none or transient	Frequently present
Neuroimaging with CT or MRI	Usually negative	Diagnostic
Natural history	Full recovery is usual; there is lack of consensus on the natural history of concussion and postconcussive symptoms	Natural history and recovery are directly related to the severity of injury and functional neuroanatomy
Case definitions and specificity of injury sequelae	Case definitions of postconcussion syndrome have low reliability and validity and show poor correlation with one another; there are high rates of these symptoms in healthy populations and high rates of "postconcussion syndrome" after non-head injuries	Injury sequelae are not debated
Predictors of persistent symptoms or disability	Psychological factors (e.g., depression, anxiety, or PTSD), compensation and litigation, and negative expectations and beliefs are the strongest risk factors	Directly related to injury characteristics
Neurocognitive testing	Often inconclusive beyond the period of acute injury	Essential and valuable component of ongoing clinical care
Neuronal-cell damage	Metabolic and ionic processes caused by axonal twisting or stretching; these can lead to secondary disconnection	Combination of cellular disruption directly related to injury and metabolic, vascular, and ionic processes
Epidemiologic evidence of causation between injury and sequelae	Inconsistent and debated	Not debated

Source: Col. Charles Hoge et al., *New England Journal of Medicine,* April 16, 2009

Hall Awarded

Lacresha Hall, M.D., of Margate, Fla., is a recipient of the 2009 Penn State Alumni Achievement Award presented by the university's Alumni Association. Hall is founder and chief executive officer of Hallway of Life Recovery Center for women in Delray Beach, Fla., and has a private psychiatric practice. The Alumni Achievement Award recognizes Penn State alumni 35 years of age and younger for their extraordinary accomplishments. ■

Ralph Hoffman, MD, and research assistant Joan Nye, view functional MR images of a patient's cortical activation during auditory hallucinations.

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IMPORTANT SAFETY INFORMATION FOR RISPERDAL® CONSTA®

WARNING: Increased Mortality in Elderly Patients with Dementia-Related Psychosis
Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of 17 placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear. RISPERDAL® CONSTA® (risperidone) is not approved for the treatment of patients with dementia-related psychosis.

Cerebrovascular Adverse Events (CAEs): CAEs, including fatalities, have been reported in elderly patients with dementia-related psychosis taking oral risperidone in clinical trials. The incidence of CAEs with risperidone was significantly higher than with placebo. RISPERDAL® CONSTA® is not approved for the treatment of patients with dementia-related psychosis.

Neuroleptic Malignant Syndrome (NMS): NMS, a potentially fatal symptom complex, has been reported with the use of antipsychotic medications, including RISPERDAL® CONSTA®. Clinical manifestations include muscle rigidity, fever, altered mental status and evidence of autonomic instability (see full Prescribing Information). Management should include immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, intensive symptomatic treatment and medical monitoring, and treatment of any concomitant serious medical problems.

Tardive Dyskinesia (TD): TD is a syndrome of potentially irreversible, involuntary, dyskinetic movements that may develop in patients treated with antipsychotic medications. The risk of developing TD and the likelihood that dyskinetic movements will become irreversible are believed to increase with duration of treatment and total cumulative dose. Elderly patients appeared to be at increased risk for TD. Prescribing should be consistent with the need to minimize the risk of TD. The syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn.

Hyperglycemia and Diabetes: Hyperglycemia, some cases extreme and associated with ketoacidosis, hyperosmolar coma or death has been reported in patients treated with atypical antipsychotics (APS), including RISPERDAL® CONSTA®. Patients starting treatment with APS who have or are at risk for diabetes should undergo fasting blood glucose testing at the beginning of and during treatment. Patients who develop symptoms of hyperglycemia should also undergo fasting blood glucose testing.

Hyperprolactinemia: As with other drugs that antagonize dopamine D_2 receptors, RISPERDAL® CONSTA® elevates prolactin levels and the elevation persists during

chronic administration. Risperidone is associated with higher levels of prolactin elevation than other antipsychotic agents.

Orthostatic Hypotension: RISPERDAL® CONSTA® may induce orthostatic hypotension associated with dizziness, tachycardia, and in some patients, syncope, especially during the initial dose-titration period. Monitoring should be considered in patients for whom this may be of concern. RISPERDAL® CONSTA® should be used with caution in patients with known cardiovascular disease, and conditions that would predispose patients to hypotension.

Potential for Cognitive and Motor Impairment: RISPERDAL® CONSTA® has the potential to impair judgment, thinking, or motor skills. Patients should be cautioned about operating hazardous machinery, including motor vehicles, until they are reasonably certain that RISPERDAL® CONSTA® does not affect them adversely.

Seizures: RISPERDAL® CONSTA® should be used cautiously in patients with a history of seizures.

Suicide: The possibility of suicide attempt is inherent in psychotic illnesses. Close supervision of high-risk patients should accompany drug therapy.

Administration: Care should be taken to avoid inadvertent injection into a blood vessel.

Extrapyramidal Symptoms (EPS): The overall incidence of EPS-related adverse events in patients treated with 25 mg and 50 mg of RISPERDAL® CONSTA® and placebo, respectively, were akathisia* (4%, 11%, 6%), Parkinsonism† (8%, 15%, 9%) and tremor (0%, 3%, 0%).

*** Akathisia and restlessness**

†Extrapyramidal disorder, musculoskeletal stiffness, muscle rigidity, and bradykinesia

Weight Gain: In a 12-week trial, the percentage of patients experiencing weight gain (>7% of baseline body weight) was 6% placebo versus 9% RISPERDAL® CONSTA®.

Maintenance Treatment: Patients should be periodically reassessed to determine the need for continued treatment.

Commonly Observed Adverse Reactions for RISPERDAL® CONSTA®: The most common adverse reactions in clinical trials (≥5%) were headache, Parkinsonism, dizziness, akathisia, fatigue, constipation, dyspepsia, sedation, weight increase, pain in extremities, and dry mouth.

01CS09051

Please see accompanying brief summary of full Prescribing Information for RISPERDAL® CONSTA®.

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Brief Summary

BEFORE PRESCRIBING RISPERDAL® CONSTA®, PLEASE SEE FULL PRESCRIBING INFORMATION, INCLUDING BOXED WARNING.

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of 17 placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear. RISPERDAL® CONSTA® (risperidone) is not approved for the treatment of patients with dementia-related psychosis. *[See Warnings and Precautions]*

RISPERDAL® CONSTA® (risperidone) is indicated for the treatment of schizophrenia *[see Clinical Studies in full PI].*

CONTRAINDICATIONS: RISPERDAL® CONSTA® (risperidone) is contraindicated in patients with a known hypersensitivity to the product.

WARNINGS AND PRECAUTIONS: Increased Mortality in Elderly Patients with Dementia-Related Psychosis

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. RISPERDAL® CONSTA® (risperidone) is not approved for the treatment of dementia-related psychosis (see Boxed Warning).

Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients with Dementia-Related Psychosis: Cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, were reported in patients (mean age 85 years; range 73-97) in trials of oral risperidone in elderly patients with dementia-related psychosis. In placebo-controlled trials, there was a significantly higher incidence of cerebrovascular adverse events in patients treated with oral risperidone compared to patients treated with placebo. RISPERDAL® CONSTA® is not approved for the treatment of patients with dementia-related psychosis *[See also Boxed Warning and Warnings and Precautions]* **Neuroleptic Malignant Syndrome (NMS):** A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. The management of NMS should include: (1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; (2) intensive symptomatic treatment and medical monitoring; and (3) treatment of any concomitant serious medical problems for which specific treatments are available. If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. **Tardive Dyskinesia:** A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. The risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. RISPERDAL® CONSTA® should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically. If signs and symptoms of tardive dyskinesia appear in a patient treated with RISPERDAL® CONSTA®, drug discontinuation should be considered. **Hyperglycemia and Diabetes Mellitus:** Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics including RISPERDAL®. Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. **Hyperprolactinemia:** As with other drugs that antagonize dopamine D_2 receptors, risperidone elevates prolactin levels and the elevation persists during chronic administration. Neither clinical studies nor epidemiologic studies conducted to date have shown an association between chronic administration of this class of drugs and tumorigenesis in humans; the available evidence is considered too limited to be conclusive at this time. **Orthostatic Hypotension:** RISPERDAL® CONSTA® may induce orthostatic hypotension associated with dizziness, tachycardia, and in some patients, syncope, especially during the initial dose-titration period with oral risperidone, probably reflecting its alpha-adrenergic antagonistic properties. Syncope was reported in 0.8% (12/1499 patients) of patients treated with RISPERDAL® CONSTA® in multiple-dose studies. Patients should be instructed in nonpharmacologic interventions that help to reduce the occurrence of orthostatic hypotension (e.g., sitting on the edge of the bed for several minutes before attempting to stand in the morning and slowly rising from a seated position). RISPERDAL® CONSTA® should be used with particular caution in (1) patients with known cardiovascular disease (history of myocardial infarction or ischemia, heart failure, or conduction abnormalities), cerebrovascular disease, and conditions which would predispose patients to hypotension, e.g., dehydration and hypovolemia, and (2) in the elderly and patients with renal or hepatic impairment. Monitoring of orthostatic vital signs should be considered in all such patients, and a dose reduction should be considered if hypotension occurs. Clinically significant hypotension has been observed with concomitant use of oral RISPERDAL® and antihypertensive medication. **Potential for Cognitive and Motor Impairment:** Somnolence was reported by 5% of patients treated with RISPERDAL® CONSTA® in multiple-dose trials. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that treatment with RISPERDAL® CONSTA® does not affect them adversely. **Seizures:** During premarketing testing, seizures occurred in 0.3% (5/1499 patients) of patients treated with RISPERDAL® CONSTA®. Therefore, RISPERDAL® CONSTA® should be used cautiously in patients with a history of seizures. **Dysphagia:** Esophageal dysmotility and aspiration have been associated with antipsychotic drug use. Aspiration pneumonia is a common cause of morbidity and mortality in patients with advanced Alzheimer's dementia. RISPERDAL® CONSTA® and other antipsychotic drugs should be used cautiously in patients at risk for aspiration pneumonia. *[See also Boxed Warning and Warnings and Precautions]* **Priapism:** Priapism has been reported during postmarketing surveillance *[see Adverse Reactions].* Severe priapism may require surgical intervention. **Thrombotic Thrombocytopenic Purpura (TTP):** A single case of TTP was reported in a 28 year-old female patient receiving oral RISPERDAL® in a large, open premarketing experience (approximately 1300 patients). She experienced jaundice, fever, and bruising, but eventually recovered after receiving plasmapheresis. The relationship to RISPERDAL® therapy is unknown. **Body Temperature Regulation:** Disruption of body temperature regulation has been attributed to antipsychotic agents. Both hyperthermia and hypothermia have been reported in association with oral RISPERDAL® or RISPERDAL® CONSTA® use. Caution is advised when prescribing RISPERDAL® CONSTA® for patients who will be exposed to temperature extremes. **Administration:** RISPERDAL® CONSTA® should be injected into the deltoid or gluteal muscle, and care must be taken to avoid inadvertent injection into a blood vessel. *[See Dosage and Administration in full PI and Adverse Reactions]* **Antiemetic Effect:** Risperidone has an antiemetic effect in animals; this effect may also occur in humans, and may mask signs and symptoms of overdosage with certain drugs or of conditions such as intestinal obstruction, Reye's syndrome, and brain tumor. **Suicide:** The possibility of a suicide attempt is inherent in schizophrenia, and close supervision of high-risk patients should accompany drug therapy. RISPERDAL® CONSTA® is to be administered by a health care professional *[see Dosage and Administration in full PI];* therefore, suicide due to an overdose is unlikely. **Use in Patients with Concomitant Illness:** Clinical experience with RISPERDAL® CONSTA® in patients with certain concomitant systemic illnesses is limited. Patients with Parkinson's Disease or Dementia with Lewy Bodies who receive antipsychotics, including RISPERDAL® CONSTA®, are reported to have an increased sensitivity to antipsychotic medications. Manifestations of this increased sensitivity have been reported to include confusion, obtundation, postural instability with frequent falls, extrapyramidal symptoms, and clinical features consistent with the neuroleptic malignant syndrome. Caution is advisable when using RISPERDAL® CONSTA® in patients with diseases or conditions that could affect metabolism or hemodynamic responses. Increased plasma concentrations of risperidone and 9-hydroxyrisperidone occur in patients with severe renal impairment (creatinine clearance <30 mL/min/1.73 m^2) treated with oral RISPERDAL®; an increase in the free fraction of risperidone is also seen in patients with severe hepatic impairment. Patients with renal or hepatic impairment should be carefully titrated on oral RISPERDAL® before treatment with RISPERDAL® CONSTA® is initiated at a dose of 25 mg. A lower initial dose of 12.5 mg may be appropriate when clinical factors warrant dose adjustment, such as in patients with renal or hepatic impairment *[see Dosage and Administration in full PI].* **Osteodystrophy and Tumors in Animals:** RISPERDAL® CONSTA® produced osteodystrophy in male and female rats in a 1-year toxicity study and a 2-year carcinogenicity study at a dose of 40 mg/kg administered IM every 2 weeks. RISPERDAL® CONSTA® produced renal tubular tumors (adenoma, adenocarcinoma) and adrenomedullary pheochromocytomas in male rats in the 2-year carcinogenicity study at 40 mg/kg administered IM every 2 weeks. In addition, RISPERDAL® CONSTA® produced an increase in a marker of cellular proliferation in renal tissue in males in the 1-year toxicity study and in renal tumor-bearing males in the 2-year carcinogenicity study at 40 mg/kg administered IM every 2 weeks. **Neither the renal or adrenal tumors, nor osteodystrophy, were seen in studies of orally administered risperidone.** Osteodystrophy was not observed in dogs at doses up to 14 times (based on AUC) the IM MRHD in a 1-year toxicity study. The renal tubular and adrenomedullary tumors in male rats and other tumor findings are described in more detail in *Nonclinical Toxicology in full PI.* The relevance of these findings to human risk is unknown. **Monitoring: Laboratory Tests:** No specific laboratory tests are recommended.

ADVERSE REACTIONS: The following are discussed in more detail in *Boxed Warning and Warnings and Precautions* sections of the labeling: • Increased mortality in elderly patients with dementia-related psychosis • Cerebrovascular adverse events, including stroke, in elderly patients with dementia-related psychosis • Neuroleptic malignant syndrome • Tardive dyskinesia • Hyperglycemia and diabetes mellitus • Hyperprolactinemia • Orthostatic hypotension • Potential for cognitive and motor impairment • Seizures • Dysphagia • Priapism • Thrombotic Thrombocytopenic Purpura (TTP) • Disruption of body temperature regulation • Avoidance of inadvertent injection into a blood vessel • Antiemetic effect • Suicide • Increased sensitivity in patients with Parkinson's disease or those with dementia with Lewy bodies • Diseases or conditions that could affect metabolism or hemodynamic responses • Osteodystrophy and tumors in animals The most common adverse reactions in clinical trials (≥ 5%) were: headache, parkinsonism, dizziness, akathisia, fatigue, constipation, dyspepsia, sedation, weight increased, pain in extremity, and dry mouth. The most common adverse reactions that were associated with discontinuation from the 12-week double-blind, placebo-controlled (causing discontinuation in ≥ 1% of patients) were agitation, depression, anxiety, and akathisia *[see Adverse Reactions].* The data described in this section are derived from a clinical trial database consisting of 2392 patients exposed to one or more doses of RISPERDAL® CONSTA® for the treatment of schizophrenia. Of these 2392 patients, 332 were patients who received RISPERDAL® CONSTA® while participating in a 12-week double-blind, placebo-controlled trial. Two hundred two (202) of the 332 were schizophrenia patients who received 25 mg or 50 mg RISPERDAL® CONSTA®. The conditions and duration of treatment with RISPERDAL® CONSTA® varied greatly and included (in overlapping categories) double-blind, fixed- and flexible-dose, placebo- or active-controlled studies and open-label phases of studies, inpatients and outpatients, and short-term (up to 12 weeks) and longer-term (up to 4 years) exposures. Safety was assessed by collecting adverse events and performing physical examinations, vital signs, body weights, laboratory analyses, and ECGs. Adverse events during exposure to study treatment were obtained by general inquiry and recorded by clinical investigators using their own terminology. Consequently, to provide a meaningful estimate of the proportion of individuals experiencing adverse events, events were grouped in standardized categories using MedDRA terminology. Throughout this section, adverse reactions are reported. Adverse reactions are adverse events that were considered to be reasonably associated with the use of RISPERDAL® CONSTA® (adverse drug reactions) based on the comprehensive assessment of the available adverse event information. A causal association for RISPERDAL® CONSTA® often cannot be reliably established in individual cases. Further, because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice. The majority of all adverse reactions were mild to moderate in severity. **Commonly-Observed Adverse Reactions in Double-Blind, Placebo-Controlled Clinical Trials:** Table 1 lists the adverse reactions reported in 2% or more of RISPERDAL® CONSTA®-treated patients with schizophrenia in one 12-week double-blind, placebo-controlled trial. **Table 1. Adverse Reactions in ≥ 2% of RISPERDAL® CONSTA®-Treated Patients with Schizophrenia in a 12-Week Double-Blind, Placebo-Controlled Trial: System Organ Class, Percentage of Patients Reporting Event RISPERDAL® CONSTA® 25mg (N=99)** first, **50 mg (N=103)** second, **Placebo (N=98)** third, **Adverse Reaction, Eye disorders:** Vision blurred 2, 3, 0; **Gastrointestinal disorders:** Constipation 5, 7, 1; Dry mouth 0, 7, 1; Dyspepsia 6, 6, 0; Nausea 3, 4, 5; Toothache 1, 3, 0: Salivary hypersecretion 4, 1, 0; **General disorders and administration site conditions:** Fatigue* 3, 9, 0; Edema peripheral 2, 3, 1; Pain 4, 1, 0; Pyrexia 2, 1, 0; **Infections and infestations:** Upper respiratory tract infection 2, 0, 1; **Investigations:** Weight increased 5, 4, 2; Weight decreased 4, 1, 1; **Musculoskeletal and connective tissue disorders:** Pain in extremity 6, 2, 1; **Nervous system disorders:** Headache 15, 21, 12; Parkinsonism* 8, 15, 9; Dizziness 7, 11, 6; Akathisia* 4, 11, 6; Sedation* 5, 6, 3; Tremor 0, 3, 0; Syncope 2, 1, 0; Hypoesthesia 2, 0, 0; **Respiratory, thoracic and mediastinal disorders:** Cough 4, 2, 3; Sinus congestion 2, 0, 0; **Skin and subcutaneous tissue disorders:** Acne 2, 2, 0; Dry skin 2, 0, 0. * Fatigue includes fatigue and asthenia. Parkinsonism includes extrapyramidal disorder, musculoskeletal stiffness, muscle rigidity, and bradykinesia. Akathisia includes akathisia and restlessness. Sedation includes sedation and somnolence. **Other Adverse Reactions Observed During the Premarketing Evaluation of RISPERDAL® CONSTA®:** The following adverse reactions occurred in < 2% of the patients in the above 12-week double-blind, placebo-controlled trial. In addition, the following also includes adverse reactions reported in RISPERDAL® CONSTA®-treated patients who participated in other studies, including double-blind, active-controlled and open-label studies in schizophrenia. **Blood and lymphatic system disorders:** anemia, neutropenia **Cardiac disorders:** tachycardia, atrioventricular block first degree, palpitations, sinus bradycardia, bundle branch block left, bradycardia, sinus tachycardia, bundle branch block right **Ear and labyrinth disorders:** ear pain, vertigo **Endocrine disorders:** hyperprolactinemia **Eye disorders:** conjunctivitis **Gastrointestinal disorders:** diarrhea, vomiting, abdominal pain, stomach discomfort, gastritis **General disorders and administration site conditions:** injection site pain, chest discomfort, chest pain, influenza like illness, sluggishness, malaise, induration, injection site induration, injection site reaction **Immune system disorders:** hypersensitivity **Infections and infestations:** nasopharyngitis, influenza, bronchitis, urinary tract infection, rhinitis, ear infection, pneumonia, lower respiratory tract infection, pharyngitis, sinusitis, viral infection, infection, localized infection, cystitis, gastroenteritis, subcutaneous abscess **Injury and poisoning:** fall, procedural pain **Investigations:** blood prolactin increased, alanine aminotransferase increased, electrocardiogram abnormal, gamma-glutamyl transferase increased, blood glucose increased, hepatic enzyme increased, aspartate aminotransferase increased **Metabolism and nutritional disorders:** increased appetite, decreased appetite **Musculoskeletal, connective tissue and bone disorders:** myalgia, back pain, arthralgia, buttock pain, muscular weakness, neck pain, musculoskeletal chest pain **Nervous system disorders:** dyskinesia, dystonia, tardive dyskinesia, drooling, paresthesia, dizziness postural, convulsion **Psychiatric disorders:** insomnia, agitation, anxiety, sleep disorder, depression, libido decreased, nervousness **Renal and urinary disorders:** urinary incontinence **Reproductive system and breast disorders:** amenorrhea, erectile dysfunction, galactorrhea, sexual dysfunction, gynecomastia **Respiratory, thoracic and mediastinal disorders:** nasal congestion, pharyngolaryngeal pain, dyspnea, rhinorrhea **Skin and subcutaneous tissue disorders:** rash, eczema, pruritus **Vascular disorders:** hypertension, hypotension, orthostatic hypotension **Discontinuations Due to Adverse Reactions:** Approximately 11% (22/202) of RISPERDAL® CONSTA®-treated patients in the 12-week double-blind, placebo-controlled trial discontinued treatment due to an adverse event, compared with 13% (13/98) who received placebo. The adverse reactions associated with discontinuation in two or more RISPERDAL® CONSTA®-treated patients were: agitation (3%), depression (2%), anxiety (1%), and akathisia (1%). **Dose Dependency of Adverse Reactions in Clinical Trials:** Extrapyramidal Symptoms: Two methods were used to measure extrapyramidal symptoms (EPS) in the 12-week double-blind, placebo-controlled trial comparing three doses of RISPERDAL® CONSTA® (25 mg, 50 mg, and 75 mg) with placebo, including: (1) the incidence of spontaneous reports of EPS symptoms; and (2) the change from baseline to endpoint on the total score (sum of the subscale scores for Parkinsonism, dystonia, and dyskinesia) of the Extrapyramidal Symptom Rating Scale (ESRS). As shown in Table 1, the overall incidence of EPS-related adverse reactions (akathisia, dystonia, Parkinsonism, and tremor) in patients treated with 25 mg RISPERDAL® CONSTA® was comparable to that of patients treated with placebo; the incidence of EPS-related adverse reactions was higher in patients treated with 50 mg RISPERDAL® CONSTA®. The median change from baseline to endpoint in total ESRS score showed no worsening in patients treated with RISPERDAL® CONSTA® compared with patients treated with placebo: 0 (placebo group); -1 (25-mg group, significantly less than the placebo group); and 0 (50-mg group). *Dystonia: Class Effect:* Symptoms of dystonia, prolonged abnormal contractions of muscle groups, may occur in susceptible individuals during the first few days of treatment. Dystonic symptoms include: spasm of the neck muscles, sometimes progressing to tightness of the throat, swallowing difficulty, difficulty breathing, and/or protrusion of the tongue. While these symptoms can occur

at low doses, they occur more frequently and with greater severity with high potency and at higher doses of first generation antipsychotic drugs. An elevated risk of acute dystonia is observed in males and younger age groups. **Changes in Body Weight:** In the 12-week double-blind, placebo-controlled trial, 9% of patients treated with RISPERDAL® CONSTA®, compared with 6% of patients treated with placebo, experienced a weight gain of >7% of body weight at endpoint. **Changes in ECG:** The electrocardiograms of 202 schizophrenic patients treated with 25 mg or 50 mg RISPERDAL® CONSTA® and 98 schizophrenic patients treated with placebo in the 12-week double-blind, placebo-controlled trial were evaluated. Compared with placebo, there were no statistically significant differences in QTc intervals (using Fridericia's and linear correction factors) during treatment with RISPERDAL® CONSTA®. **Pain Assessment and Local Injection Site Reactions:** The mean intensity of injection pain reported by patients using a visual analog scale (0 = no pain to 100 = unbearably painful) decreased in all treatment groups from the first to the last injection (placebo: 16.7 to 12.6; 25 mg: 12.0 to 9.0; 50 mg: 18.2 to 11.8). After the sixth injection (Week 10), investigator ratings indicated that 1% of patients treated with 25 mg or 50 mg RISPERDAL® CONSTA® experienced redness, swelling, or induration at the injection site. In a separate study to observe local-site tolerability in which RISPERDAL® CONSTA® was administered into the deltoid muscle every 2 weeks over a period of 8 weeks, no patient discontinued treatment due to local injection site pain or reaction. Clinician ratings indicated that only mild redness, swelling, or induration at the injection site was observed in subjects treated with 37.5 mg or 50 mg RISPERDAL® CONSTA® at 2 hours after deltoid injection. All ratings returned to baseline at the predose assessment of the next injection 2 weeks later. No moderate or severe reactions were observed in any subject. **Postmarketing Experience:** The following adverse reactions have been identified during postapproval use of risperidone; because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency: agranulocytosis, alopecia, anaphylactic reaction, angioedema, atrial fibrillation, diabetic ketoacidosis in patients with impaired glucose metabolism, inappropriate antidiuretic hormone secretion, hypothermia, intestinal obstruction, jaundice, mania, pancreatitis, priapism, QT prolongation, sleep apnea syndrome, thrombocytopenia, and water intoxication. In addition, the following adverse reactions have been observed during postapproval use of RISPERDAL® CONSTA®: cerebrovascular disorders, including cerebrovascular accidents, and diabetes mellitus aggravated. Retinal artery occlusion after injection of RISPERDAL® CONSTA® has been reported during postmarketing surveillance. This has been reported in the presence of abnormal arteriovenous anastomosis. Serious injection site reactions including abscess, cellulitis, cyst, hematoma, necrosis, nodule, and ulcer have been reported with RISPERDAL® CONSTA® during postmarketing surveillance. Isolated cases required surgical intervention.

DRUG INTERACTIONS: The interactions of RISPERDAL® CONSTA® with coadministration of other drugs have not been systematically evaluated. The drug interaction data provided in this section is based on studies with oral RISPERDAL®. **Centrally-Acting Drugs and Alcohol:** Given the primary CNS effects of risperidone, caution should be used when RISPERDAL® CONSTA® is administered in combination with other centrally-acting drugs or alcohol. **Drugs with Hypotensive Effects:** Because of its potential for inducing hypotension, RISPERDAL® CONSTA® may enhance the hypotensive effects of other therapeutic agents with this potential. **Levodopa and Dopamine Agonists:** RISPERDAL® CONSTA® may antagonize the effects of levodopa and dopamine agonists. **Amitriptyline:** Amitriptyline did not affect the pharmacokinetics of risperidone or of risperidone and 9-hydroxyrisperidone combined following concomitant administration with oral RISPERDAL®. **Cimetidine and Ranitidine:** Cimetidine and ranitidine increased the bioavailability of oral risperidone by 64% and 26%, respectively. However, cimetidine did not affect the AUC of risperidone and 9-hydroxyrisperidone combined, whereas ranitidine increased the AUC of risperidone and 9-hydroxyrisperidone combined by 20%. **Clozapine:** Chronic administration of clozapine with risperidone may decrease the clearance of risperidone. **Lithium:** Repeated doses of oral RISPERDAL® (3 mg twice daily) did not affect the exposure (AUC) or peak plasma concentrations (C_{max}) of lithium (n=13). **Valproate:** Repeated doses of oral RISPERDAL® (4 mg once daily) did not affect the pre-dose or average plasma concentrations and exposure (AUC) of valproate (1000 mg/day in three divided doses) compared to placebo (n=21). However, there was a 20% increase in valproate peak plasma concentration (C_{max}) after concomitant administration of oral RISPERDAL®. **Digoxin:** Oral RISPERDAL® (0.25 mg twice daily) did not show a clinically relevant effect on the pharmacokinetics of digoxin. **Topiramate:** Oral RISPERDAL® administered at doses from 1-6 mg/day concomitantly with topiramate 400 mg/day resulted in a 23% decrease in risperidone Cmax and a 33% decrease in risperidone $AUC_{0\text{-}12\,hour}$ at steady state. Minimal reductions in the exposure to risperidone and 9-hydroxyrisperidone combined, and no change for 9-hydroxyrisperidone were observed. This interaction is unlikely to be of clinical significance. There was no clinically relevant effect of oral RISPERDAL® on the pharmacokinetics of topiramate. **Drugs That Inhibit CYP 2D6 and Other CYP Isozymes:** Risperidone is metabolized to 9-hydroxyrisperidone by CYP 2D6, an enzyme that is polymorphic in the population and that can be inhibited by a variety of psychotropic and other drugs *[see Clinical Pharmacology in full PI]*. Drug interactions that reduce the metabolism of risperidone to 9-hydroxyrisperidone would increase the plasma concentrations of risperidone and lower the concentrations of 9-hydroxyrisperidone. Analysis of clinical studies involving a modest number of poor metabolizers (n≅70 patients) does not suggest that poor and extensive metabolizers have different rates of adverse effects. No comparison of effectiveness in the two groups has been made. *In vitro* studies showed that drugs metabolized by other CYP isozymes, including 1A1, 1A2, 2C9, 2C19, and 3A4, are only weak inhibitors of risperidone metabolism. Fluoxetine and Paroxetine: Fluoxetine (20 mg once daily) and paroxetine (20 mg once daily), CYP 2D6 inhibitors, have been shown to increase the plasma concentration of risperidone 2.5-2.8 fold and 3-9 fold respectively. Fluoxetine did not affect the plasma concentration of 9-hydroxyrisperidone. Paroxetine lowered the concentration of 9-hydroxyrisperidone by about 10%. When either concomitant fluoxetine or paroxetine is initiated or discontinued, the physician should re-evaluate the dose of RISPERDAL® CONSTA®. When initiation of fluoxetine or paroxetine is considered, patients may be placed on a lower dose of RISPERDAL® CONSTA® between 2 to 4 weeks before the planned start of fluoxetine or paroxetine therapy to adjust for the expected increase in plasma concentrations of risperidone. When fluoxetine or paroxetine is initiated in patients receiving the recommended dose of 25 mg RISPERDAL® CONSTA®, it is recommended to continue treatment with the 25-mg dose unless clinical judgment necessitates lowering the RISPERDAL® CONSTA® dose to 12.5 mg or necessitates interruption of RISPERDAL® CONSTA® treatment. When RISPERDAL® CONSTA® is initiated in patients already receiving fluoxetine or paroxetine, a starting dose of 12.5 mg can be considered. The efficacy of the 12.5 mg dose has not been investigated in clinical trials. *[See also Dosage and Administration in full PI]*. The effects of discontinuation of concomitant fluoxetine or paroxetine therapy on the pharmacokinetics of risperidone and 9-hydroxyrisperidone have not been studied. Erythromycin: There were no significant interactions between oral RISPERDAL® and erythromycin. **Carbamazepine and Other CYP 3A4 Enzyme Inducers:** Carbamazepine co-administration with oral RISPERDAL® decreased the steady-state plasma concentrations of risperidone and 9-hydroxyrisperidone by about 50%. Plasma concentrations of carbamazepine did not appear to be affected. Co-administration of other known CYP 3A4 enzyme inducers (e.g., phenytoin, rifampin, and phenobarbital) with risperidone may cause similar decreases in the combined plasma concentrations of risperidone and 9-hydroxyrisperidone, which could lead to decreased efficacy of RISPERDAL® CONSTA® treatment. At the initiation of therapy with carbamazepine or other known hepatic enzyme inducers, patients should be closely monitored during the first 4–8 weeks, since the dose of RISPERDAL® CONSTA® may need to be adjusted. A dose increase, or additional oral RISPERDAL®, may need to be considered. On discontinuation of carbamazepine or other CYP 3A4 hepatic enzyme inducers, the dosage of RISPERDAL® CONSTA® should be re-evaluated and, if necessary, decreased. Patients may be placed on a lower dose of RISPERDAL® CONSTA® between 2 to 4 weeks before the planned discontinuation of carbamazepine or other CYP 3A4 enzyme inducers to adjust for the expected increase in plasma concentrations of risperidone plus 9-hydroxyrisperidone. For patients treated with the recommended dose of 25 mg RISPERDAL® CONSTA® and discontinuing from carbamazepine or other CYP 3A4 enzyme inducers, it is recommended to continue treatment with the 25-mg dose unless clinical judgment necessitates lowering the RISPERDAL® CONSTA® dose to 12.5 mg or necessitates interruption of RISPERDAL® CONSTA® treatment. The efficacy of the 12.5 mg dose has not been investigated in clinical trials. *[See also Dosage and Administration in full PI]* **Drugs Metabolized by CYP 2D6:** *In vitro* studies indicate that risperidone is a relatively weak inhibitor of CYP 2D6. Therefore, RISPERDAL® CONSTA® is not expected to substantially inhibit the clearance of drugs that are metabolized by this enzymatic pathway. In drug interaction studies, oral RISPERDAL® did not significantly affect the pharmacokinetics of donepezil and galantamine, which are metabolized by CYP 2D6.

USE IN SPECIFIC POPULATIONS: Pregnancy: Pregnancy Category C.: The teratogenic potential of oral risperidone was studied in three embryofetal development studies in Sprague-Dawley and Wistar rats (0.63-10 mg/kg or 0.4 to 6 times the oral maximum recommended human dose [MRHD] on a mg/m² basis) and in one embryofetal development study in New Zealand rabbits (0.31-5 mg/kg or 0.4 to 6 times the oral MRHD on a mg/m² basis). The incidence of malformations was not increased compared to control in offspring of rats or rabbits given 0.4 to 6 times the oral MRHD on a mg/m² basis. In three reproductive studies in rats (two peri/post-natal development studies and a multigenerational study), there was an increase in pup deaths during the first 4 days of lactation at doses of 0.16-5 mg/kg or 0.1 to 3 times the oral MRHD on a mg/m² basis. It is not known whether these deaths were due to a direct effect on the fetuses or pups or to effects on the dams. There was no no-effect dose for increased rat pup mortality. In one peri/post-natal development study, there was an increase in stillborn rat pups at a dose of 2.5 mg/kg or 1.5 times the oral MRHD on a mg/m² basis. In a cross-fostering study in Wistar rats, toxic effects on the fetus or pups, as evidenced by a decrease in the number of live pups and an increase in the number of dead pups at birth (Day 0), and a decrease in birth weight in pups of drug-treated dams were observed. In addition, there was an increase in deaths by Day 1 among pups of drug-treated dams, regardless of whether or not the pups were cross-fostered. Risperidone also appeared to impair maternal behavior in that pup body weight gain and survival (from Days 1 to 4 of lactation) were reduced in pups born to control but reared by drug-treated dams. These effects were all noted at the one dose of risperidone tested, i.e., 5 mg/kg or 3 times the oral MRHD on a mg/m² basis. No studies were conducted with RISPERDAL® CONSTA®. Placental transfer of risperidone occurs in rat pups. There are no adequate and well-controlled studies in pregnant women. However, there was one report of a case of agenesis of the corpus callosum in an infant exposed to risperidone *in utero*. The causal relationship to oral RISPERDAL® therapy is unknown. Reversible extrapyramidal symptoms in the neonate were observed following postmarketing use of risperidone during the last trimester of pregnancy. RISPERDAL® CONSTA® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Labor and Delivery:** The effect of RISPERDAL® CONSTA® on labor and delivery in humans is unknown. **Nursing Mothers:** Risperidone and 9-hydroxyrisperidone are also excreted in human breast milk. Therefore, women should not breast-feed during treatment with RISPERDAL® CONSTA® and for at least 12 weeks after the last injection. **Pediatric Use:** RISPERDAL® CONSTA® has not been studied in children younger than 18 years old. **Geriatric Use:** In an open-label study, 57 clinically stable, elderly patients (≥ 65 years old) with schizophrenia or schizoaffective disorder received RISPERDAL® CONSTA® every 2 weeks for up to 12 months. In general, no differences in the tolerability of RISPERDAL® CONSTA® were observed between otherwise healthy elderly and nonelderly patients. Therefore, dosing recommendations for otherwise healthy elderly patients are the same as for nonelderly patients. Because elderly patients exhibit a greater tendency to orthostatic hypotension than nonelderly patients, elderly patients should be instructed in nonpharmacologic interventions that help to reduce the occurrence of orthostatic hypotension (e.g., sitting on the edge of the bed for several minutes before attempting to stand in the morning and slowly rising from a seated position). In addition, monitoring of orthostatic vital signs should be considered in elderly patients for whom orthostatic hypotension is of concern *[see Warnings and Precautions]*. Concomitant use with Furosemide in Elderly Patients with Dementia-Related Psychosis: In two of four placebo-controlled trials in elderly patients with dementia-related psychosis, a higher incidence of mortality was observed in patients treated with furosemide plus oral risperidone when compared to patients treated with oral risperidone alone or with oral placebo plus furosemide. No pathological mechanism has been identified to explain this finding, and no consistent pattern for cause of death was observed. An increase of mortality in elderly patients with dementia-related psychosis was seen with the use of oral risperidone regardless of concomitant use with furosemide. RISPERDAL® CONSTA® is not approved for the treatment of patients with dementia-related psychosis. *[See Boxed Warning and Warnings and Precautions]*

PATIENT COUNSELING INFORMATION: Physicians are advised to discuss the following issues with patients for whom they prescribe RISPERDAL® CONSTA®. **Orthostatic Hypotension:** Patients should be advised of the risk of orthostatic hypotension and instructed in nonpharmacologic interventions that help to reduce the occurrence of orthostatic hypotension (e.g., sitting on the edge of the bed for several minutes before attempting to stand in the morning and slowly rising from a seated position) *[see Warnings and Precautions]*. **Interference with Cognitive and Motor Performance:** Because RISPERDAL® CONSTA® has the potential to impair judgment, thinking, or motor skills, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that treatment with RISPERDAL® CONSTA® does not affect them adversely *[see Warnings and Precautions]*. **Pregnancy:** Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy and for at least 12 weeks after the last injection of RISPERDAL® CONSTA® *[see Use in Specific Populations]*. **Nursing:** Patients should be advised not to breast-feed an infant during treatment and for at least 12 weeks after the last injection of RISPERDAL® CONSTA® *[see Use in Specific Populations]*. **Concomitant Medication:** Patients should be advised to inform their physicians if they are taking, or plan to take, any prescription or over-the-counter drugs, since there is a potential for interactions *[see Drug Interactions]*. **Alcohol:** Patients should be advised to avoid alcohol during treatment with RISPERDAL® CONSTA® *[see Drug Interactions]*.

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Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc.

Risperidone is manufactured by:
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RISPERDAL® CONSTA® is manufactured for:
Janssen, Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc.
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01CS09024B

COMPILED BY JUN YAN

Regulatory Briefs

• The Food and Drug Administration (FDA) approved combination ***olanzapine/fluoxetine*** capsules (Symbyax) for the acute treatment of treatment-resistant depression, defined as "major depressive disorder in adults who do not respond to two separate trials of different antidepressants of adequate dose and duration in the current episode," according to an Eli Lilly announcement on March 23.

This is the first drug therapy approved for this indication. The combination was also approved for depressive episodes associated with bipolar I disorder in adults. In addition, the individual labels of fluoxetine, which is currently available in generic form, and olanzapine now contain approved indications for treatment-resistant depression and bipolar I depression if each drug is taken in combination with the other. The labels of the combination drug and olanzapine alone were also revised to contain clinical trial findings regarding weight gain, hyperglycemia, and increased cholesterol associated with the antipsychotic.

• The labels of all ***selective serotonin-reuptake inhibitor (SSRI) and serotonin- and norepinephrine-reuptake inhibitor (SNRI) antidepressants*** were updated in January, as mandated by the FDA, with warnings about the risk of serotonin syndrome or neuroleptic malignant syndrome-like reactions. The warning cautions that concomitant use of SSRIs or SNRIs with monoamine oxidase inhibitors, serotonergic drugs such as triptans (5-hydroxytryptamine receptor agonists), antipsychotics, or dopamine antagonists may exacerbate the risk of these potentially life-threatening adverse events and require careful monitoring.

• The FDA posted changes to the "Warnings and Precautions" and "Adverse Reactions" sections of the label for ***duloxetine delayed-release capsules*** (Cymbalta) in March. The updated wording warns of adverse reactions reported in clinical trials and postmarketing reports. These reactions include tinnitus, poor sleep quality, polyuria, aggression and anger (particularly early in treatment or after discontinuation), restless legs syndrome, and other adverse events.

• The FDA's Division of Drug Marketing, Advertising, and Communications (DDMAC) sent letters to 14 companies requesting that inappropriate and unlawful drug-promotional Internet links be removed because they omitted risk information or contained misleading claims. The DDMAC appears to be stepping up its monitoring and regulation of online drug and medical-device advertising in recent months. This batch of warning letters focused on company-sponsored links on Internet search engines that are intended to draw Internet users to Web sites focused on these drugs, including ***duloxetine***.

Legal Briefs

• A proposed settlement of a lawsuit involving ***paroxetine extended-release tablets*** may entitle patients and third-party payers to reimbursement for buying Paxil CR tablets that were manufactured by GlaxoSmithKline from April 1, 2002, to March 4, 2005. The lawsuit claimed that these tablets were defective and tended to split apart. If the proposed settlement is approved in the final hearing, scheduled for July, the company will pay up to $28 million to settle claims. The manufacturer has denied any liability in the suit.

Details of the settlement are posted at <www.simonetpaxilcrsettlement.com>.

• IMS Health and SDI filed a petition with the U.S. Supreme Court on March 27, seeking to overturn a New Hampshire law that restricts prescription data mining. Both are large data-gathering companies that collect, analyze, and sell health care market data, including prescription data that allow pharmaceutical companies to monitor prescribing patterns of physicians and other prescribers and identify and target specific prescribers in marketing efforts. New Hampshire, Maine, and Vermont have passed laws to ban this type of data mining, but they were struck down or tied up in lower courts based on First Amendment arguments. However, in November 2008 a federal appellate court overturned a lower court ruling and upheld the New Hampshire Prescription Confidentiality Act and in April Vermont's law was upheld in U.S. District Court.

Industry and R&D Briefs

• Eli Lilly announced inconclusive results from a phase 2 study of ***LY2140023***, a glutamate mGlu2/3 receptor agonist and a candidate drug to treat schizophrenia. The finding was somewhat unexpected, as the compound appeared to be a promising first-in-kind antipsychotic with positive efficacy data in a previous phase 2a study in 2007.

In this randomized, placebo-controlled trial, 393 patients with schizophrenia completed four weeks of treatment with LY2140023, olanzapine, or placebo. The placebo group had an unexpectedly high response rate, according to the company announcement, and neither olanzapine 15 mg daily nor LY2140023 led to a statistically significant reduction in patients' symptoms compared with placebo. Lilly said it would continue the clinical development of LY2140023 and would conduct another phase 2 trial to determine the molecule's efficacy.

• Cephalon announced positive results from a phase 3 trial of ***armodafinil*** for the treatment of excessive sleepiness in jet-lag disorder on April 6. An *R*-enantiomer of modafinil, armodafinil is currently approved for promoting wakefulness in patients with excessive sleepiness associated with obstructive sleep apnea/hypopnea syndrome, narcolepsy, and shift-work sleep disorder.

The randomized, double-blind, placebo-controlled trial was conducted in 427 healthy adults with a history of jet-lag symptoms during the previous five years. Study participants traveled eastbound from the United States to France and received either armodafinil or placebo for three days. The drug was generally well tolerated and was shown to be more effective than placebo in reducing excessive sleepiness. The company said it would file a supplemental new drug application with the FDA later this year for this indication.

• A modified-release formulation of ***eszopiclone***, a nonbenzodiazepine drug currently approved to treat insomnia, failed a phase 2 clinical trial to evaluate its efficacy in patients with generalized anxiety disorder (GAD), according to a March 5 announcement by its maker Sepracor. In this 440-patient trial, the drug did not meet the primary endpoint in reducing the symptoms of GAD.

• Repligen Corp. announced on March 31 that it licensed the patent rights to the use of ***uridine*** to treat bipolar disorder from McLean Hospital in Belmont, Mass. An oral formulation of uridine is currently in phase 2 clinical development by the company for treatment of bipolar depression.

• Switzerland-based Roche and Germany-based Evotec announced a plan to co-develop a group of compounds that belong to the category of N-methyl D-aspartate receptor NR2B subtype selective antagonists. These molecules act on a type of glutamate receptor and may become candidates for treating a number of central nervous system disorders, including Alzheimer's disease and Parkinson's disease. One of these drug candidates, ***EVT 101***, is currently in phase 2 clinical development for treatment-resistant depression.

• A once-daily formulation of ***bupropion hydrobromide extended-release tablets***, marketed under the brand name Aplenzin, has entered the U.S. market, said the manufacturer Sanofi-Aventis on April 7. The highest dosage form, 522 mg, delivers the equivalent of a 450 mg bupropion hydrochloride tablet. Approved by the FDA for marketing in April 2008, the tablet was developed by Biovail and has shown bioequivalence to other formulations of bupropion tablets.

• Shire announced on March 16 that it has decided to withdraw a previous application to European regulators to market ***methylphenidate transdermal system*** (Daytrana), a medicated patch approved in the United States to treat attention-deficit/hyperactivity disorder. The European authority had asked the company to conduct additional clinical trials.

• A phase 3 study of ***vilazodone***, an investigational antidepressant developed by Clinical Data Inc., showed positive outcomes in the treatment of major depressive disorder, according to a study published in the March *Journal of Clinical Psychiatry*. In the randomized, double-blind, placebo-controlled study, 198 patients with depression received vilazodone and 199 received placebo for eight weeks. The mean Montgomery-Asberg Depression Rating Scale scores were reduced from baseline by 12.9 points in the vilazodone group and 9.6 points in the placebo group after eight weeks, and the difference was statistically significant. The reductions in 17-item Hamilton Rating Scale for Depression scores from baseline were 10.4 points and 8.6 points in the vilazodone and placebo groups, respectively, also a statistically significant difference. The most frequent adverse events associated with vilazodone included diarrhea, nausea, and somnolence. Vilazodone is an SSRI and a partial agonist of the $5HT_{1A}$ receptor.

An abstract of "Evidence for Efficacy and Tolerability of Vilazodone in the Treatment of Major Depressive Disorder: A Randomized, Double-Blind, Placebo-Controlled Trial" is posted at <www.psychiatrist.com/abstracts/abstracts.asp?abstract=200903/030903.htm>.

• Janssen, a division of Johnson and Johnson, announced on April 1 that results from a clinical trial of ***paliperidone extended-release tablets*** for the treatment of schizoaffective disorder were presented by the company at the 12th International Congress on Schizophrenia Research in San Diego. In the randomized, double-blind, placebo-controlled study, 311 patients with acute symptoms were treated with either paliperidone or placebo for six weeks. The reduction in Positive and Negative Syndrome Scale total score in the paliperidone group was significantly more than that in the placebo group. The most common adverse events were headache, dizziness, insomnia, akathisia, and dyspepsia, according to the company.

Paliperidone is approved to treat schizophrenia. In February Janssen submitted an application to the FDA seeking approval to use paliperidone to treat schizoaffective disorder. ■

ECP Issues

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abuse who are left to protect themselves however they can.

Despite the differences between practices in Cuba and the United States, there are similarities as well. As in the United States, stigma is an issue in Cuba's mental health system.

My visit to Cuba was certainly a humbling experience, and I realized how much I take for granted in our country. Such simple things as bandages are readily available, but in Cuba they are nearly impossible to obtain. I was also able to learn the Cuban approaches to mental health services. With the path my career has taken and the therapeutic approaches I have learned in Cuba, I plan to incorporate this expanded base of knowledge in my future mental health practice. ■

Immune System May Hold Key To New Depression Treatments

Vaccination may open a new route in the quest for a way to prevent or improve treatment of depressive disorders.

BY AARON LEVIN

Researchers around the world continue knitting together connections between the immune system, the brain, and psychiatric disorders.

Several streams of thought over the last two decades have contributed to a more solid understanding of those complex interrelationships, said Esther Sternberg, M.D., chief of the Section on Neuroendocrine Immunology and Behavior at the National Institute of Mental Health.

"One area is the study of autoimmune diseases in the brain, like multiple sclerosis, vasculitis, and lupus," said Sternberg in an interview with *Psychiatric News*.

For a long time, it was believed that immunological response to central nervous system injury was a leading agent in the death of nerve cells, she said. Today that picture is more complex. In the right circumstances, immune molecules and immune cells can help prevent cell death, depending on the extent and timing of the stimulus to the immune system relative to the injury.

A second track explores sickness behavior. The withdrawal, loss of appetite, impaired cognition, and changes in mood that accompany fever are caused by the immune response to it and mimic depression, said Sternberg.

A recent test in an animal model used a vaccine to immunize rats against analogues of depression. It provides the "first demonstration that immune activity could be harnessed in a safe and efficient manner to treat depression," reported Michal Schwartz, Ph.D., a professor of neurobiology at the Weizmann Institute of Science in Rehovot, Israel, and colleagues in the February 15 *Biological Psychiatry*.

Molecular Targets for New Treatment?

The results "open a whole new set of molecular targets" for possible treatments, said Sternberg. "This is the most exciting area of research into depression."

The research grew out of Schwartz's earlier work on spinal-cord damage, in which she observed that sensitized T cells generated by injury could either damage or protect neurons, depending on when they were activated.

Still other work indicated that autoreactive T cells help protect injured central nervous system tissue, maintain hippocampal neurogenesis, and increase expression of brain-derived neurotrophic factor (BDNF).

The researchers vaccinated rats with altered myelin basic protein peptide (A91), chosen because it was already known to activate T cells.

Just as vaccines that prevent infectious diseases use attenuated viruses to stimulate the body's defenses, Schwartz and colleagues used this weakened agonist to stimulate T cells but not make the immune system overreact and cause autoimmune disease in brain neurons.

To begin with, immunization proved to have no effect on naïve, unstressed rats.

Next, Lewis rats (a type frequently used to study autoimmune diseases) were stressed with a varying mix of strobe lights, intermittent white noise, food or water deprivation, a cage tilt of 45 degrees, and other stimuli. This chronic mild stress caused a reduction in two measures of behavior analogous to depressive symptoms: sucrose preference—considered a measure of anhedonia—and reduced mobility in the forced swim test—a test of motivation.

Control rats were injected with a saline solution. Immunized Lewis rats showed a higher sucrose preference compared with that of controls, but no improvement in the forced swim test.

Since Lewis rats have a blunted HPA-axis response to stress, the researchers then repeated the experiment with Sprague-Dawley rats, more commonly used in tests of chronic mild stress. In this group, immunized animals had significantly better scores on both the sucrose preference and forced swim tests than did control rats. However, both groups did equally well on other tests of movement in the home-cage or a novel environment, indicating lessened motivation by the saline-injected control animals but not reduced basic locomotor activity, Schwartz said.

Brain Findings Evaluated

The researchers also examined the rats' brains to observe the levels of BDNF in the dentate gyrus of the hippocampus. Hippocampal BDNF and neurogenesis are known to decrease following chronic mild stress, but stressed rats immunized with A91 had significantly higher levels of BDNF and more cell proliferation than controls.

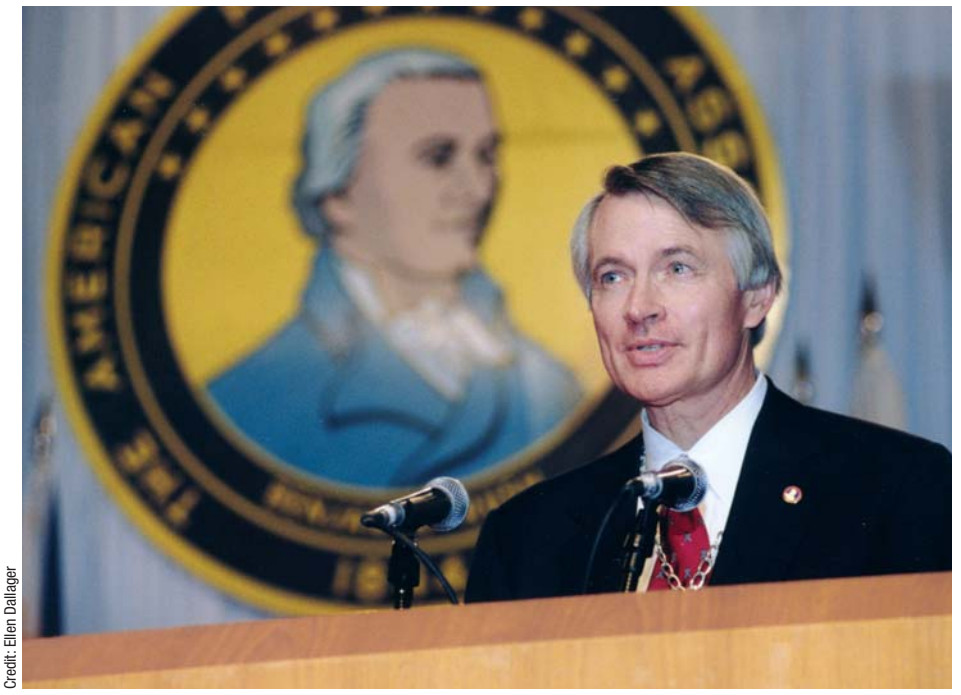
This finding may further explain the observation in humans that antidepressant drugs take several weeks to work because their effect depends on growth of new neurons in the hippocampus.

Both Schwartz and colleagues and Sternberg acknowledged that a good deal of refinement will be needed to turn these initial results into therapy.

"In terms of a proof-of-principle, it is a well-designed trial," said Sternberg. "The question is not if it works. It does, but a lot more work needs to be done before immunization could be used for patients."

"Further studies are necessary to identify the best antigen, regimen, timing, and carrier capable of providing the most effective and risk-free therapeutic vaccination for the protection against chronic stress that often leads to depression," the authors concluded.

An abstract of "Vaccination as a Novel Approach for Treating Depressive Behavior" is posted at <www.journals.elsevierhealth.com/periodicals/bps/article/S0006-3223(08)00832-9/abstract>. ■


Credit: Ellen Dallager

Richard Harding, M.D., is president of the American Psychiatric Foundation. Harding, a former APA president, is shown giving his presidential address at APA's 2002 annual meeting in Philadelphia.

Healthy Minds

continued from page 1

tion's executive director, met last year with APA's Committee on Public Affairs to discuss ways to promote the foundation's projects, Burke and Borenstein—who spoke at the meeting about "Healthy Minds"—knew they had an opportunity on their hands.

For the 2008-2009 season, Borenstein and the staff at WLIW were interested in producing shows on adolescent mental health and mental health issues among returning military personnel—two areas in which the foundation has important projects. With the help of the foundation, shows were produced that featured the foundation's "Typical or Troubled" program, which is designed to help educators identify adolescents with mental health problems, and the "Give an Hour" program, in which psychiatrists and mental health professionals are encouraged to donate time to evaluate and treat military personnel returning from Iraq and Afghanistan and their families.

"We feel a palpable increase in the demand for quality mental health public education coming from all aspects of American life and society," Burke told *Psychiatric News*. "As the public-educational arm of APA, we were looking for ways to advance awareness of our programs, and we saw 'Healthy Minds' as a showcase. And we collectively realized that a valued endorsement from APA would add credibility to the 'Healthy Minds' episodes."

The foundation also agreed to fund the national distribution of the entire 13-episode 2008-2009 season and three episodes from the show's first season. While it is up to each public television station to broadcast the shows, they are expected to begin airing in September.

Borenstein said the format of each show includes interviews with expert clinicians and researchers, as well as with patients and families. The current season of shows to be nationally distributed begins with a two-part special on autism in which five families with children diagnosed with autism spectrum disorder share personal stories about diagnosis, early intervention, and treatment.

In addition to the shows on PTSD and military personnel and adolescent mental health, the new season covers schizophrenia, recovery from abuse, minority mental health, mental health in the workplace, eating disorders, obsessive-compulsive disorder, chemical dependency, and neurogenesis. Special guests include, among others, Judith Rapoport, M.D., a senior investigator at the National Institute of Mental Health; Nobel Prize–winner Eric Kandel, M.D.; and Jeffrey Lieberman, M.D., chair of psychiatry at Columbia University College of Physicians and Surgeons.

Borenstein and Burke said that they hope APA members will look for the show on a public broadcasting station near them and urge their local station to air the show if it is not already.

"We want to encourage people to watch the series," Borenstein said. "Psychiatrists may get queries about the shows, which will offer another opportunity to educate the public. We have gotten very good feedback about the series, and one common thread is that it opens up discussions in families where previously there was no discussion about mental health. We think that is very powerful."

More information about "Healthy Minds," including streaming videos of the new episodes, can be accessed at <www.wliw.org/productions/local/healthy-minds/season-two-overview/164>. ■

letters to the editor

Add N.H. to List

I wanted to comment on the article "State Hospital Admissions on Unexpected Upswing" in the February 6 issue. New Hampshire is another state that has showed a steady increase in admissions to their state hospital, and we are doing our best to meet this challenge.

New Hampshire Hospital (NHH), a 212-bed state hospital in New Hampshire, has had a consistent increase in admissions for many years. In 1990 NHH had 850 admissions. In 2008 NHH had 2,260 admissions—this, with an increase of 36 inpatient beds over that time period.

The reasons for this dramatic increase are many and include reduced voluntary inpatient psychiatric beds, decreased community crisis-bed availability, reduced designated receiving facility (involuntary) beds throughout the state, reduced funding for outpatient community mental health centers, diminished outpatient treatment options, and limited housing for our most vulnerable mentally ill patients.

Our hospital, for which I am associate medical director, is seen as the inpatient treatment of choice by an increasing number of patients as mental health services are cut back and eliminated in communities. We deal with increasingly diverse patients with complex medical and psychiatric needs. New Hampshire Hospital's adult admission units are acute care settings where half of all patients admitted are discharged within eight days. Rapid stabilization and return to the community is the norm.

The state of New Hampshire and the Dartmouth Medical School Department of Psychiatry have partnered for 20 years to provide comprehensive patient-centered programming at NHH, and this has benefited our patients greatly. The challenges of providing and maintaining excellent psychiatric care, while addressing multiple demands, are many.

ALEXANDER DE NESNERA, M.D.
Concord, N.H.

Readers are invited to submit letters not more than 500 words long for possible publication. *Psychiatric News* reserves the right to edit letters and to publish them in all editions, print, electronic, or other media. Receipt of letters is not acknowledged. Letters should be sent by mail to *Psychiatric News*, APA, Suite 1825, 1000 Wilson Boulevard, Arlington, Va. 22209 or by e-mail to pnews@psych.org. Clinical opinions are not peer reviewed and thus should be independently verified.

clinical & research news

Antipsychotics

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recognize these metabolic changes associated with antipsychotics in younger patients, it has taken longer for us to realize they occur in elderly patients as well."

He continued, "The weight gain and metabolic effects were seen as early as 12 weeks into treatment and continued with longer use." He noted that past clinical trials of SGAs, many sponsored by pharmaceutical companies, often lasted only six to eight weeks and did not adequately monitor metabolic effects.

None of the SGAs is approved by the FDA for treating symptoms of dementia. Despite the lack of evidence for efficacy from studies such as CATIE-AD, antipsychotics are often prescribed for dementia-related behavioral disturbances for which there is no approved drug therapy. A standard black-box warning is currently required by the FDA in the labels of all antipsychotics that warns "elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death" based on data from clinical trials.

The mounting evidence of potential harm, "in the context of these drugs not working very well," should give clinicians pause for prescribing antipsychotics to dementia patients, Schneider suggested.

"Metabolic Changes Associated With Second-Generation Antipsychotic Use in Alzheimer's Disease Patients: The CATIE-AD Study" is posted at <ajp.psychiatryonline.org/cgi/reprint/appi.ajp.2008.08081218v1>. ■

APA/Shire Fellows Selected for 2009-10

Five psychiatry residents have been selected for the 2009-2010 APA/Shire Child and Adolescent Psychiatry Fellowship:

Margaret Cary, M.D., M.P.H.
Psychiatry Residency Training Program
University of Washington School of Medicine, Seattle, Wash.

Erikka Daniene Dzirasa, M.D., M.P.H.
Duke University Child and Adolescent Psychiatry Program
Duke University School of Medicine, Durham, N.C.

Julie Chilton, M.D.
Adult Psychiatry Residency, Pediatric Concentration
Children's Hospital of Philadelphia, Philadelphia, Pa.

Tresha Ann Gibbs, M.D.
Psychiatry Residency Program
New York Presbyterian Hospital and New York State Psychiatric Institute, New York, N.Y.

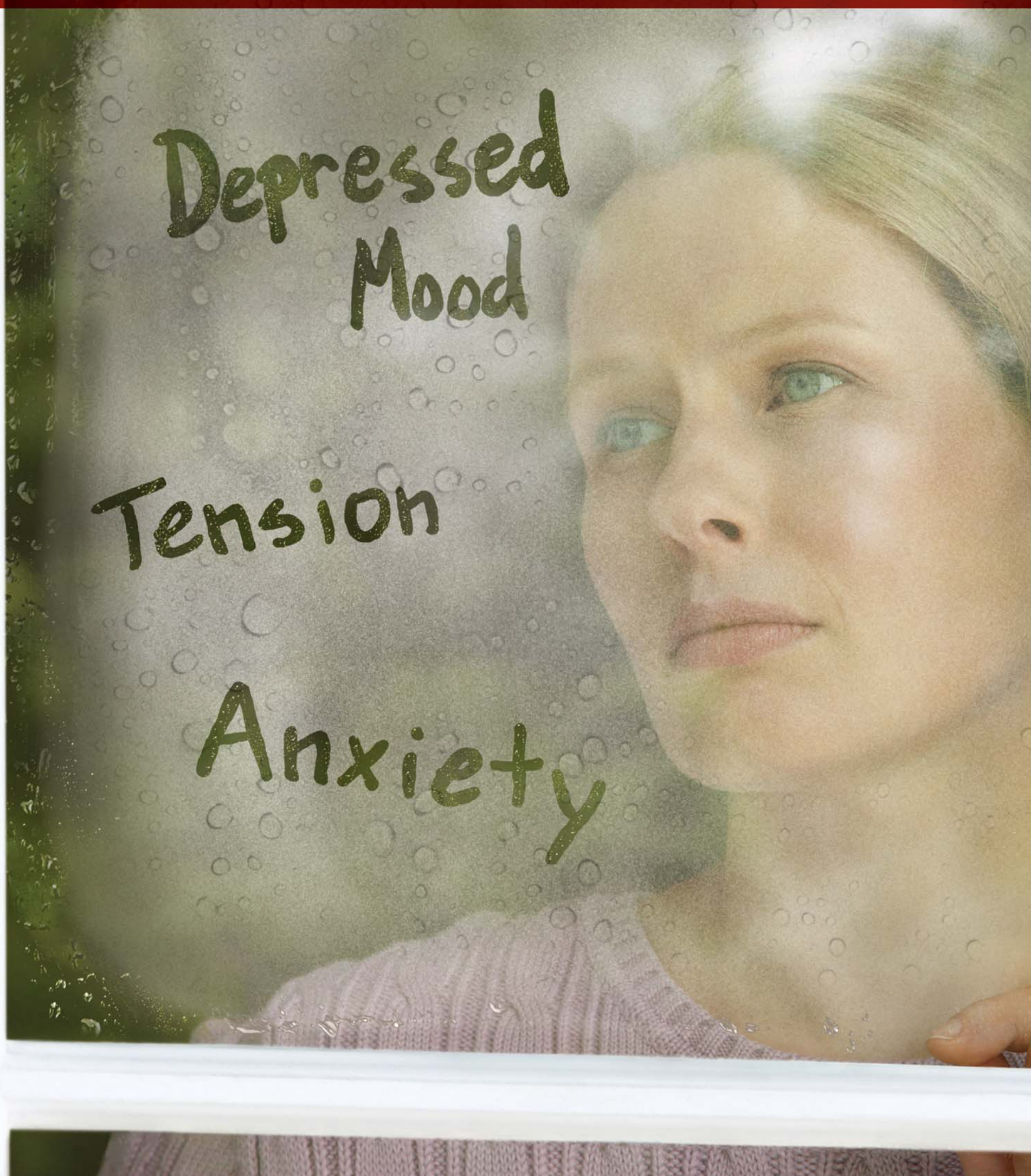
Soonjo Hwang, M.D.
Psychiatry Residency Program
New York Medical College at Westchester Medical Center, Valhalla, N.Y.

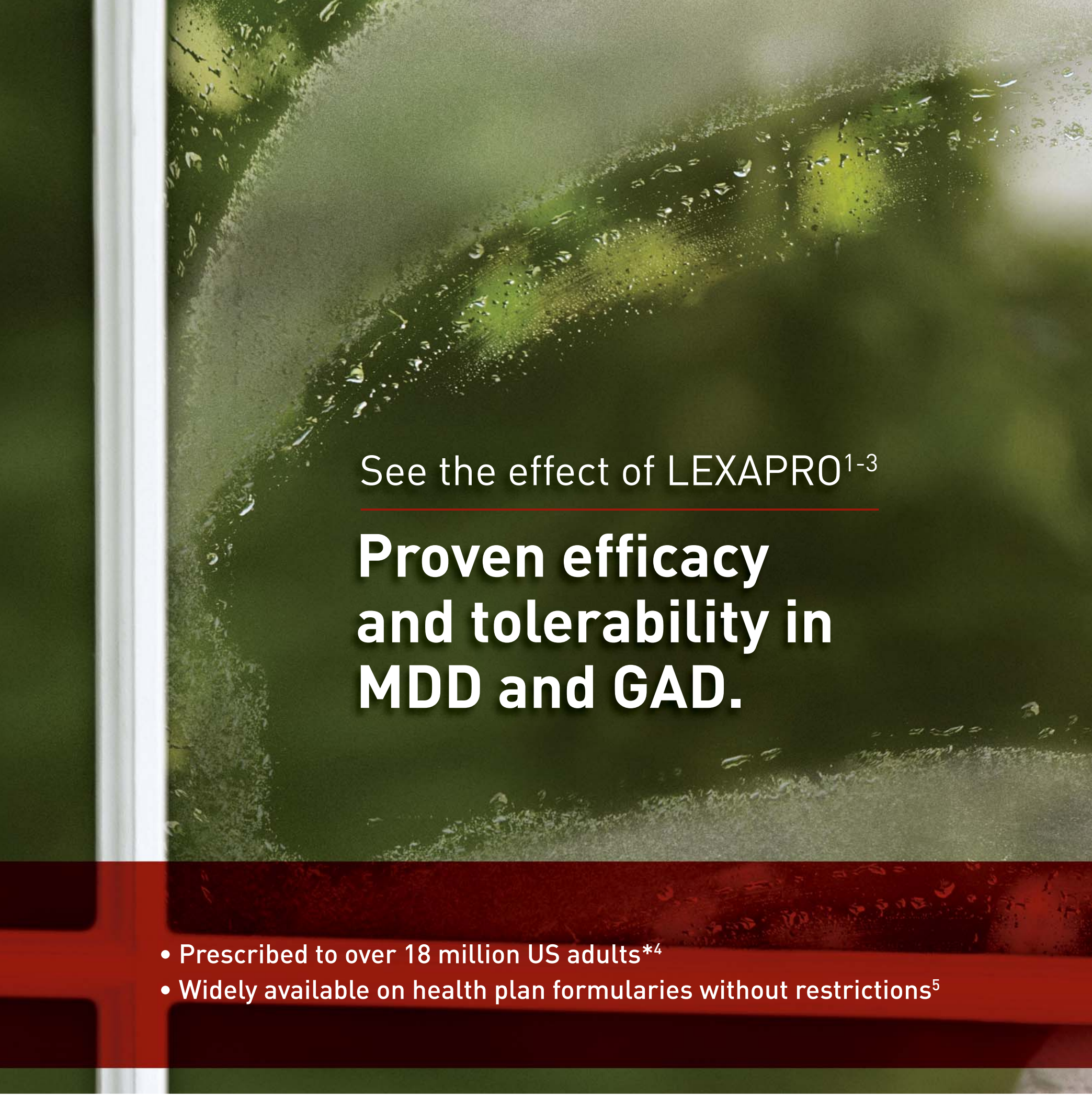
The APA/Shire Child and Adolescent Psychiatry Fellowships are awarded to psychiatry residents (PGY-1 to PGY-3) each year to support their attendance at two APA annual meetings and to develop their interests in pursuing careers in child and adolescent psychiatry. These residents are mentored by noted child and adolescent psychiatrists and are required to submit program proposals to the annual meeting's Scientific Program Committee for their second year.

More information about the APA/Shire Child and Adolescent Psychiatry Fellowships and other APA fellowships can be accessed at <www.psych.org/MainMenu/EducationCareerDevelopment/ResidentsMembersinTraining/AwardsandFellowships.aspx>.

Treat core symptoms[1,2]

of Major Depressive Disorder (MDD) & Generalized Anxiety Disorder (GAD)





*Lexapro Market Overview. Patient level report based on longitudinal analysis of US electronic pharmacy claims submitted for third-party reimbursement. Patients projected based on their activity in retail pharmacies.

IMPORTANT SAFETY INFORMATION
Lexapro is approved for the treatment of major depressive disorder (MDD) and generalized anxiety disorder (GAD).

Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Antidepressants increased the risk of suicidality (suicidal thinking and behavior) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of antidepressants in children, adolescents or young adults must balance the risk to clinical need. Patients of all ages started on antidepressant therapy should be closely monitored and observed for clinical worsening, suicidality or unusual changes in behavior, especially at the beginning of therapy or at the time of dose changes. This risk may persist until significant remission occurs. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Lexapro is not approved for use in pediatric patients.

Lexapro is contraindicated in patients taking monoamine oxidase inhibitors (MAOIs), pimozide, or in patients with hypersensitivity to escitalopram or citalopram. As with other SSRIs, caution is indicated in the coadministration of tricyclic antidepressants (TCAs) with Lexapro. SSRIs and SNRIs (including Lexapro) may increase the risk of bleeding events. Patients should be cautioned that concomitant use of aspirin, NSAIDs, warfarin and other anticoagulants may add to the risk. As with all drugs effective in the treatment of major depressive disorder, Lexapro should be used cautiously in patients with a history of mania or with a history of seizure disorder. Lexapro should be used with caution in patients with severe renal impairment. SSRIs and SNRIs have been associated with clinically significant hyponatremia. Elderly patients or patients taking diuretics or who are otherwise volume-depleted appear to be at a greater risk. Discontinuation of Lexapro should be considered in patients with symptomatic hyponatremia and appropriate medical intervention should be instituted. The concomitant use of Lexapro with other SSRIs, SNRIs, triptans, tryptophan, antipsychotics or other dopamine antagonists is not recommended due to the potential for development of life-threatening serotonin syndrome or neuroleptic malignant syndrome (NMS)-like reactions. The management of these events should include immediate discontinuation of Lexapro and the concomitant agent. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that Lexapro therapy does not affect their ability to engage in such activities. For pregnant and nursing mothers, Lexapro should be used only if the potential benefit justifies the potential risk to the fetus or child. The most common adverse events with Lexapro treatment versus placebo (approximately 5% or greater and approximately 2x placebo) were nausea, insomnia, ejaculation disorder, somnolence, increased sweating, fatigue, decreased libido, and anorgasmia. Patients should be monitored for adverse events when discontinuing treatment with Lexapro. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible.

References: 1. Burke WJ, Gergel I, Bose A. Fixed-dose trial of the single isomer SSRI escitalopram in depressed outpatients. *J Clin Psychiatry.* 2002;63: 331-336. **2.** Davidson JRT, Bose A, Korotzer A, Zheng H. Escitalopram in the treatment of generalized anxiety disorder: double-blind, placebo controlled, flexible-dose study. *Depress Anxiety.* 2004;19:234-240. **3.** LEXAPRO [package insert]. St. Louis, Mo: Forest Pharmaceuticals, Inc.; 2009. **4.** Surveillance Data, Inc. (SDI), April 2008. **5.** Data on file, Forest Laboratories, Inc.

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Suicidality and Antidepressant Drugs Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of Lexapro or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Lexapro is not approved for use in pediatric patients. (See WARNINGS: Clinical Worsening and Suicide Risk, PRECAUTIONS: Information for Patients, and PRECAUTIONS: Pediatric Use)

INDICATIONS AND USAGE Major Depressive Disorder Lexapro (escitalopram) is indicated for the treatment of major depressive disorder. The efficacy of Lexapro in the treatment of major depressive disorder was established in three, 8-week, placebo-controlled trials of outpatients whose diagnoses corresponded most closely to the DSM-IV category of major depressive disorder (see **CLINICAL PHARMACOLOGY**). A major depressive episode (DSM-IV) implies a prominent and relatively persistent (nearly every day for at least 2 weeks) depressed or dysphoric mood that usually interferes with daily functioning, and includes at least five of the following nine symptoms: depressed mood, loss of interest in usual activities, significant change in weight and/or appetite, insomnia or hypersomnia, psychomotor agitation or retardation, increased fatigue, feelings of guilt or worthlessness, slowed thinking or impaired concentration, a suicide attempt or suicidal ideation. The efficacy of Lexapro in hospitalized patients with major depressive disorders has not been adequately studied. The efficacy of Lexapro in maintaining a response, in patients with major depressive disorder who responded during an 8-week, acute-treatment phase while taking Lexapro and were then observed for relapse during a period of up to 36 weeks, was demonstrated in a placebo-controlled trial (see **Clinical Efficacy Trials** under **CLINICAL PHARMACOLOGY**). Nevertheless, the physician who elects to use Lexapro for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient (see **DOSAGE AND ADMINISTRATION**). **Generalized Anxiety Disorder** Lexapro is indicated for the treatment of Generalized Anxiety Disorder (GAD). The efficacy of Lexapro was established in three, 8-week, placebo-controlled trials in patients with GAD (see **CLINICAL PHARMACOLOGY**). Generalized Anxiety Disorder (DSM-IV) is characterized by excessive anxiety and worry (apprehensive expectation) that is persistent for at least 6 months and which the person finds difficult to control. It must be associated with at least 3 of the following symptoms: restlessness or feeling keyed up or on edge, being easily fatigued, difficulty concentrating or mind going blank, irritability, muscle tension, and sleep disturbance. The efficacy of Lexapro in the long-term treatment of GAD, that is, for more than 8 weeks, has not been systematically evaluated in controlled trials. The physician who elects to use Lexapro for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient. **CONTRAINDICATIONS** Concomitant use in patients taking monoamine oxidase inhibitors (MAOIs) is contraindicated (see **WARNINGS**). Concomitant use in patients taking pimozide is contraindicated (see **Drug Interactions – Pimozide and Celexa**). Lexapro is contraindicated in patients with a hypersensitivity to escitalopram or citalopram or any of the inactive ingredients in Lexapro. **WARNINGS WARNINGS-Clinical Worsening and Suicide Risk Clinical Worsening and Suicide Risk** Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. There has been a long-standing concern, however, that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients during the early phases of treatment. Pooled analyses of short-term placebo-controlled trials of antidepressant drugs (SSRIs and others) showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18-24) with major depressive disorder (MDD) and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction with antidepressants compared to placebo in adults aged 65 and older. The pooled analyses of placebo-controlled trials in children and adolescents with MDD, obsessive compulsive disorder (OCD), or other psychiatric disorders included a total of 24 short-term trials of 9 antidepressant drugs in over 4400 patients. The pooled analyses of placebo-controlled trials in adults with MDD or other psychiatric disorders included a total of 295 short-term trials (median duration of 2 months) of 11 antidepressant drugs in over 77,000 patients. There was considerable variation in risk of suicidality among drugs, but a tendency toward an increase in the younger patients for almost all drugs studied. There were differences in absolute risk of suicidality across the different indications, with the highest incidence in MDD. The risk differences (drug vs placebo), however, were relatively stable within age strata and across indications. These risk differences (drug-placebo difference in the number of cases of suicidality per 1000 patients treated) are provided in **Table 1. TABLE 1: Age Range and Drug-Placebo Difference in Number of Cases of Suicidality per 1000 Patients Treated:** Increases Compared to Placebo; <18 (14 additional cases); 18-24 (5 additional cases); Decreases Compared to Placebo; 25-64 (1 fewer case); ≥65 (6 fewer cases). No suicides occurred in any of the pediatric trials. There were suicides in the adult trials, but the number was not sufficient to reach any conclusion about drug effect on suicide. It is unknown whether the suicidality risk extends to longer-term use, i.e., beyond several months. However, there is substantial evidence from placebo-controlled maintenance trials in adults with depression that the use of antidepressants can delay the recurrence of depression. **All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases.** The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality. Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse, or who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms. If the decision has been made to discontinue treatment, medication should be tapered, as rapidly as is feasible, but with recognition that abrupt discontinuation can be associated with certain symptoms (see **PRECAUTIONS and DOSAGE AND ADMINISTRATION—Discontinuation of Treatment with Lexapro**, for a description of the risks of discontinuation of Lexapro). **Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to healthcare providers. Such monitoring should include daily observation by families and caregivers.** Prescriptions for Lexapro should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose. **Screening Patients for Bipolar Disorder:** A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled trials) that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Whether any of the symptoms described above represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that Lexapro is not approved for use in treating bipolar depression. **Potential for Interaction with Monoamine Oxidase Inhibitors In patients receiving serotonin reuptake inhibitor drugs in combination with a monoamine oxidase inhibitor (MAOI), there have been reports of serious, sometimes fatal, reactions including hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that include extreme agitation progressing to delirium and coma. These reactions have also been reported in patients who have recently discontinued SSRI treatment and have been started on an MAOI. Some cases presented with features resembling neuroleptic malignant syndrome. Furthermore, limited animal data on the effects of combined use of SSRIs and MAOIs suggest that these drugs may act synergistically to elevate blood pressure and evoke behavioral excitation. Therefore, it is recommended that Lexapro should not be used in combination with an MAOI, or within 14 days of discontinuing treatment with an MAOI. Similarly, at least 14 days should be allowed after stopping Lexapro before starting an MAOI. Serotonin syndrome has been reported in two patients who were concomitantly receiving linezolid, an antibiotic which is a reversible non-selective MAOI. Serotonin Syndrome or Neuroleptic Malignant Syndrome (NMS)-like Reactions:** The development of a potentially life-threatening serotonin syndrome or Neuroleptic Malignant Syndrome (NMS)-like reactions have been reported with SNRIs and SSRIs alone, including Lexapro treatment, but particularly with concomitant use of serotonergic drugs (including triptans) with drugs which impair metabolism of serotonin (including MAOIs), or with antipsychotics or other dopamine antagonists. Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination) and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). Serotonin syndrome, in its most severe form can resemble neuroleptic malignant syndrome, which includes hyperthermia, muscle rigidity, autonomic instability with possible rapid fluctuation of vital signs, and mental status changes. Patients should be monitored for the emergence of serotonin syndrome or NMS-like signs and symptoms. The concomitant use of Lexapro with MAOIs intended to treat depression is contraindicated. If concomitant treatment of Lexapro with a 5-hydroxytryptamine receptor agonist (triptan) is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. The concomitant use of Lexapro with serotonin precursors (such as tryptophan) is not recommended. Treatment with Lexapro and any concomitant serotonergic or antidopaminergic agents, including antipsychotics, should be discontinued immediately if the above events occur and supportive symptomatic treatment should be initiated. **PRECAUTIONS General** Discontinuation of Treatment with Lexapro During marketing of Lexapro and other SSRIs and SNRIs (serotonin and norepinephrine reuptake inhibitors), there have been spontaneous reports of adverse events occurring upon discontinuation of these drugs, particularly when abrupt, including the following: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesias such as electric shock sensations), anxiety, confusion, headache, lethargy, emotional lability, insomnia, and hypomania. While these events are generally self-limiting, there have been reports of serious discontinuation symptoms. Patients should be monitored for these symptoms when discontinuing treatment with Lexapro. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose but at a more gradual rate (see **DOSAGE AND ADMINISTRATION**). Abnormal Bleeding SSRIs and SNRIs, including Lexapro, may increase the risk of bleeding events. Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs, warfarin, and other anticoagulants may add to the risk. Case reports and epidemiological studies (case-control and cohort design) have demonstrated an association between use of drugs that interfere with serotonin reuptake and the occurrence of gastrointestinal bleeding. Bleeding events related to SSRI and SNRI use have ranged from ecchymoses, hematomas, epistaxis, and petechiae to life-threatening hemorrhages. Patients should be cautioned about the risk of bleeding associated with the concomitant use of Lexapro and NSAIDs, aspirin, or other drugs that affect coagulation. Hyponatremia Hyponatremia may occur as a result of treatment with SSRIs and SNRIs, including Lexapro. In many cases, this hyponatremia appears to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH), and was reversible when Lexapro was discontinued. Cases with serum sodium lower than 110 mmol/L have been reported. Elderly patients may be at greater risk of developing hyponatremia with SSRIs and SNRIs. Also, patients taking diuretics or who are otherwise volume depleted may be at greater risk (see **Geriatric Use**). Discontinuation of Lexapro should be considered in patients with symptomatic hyponatremia and appropriate medical intervention should be instituted. Signs and symptoms of hyponatremia include headache, difficulty concentrating, memory impairment, confusion, weakness, and unsteadiness, which may lead to falls. Signs and symptoms associated with more severe and/or acute cases have included hallucination, syncope, seizure, coma, respiratory arrest, and death. Activation of Mania/Hypomania In placebo-controlled trials of Lexapro in major depressive disorder, activation of mania/hypomania was reported in one (0.1%) of 715 patients treated with Lexapro and in none of the 592 patients treated with placebo. One additional case of hypomania has been reported in association with Lexapro treatment. Activation of mania/hypomania has also been reported in a small proportion of patients with major affective disorders treated with racemic citalopram and other marketed drugs effective in the treatment of major depressive disorder. As with all drugs effective in the treatment of major depressive disorder, Lexapro should be used cautiously in patients with a history of mania. Seizures Although anticonvulsant effects of racemic citalopram have been observed in animal studies, Lexapro has not been systematically evaluated in patients with a seizure disorder. These patients were excluded from clinical studies during the product's premarketing testing. In clinical trials of Lexapro, cases of convulsion have been reported in association with Lexapro treatment. Like other drugs effective in the treatment of major depressive disorder, Lexapro should be introduced with care in patients with a history of seizure disorder. Interference with Cognitive and Motor Performance In a study in normal volunteers, Lexapro 10 mg/day did not produce impairment of intellectual function or psychomotor performance. Because any psychoactive drug may impair judgment, thinking, or motor skills, however, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that Lexapro therapy does not affect their ability to engage in such activities. Use in Patients with Concomitant Illness Clinical experience with Lexapro in patients with certain concomitant systemic illnesses is limited. Caution is advisable in using Lexapro in patients with diseases or conditions that produce altered metabolism or hemodynamic responses. Lexapro has not been systematically evaluated in patients with a recent history of myocardial infarction or unstable heart disease. Patients with these diagnoses were generally excluded from clinical studies during the product's premarketing testing. In subjects with hepatic impairment, clearance of racemic citalopram was decreased and plasma concentrations were increased. The recommended dose of Lexapro in hepatically impaired patients is 10 mg/day (see **DOSAGE AND ADMINISTRATION**). Because escitalopram is extensively metabolized, excretion of unchanged drug in urine is a minor route of elimination. Until adequate numbers of patients with severe renal impairment have been evaluated during chronic treatment with Lexapro, however, it should be used with caution in such patients (see **DOSAGE AND ADMINISTRATION**). **Information for Patients** Physicians are advised to discuss the following issues with patients for whom they prescribe Lexapro. Patients should be cautioned about the risk of serotonin syndrome with the concomitant use of Lexapro and triptans, tramadol or other serotonergic agents. In a study in normal volunteers, Lexapro 10 mg/day did not impair psychomotor performance. The effect of Lexapro on psychomotor coordination, judgment, or thinking has not been systematically examined in controlled studies. Because psychoactive drugs may impair judgment, thinking, or motor skills, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that Lexapro therapy does not affect their ability to engage in such activities. Patients should be told that, although Lexapro has not been shown in experiments with normal subjects to increase the mental and motor skill impairments caused by alcohol, the concomitant use of Lexapro and alcohol in depressed patients is not advised. Patients should be made aware that escitalopram is the active isomer of Celexa (citalopram hydrobromide) and that the two medications should not be taken concomitantly. Patients should be advised to inform their physician if they are taking, or plan to take, any prescription or over-the-counter drugs, as there is a potential for interactions. Patients should be cautioned about the concomitant use of Lexapro and NSAIDs, aspirin, warfarin, or other drugs that affect coagulation since combined use of psychotropic drugs that interfere with serotonin reuptake and these agents has been associated with an increased risk of bleeding. Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy. Patients should be advised to notify their physician if they are breastfeeding an infant. While patients may notice improvement with Lexapro therapy in 1 to 4 weeks, they should be advised to continue therapy as directed. Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with Lexapro and should counsel them in its appropriate use. A patient Medication Guide about "Antidepressant Medicines, Depression and other Serious Mental Illness, and Suicidal Thoughts or Actions" is available for Lexapro. The prescriber or health professional should instruct patients, their families, and their caregivers to read the Medication Guide and should assist them in understanding its contents. Patients should be given the opportunity to discuss the contents of the Medication Guide and to obtain answers to any questions they may have. Patients should be advised of the following issues and asked to alert their prescriber if these occur while taking Lexapro. **Clinical Worsening and Suicide Risk:** Patients, their families, and their caregivers should be encouraged to be alert to the emergence of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, mania, other unusual changes in behavior, worsening of depression, and suicidal ideation, especially early during antidepressant treatment and when the dose is adjusted up or down. Families and caregivers of patients should be advised to look for the emergence of such symptoms on a day-to-day basis, since changes may be abrupt. Such symptoms should be reported to the patient's prescriber or health professional, especially if they are severe, abrupt in onset, or were not part of the patient's presenting symptoms. Symptoms such as these may be associated with an increased risk for suicidal thinking and behavior and indicate a need for very close monitoring and possibly changes in the medication. **Laboratory Tests** There are no specific laboratory tests recommended. **Concomitant Administration with Racemic Citalopram** Citalopram - Since escitalopram is the active isomer of racemic citalopram (Celexa), the two agents should not be coadministered. **Drug Interactions Serotonergic Drugs:** Based on the mechanism of action of SNRIs and SSRIs including Lexapro, and the potential for serotonin syndrome, caution is advised when Lexapro is coadministered with other drugs that may affect the serotonergic neurotransmitter systems, such as triptans, linezolid (an antibiotic which is a reversible non-selective MAOI), lithium, tramadol, or St. John's Wort (see **WARNINGS-Serotonin Syndrome**). The concomitant use of Lexapro with other SSRIs, SNRIs or tryptophan is not recommended (see **PRECAUTIONS - Drug Interactions**). **Triptans:** There have been rare postmarketing reports of serotonin syndrome with use of an SSRI and a triptan. If concomitant treatment of Lexapro with a triptan is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases (see **WARNINGS - Serotonin Syndrome**). CNS Drugs - Given the primary CNS effects of escitalopram, caution should be used when it is taken in combination with other centrally-acting drugs. Alcohol - Although Lexapro did not potentiate the cognitive and motor effects of alcohol in a clinical trial, as with other psychotropic medications, the use of alcohol by patients taking Lexapro is not recommended. Monoamine Oxidase Inhibitors (MAOIs) - See **CONTRAINDICATIONS** and **WARNINGS**. **Drugs That Interfere With Hemostasis (NSAIDs, Aspirin, Warfarin, etc.)** Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies of the case-control and cohort design that have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding have also shown that concurrent use of an NSAID or aspirin may potentiate the risk of bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when SSRIs and SNRIs are coadministered with warfarin. Patients receiving warfarin therapy should be carefully monitored when Lexapro is initiated or discontinued. Cimetidine - In subjects who had received 21 days of 40 mg/day racemic citalopram, combined administration of 400 mg/day cimetidine for 8 days resulted in an increase in citalopram AUC and C_{max} of 43% and 39%, respectively. The clinical significance of these findings is unknown. Digoxin - In subjects who had received 21 days of 40 mg/day racemic citalopram, combined administration of citalopram and digoxin (single dose of 1 mg) did not significantly affect the pharmacokinetics of either citalopram or digoxin. Lithium - Coadministration of racemic citalopram (40 mg/day for 10 days) and lithium (30 mmol/day for 5 days) had no significant effect on the pharmacokinetics of citalopram or lithium. Nevertheless, plasma lithium levels should be monitored with appropriate adjustment to the lithium dose in accordance with standard clinical practice. Because lithium may enhance the serotonergic effects of escitalopram, caution should be exercised when Lexapro and lithium are coadministered. Pimozide and Celexa - In a controlled study, a single dose of pimozide 2 mg co-administered with racemic citalopram 40 mg given once daily for 11 days was associated with a mean increase in QTc values of approximately 10 msec compared to pimozide given alone. Racemic citalopram did not alter the mean AUC or C_{max} of pimozide. The mechanism of this pharmacodynamic interaction is not known. Sumatriptan - There have been rare postmarketing reports describing patients with weakness, hyperreflexia, and incoordination following the use of an SSRI and sumatriptan. If concomitant treatment with sumatriptan and an SSRI (e.g., fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram, escitalopram) is clinically warranted, appropriate observation of the patient is advised. Theophylline - Combined administration of racemic citalopram (40 mg/day for 21 days) and the CYP1A2 substrate theophylline (single dose of 300 mg) did not affect the pharmacokinetics of theophylline. The effect of theophylline on the pharmacokinetics of citalopram was not evaluated. Warfarin - Administration of 40 mg/day racemic citalopram for 21 days did not affect the pharmacokinetics of warfarin, a CYP3A4 substrate. Prothrombin time was increased by 5%, the clinical significance of which is unknown. Carbamazepine - Combined administration of racemic citalopram (40 mg/day for 14 days) and carbamazepine (titrated to 400 mg/day for 35 days) did not significantly affect the pharmacokinetics of carbamazepine, a CYP3A4 substrate. Although trough citalopram plasma levels were unaffected, given the enzyme-inducing properties of carbamazepine, the possibility that carbamazepine might increase the clearance of escitalopram should be considered if the two drugs are coadministered. Triazolam - Combined administration of racemic citalopram (titrated to 40 mg/day for 28 days) and the CYP3A4 substrate triazolam (single dose of 0.25 mg) did not significantly affect the pharmacokinetics of either citalopram or triazolam. Ketoconazole - Combined administration of racemic citalopram (40 mg) and ketoconazole (200 mg), a potent CYP3A4 inhibitor, decreased the C_{max} and AUC of ketoconazole by 21% and 10%, respectively, and did not significantly affect the pharmacokinetics of citalopram. Ritonavir - Combined administration of a single dose of ritonavir (600 mg), both a CYP3A4 substrate and a potent inhibitor of CYP3A4, and escitalopram (20 mg) did not affect the pharmacokinetics of either ritonavir or escitalopram. CYP3A4 and -2C19 Inhibitors - *In vitro* studies indicated that CYP3A4 and -2C19 are the primary enzymes involved in the metabolism of escitalopram. However, coadministration of escitalopram (20 mg) and ritonavir (600 mg), a potent inhibitor of CYP3A4, did not significantly affect the pharmacokinetics of escitalopram. Because escitalopram is metabolized by multiple enzyme systems, inhibition of a single enzyme may not appreciably decrease escitalopram clearance. Drugs Metabolized by Cytochrome P4502D6 - *In vitro* studies did not reveal an inhibitory effect of escitalopram on CYP2D6. In addition, steady state levels of racemic citalopram were not significantly different in poor metabolizers and extensive CYP2D6 metabolizers after multiple-dose administration of citalopram, suggesting that coadministration, with escitalopram, of a drug that inhibits CYP2D6, is unlikely to have clinically significant effects on escitalopram metabolism. However, there are limited *in vivo* data suggesting a modest CYP2D6 inhibitory effect for escitalopram, i.e., coadministration of escitalopram (20 mg/day for 21 days) with the tricyclic antidepressant desipramine (single dose of 50 mg), a substrate for CYP2D6, resulted in a 40% increase in C_{max} and a 100% increase in AUC of desipramine. The clinical significance of this finding is unknown. Nevertheless, caution is indicated in the coadministration of escitalopram and drugs metabolized by CYP2D6. Metoprolol - Administration of 20 mg/day Lexapro for 21 days in healthy volunteers resulted in a 50% increase in C_{max} and 82% increase in AUC of the beta-adrenergic blocker metoprolol (given in a single dose of 100 mg). Increased metoprolol plasma levels have been associated with decreased cardioselectivity. Coadministration of Lexapro and metoprolol had no clinically significant effects on blood pressure or heart rate. Electroconvulsive Therapy (ECT) - There are no clinical studies of the combined use of ECT and escitalopram. **Carcinogenesis, Mutagenesis, Impairment of Fertility** Carcinogenesis Racemic citalopram was administered in the diet to NMRI/BOM strain mice and COBS WI strain rats for 18 and 24 months, respectively. There was no evidence for carcinogenicity of racemic citalopram in mice receiving up to 240 mg/kg/day. There was an increased incidence of small intestine carcinoma in rats receiving 8 or 24 mg/kg/day racemic citalopram. A no-effect dose for this finding was not established. The relevance of these findings to humans is unknown. Mutagenesis Racemic citalopram was mutagenic in the *in vitro* bacterial reverse mutation assay (Ames test) in 2 of 5 bacterial strains (Salmonella TA98 and TA1537) in the absence of metabolic activation. It was clastogenic in the *in vitro* Chinese hamster lung cell assay for chromosomal aberrations in the presence and absence of metabolic activation. Racemic citalopram was not mutagenic in the *in vitro* mammalian forward gene mutation assay (HPRT) in mouse lymphoma cells or in a coupled *in vitro/in vivo* unscheduled DNA synthesis (UDS) assay in rat liver. It was not clastogenic in the *in vitro* chromosomal aberration assay in human lymphocytes or in two *in vivo* mouse micronucleus assays. Impairment of Fertility When racemic citalopram was administered orally to 16 male and 24 female rats prior to and throughout mating and gestation at doses of 32, 48, and 72 mg/kg/day, mating was decreased at all doses, and fertility was decreased at doses ≥32 mg/kg/day. Gestation duration was increased at 48 mg/kg/day. **Pregnancy** Pregnancy Category C In a rat embryo/fetal development study, oral administration of escitalopram (56, 112, or 150 mg/kg/day) to pregnant animals during the period of organogenesis resulted in decreased fetal body weight and associated delays in ossification at the two higher doses (approximately ≥56 times the maximum recommended human dose [MRHD] of 20 mg/day on a body surface area [mg/m^2] basis). Maternal toxicity (clinical signs and decreased body weight gain and food consumption), mild at 56 mg/kg/day, was present at all dose levels. The developmental no-effect dose of 56 mg/kg/day is approximately 28 times the MRHD on a mg/m^2 basis. No teratogenicity was observed at any of the doses tested (as high as 75 times the MRHD on a mg/m^2 basis). When female rats were treated with escitalopram (6, 12, 24, or 48 mg/kg/day) during pregnancy and through weaning, slightly increased offspring mortality and growth retardation were noted at 48 mg/kg/day which is approximately 24 times the MRHD on a mg/m^2 basis. Slight maternal toxicity (clinical signs and decreased body weight gain and food consumption) was seen at this dose. Slightly increased offspring mortality was seen at 24 mg/kg/day. The no-effect dose was 12 mg/kg/day which is approximately 6 times the MRHD on a mg/m^2 basis. In animal reproduction studies, racemic citalopram has been shown to have adverse effects on embryo/fetal and postnatal development, including teratogenic effects, when administered at doses greater than human therapeutic doses. In two rat embryo/fetal development studies, oral administration of racemic citalopram (32, 56, or 112 mg/kg/day) to pregnant animals during the period of organogenesis resulted in decreased embryo/fetal growth and survival and an increased incidence of fetal abnormalities (including cardiovascular and skeletal defects) at the high dose. This dose was also associated with maternal toxicity (clinical signs, decreased body weight gain). The developmental no-effect dose was 56 mg/kg/day. In a rabbit study, no adverse effects on embryo/fetal development were observed at doses of racemic citalopram of up to 16 mg/kg/day. Thus, teratogenic effects of racemic citalopram were observed at a maternally toxic dose in the rat and were not observed in the rabbit. When female rats were treated with racemic citalopram (4.8, 12.8, or 32 mg/kg/day) from late gestation through weaning, increased offspring mortality during the first 4 days after birth and persistent offspring growth retardation were observed at the highest dose. The no-effect dose was 12.8 mg/kg/day. Similar effects on offspring mortality and growth were seen when dams were treated throughout gestation and early lactation at doses ≥24 mg/kg/day. A no-effect dose was not determined in that study. There are no adequate and well-controlled studies in pregnant women; therefore, escitalopram should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Pregnancy-Nonteratogenic Effects** Neonates exposed to Lexapro and other SSRIs or SNRIs, late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Such complications can arise immediately upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. These features are consistent with either a direct toxic effect of SSRIs and SNRIs or, possibly, a drug discontinuation syndrome. It should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome (see **WARNINGS**). Infants exposed to SSRIs in late pregnancy may have an increased risk for persistent pulmonary hypertension of the newborn (PPHN). PPHN occurs in 1-2 per 1000 live births in the general population and is associated with substantial neonatal morbidity and mortality. In a retrospective, case-control study of 377 women whose infants were born with PPHN and 836 women whose infants were born healthy, the risk for developing PPHN was approximately six-fold higher for infants exposed to SSRIs after the 20th week of gestation compared to infants who had not been exposed to antidepressants during pregnancy. There is currently no corroborative evidence regarding the risk for PPHN following exposure to SSRIs in pregnancy; this is the first study that has investigated the potential risk. The study did not include enough cases with exposure to individual SSRIs to determine if all SSRIs posed similar levels of PPHN risk. When treating a pregnant woman with Lexapro during the third trimester, the physician should carefully consider both the potential risks and benefits of treatment (see **DOSAGE AND ADMINISTRATION**). Physicians should note that in a prospective longitudinal study of 201 women with a history of major depression who were euthymic at the beginning of pregnancy, women who discontinued antidepressant medication during pregnancy were more likely to experience a relapse of major depression than women who continued antidepressant medication. **Labor and Delivery** The effect of Lexapro on labor and delivery in humans is unknown. **Nursing Mothers** Racemic citalopram, like many other drugs, is excreted in human breast milk. There have been two reports of infants experiencing excessive somnolence, decreased feeding, and weight loss in association with breastfeeding from a citalopram-treated mother; in one case, the infant was reported to recover completely upon discontinuation of citalopram by its mother and, in the second case, no follow-up information was available. The decision whether to continue or discontinue either nursing or Lexapro therapy should take into account the risks of citalopram exposure for the infant and the benefits of Lexapro treatment for the mother. **Pediatric Use** Safety and effectiveness in the pediatric population have not been established (see **BOXED WARNING** and **WARNINGS—Clinical Worsening and Suicide Risk**). One placebo-controlled trial in 264 pediatric patients with MDD has been conducted with Lexapro, and the data were not sufficient to support a claim for use in pediatric patients. Anyone considering the use of Lexapro in a child or adolescent must balance the potential risks with the clinical need. **Geriatric Use** Approximately 6% of the 1144 patients receiving escitalopram in controlled trials of Lexapro in major depressive disorder and GAD were 60 years of age or older; elderly patients in these trials received daily doses of Lexapro between 10 and 20 mg. The number of elderly patients in these trials was insufficient to adequately assess for possible differential efficacy and safety measures on the basis of age. Nevertheless, greater sensitivity of some elderly individuals to effects of Lexapro cannot be ruled out. SSRIs and SNRIs, including Lexapro, have been associated with cases of clinically significant hyponatremia in elderly patients, who may be at greater risk for this adverse event (see **PRECAUTIONS**, Hyponatremia). In two pharmacokinetic studies, escitalopram half-life was increased by approximately 50% in elderly subjects as compared to young subjects and C_{max} was unchanged (see **CLINICAL PHARMACOLOGY**). 10 mg/day is the recommended dose for elderly patients (see **DOSAGE AND ADMINISTRATION**). Of 4422 patients in clinical studies of racemic citalopram, 1357 were 60 and over, 1034 were 65 and over, and 457 were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but again, greater sensitivity of some elderly individuals cannot be ruled out. **ADVERSE REACTIONS** Adverse event information for Lexapro was collected from 715 patients with major depressive disorder who were exposed to escitalopram and from 592 patients who were exposed to placebo in double-blind, placebo-controlled trials. An additional 284 patients with major depressive disorder were newly exposed to escitalopram in open-label trials. The adverse event information for Lexapro in patients with GAD was collected from 429 patients exposed to escitalopram and from 427 patients exposed to placebo in double-blind, placebo-controlled trials. Adverse events during exposure were obtained primarily by general inquiry and recorded by clinical investigators using terminology of their own choosing. Consequently, it is not possible to provide a meaningful estimate of the proportion of individuals experiencing adverse events without first grouping similar types of events into a smaller number of standardized event categories. In the tables and tabulations that follow, standard World Health Organization (WHO) terminology has been used to classify reported adverse events. The stated frequencies of adverse events represent the proportion of individuals who experienced, at least once, a treatment-emergent adverse event of the type listed. An event was considered treatment-emergent if it occurred for the first time or worsened while receiving therapy following baseline evaluation. **Adverse Events Associated with Discontinuation of Treatment Major Depressive Disorder** Among the 715 depressed patients who received Lexapro in placebo-controlled trials, 6% discontinued treatment due to an adverse event, as compared to 2% of 592 patients receiving placebo. In two fixed-dose studies, the rate of discontinuation for adverse events in patients receiving 10 mg/day Lexapro was not significantly different from the rate of discontinuation for adverse events in patients receiving placebo. The rate of discontinuation for adverse events in patients assigned to a fixed dose of 20 mg/day Lexapro was 10%, which was significantly different from the rate of discontinuation for adverse events in patients receiving 10 mg/day Lexapro (4%) and placebo (3%). Adverse events that were associated with the discontinuation of at least 1% of patients treated with Lexapro, and for which the rate was at least twice that of placebo, were nausea (2%) and ejaculation disorder (2% of male patients). **Generalized Anxiety Disorder** Among the 429 GAD patients who received Lexapro 10-20 mg/day in placebo-controlled trials, 8% discontinued treatment due to an adverse event, as compared to 4% of 427 patients receiving placebo. Adverse events that were associated with the discontinuation of at least 1% of patients treated with Lexapro, and for which the rate was at least twice the placebo rate, were nausea (2%), insomnia (1%), and fatigue (1%). **Incidence of Adverse Events in Placebo-Controlled Clinical Trials Major Depressive Disorder Table 2** enumerates the incidence, rounded to the nearest percent, of treatment-emergent adverse events that occurred among 715 depressed patients who received Lexapro at doses ranging from 10 to 20 mg/day in placebo-controlled trials. Events included are those occurring in 2% or more of patients treated with Lexapro and for which the incidence in patients treated with Lexapro was greater than the incidence in placebo-treated patients. The prescriber should be aware that these figures cannot be used to predict the incidence of adverse events in the course of usual medical practice where patient characteristics and other factors differ from those which prevailed in the clinical trials. Similarly, the cited frequencies cannot be compared with figures obtained from other clinical investigations involving different treatments, uses, and investigators. The cited figures, however, do provide the prescribing physician with some basis for estimating the relative contribution of drug and non-drug factors to the adverse event incidence rate in the population studied. The most commonly observed adverse events in Lexapro patients (incidence of approximately 5% or greater and approximately twice the incidence in placebo patients) were insomnia, ejaculation disorder (primarily ejaculatory delay), nausea, sweating increased, fatigue, and somnolence (see **TABLE 2**). **TABLE 2: Treatment-Emergent Adverse Events: Incidence in Placebo-Controlled Clinical Trials for Major Depressive Disorder* (Percentage of Patients Reporting Event) Body System/Adverse Event [Lexapro (N=715) and Placebo (N=592)]: Autonomic Nervous System Disorders:** Dry Mouth (6% and 5%); Sweating Increased (5% and 2%). **Central & Peripheral Nervous System Disorders:** Dizziness (5% and 3%). **Gastrointestinal Disorders:** Nausea (15% and 7%); Diarrhea (8% and 5%); Constipation (3% and 1%); Indigestion (3% and 1%); Abdominal Pain (2% and 1%). **General:** Influenza-like Symptoms (5% and 4%); Fatigue (5% and 2%). **Psychiatric Disorders:** Insomnia (9% and 4%); Somnolence (6% and 2%); Appetite Decreased (3% and 1%); Libido Decreased (3% and 1%). **Respiratory System Disorders:** Rhinitis (5% and 4%); Sinusitis (3% and 2%). **Urogenital:** Ejaculation Disorder[1,2] (9% and <1%); Impotence[2] (3% and <1%); Anorgasmia[3] (2% and <1%).*Events reported by at least 2% of patients treated with Lexapro are reported, except for the following events which had an incidence on placebo ≥ Lexapro: headache, upper respiratory tract infection, back pain, pharyngitis, inflicted injury, anxiety. [1]Primarily ejaculatory delay. [2]Denominator used was for males only (N=225 Lexapro; N=188 placebo). [3]Denominator used was for females only (N=490 Lexapro; N=404 placebo). **Generalized Anxiety Disorder Table 3** enumerates the incidence, rounded to the nearest percent of treatment-emergent adverse events that occurred among 429 GAD patients who received Lexapro 10 to 20 mg/day in placebo-controlled trials. Events included are those occurring in 2% or more of patients treated with Lexapro and for which the incidence in patients treated with Lexapro was greater than the incidence in placebo-treated patients. The most commonly observed adverse events in Lexapro patients (incidence of approximately 5% or greater and approximately twice the incidence in placebo patients) were nausea, ejaculation disorder (primarily ejaculatory delay), insomnia, fatigue, decreased libido, and anorgasmia (see **TABLE 3**). **TABLE 3: Treatment-Emergent Adverse Events: Incidence in Placebo-Controlled Clinical Trials for Generalized Anxiety Disorder* (Percentage of Patients Reporting Event) Body System/Adverse Event [Lexapro (N=429) and Placebo (N=427)]: Autonomic Nervous System Disorders:** Dry Mouth (9% and 5%); Sweating Increased (4% and 1%). **Central & Peripheral Nervous System Disorders:** Headache (24% and 17%); Paresthesia (2% and 1%). **Gastrointestinal Disorders:** Nausea (18% and 8%); Diarrhea (8% and 6%); Constipation (5% and 4%); Indigestion (3% and 2%); Vomiting (3% and 1%); Abdominal Pain (2% and 1%); Flatulence (2% and 1%); Toothache (2% and 0%). **General:** Fatigue (8% and 2%); Influenza-like symptoms (5% and 4%). **Musculoskeletal:** Neck/Shoulder Pain (3% and 1%). **Psychiatric Disorders:** Somnolence (13% and 7%); Insomnia (12% and 6%); Libido Decreased (7% and 2%); Dreaming Abnormal (3% and 2%); Appetite Decreased (3% and 1%); Lethargy (3% and 1%); Yawning (2% and 1%). **Urogenital:** Ejaculation Disorder[1,2] (14% and 2%); Anorgasmia[3] (6% and <1%); Menstrual Disorder (2% and 1%). *Events reported by at least 2% of patients treated with Lexapro are reported, except for the following events which had an incidence on placebo ≥ Lexapro: inflicted injury, dizziness, back pain, upper respiratory tract infection, rhinitis, pharyngitis. [1]Primarily ejaculatory delay. [2]Denominator used was for males only (N=182 Lexapro; N=195 placebo). [3]Denominator used was for females only (N=247 Lexapro; N=232 placebo). **Dose Dependency of Adverse Events** The potential dose dependency of common adverse events (defined as an incidence rate of ≥ 5% in either the 10 mg or 20 mg Lexapro groups) was examined on the basis of the combined incidence of adverse events in two fixed-dose trials. The overall incidence rates of adverse events in 10 mg Lexapro-treated patients (66%) was similar to that of the placebo-treated patients (61%), while the incidence rate in 20 mg/day Lexapro-treated patients was greater (86%). **Table 4** shows common adverse events that occurred in the 20 mg/day Lexapro group with an incidence that was approximately twice that of the 10 mg/day Lexapro group and approximately twice that of the placebo group. **TABLE 4: Incidence of Common Adverse Events* in Patients with Major Depressive Disorder Receiving Placebo (N=311), 10 mg/day Lexapro (N=310), 20 mg/day Lexapro (N=125): Insomnia** (4%, 7%, 14%); **Diarrhea** (5%, 6%, 14%); **Dry Mouth** (3%, 4%, 9%); **Somnolence** (1%, 4%, 9%); **Dizziness** (2%, 4%, 7%); **Sweating Increased** (<1%, 3%, 8%); **Constipation** (1%, 3%, 6%); **Fatigue** (2%, 2%, 6%); **Indigestion** (1%, 2%, 6%).*Adverse events with an incidence rate of at least 5% in either of the Lexapro groups and with an incidence rate in the 20 mg/day Lexapro group that was approximately twice that of the 10 mg/day Lexapro group and the placebo group. **Male and Female Sexual Dysfunction with SSRIs** Although changes in sexual desire, sexual performance, and sexual satisfaction often occur as manifestations of a psychiatric disorder, they may also be a consequence of pharmacologic treatment. In particular, some evidence suggests that SSRIs can cause such untoward sexual experiences. Reliable estimates of the incidence and severity of untoward experiences involving sexual desire, performance, and satisfaction are difficult to obtain, however, in part because patients and physicians may be reluctant to discuss them. Accordingly, estimates of the incidence of untoward sexual experience and performance cited in product labeling are likely to underestimate their actual incidence. **Table 5** shows the incidence rates of sexual side effects in patients with major depressive disorder and GAD in placebo-controlled trials. **TABLE 5: Incidence of Sexual Side Effects in Placebo-Controlled Clinical Trials** [In Males Only: **Adverse Event: Lexapro** (N=407) **and Placebo** (N=383)]: Ejaculation Disorder (primarily ejaculatory delay) (12% and 1%); Libido Decreased (6% and 2%); Impotence (2% and <1%). [In Females Only**: Lexapro** (N=737) **and Placebo** (N=636)]: Libido Decreased (3% and 1%); Anorgasmia (3% and <1%). There are no adequately designed studies examining sexual dysfunction with escitalopram treatment. Priapism has been reported with all SSRIs. While it is difficult to know the precise risk of sexual dysfunction associated with the use of SSRIs, physicians should routinely inquire about such possible side effects. **Vital Sign Changes** Lexapro and placebo groups were compared with respect to (1) mean change from baseline in vital signs (pulse, systolic blood pressure, and diastolic blood pressure) and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses did not reveal any clinically important changes in vital signs associated with Lexapro treatment. In addition, a comparison of supine and standing vital sign measures in subjects receiving Lexapro indicated that Lexapro treatment is not associated with orthostatic changes. **Weight Changes** Patients treated with Lexapro in controlled trials did not differ from placebo-treated patients with regard to clinically important change in body weight. **Laboratory Changes** Lexapro and placebo groups were compared with respect to (1) mean change from baseline in various serum chemistry, hematology, and urinalysis variables, and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed no clinically important changes in laboratory test parameters associated with Lexapro treatment. **ECG Changes** Electrocardiograms from Lexapro (N=625), racemic citalopram (N=351), and placebo (N=527) groups were compared with respect to (1) mean change from baseline in various ECG parameters and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed (1) a decrease in heart rate of 2.2 bpm for Lexapro and 2.7 bpm for racemic citalopram, compared to an increase of 0.3 bpm for placebo and (2) an increase in QTc interval of 3.9 msec for Lexapro and 3.7 msec for racemic citalopram, compared to 0.5 msec for placebo. Neither Lexapro nor racemic citalopram were associated with the development of clinically significant ECG abnormalities. **Other Events Observed During the Premarketing Evaluation of Lexapro** Following is a list of WHO terms that reflect treatment-emergent adverse events, as defined in the introduction to the **ADVERSE REACTIONS** section, reported by the 1428 patients treated with Lexapro for periods of up to one year in double-blind or open-label clinical trials during its premarketing evaluation. All reported events are included except those already listed in **Tables 2 & 3**, those occurring in only one patient, event terms that are so general as to be uninformative, and those that are unlikely to be drug related. It is important to emphasize that, although the events reported occurred during treatment with Lexapro, they were not necessarily caused by it. Events are further categorized by body system and listed in order of decreasing frequency according to the following definitions: frequent adverse events are those occurring on one or more occasions in at least 1/100 patients; infrequent adverse events are those occurring in less than 1/100 patients but at least 1/1000 patients. Cardiovascular - *Frequent:* palpitation, hypertension. *Infrequent:* bradycardia, tachycardia, ECG abnormal, flushing, varicose vein. Central and Peripheral Nervous System Disorders - *Frequent:* light-headed feeling, migraine. *Infrequent:* tremor, vertigo, restless legs, shaking, twitching, dysequilibrium, tics, carpal tunnel syndrome, muscle contractions involuntary, sluggishness, coordination abnormal, faintness, hyperreflexia, muscular tone increased. Gastrointestinal Disorders - *Frequent:* heartburn, abdominal cramp, gastroenteritis. *Infrequent:* gastroesophageal reflux, bloating, abdominal discomfort, dyspepsia, increased stool frequency, belching, gastritis, hemorrhoids, gagging, polyposis gastric, swallowing difficult. General - *Frequent:* allergy, pain in limb, fever, hot flushes, chest pain. *Infrequent:* edema of extremities, chills, tightness of chest, leg pain, asthenia, syncope, malaise, anaphylaxis, fall. Hemic and Lymphatic Disorders - *Infrequent:* bruise, anemia, nosebleed, hematoma, lymphadenopathy cervical. Metabolic and Nutritional Disorders - *Frequent:* increased weight. *Infrequent:* decreased weight, hyperglycemia, thirst, bilirubin increased, hepatic enzymes increased, gout, hypercholesterolemia. Musculoskeletal System Disorders - *Frequent:* arthralgia, myalgia. *Infrequent:* jaw stiffness, muscle cramp, muscle stiffness, arthritis, muscle weakness, back discomfort, arthropathy, jaw pain, joint stiffness. Psychiatric Disorders - *Frequent:* appetite increased, lethargy, irritability, concentration impaired. *Infrequent:* jitteriness, panic reaction, agitation, apathy, forgetfulness, depression aggravated, nervousness, restlessness aggravated, suicide attempt, amnesia, anxiety attack, bruxism, carbohydrate craving, confusion, depersonalization, disorientation, emotional lability, feeling unreal, tremulousness nervous, crying abnormal, depression, excitability, auditory hallucination, suicidal tendency. Reproductive Disorders/Female* - *Frequent:* menstrual cramps, menstrual disorder. *Infrequent:* menorrhagia, breast neoplasm, pelvic inflammation, premenstrual syndrome, spotting between menses. *% based on female subjects only: N=905 Respiratory System Disorders - *Frequent:* bronchitis, sinus congestion, coughing, nasal congestion, sinus headache. *Infrequent:* asthma, breath shortness, laryngitis, pneumonia, tracheitis. Skin and Appendages Disorders - *Frequent:* rash. *Infrequent:* pruritus, acne, alopecia, eczema, dermatitis, dry skin, folliculitis, lipoma, furunculosis, dry lips, skin nodule. Special Senses - *Frequent:* vision blurred, tinnitus. *Infrequent:* taste alteration, earache, conjunctivitis, vision abnormal, dry eyes, eye irritation, visual disturbance, eye infection, pupils dilated, metallic taste. Urinary System Disorders - *Frequent:* urinary frequency, urinary tract infection. *Infrequent:* urinary urgency, kidney stone, dysuria, blood in urine. **Events Reported Subsequent to the Marketing of Escitalopram** - Although no causal relationship to escitalopram treatment has been found, the following adverse events have been reported to have occurred in patients and to be temporally associated with escitalopram treatment during postmarketing spontaneous and clinical trial experience and were not observed during the premarketing evaluation of escitalopram: Blood and Lymphatic System Disorders: hemolytic anemia, leukopenia, thrombocytopenia. Cardiac Disorders: atrial fibrillation, cardiac failure, myocardial infarction, torsade de pointes, ventricular arrhythmia, ventricular tachycardia. Endocrine Disorders: diabetes mellitus, hyperprolactinemia, SIADH. Eye Disorders: diplopia, glaucoma. Gastrointestinal Disorders: gastrointestinal hemorrhage, pancreatitis, rectal hemorrhage. General Disorders and Administration Site Conditions: abnormal gait. Hepatobiliary Disorders: fulminant hepatitis, hepatic failure, hepatic necrosis, hepatitis. Immune System Disorders: allergic reaction. Investigations: electrocardiogram QT prolongation, INR increased, prothrombin decreased. Metabolism and Nutrition Disorders: hypoglycemia, hypokalemia. Musculoskeletal and Connective Tissue Disorders: rhabdomyolysis. Nervous System Disorders: akathisia, choreoathetosis, dysarthria, dyskinesia, dystonia, extrapyramidal disorders, grand mal seizures (or convulsions), hypoaesthesia, myoclonus, nystagmus, seizures, tardive dyskinesia. Pregnancy, Puerperium and Perinatal Conditions: spontaneous abortion. Psychiatric Disorders: acute psychosis, aggression, anger, delirium, delusion, nightmare, paranoia, visual hallucinations. Renal and Urinary Disorders: acute renal failure. Reproductive System and Breast Disorders: priapism. Respiratory, Thoracic and Mediastinal Disorders: pulmonary embolism. Skin and Subcutaneous Tissue Disorders: angioedema, ecchymosis, erythema multiforme, photosensitivity reaction, Stevens Johnson Syndrome, toxic epidermal necrolysis, urticaria. Vascular Disorders: deep vein thrombosis, hypotension, orthostatic hypotension, phlebitis, thrombosis.

Cardiac Risks

continued from page 2

the advisory committee members voted "no" on the agency's question of whether sertindole is acceptably safe for the "broad treatment of schizophrenia." If the company implements strong warnings and risk-management guidelines on the labels for prescribers and patients, however, eight members voted "yes" on the question of whether sertindole can be approved for use in certain subgroups of patients, while two voted "no" and three abstained. The committee agreed that sertindole should not be used as first-line treatment because of the small but potentially fatal cardiac risk.

The suicide claim for sertindole was given a thumbs-down by the committee because of marginal statistical results from the SCoP trial. The analyses related to the rates of suicide attempts, based on standardized criteria, did not reach statistical significance despite numerically lower rates in the sertindole group.

Cardiac risk also made the committee reluctant to support the expansion of quetiapine indications to MDD and GAD.

At an April 8 meeting, AstraZeneca presented clinical trial data in which quetiapine XR was shown to be more effective than placebo as monotherapy for MDD and GAD and as adjunctive therapy for MDD. Wayne Ray, Ph.D., director of the Division of Pharmacoepidemiology and a professor of preventive medicine at Vanderbilt University School of Medicine, was brought in by the FDA to discuss higher rates of sudden cardiac death associated with antipsychotics observed in a large case-control study he and his colleagues had conducted. The study was published in the January 15 *New England Journal of Medicine* (*Psychiatric News*, March 6).

In that study, the rates of sudden cardiac death were similar between patients taking first-generation and second-generation antipsychotics.

Quetiapine is currently approved for treating schizophrenia and bipolar disorder. An approval for MDD and GAD indications would substantially increase the drug's market share since it would then likely be prescribed more often by primary care physicians. The potentially large expansion of the patient population taking quetiapine also was worrisome because of weight gain and negative metabolic effects associated with the drug, some committee members indicated.

Most but not all of the advisory committee members agreed that the efficacy of quetiapine XR in MDD and GAD patients was demonstrated by the company. Six members voted "yes" and three voted "no" to the question of whether the safety of monotherapy quetiapine XR was demonstrated as an adjunct treatment for MDD. The drug was not studied for adjunct treatment for GAD.

However, the committee unanimously rejected the claim that the drug is acceptably safe as a monotherapy for the broad treatment for MDD and GAD. If certain conditions are met, however, such as the addition of strongly worded label warnings, some committee members were in favor of declaring quetiapine XR safe enough to be approved as a monotherapy, but not first-line treatment, for treating either disorder. The vote on this issue was 4-4.

The FDA usually—but not always—follows advisory committee recommendations. ■

professional news

Traditions

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Roessel thought about veterinary school, but later chose medical school at the University of Minnesota. She first considered family medicine as a possible specialty, drawn to it as a way of being of service.

"But after a psychiatry rotation in my third year, I felt that psychiatry was a more holistic way of dealing with people, like the Navajo culture," she said.

Today she is based at the Santa Fe, N.M., Indian Hospital but spends several days a month at the Santa Clara and Santa Domingo pueblos. There she attends clinics, makes some home visits, and trains tribal staff members.

Adapting contemporary psychiatry to another culture is more complex than simply pushing a switch, she said.

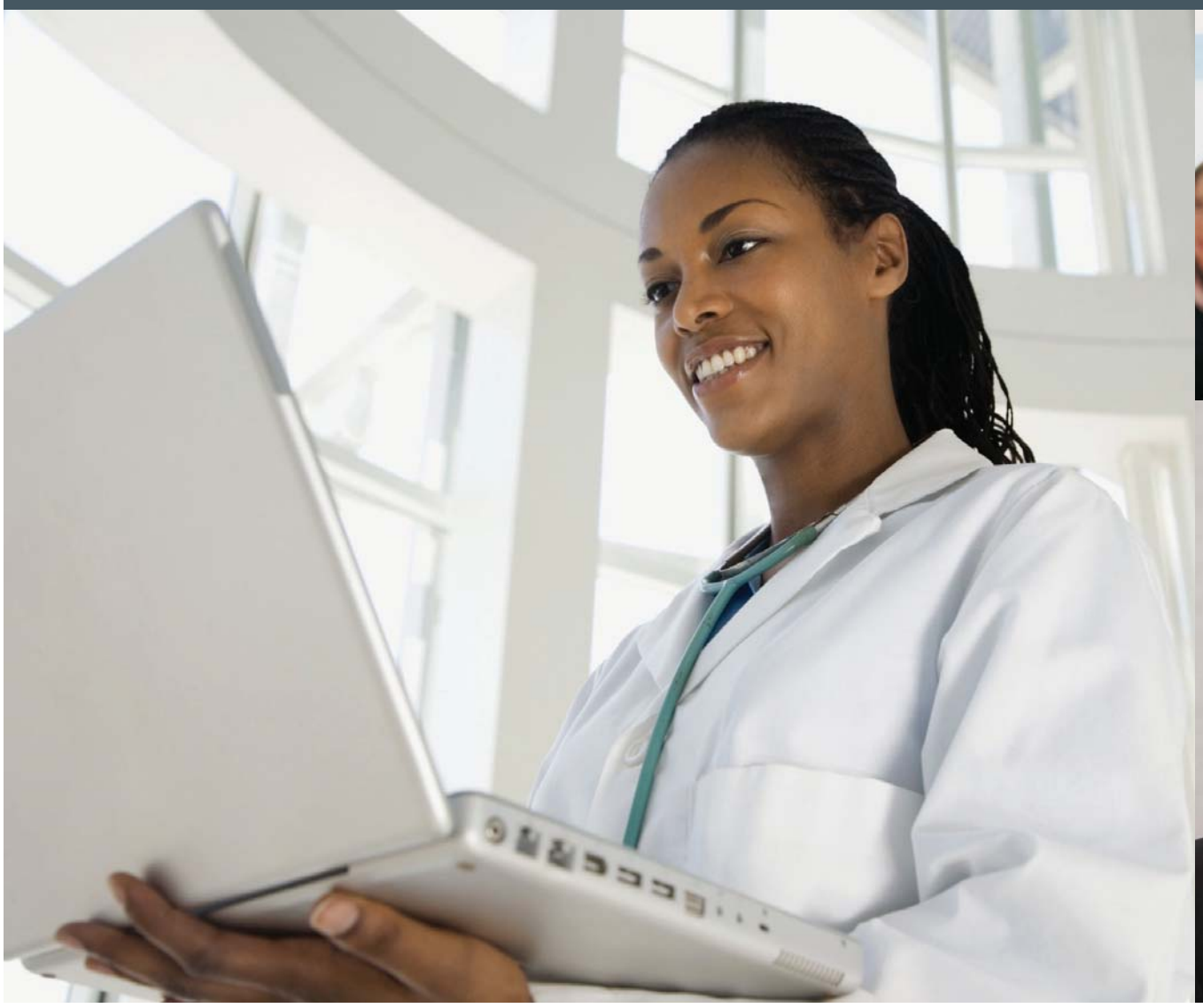
"It means thinking about patients' culture of origin, their language, and how they identify themselves," she said. "How do they look at their illness from both medical and cultural perspectives?"

Knowing the long view of history is critical, too. The physical destruction and dislocation of American Indians in the 19th century may be known to most non-Indians. However, a variety of policies of the 20th century, like the boarding school system that removed children from their homes, left many Indians adrift, stripped of their culture and caught in a pattern of ongoing intergenerational trauma, she said.

With that in the background of every conversation, patients frequently find it a relief to talk to someone like Roessel, who shares their perspective on the world. In fact, 75 percent will see a traditional healer first before coming to a psychiatrist, she said.

Roessel also takes a long-term view of improving access to medical and psychiatric care for the population she serves. She makes presentations at local high schools on science and medicine and mentors students through the Association of American Indian Physicians.

Having a foot in two worlds coupled with a desire to help patients sustained her through rough patches in medical school, and does so today, she said. "I can see both the Navajo and the Western points of view, and that has given me a more holistic world view and made me more accepting of people's differences." ■



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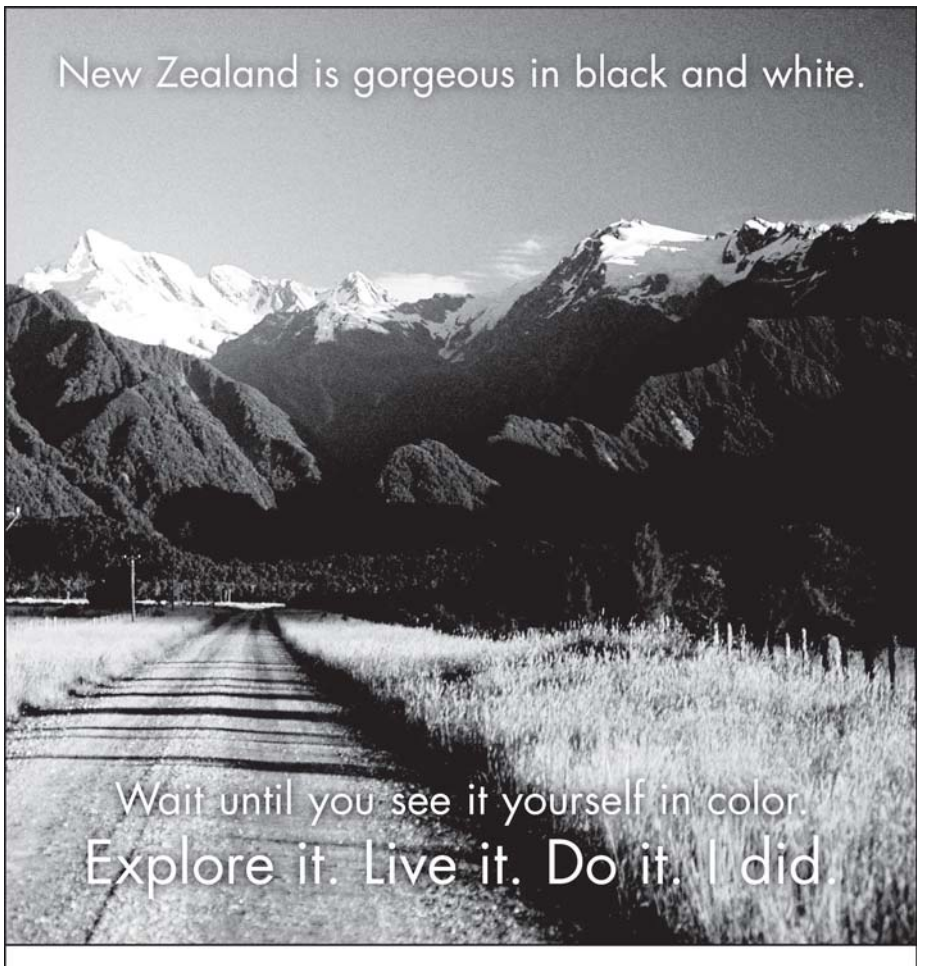

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Director, M.I.N.D. Institute

The University of California, Davis, is searching for a Director of the Medical Investigation of Neurodevelopmental Disorders (M.I.N.D.) Institute. This is a tenured, ladder rank position with a state FTE.

The individual selected will also hold the Tsakopoulos-Vismara Endowed Chair. The M.I.N.D. Institute is a multidisciplinary research and clinical center that focuses on the causes and treatment of neurodevelopmental disorders such as autism, fragile-X syndrome, ADHD, Tourette syndrome, 22q deletion syndrome and other disorders.

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Institute.

The search committee is looking for a visionary leader who could develop and refine the direction for the M.I.N.D. Institute for the next decade. The candidate should have a background in fundraising activities and building community relationships. The candidate should also be committed to fostering diversity among faculty and staff.

The successful candidate should be a prominent N.I.H.-funded investigator whose research has focused on neurodevelopmental disorders. It is preferable that the candidate be a physician who is license eligible in the State of California; however, applications from Ph.D. investigators will also be considered.

The candidate should have had significant leadership and administrative experience directing a center, department or clinical service. A history of mentoring junior faculty and facilitating interdisciplinary approaches to research are also highly desirable attributes.

For more information, please review the M.I.N.D. Institute'swebsite at **http://www.ucdmc.ucdavis.edu/mindinstitute/** or contact the search committee chair, Robert E. Hales, M.D. at **rehales@ucdavis.edu.**

For full consideration, applications must be received by September 30, 2009. Position is open until filled, but no later than April 1, 2010. Interested candidates should email a curriculum vitae and letter of interest in response to Position #AD-01R-09 to Megan Rott at megan.rott@ucdmc.ucdavis.edu.

In conformance with applicable law and University policy, the University of California, Davis, is an equal opportunity/affirmative action employer.

Alberta Health Services

Alberta Health Services (AHS) is the provincial health authority responsible for overseeing the planning and delivery of health services and support to 3.5 million Albertans. It is one of the world's largest health systems, and with 90,000 staff and 7,000 physicians, is one of Canada's largest employers. Together, we will create accessible, sustainable and patient-focused health care across rural, urban and academic settings.

The Regional Mental Health Program has over 2,200 staff providing a full spectrum of services through urban and suburban clinics, funded agencies, mobile crisis teams, community partnerships, a specialized psychiatric hospital and all of the general hospitals within the Region. Our staff exemplify commitment, caring and collegial sharing of clinical expertise. The Regional Mental Health Program is a leader in health care excellence and innovation.

AHS' Regional Mental Health Program is actively recruiting Psychiatrists for the following positions:

Addiction Psychiatrist

Child & Adolescent Psychiatrists

- Acute Care
- Addiction
- Community Clinics
- Consultation/Liaison
- General
- Infant & Preschool

Clinical Director, General Adult Psychiatry

Consultation/Liaison Psychiatrists

Emergency Department Psychiatrists

Forensic Psychiatrist, Sex Offender Treatment Program

Forensic Psychiatrist, General

Geriatric Psychiatrists

Operational Stress Injury (OSI) Psychiatrist

Staff Psychiatrist, Psychodynamic Psychotherapy

Site Chief, Psychiatry

The successful candidate must have or be eligible for licensure with the College of Physicians and Surgeons of Alberta. Preference will be given to candidates with specialist qualifications, FRCPC or equivalent.

Visit us at the APA 162nd Annual Meeting Career Fair (Booth #2210) – SEE YOU THERE!

Apply online at: www.capitalhealth.ca/physicians • Learn about the City of Edmonton at: www.movetoedmonton.com

www.albertahealthservices.ca

DEPARTMENT OF VETERANS AFFAIRS
MEDICAL CENTER
DAYTON, OHIO

PSYCHIATRISTS

The Department of Veterans Affairs Medical Center, Dayton, Ohio, seeks three full-time and one part-time Psychiatrist, to provide direct patient care in both inpatient and outpatient settings.

The incumbents must be well versed in the major treatment modalities for diagnosing and treating a wide variety of psychiatric disorders in Veterans. Positions will be available in the Substance Abuse Program and the Community Living Center (Nursing Home). The Medical Center is a 539-bed multi-specialty Dean's Committee Hospital.

Applicants should be board-certified or board-eligible. Graduating residents and fellows may apply; have a license from one of the 50 states; and be a citizen or permanent resident or the USA.

Dayton, the birthplace of flight, is located in the beautiful rolling hills of Southwestern Ohio and offers the convenience of a city, without the hassles. The metropolitan area has five universities, excellent school systems, museums, theaters, and other recreational opportunities, and is the home of Wright-Patterson Air Force Base.

-Dayton VAMC employees enjoy excellent federal benefits and competitive salaries.

-External applicants selected for this position may be eligible to apply for an educational loan reimbursement award under the provisions of the Education Debt Reduction Program (EDRP) subject to availability of EDRP funding.

-Recruitment incentive and moving/relocation expenses may be authorized.

-Medical Malpractice Claims coverage is provided under the Federal Tort Claims Act.

Send curriculum vitae with three references to:

Dayton VA Medical Center
Richard Morvatz (11d)
4100 West Third Street, Dayton, OH 45428

E-mail: Richard.Morvatz@va.gov
Tel: 937-262-2106 or Fax: 937-262-2179
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Adult Psychiatrists
Bremerton, Tacoma, Olympia, WA

Group Health Permanente is currently seeking BE/BC Adult Psychiatrists. Group Health is dedicated to providing comprehensive, innovative & patient-centered care to communities throughout WA. We offer flexible schedules with generous benefits & competitive salaries

- Ideal candidate will have knowledge & skills in medication management and team consultation
- 100% outpatient opportunity perfect for those with experience working with diverse patient populations
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For additional information or to submit your CV, please contact:

Cayley Crotty – crotty.c@ghc.org
206-448-6519

EOE/AA

www.ghc.org/greatjob

GroupHealth

PSYCHIATRIC LOCUM TENENS

PINE REST Christian Mental Health Services

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www.pinerest.org

Pine Rest Christian Mental Health Services is seeking Psychiatrists in West Michigan.

Pine Rest is one of the five largest free-standing behavioral health providers in the U.S. In addition to our main campus in Grand Rapids, Pine Rest also has 20 outpatient locations throughout West Michigan and 2 in Iowa.

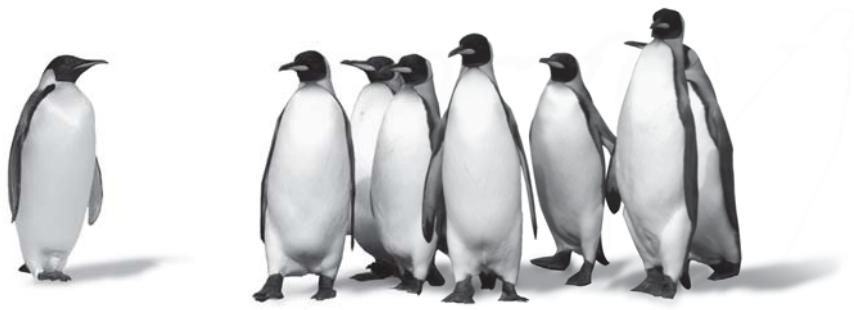
Pine Rest Christian Mental Health Services is seeking psychiatrists for inpatient, outpatient and residential settings. A full continuum of services is offered, which includes addiction treatment and recovery, extensive child and adolescent programs, senior care services, consultation liaison, and ECT Clinic. Pine Rest is the preferred behavioral health provider for over 20 regional community mental health offices.

Board certification is preferred, specialty training is highly desired. Qualified candidates must possess a current license to practice in Michigan at the time of appointment. There are full-time and part-time positions available.

Pine Rest Christian Mental Health Services offers a competitive compensation package, comprehensive benefits, and is an equal opportunity employer.

Direct Contact Information:
If you would like to explore an opportunity with Pine Rest, please contact Trisha Fite, Physician Recruiter, at 616/281-6363, x-2113 or email trisha.fite@pinerest.org.

We will see you at the 162nd Annual Meeting of the American Psychiatric Association
May 16-21, 2009 • San Francisco, CA



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Adult, Child & Adolescent

Turn your world upside down for all the right reasons – work environment, colleagues and an unparalleled quality of life.

Timaru Hospital is a secondary level hospital situated on the east coast of the South Island of New Zealand. You've high country rivers, lakes, four ski fields and the cities of Christchurch and Dunedin within two hours drive, affordable housing and superb schooling. There is something for everyone here – professionally and personally.

The service, staffed by two long serving psychiatrists, Clinical Director and locums, works within budget, has no waiting lists and is well resourced. Working in the Child and Adolescent Service (0.5), you will also cover the Adult (0.5) and on call weekend work, using the "Strengths Model" approach to assist client recovery. Eligible for registration in New Zealand you'll be US Board Certified and have experience with adults, adolescents and children.

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South Canterbury District Health Board

www.scdhb.co.nz

We are recruiting Psychiatrists!

dhhs NC DEPARTMENT OF HEALTH AND HUMAN SERVICES
www.ncdhhs.gov

Complex cases…specialized treatment…an opportunity for the best of the best to rise to the challenge! If altruism…compassion…and a strong desire to make a dramatic difference in the lives of your patients matters to you …then consider joining our team.

As a Psychiatrist at one of our facilities, you will serve as an integral member of an interdisciplinary team, developing comprehensive treatment plans to address the individual, social, medical, and vocational needs of patients.

In addition, you will work in affiliation with prominent residency programs such as the University of North Carolina-Chapel Hill, Duke University, and East Carolina University. We offer child adolescent, adult admissions, forensic and rehabilitation services at our hospitals.

From the mountains to the coast, we employ Psychiatrists at the following Hospitals and Alcohol & Drug Abuse Treatment Centers (ADATC):
•Broughton Hospital • Central Regional Hospital • Cherry Hospital
•Walter B. Jones ADATC •R.J. Blackley ADATC • Julian F. Keith ADATC

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UF UNIVERSITY of FLORIDA

Community Psychiatry Fellowship

The University of Florida College of Medicine Department of Psychiatry is currently accepting applications for a PGY-5 Fellowship in Community Psychiatry to start July 1, 2009.

This fellowship in Community Psychiatry is under the guidance of Richard Christensen, MD, Chief of Public Psychiatry, and Wayne L. Creelman, MD, McCabe Clinical Eminent Scholar Chair in Psychiatry & Community Mental Health.

The fellowship offers consultation-liaison training in a wide variety of settings. These clinical experiences are accompanied by didactics, interviewing and psychotherapy instruction. Training is tailored according to the fellow's area of interest and career goals. The fellowship is based in spectacular Vero Beach, Florida, at the University's Center for Psychiatry & Addiction Medicine.

Qualified applicants will have completed an accredited psychiatry residency in the U.S. have passed all necessary exams to obtain a Medical License in the state of Florida and be Board Certified or Board Eligible. This is a one or two-year position. Applications are now being accepted for the 2009/2010 academic year.

Application deadline to apply is June 12, 2009.

Interested individuals should send a letter of interest and current CV to:

Wayne L. Creelman, MD
Center for Psychiatry & Addiction Medicine
840 37th Place, Suite 2
Vero Beach, FL 32960

An Equal Opportunity Institution

PSYCHIATRISTS

SF Bay Area – Santa Clara Valley Medical Center Dept of Psychiatry is looking for salaried full- and part-time BE/BC psychiatrists to staff ambulatory clinics.

Also, contract physician positions available in psychiatric emergency room. All positions available immediately. Very competitive salary and excellent benefit pkg.

Current California licensure mandatory.

Contact:

Tiffany Ho, M.D., Medical Director
Outpatient Specialty Mental Health
Ph: 408.885.5767
Fax C.V. to: 408.293.4889

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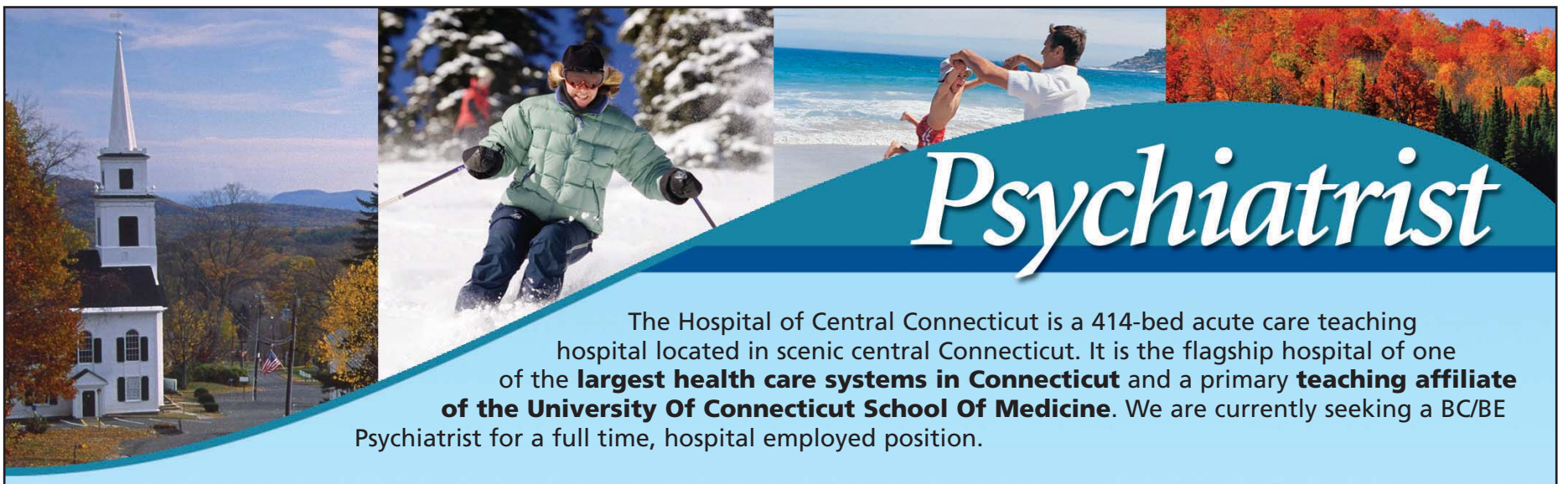

Psychiatrist

The Hospital of Central Connecticut is a 414-bed acute care teaching hospital located in scenic central Connecticut. It is the flagship hospital of one of the **largest health care systems in Connecticut** and a primary **teaching affiliate of the University Of Connecticut School Of Medicine**. We are currently seeking a BC/BE Psychiatrist for a full time, hospital employed position.

THIS POSITION OFFERS:

- A rewarding and challenging patient mix
- The opportunity to work with a talented, multidisciplinary team of clinical professionals
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- 22-bed inpatient unit and multiple outpatient programs
- Room for professional advancement in future-Director of Substance Abuse

In addition to the **exceptional pay and benefits** offered by the hospital, central Connecticut offers an **attractive lifestyle with ready access to Boston and New York City, Vermont skiing, a magnificent coastline, and some of the finest schools in the nation.** Interested candidates should contact Patricia Lowicki, Director of Physician Recruitment at 860-224-5576. Or email plowicki@thocc.org.

The Hospital of Central Connecticut
at New Britain General and Bradley Memorial

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Issue	Deadline (Friday, 2 p.m. E.T.)
June 5	May 22
June 19	June 6

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ALABAMA

The Daily Center

A well-established private practice located in Florence, AL is seeking a BC/BE **Child & Adolescent** and/or **Adult Psychiatrist.** All outpatient, 4-day work week. Excellent salary, benefits and full administrative services included. Send CV to: thedailycenter@msn.com or fax to: (256) 767-7991.

Outpatient Center Seeks Psychiatrist to work w/ 4 Psychologists & 2 Counselors. We are the longest-standing counseling center in Birmingham, AL. Incredible family atmosphere, w/ exceptional staff and support staff. Contact Dr. Bowman at www.personalrelationships.com

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Assistant/Associate Professor of Psychiatry

The University of Alabama - College of Community Health Sciences (CCHS) (University of Alabama School of Medicine -Tuscaloosa Campus) offers a unique opportunity for the Psychiatrist, non-tenure earning clinical track, interested in working in a multi-specialty group practice and participate in the education of medical students and family medicine residents, and focusing clinical care in college mental health. The University of Alabama, with an enrollment of over 27,000 offers significant diversity in diagnosis.

CCHS is one of three clinical campuses of the University of Alabama, School of Medicine providing clinical training for third and fourth year medical students. In addition, for over 25 years the College has administered one of the most prestigious and successful Family Practice Residency programs in the Southeast. The College is located on the main campus of the University of Alabama, a comprehensive research institution that offers a wide variety of opportunities for faculty and their families. Located in Tuscaloosa, Alabama, a community of approximately 150,000 there are many exceptional cultural and recreational opportunities. The Campus is located one hour from Birmingham, three hours from Atlanta, and five hours from the Gulf of Mexico.

Salary is commensurate with experience and includes a generous benefits package. Candidates must be Board Certified in General and/or Child & Adolescent Psychiatry, meet requirements for an academic appointment at the UA and be eligible for licensure in the State of Alabama.

Screening is on-going. Applications will be accepted until the position is filled. Interested candidates should submit application and include CV, letter of interest and three letters of recommendation to:
http://facultyjobs.ua.edu

For additional information, contact: Susan Arnold, MD, Chair, Search Committee at sarnold1@cchs.ua.edu.

Please see our website at http://cchs.ua.edu/
The University of Alabama is an Equal Opportunity Affirmative Action Employer. Women and minorities are encouraged to apply.

ARIZONA

The Phoenix VA Health Care System at Phoenix seeks Staff Psychiatrists. Become a part of a tradition of excellence with new and rewarding challenges. Mental Health is currently offering inpatient and outpatient positions concentrating on the readjustment of veterans from the recent conflicts in Afghanistan and Iraq and on the treatment of veterans with posttraumatic stress disorder, and substance abuse care positions concentrating on the treatment of addictions directly related to veteran mental health care. Candidates must be highly motivated, flexible and able to work as part of an integrated team. Previous experience with combat-related posttraumatic stress disorder is a plus. We offer competitive salaries and an excellent benefit plan, including medical coverage, malpractice coverage, retirement plan, and MORE! Psychiatrists may have licensure in any state. Either board certified or board eligible. Please send your curriculum vitae to: Human Resources Management Service (05B1), 650 E. Indian School Road, Phoenix, Arizona 85012, 602-277-5551 ext 3021 or Fax 602-222-6554. The VA is an equal opportunity employer.

Mohave Mental Health Clinic, Inc is located in Northwestern Arizona. We are a private, not for profit community health center providing services to residents of Mohave County, with clinics in Kingman, Bullhead City, and Lake Havasu City.

We have an immediate opening based in Kingman, AZ. for a Psychiatrist. Requirements: Medical physician trained in General Psychiatry, 4 years (verified). Fulfillment of required 20 hours Continuing Medical Education (CME) per year (on file). Current Arizona physician license. Satisfactory completion of 4 year general psychiatry residency program. Experience in Mental Health field preferred, but will train the right candidate.

Our mission is to improve, enhance and promote the emotional well being of Mohave County residents who experience life disrupting problems, and to strengthen the quality personal, family and community life.

We provide services to the Seriously Mentally Ill, children and families, substance abuse adults and individuals requiring crisis support.

Salary DOE and is negotiable.

Excellent medical benefits, 401k, and liberal vacation. Great outdoor activities, just a few hours from Phoenix, Las Vegas and the Grand Canyon.

If interested, contact the Human Resource Department at 928-757-8111 ext 3336 or 3334. Fax resume to 928-757-8705 or mail to 1743 Sycamore Ave. Kingman, AZ 86409.

Ninety Minutes to Vegas, Arizona
Join a successful non-profit community mental health center. High quality life style opportunity. 100% outpatient, with a light call schedule of 1:13, which is phone back up. Full support staff, moderate caseload, and professional medical staff. Loan Repayment is Available. Scenic hiking, historic charm, great cafes and restaurants combine to make this a remarkable destination.

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800.504-3411 jhock@alphamg.org
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ARKANSAS

FAYETTEVILLE & LITTLE ROCK - General & Child Psychiatrists. State of the art new hospital in Fayetteville opening Fall 2009. Admin/Clinical & Staff positions. Inpatient & partial programs. Fulltime or part-time positions offering very competitive salary & benefits. Contact Joy Lankswert @ 866-227-5415 or email joy.lankswert@uhsinc.com

CALIFORNIA

Karl E. Douyon, M.D., Inc.
Psychiatrists are needed as independent contractors for Locum Tenens positions in California. Pay is $175 per hour depending on location. On call pay is extra. Hours are flexible for weekdays and some weekends. Call 805-644-4093. Fax resumes to 805-830-6300. karledouyonmd.com

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Research Psychiatrist position is open in the Laboratory of Clinical Psychopharmacology at The Scripps Research Institute, La Jolla, CA to participate in an active program of NIH-funded clinical trials involving alcohol and cannabis dependence. To view job description and submit resume online, go to www.scripps.edu

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GREATER BAY AREA - Modesto, California

General & Child Psychiatrists needed, for unique, stable County Mental Health system in a welcoming community. Serve both public & private sector patients, in both inpatient/outpatient settings that have been benchmarked for their quality. Possibilities for Resident teaching & consultation with a full range of providers. When patients require hospitalization, inpatient & outpatient staff work **TOGETHER** to optimize care. Stanislaus County is located only 1 1/2 hours from both San Francisco and Yosemite, enjoying the best of both worlds.

Excellent salary scale, with steps from $171K to $208K; **PLUS** full benefits; **PLUS** 5% additional for Inpatient, and General Boards or Child Boards; **PLUS** extra for limited On-Call; **PLUS** Union-negotiated increases already set for next few years. Negotiable hourly contract also an option. Fax CV to Uday Mukherjee, MD, 209-525-6291 or call 209-525-6121.

CALIFORNIA
BC/BE STAFF PSYCHIATRIST

Patton State Hospital is recruiting board certified/eligible psychiatrists. Patton is a Joint Commission accredited, 1500 bed, adult f orensic psychiatric hospital, with an extremely interesting and challenging patient population. The hospital is nestled below Arrowhead and the San Bernardino Mountains, 65 miles east of Los Angeles; an hour's drive to beaches, Palm Springs, or mountain lakes and skiing. Salary with Board Certification starts at **$18,622 and goes to $21,311 monthly.** Salary for Board Eligible starts at **$18,146 and goes to $20,711 monthly.** In addition, Patton offers excellent benefits (health, dental, and vision; license renewal; malpractice insurance; tax-deferred compensation; paid annual leave and 12 holidays (plus one personal holiday), as well as seven days per fiscal year of Continuing Medical Education leave). Voluntary on call duty is compensated on an hourly basis over and above base salary. We provide civil service security and retirement plans (including safety retirement). For c onfidential consideration, send CV to Wadsworth Murad, D.O., (A) Medical Director, 3102 East Highland Avenue, Patton, California 92369, (909) 425-7326 or Fax (909) 425-6635.

Contract psychiatrists are needed to work 10 hours, 4 days wkly at Coalinga State Hospital, CA, at hrly rate of $180. Call 800-758-7012 or fax CV to 800-758-7013 or e-mail hahacorp@gmail.com if interested. CA license, and insurance needed. We will work with recruiter for a fee.

Psychiatrist
Modesto, CA

Gould Medical Group, Inc has an excellent opportunity for a BC/ BE Psychiatrist who will be joining group practice as a lead provider of psychiatry services for the group. Gould Medical group is 230+ member physicians owned multispecialty group affiliated with Sutter Medical Foundation.
Responsibilities include:
- Primarily Outpatient setting
- General adult population
- Call will be discussed
- Full support staff
- Opportunity for shareholder track
- Competitive Benefits and Relocation Package

Modesto is a growing community of 210,000; about 90 minutes drive from San Francisco and Yosemite National park; located on Highway99 and is easily accessible from throughout Northern California.

Send CV to GMGrecruiting@sutterhealth.org
or Fax at 209-550-4892
Visit our website for details
www.suttergould.org
Contact: C.V. Allen M.D., 209-574-4407

Southern CA - Lancaster: Join established private practice. Combined inpatient & outpatient practice with shared call. Competitive compensation with partnership track. Contact Kimberly Lanzilotti at 866-227-5415 or email kimberly.lanzillotti@uhsinc.com

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Easy Access to San Francisco - 100% Outpatient
Dynamic Group Practice offering established client base and exclusive referral sources seeks an Adult and a Child / Adolescent Psychiatrist. Positions are 100% outpatient, minimal call with a moderate caseload. Benefit from a comprehensive support staff. Ideal candidate will possess strong psycho-pharmacology skills and the ability to work within a team setting. ECT experience is a plus, but not required. Community offers affordable housing, numerous educational opportunities and easy access to San Francisco.

Rosa Herring
Alpha Medical Group
800.504-3411 rherring@alphamg.org
View available opportunities at
www.alphaps.org
Visit us at APA, Booth 2003

California Psychiatric Transitions - MHRC, located in the Modesto area is seeking a staff psychiatrist with experience in the treatment of the chronic, severely mentally ill. Experience with Clozaril, strong psycho-pharmacology skills, experience in treating co-morbid personality disorders, substance abuse and developmental disabilities are essential. Good supportive psycho therapy skills are strongly encouraged and the ability to supervise treatment team and milieu therapy required. Salary and benefits are negotiable D.O.E. Flexible scheduling/half-time positions available.

Please contact:
John T. Hackett M.D.
Medical Director
Tel. (209) 667-9304 ext. 102
Fax. (209) 669-3978
OR
James T. Drayton
Administrator
(209) 667-9304 ext. 103
jdrayton@cptmhrc.com

INPATIENT PSYCHIATRIST-INDEPENDENT CONTRACTOR: DOMINICAN HOSPITAL is seeking a board certified or board eligible psychiatrist as an independent contractor to provide services 40 hours/week. Santa Cruz is a coastal community located on the Monterey Bay, 11/2 hours away from San Francisco and UC Berkeley, less than an hour from Stanford University. Santa Cruz enjoys temperate climate, outdoor activities such as bicycling, surfing, hiking, cultural events such as Shakespeare Santa Cruz, the Santa Cruz, Symphony, music and art and wine festivals just to mention a few. We are looking for a Psychiatrist to join the Inpatient Team which also provides services to our Partial Hospitalization and Consult Liaison services. Strong background in Psychopharmacology and an ability to work well in a multidisciplinary setting are essential. Compensation???
Contact: Frances Kashino (831) 462-7511
E-mail: fkashino@chw.edu

Immediately hiring 2 Board Certified Psychiatrists to join a new inpatient facility located in CA. Excellent compensation, benefits, and relo, 40hrs/week. Ideal candidate: 2-5 years experience, management a +. Contact Linda Kelley, 239-561-0945, Hope4U2911@comcast.net

CONNECTICUT

STAFF PSYCHIATRIST, FULL-TIME - At the Hospital of Saint Raphael, a 511-bed community teaching hospital in New Haven, CT, our vision is to provide the highest quality care and the most balanced, caring and professional environment possible to each face that walks through our doors. Full-time staff psychiatrist will provide services on our Adult Inpatient Unit as well as in the PHP/IOP. One out of four weekends call schedule. Board Certified or eligible in Psychiatry required. We offer a competitive salary and a supportive, friendly environment. Please call Travis Taigen to learn more about these opportunities at **1-800-322-2380** or contact at **ttaigen@srhs.org.** For consideration, please apply online at: www.srhs.org/career. Committed to equal opportunity and an environment that celebrates diversity.

Hospital of Saint Raphael

Full time psychiatrist, inpatient or outpatient service. Dept of Psychiatry at outstanding community hospital in central CT. Experienced, collegial, professional, multidisciplinary team. Reasonable call, competitive salary & benefits. Respond in confidence to Robert Grillo MD, Chairman Dept Psychiatry Middlesex Hospital robert_grillo_md@midhosp.org

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BEAUTIFUL SUBURBAN CT/ 1 ¼ HRS FROM NYC

CT licensed BC/BE Psychiatrist to join a 30 year well established multi-disciplinary practice providing adult psychiatric services. Excellent Compensation. Send CV/cover letter by fax 203-797-0877 or Email: afrymd@yahoo.com. Any questions, contact Sam at 203-792-6060 x15.

Yale University Department of Psychiatry

The Yale Department of Psychiatry seeks to hire a forensic psychiatrist to provide psychiatric services to inmates in state correctional institutions and to perform revenue generating forensic work, i.e. state court, federal court, probation and private attorney referrals in civil and criminal cases. Some academic time for teaching and research activities is included. The position carries a faculty appointment at the rank of Assistant Professor. Requirements include Board Certification in Psychiatry, a license to practice in Connecticut, and completion of a formal program of training in forensic psychiatry. Interested parties should send a letter of interest and curriculum vitae no later than June 15, 2009 to:

Howard Zonana, M.D.
Law & Psychiatry Division
CT Mental Health Center
34 Park Street
New Haven, CT 06519
Howard.zonana@yale.edu
(203) 974-7158

FULL-TIME/PART-TIME/PER DIEM ADULT PSYCHIATRIST
Central Connecticut

Full-time/Part-time/Per Diem opportunity for BC/BE adult psychiatrist at Saint Francis Hospital and Medical Center. You'll work in the adult psychiatric unit with a skilled, multi-disciplinary team of Master's-level therapists, nurses and mental health workers treating a broad spectrum of psychiatric patients. Additional responsibilities may include treating adult patients in a partial hospital or intensive outpatient setting. We offer flexible hours with an opportunity for permanent PT/FT position.

Our central Connecticut location offers a wide range of upscale suburban living choices and all the amenities of the New England region, including first-rate schools, and the pleasures of country and coastal environments. Close proximity to professional sporting events, concerts, ballet, theatres, skiing and boating, and less than two hours to Boston and New York.

For more information about this opportunity, please contact Christine Bourbeau in the Recruitment Office at 800.892.3846 or fax/email your CV to 860.714.8835

Email address: cdoughti@stfranciscare.org
Please visit our website at:
www.saintfranciscare.com

EEO/AA - A/F/D/V, pre-employment drug testing

FLORIDA

Gulf Coast, Florida - Outstanding Income Potential
Specializing in Family counseling, substance abuse and the treatment of mental illness, this comprehensive behavioral health center provides services to over 9,000 individuals and families each year in several gulf coast communities. 85%-90% outpatient with a starting salary of $175,000. Certification and experience will be rewarded with additional salary. Patient load is very manageable, which allows for a low stress work environment.

Tammie Pepin
Alpha Medical Group
800.504-3411 tpepin@alphamg.org
View available opportunities at
www.alphaps.org
Visit us at APA, Booth 2003

LEAD PSYCHIATRIST / MEDICAL DIRECTOR

Daniel Memorial, Inc. (daniel), a private non-profit agency located in Jacksonville, Florida, is seeking a BE/BC Child and Adolescent Psychiatrist to become an active member of our senior executive team and to provide administrative and clinical oversight over agency services, including our Residential Treatment Center/ Statewide Inpatient Psychiatric Program. daniel offers a competitive compensation package, including benefits, paid malpractice insurance, and compensation for on-call responsibilities. For more information, please see our website: http://www.danielkids.org or contact HR by email: hr@danielkids.org or fax your CV to (904) 296-1953.

PSYCHIATRIST

Board certified (or eligible) Child Psychiatrist to work with both inpatient/outpatient clients. Must be FL licensed and able to work in a fast-paced, multidisciplinary, team environment. Full-time position. Spanish speaking a plus. Designated area of need for loan repayment and other waiver programs. We offer a competitive salary and benefits package. For consideration, please send resume to: Manatee Glens, P.O. Box 9478, 391 Sixth Avenue W., Bradenton, FL 34206. FAX: (941) 782-4301 o Email: hr@manateeglens.org Ph: (941) 782-4299 Pre-employment drug test required. www.manateeglens.org EOE M/F/D/V

MANATEE GLENS

DAYTONA - MELBOURNE - ORLANDO - MIAMI - FORT LAUDERDALE - PALM BEACH - OCALA - GAINESVILLE - FORT MYERS - SARASOTA - PENSECOLA - JACKSONVILLE - Psychiatrists needed for rapidly expanding Nursing Home Service. Great support. No call. Average Salary 210K + benefits. Part-time available. Some travel required. Must have FL Medicare & FL Medicaid individual provider #s. No Restrictions (H1B Candidates Considered). Call our administrator, Christy, at 866-936-5250.

GEORGIA

Child and Adolescent Psychiatrist
Medical College of Georgia
Augusta, Georgia

With expanding programs and financial stability the Medical College of Georgia (MCG), Department of Psychiatry and Health Behavior is seeking a BE/BC child and adolescent psychiatrist for a faculty position in its Division of Child, Adolescent and Family Psychiatry at rank of Assistant, Associate or Professor level. Competitive salary and benefits package commensurate with experience and qualifications. Responsibilities in a collegial academic division to include supervision/teaching of medical students and general and child and adolescent psychiatry residents, clinical leadership opportunities in inpatient/outpatient programs, and collaborative research at departmental and institutional levels (psychopharmacology, imaging, genetics, developmental neurobiology, treatment outcomes, translational research). Faculty leadership is extensively involved in the national arena. MCG has a long standing fully accredited child and adolescent psychiatry training program with a resident complement.

Augusta, home of the Master's golf tournament and a charming Southern city, is a superb place to live! Low cost of living, close to Georgia/Carolina mountains and Georgia/Carolina/Florida coast. The Medical College of Georgia is an equal employment, equal access, and equal educational opportunity and affirmative action institution.

Contact: Sandra B. Sexson, MD, Chief, Division of Child, Adolescent and Family Psychiatry, Medical College of Georgia, Department of Psychiatry and Health Behavior, 997 St. Sebastian Way, Augusta, GA 30912, Phone (706) 721-6699, Fax (706) 721-3593, ssexson@mcg.edu. See www.mcg.edu/som/psychiatry for more information.

Atlanta Psych Consultants, an established multidisciplinary private practice strategically located in Atlanta, has an immediate need for an Adult Psychiatrist to affiliate with a psychiatrist and 5 psychologists. Full service practice is located in class 'A' medical building near 3 major hospitals. Collegial atmosphere with great potential for a clinical practice through medication management for current patients, referral sharing and joint marketing. Please email CV to consula@bellsouth.net or call Kim Oppenheimer, Ph.D. at 404-847-9560.

FLOYD℠
Behavioral Health Center

Hospitalist Psychiatrist position with a dynamic and expanding 53-bed, adult behavioral health center. Programs include adult psychiatry, chemical dependency and geriatrics, and all patients are admitted on a voluntary basis.

Nestled in the foothills of northwestern Georgia, Rome is surrounded by seven hills and the Coosa, Etowah and Oostanaula Rivers. Rome is a unique small city that has been recognized as the "Number One Small City in the Southeast" and is an hour from Atlanta as well as Chattanooga. Rome boasts a flourishing health care community with more than 350 practicing physicians. Our area enjoys a mild climate and offers quality educational and cultural opportunities.

Floyd offers a competitive salary with great benefits and bonus opportunities. This position is available for J-1 Visa candidates and the qualified candidate will be joining a successful, experienced psychiatric physician already practicing in this role. Outstanding compensation includes full benefits and relocation for the right executive. For confidential consideration, please apply online at www.floyd.org. For more information email Cami Legacy (clegacy@floyd.org) or call 706.509.3964.

Georgia - Southern Charm and Hospitality
Established, financially stable outpatient practice seeks an additional Psychiatrist. Full support staff including a PA. Employed position. Base salary of $180,000 plus complete benefits. University town with a high standard of living and an award winning school system. Its southern charm and hospitality make it a wonderful place to raise your family.

Jim Hock
Alpha Medical Group
800.504-3411 jhock@alphamg.org
View available opportunities at
www.alphaps.org
Visit us at APA, Booth 2003

Augusta, Georgia
Growing Department Seeks New Faculty

With expanding programs and financial stability the Medical College of Georgia (MCG), Department of Psychiatry and Health Behavior is seeking a BE/BC psychiatrist in the area of Consultation Liaison for a faculty position at rank of Assistant, Associate or Professor level. Competitive salary and benefits package commensurate with experience and qualifications. Responsibilities in a collegial academic division to include supervision/teaching of medical students and general and child and adolescent psychiatry residents, clinical leadership opportunities in inpatient/outpatient programs, and collaborative research at departmental and institutional levels (psychopharmacology, imaging, genetics, developmental neurobiology, treatment outcomes, translational research). Position will be involved in shaping service by working with non-psychiatric disciplines to develop an integrated system for delivering psychiatric/psychological and general medical care throughout the institution. Current and potential liaisons with medical/surgical services include the areas of depression, chronic pain, women's health, neurology, heart transplant and the rapidly expanding cancer center and clinic.

Augusta, home of the Master's golf tournament and a charming Southern city, is a superb place to live! Low cost of living, close to Georgia/Carolina mountains and Georgia/Carolina/Florida coast. The Medical College of Georgia is an equal employment, equal access, and equal educational opportunity and affirmative action institution. **See www.mcg.edu for more information. Contact: Peter F. Buckley, M.D., Chairman, pbuckley@mcg.edu, (706) 721-6719.**

ATLANTA: General/Addiction Psychiatrist - Inpatient & partial program. Fulltime position offering salary, benefits & more. **Child Psychiatrist** - part-time position for Residential Treatment Center. Flexible hours. Joy Lankswert @ 866-227-5415 or email joy.lankswert@uhsinc.com

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BEAUTIFUL AREA - VERY CLOSE TO TALLAHASSEE, FL - Seeking another Psychiatrist to work on adult and C/A psychiatric services (inpatient, PHP & outpatient) in an impressive hospital in Thomasville, GA. Offering attractive salary w/benefits. Great quality of life: great climate; great opportunity. Please **call Terry B. Good at 1-804-684-5661,** Fax #: 804-684-5663; Email: terry.good@psysolutions.com.

Child & Adolescent Psychiatrist - Metro-Atlanta

Cobb-Douglas Community Services Board, a behavioral healthcare organization in metro Atlanta, seeks a part-time, BC/BE, Child & Adolescent Psychiatrist for Community Outpatient Behavioral Health clinic. Please send CV to cholt@cobbcsb.com or fax to Cheryl Holt at 770-948-6147.

ILLINOIS

BE/BC Psychiatrist wanted to do consultations on inpatients and SNF plus outpatient and inpatient work. Flexible hours and unlimited income potential. NWChicago/suburbs. Mentalhealthchicago.com Fax 847 387-3419 or email Blaise2001@aol.com

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GENERAL PSYCHIATRIST
Board Certified for growing practice. Compensation-70%of all fees collected. No overhead. Excellent Referrals.

E-mail vita to WDRWEB@AOL@COM

INDIANA

UNDER AN HOUR FROM INDIANAPOLIS & DAYTON-
Please see our ad under Ohio for position "Attractive Salary Plus Generous Sign-on Bonus". Terry Good, Horizon Health, 1-804-684-5661; terry.good@psysolutions.com.

KANSAS

Supervisory Psychiatrist (Chief of Psychiatry) - Topeka, KS
The VA Eastern Kansas Health Care System is seeking a Chief of Psychiatry to serve as an executive supervisor of behavioral health prescription providers. The manager will demonstrate leadership and direction for effective, uniform and economical accomplishment of Behavioral Health Service Line functions within Eastern Kansas Health Care System at both Topeka and Leavenworth sites. This position is responsible for all aspects of administrative and clinical duties relating to prescription providers located within EKHCS. The manager will work with the Quality Management Coordinator, manage quality assurance and improvement activities for all programs and ensure compliance with all applicable JCAHO standards. Additionally, the manager will participate fully in management discussions, decisions, policymaking and shares in the responsibility to top management actions covering activities related to the Behavioral Health Service Line. English language proficiency and US citizenship required, BC/BE in Psychiatry, possess a valid, unrestricted license, have training or experience in psychopharmacology, and be eligible for academic appointment. VA Healthcare providers are entitled to immunity from medical malpractice claims as provided by the Federal Tort Claims Act. In addition to an attractive salary, we offer vacation/sick leave, health/life insurance coverage and a retirement package including a tax-deferred savings plan. Interested candidates should send current CV and references to James Marfield at james.marfield@va.gov. EOE.

KENTUCKY

Child & Adolescent Psychiatrist Wanted

Competitive salary and fringe benefits

Kentucky River Community Care, Inc., a progressive, private, nonprofit Community Mental Health Center in beautiful southeastern Kentucky, is offering an exciting opportunity for a licensed BC/BE psychiatrist to join a team of dedicated behavioral health staff.

The ideal candidate will:
- Provide assessment and treatment in a challenging and rewarding environment.
- Contribute to program development within a growing comprehensive Community Mental Health Center.

We offer:
- Reimbursement of eligible relocation expenses.
- An outpatient setting with minimum on-call duties.
- **NHSC loan repayment designated site.**

Please send letter of interest and resume or C.V. to:
Kentucky River Community Care, Inc.
Human Resources Department
115 Rockwood Lane
Hazard, KY 41701

www.krcccares.com
EOE/AA

GENERAL ADULT PSYCHIATRIST: The HAZARD ARH REGIONAL MEDICAL CENTER, a 308 bed community medical center located in Hazard, Kentucky is seeking a compassionate, motivated BE/BC psychiatrist for its 100 bed psychiatric inpatient unit. The psychiatrist will lead a team of professionals in the evaluation and treatment of adults with mental, emotional and behavioral problems. Center units include dual diagnosis, rehab, and general psychiatry. The salary range is $185,000-$200,000 per annum depending upon experience and board certification. At full staff, the call is 1 in 6 with weekend rotation. Opportunities for teaching with nearby affiliated educational programs are available. Experience a rural lifestyle with abundant outdoor recreational opportunities. Also, another psychiatrist vacancy (OP/IP) exists in Harlan, Kentucky with our Harlan ARH Hospital with an excellent compensation package. E-mail your C.V. to: Kyle Hoskins, khoskins@arh.org or Christi Yercine: cyercine@arh.org or mail CV to Appalachian Regional Healthcare, Attn: G. Smock, 2285 Executive Drive, Suite 400, Lexington, Kentucky 40505 Tel: 1-800-888-7045 Our web address is www.arh.org. EOE

ARH®

LOUISIANA

BC/BE Psychiatrist

OCHSNER ST. ANNE GENERAL HOSPITAL is seeking:

- A BC/BE Psychiatrist for an employed position in Raceland, Louisiana
- Located 40 miles from New Orleans with a population of approximately 40,000
- Not-for-profit critical access hospital providing inpatient & outpatient services with high quality, cost-effective emergency, medical & surgical care
- Part of nationally renowned health system of 7 hospitals, 700+ member physician group, and 40 health centers
- Very competitive salary and benefits
- Family-oriented community with year-round outdoor activities
- Favorable malpractice environment in Louisiana
- Ochsner Health System is an equal opportunity employer.

Please email CVs to: profrecruiting@ochsner.org or call (800) 488-2240. Ref# APSTA09. EOE.

Inpatient Adult Psychiatrist

The Department of Psychiatry at Louisiana State University Health Sciences Center in Shreveport is seeking applicants for **Inpatient Adult Psychiatrist.** Applicants must be board eligible or board certified and able to obtain a Louisiana medical license. Basic responsibilities include direct patient care, teaching residents and medical students, and research. Department resources include a clinical trials unit, biological psychiatry lab, research access to MRI and PET scanners, 51-bed inpatient adult unit, 20 bed crisis unit, and private and public outpatient clinics. ACGME approved training programs include general psychiatry residency and advanced training in Psychosomatic, Forensic, and Child and Adolescent Psychiatry. Positions may be clinical or tenure tracked. Competitive university base salary, practice plan participation, and academic rank will be commensurate with training and experience. Shreveport is located in the northwest corner of Louisiana and offers diverse cultural and recreational opportunities in a pleasant climate. LSU HSC-S is an equal opportunity employer. Applicants should submit curriculum vitae with three professional references to:

LSU HSC-S
Rita Y. Horton, MD, Acting Chairman
Department of Psychiatry
1501 Kings Highway
Shreveport, LA 71103
Email: rhort1@lsuhsc.edu
Fax: 318-675-6148

MAINE

SOUTHERN MAINE

How would you like to be valued as part of a professional team for one of Southern Maine's largest mental health and community service based agencies where there is a strong commitment to staff, clients, and their agency mission?

Counseling Services, Inc. is a comprehensive and integrated community mental health center serving adults and children with serious mental health and substance abuse problems. Our programs include Complementary Therapies, Child and Family Primary Care Services, Adult and Family Primary Care Services, Primary Care Support Services, Psychiatric Services, Assessment Referral and Treatment, and Crisis Response Services.

We are currently recruiting for a part-time (up to 20 hours per week) psychiatrist to work with children and/or adults. The position will involve direct patient care at one or more of our community mental health centers located in Kittery, Springvale, Biddeford, and Westbrook. The physician will work with a multi-disciplinary team providing outpatient services to a variety of programs.

If you are aware of a qualified individual who would want to explore this exciting opportunity, please contact the Human Resources Department at 207-294-7104. A resume and cover etter may be sent to: Counseling Services, Inc., P.O. Box 1010, Saco, Maine 04072 or human.resources@csimaine.com. We are an equal opportunity employer.

Maine - Beautiful Northern
Leading behavioral health organization in Northern Maine seeks a Psychiatrist. Flexible schedule, 100% outpatient and limited call. Salary of $180,000 - 200,000, generous bonus structure and full and comprehensive benefit package. Full Support Staff. Can support visa requirements. Enjoy pristine living in this community offering year round activities, fine arts and nationally ranked schools.

Tammie Pepin
Alpha Medical Group
800.504-3411 tpepin@alphamg.org
View available opportunities at **www.alphaps.org**
Visit us at APA, Booth 2003

Adult and Child/Adolescent Psychiatrists
Nation's 1st Psychiatric Magnet Hospital seeking BC/BE psychiatrists for both our adult and child/adolescent inpatient and outpatient programs. We are a thriving, non-profit, private community-based hospital offering acute psychiatric care for adults and children, as well as chemical dependency programs. One of only two private psychiatric hospitals in Maine. We offer physicians clinical practice in a highly collaborative, multi-disciplinary setting. Competitive salary/benefit package. Send CV to: VP of Medical Affairs, The Acadia Hospital, P.O. Box 422, Bangor, ME 04402-0422.
www.acadiahospital.org

MARYLAND

"THE MARYLAND PLAN" is a nationally acclaimed program in public psychiatry. Positions are available for child and adult psychiatrists. Academic involvement with med. schools in your area of interest is encouraged. Please e-mail CV with area of interest and geographic preference to: GJordanRandolph@dhmh.state.md.us or mail to: Gayle Jordan-Randolph, M.D., Mental Hygiene Administration, Spring Grove Hospital, Dix Building, 55 Wade Avenue, Catonsville, MD 21228.

ARCC is looking for a Consulting Board Certified Psychiatrist to work in this fully integrated Co-Occurring Disorder Program servicing individuals who are substance addicted and mentally ill. Candidate will be responsible for evaluations, medication mgmt, case/team consultation, & training. Position is for a Psychiatrist/Medical Director 20-23 hours a week. Send cover letter & resume to Laura Winton at lauraw@rhd.org E.O.E

MASSACHUSETTS

High Point Treatment Center is seeking a 40 hr week psychiatrist for a 16-bed Inpatient Psychiatric Unit located in Plymouth, MA. Salary ranging from $170,000 - $190,000. No weekends, paid holidays and leave time. Health benefits available. If willing to work an additional 1 hr per day salary range would be $200,000 - $215,000. If interested, please contact Jim Horvath at 508-503-2455 or email to jim.horvath@hptc.org.

CAMBRIDGE: Adult Psychiatry

Positions available at Cambridge Health Alliance. The Department of Psychiatry at Cambridge Health Alliance is an appointing department at Harvard Medical School with excellent residencies in adult and child psychiatry. Our public health commitment to improving the health of our communities, coupled with a strong academic tradition, make this an ideal opportunity for candidates interested in caring for underserved populations in a rich clinical environment.

Adult Inpatient Psychiatrist - We are seeking a psychiatrist to join a collegial team and become an active member of a rich clinical department. This opportunity is a full-time inpatient psychiatrist position with clinical and teaching responsibilities for an inpatient team on an active community training service. Clinical care is provided through a multidisciplinary team approach with psychiatrist leadership. Academic appointment, as determined by the criteria of Harvard Medical School, is available for qualified candidates.

Weekend Moonlighting Psychiatrists: Lucrative and flexible opportunities available for attending psychiatrists to provide weekend/holiday coverage of inpatient units.

Qualifications: BE/BC, demonstrated commitment to public sector populations, strong clinical skills, team oriented, problem solver. Interest and/or experience with dual diagnosis patients a plus. Cambridge Health Alliance is an Equal Employment Opportunity employer, and women and minority candidates are strongly encouraged to apply. CV & letter to Susan Lewis, Department of Psychiatry, 1493 Cambridge Street, Cambridge, MA; Fax: 617-665-1204. **Email preferred: SLewis@challiance.org.**

INPATIENT PSYCHIATRY POSITION

Beth Israel Deaconess Medical Center in Boston, a 400 bed tertiary care teaching hospital of Harvard Medical School, is seeking an Inpatient Staff Psychiatrist to start July 1, 2009. The successful candidate will participate actively in clinical care and teaching on a 25 bed unit. The service is a major teaching site for Harvard Medical School and the Harvard Longwood Psychiatry Residency Training Program. Interest and experience in research is desirable. Women and underrepresented minorities are encouraged to apply. A Harvard Medical School appointment at the rank of Instructor, Assistant or Associate Professor is available commensurate with experience. Please send a letter of interest with three references and a CV to Rohn Friedman, M.D., Vice-Chairman of Psychiatry, 185 Pilgrim Road, Boston, MA 02215, Tel 617-632-0907, Fax 617-632-7990 or email rfriedma@bidmc.harvard.edu.

MEDICAL DIRECTOR - 80 bed hospital. General psychiatric, dual diagnoses & specialty programs for adults. Very competitive salary, benefits & opportunity for additional income over base. **No call.** Contact Joy Lankswert @ 866-227-5415; OR email joy.lankswert@uhsinc.com

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Starr Psychiatric Center seeks a 20-30 hr psychiatrist for dynamic established psychiatric practice On Boston's South Shore. Medical model, multi-disciplinary staff. Stimulating environment, good pay. Clinic has a reputation for successful care, where others have failed. Email davidzstarr@juno.com or call 508.580.2211.

South End Community Health Center seeks a part-time board certified or board eligible Psychiatrist to provide psychiatric/medical evaluation and medication follow up for an adult population at a behavioral health clinic in a Community Health Center. The population served by the clinic is a diverse racial, ethnic and socio-economic population with a range of mental health diagnosis. Bilingual in Spanish a plus. Send resume with salary requirements to hrdept@sechc.org, fax to 617-425-2090, or mail to South End Community Health, Attn: Human Resources, 1601 Washington Street, Boston, MA 02118. No phone calls please. Equal Opportunity Employer.

MARLBOROUGH, MASSACHUSETTS - UMass Department of Psychiatry is seeking candidates for a full time psychiatrist at its affiliated general hospital in Marlborough, Massachusetts. The position primarily involves providing treatment and clinical care supervision on the unit's superb partial hospital program and some amount of inpatient coverage. Our Department of Psychiatry has a large clinical faculty with clinical, teaching and academic opportunities at a wide variety of inpatient and outpatient programs. We have faculty development programs, commitment to our care, training and research missions, and a great living and learning environment in Central Massachusetts. If you want to know more about job opportunities or the department in general, please email psychiatryrecruitment@umassmemorial.org or fax to 508-856-5990. AA/EOE

BOSTON areas - Brookline, Jamaica Plain (Latino Program), & Westwood! Child & General Psychiatrists. Inpatient/partial programs. Staff & Admin/clinical positions. Salary, benefits & incentive plans. **NO CALL.** Contact Courtney Williams @ 866-227-5415 or email courtney.williams@uhsinc.com

MICHIGAN

GRAND RAPIDS - Staff Psychiatrist. 62 bed established private hospital with inpatient, partial & outpatient services. Collegial clinical care & work environment. Very competitive salary & full benefits. Contact Joy Lankswert @ 866-227-5415 or email joy.lankswert@uhsinc.com

Horizon Health seeks an **Associate Medical Director** for a 15-bed Adult Inpatient Psychiatric Program in **Alpena, MI.** Enjoy your practice in a state-of-the-art, 146-bed acute care facility with nearly 100 physicians, over 900 employees and approximately 300 volunteers. Federally-designated as a rural Regional Referral Center for all of Northeastern Michigan.

Practice opportunity includes easily attainable income of up to **$240-265K,** inclusive of salary and call reimbursement. In addition, **Productivity Bonus, Sign-On Bonus** and **Loan Repayment** included!

Alpena overlooks Lake Huron's picturesque Thunder Bay in northern Michigan, and is located on the Sunrise Side Coastal Highway, a 200-mile stretch of US 23 graced with scenic views, undeveloped wild areas, roomy beaches and recreational areas for hiking, biking, cross-country skiing and snowmobiling. Great place to raise a family and excellent quality of life! Contact: Mark Blakeney, Horizon Health, 972-420-7473, fax CV: 972-420-8233, or email mark.blakeney@horizonhealth.com. EOE.

MISSOURI

Staff Psychiatrist. Long-term inpatient. Scheduled admissions, no ER. Modern facility, dictated progress notes. Very competitive income with a low cost of living. Moving expenses and student loan payment available. Health and malpractice provided. Small city setting, less than an hour from Kansas City, 1/2 hour from K.C. airport. Medical school affiliation. Call: **James B. Reynolds, M.D. (816) 387-2503**

Commutable from Springfield -
Horizon Health is seeking a Psychiatrist for inpatient and outpatient work or all outpatient work in a very impressive general hospital in southwest MO. Unit is a 10-bed geropsychiatric program. Can offer salary w/benefits, or income guarantee, or contract with local physician's practice. Please **call Terry B. Good at 1-804-684-5661,** Fax #: 804-684-5663; Email: terry.good@psysolutions.com.

MONTANA

APRN or Psychiatrist

Intermountain Children's Home is an accredited, nationally-recognized MT non-profit agency that provides nurturing therapeutic environments for children under severe emotional distress. The main campus is nestled at the foot of the mountains on a 40 acre campus in beautiful Helena Montana and has dedicated the past 100 years to serving children throughout the country. Our outpatient clinic, serving children and adolescents, ages 5-21, is currently expanding services to better meet the needs of the Helena community and Tri-County area. We are now recruiting for a dynamic, highly-motivated, psychiatric APRN or Psychiatrist to provide outpatient assessments and psychotropic medication management, initially on a part time basis, with the potential for full time in the near future. The person hired for this position will be considered an employee of Intermountain, with liability insurance provided, an excellent benefit package, and competitive salary. If you are interested in restoring hope for these kids, please submit a resume to: Intermountain, 500 South Lamborn, Helena, MT 59601 or e-mail: mardieg@intermountain.org.
Please visit our web site for further information: www.intermountain.org Position is open until filled.

Horizon Health invites you to consider an exciting new practice opportunity for two NEW distinct **Adult** and **Geriatric** Inpatient Psychiatric Units, comprised of **26** total beds in **Helena, MT.** Nestled beneath the foothills of the Montana Rockies, **Helena,** the Capital of Montana, is alive with history and culture. This charming and beautiful Victorian city of 70,000 people provides a diverse attraction with many street festivals, theater, museums, symphonies, fairs and rodeos. There is truly something for everyone here! Excellent practice opportunity with great income ($200K+) and unparalleled quality of life! For more information contact: Mark Blakeney, Voice: 972-420-7473, Fax: 972-420-8233; email: mark.blakeney@horizonhealth.com EOE.

NEW JERSEY

Child/Adol. or Adult Psychiatrists

Child/Adol. or Adult Psychiatrists - needed for multi-disciplinary group in affluent communities in North/Central N.J. NO Managed Care! Call Dr. S. Reiter at 908-598-2400 x1 and fax CV to 908-598-2408.

P/T Adolescent/Adult Psychiatrist for small non-profit counseling center-6 hours per week - providing psychiatric evaluations and medication monitoring. Please send CV to: Irvcounseling@aol.com or Irvington Counseling Ctr, 21-29 Wagner Pl, Irv, NJ 07111 or fax to 973-399-7552

NEW YORK CITY & AREA

ALBERT EINSTEIN COLLEGE OF MEDICINE Of Yeshiva University Department of Psychiatry and Behavioral Sciences

The Sound View Throgs Neck Community Mental Health Center

PSYCHIATRISTS - Full-Time and Part-Time Adult Outpatient Program and Continuing Day Treatment and MICA Program. These Programs seek psychiatrists experienced in diagnostic evaluation and psychopharmacology to provide clinical care, supervise a team and teach medical students, psychiatry residents and clinical fellows. New York State License, Board Certified/Board Eligible in Psychiatry. DEA Registration. These positions carry a faculty appointment. Knowledge of Spanish a plus.

In return for your expertise, we offer a competitive salary, outstanding benefits package and a professional work environment offering career growth potential. For consideration, please submit your CV with salary history to: **Thomas F. Betzler, M.D., Executive Director, Sound View Throgs Neck Community Mental Health Center, 2527 Glebe Avenue, Room 304, Bronx, NY 10461; Fax: (718) 931-7307; Email: tbetzler@aecom.yu.edu . Equal Opportunity Employer.**

PSYCHIATRISTS

The City of New York Human Resources Administration's Customized Assistance Services is recruiting Psychiatrists for a unique program providing home-based psychiatric evaluation and crisis-intervention services. In this role, you will utilize a team approach to provide consultative evaluations throughout the City's five boroughs. This will often involve working on geriatric, emergency, and consult/liaison issues. Psychiatrists must possess a valid license to practice medicine in the State of New York, must have completed an approved residency training program in Psychiatry, and be Board Eligible/Certified.
This position offers regular hours, competitive pay, a collegial atmosphere, a minimum of paperwork, no managed care, and optional on-call duties for additional pay. Fringe benefits include health insurance, 401K, 457, defined benefit pension plans, and paid vacations and sick leave. Physician Loan Forgiveness programs may be available to eligible candidates.
Interested individuals should submit their curriculum vitae and a copy of their New York State Registration(s) to: **Johnny Bon, Director of Personnel Services, NYC Human Resources Administration, Customized Assistance Services, 2 Washington Street - 17th Floor, New York, New York 10004, E-mail: bonj@hra.nyc.gov, Fax: (212) 495-2931.** ***HRA/City of New York, an Equal Opportunity Employer***

Child and Adolescent Psychiatrist
P/T - 10-15 hours per week (evenings and/or weekends) in a Child and Family Mental Health Center in Brooklyn. Excellent compensation. No call. Fax resume to (718) 553-6769, or email to clinicaldirector@nypcc.org

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Manhattan OR Westchester-1 location
Child/Adolescent Assoc Medical Director
Inpt academic clinical care with leadership, & teaching. Daytime hrs; no call/wkends/ev's! 25 day LOS, little mg'd care, MD-ledstaff. AdolMD@gmail.com or 917-710-2456

Consult Liaison Psychiatrist

The Department of Psychiatry at The Mount Sinai Medical Center in the heart of NYC, has an opening for a CL Psychiatrist beginning July 1, 2009. The position includes both inpatient and outpatient consultation liaison work, supervision of residents and fellows and opportunities for teaching and clinical research. The position will include an academic appointment commensurate with experience. Qualified candidates will possess an MD or DO degree, be board eligible or certified in General Adult Psychiatry and preferably have advanced training in Psychosomatic Medicine. The Mount Sinai Medical Center is a premier 1,171 bed tertiary-care facility internationally acclaimed for excellence in clinical care, education and scientific research in nearly every aspect of medicine.

Interested applicants should contact Dr. Kim Klipstein, Director of Behavioral Medicine and Consultation Psychiatry at 212-659-8712 or email kim.klipstein@msssm.edu.

Premier HealthCare

BC/BE Psychiatrists

Child/Adolescent or Adult
Throggs Neck, Bronx or Sheepshead Bay, Brooklyn or Queens, NY
Half Time or Fee for Service

YAI/Premier HealthCare is a nationally recognized, well-established NYC diagnostic & treatment center for people with developmental disabilities and their families.
Sheepshead Bay, Brooklyn; Throggs Neck, Bronx or Queens, New York.
This is an opportunity to work with a professional staff of doctors and nurses in a multi-cultural, team environment. Growing field for learning. Send CV to: Karen Meyers, Clinical Recruiter, Premier HealthCare, 460 West 34 Street, N.Y., N.Y. 10001 Fax 212-563-4836 Email: kmeyers@yai.org

NEW YORK STATE

ELMIRA PSYCHIATRIC CENTER
Adult and Adolescent Psychiatrists

Board Certified - $172,269 - $176,903
Licensed Physician - $141,751
Limited Permit - $107, 318 - $115,905

- All positions **M-F 8-4:30** with **no managed care insurance demands**
- **Optional** participation in a low stress on-call program with **potential** to earn up to an **extra $74,000/year**
- Student loan repayment available
- Excellent NYS benefits package
- Inpatient, Outpatient and Day Treatment services
- Our location offers: quality housing prices; little traffic; regional airport; Cornell University; 4hr drive to NYC, Toronto & Philadelphia; 5 ½ hr drive to Boston & DC; less than 1hr to Finger Lakes

For further info contact: Patricia Santulli, Director of Human Resources at: Elmira Psychiatric Center, 100 Washington Street, Elmira, NY 14901 or e-mail: elpopms@omh.state.ny.us or
call: (607) 737-4726 or fax: (607) 737-4722
An AA//EOE Employer

New York - Beautiful Upstate
Psychiatrist sought to join a community-based Psychiatric service. Sub-specialty training in C&A, Geriatric or Addiction will be considered. Salaried position with income potential in excess of $250,000. 100% outpatient with no call. Comprehensive benefit package includes paid time off, CME, malpractice, all insurances, and relocation assistance.

Jim Hock
Alpha Medical Group
800.504-3411 jhock@alphamg.org
View available opportunities at
www.alphaps.org
Visit us at APA, Booth 2003

GLENS FALLS - SARATOGA SPRINGS, NY - Glens Falls Hospital seeks a BC/BE Psychiatrist to join an integrated outpatient psychiatry team consisting of 8 Psychiatrists, and a team of nurses, and social workers. Primary duty is outpatient psychiatry; also provide consults to general medical units and back up to inpatient Behavioral Health Unit. Call is 1:6 with primary ED response by dedicated adjunct staff. Competitive salary and full benefits package. Situated near the Adirondacks, Lake George, and Saratoga, you have access to hiking, boating, skiing, and numerous cultural opportunities year-round. Only 3 hours to NYC, Boston, and Montreal. Send CV to Jennifer Metivier, Physician Recruiter at 518-926-1946 or jmetivier@glensfallshosp.org.

Child Psychiatry/Adult Psychiatry: St. Lawrence Psychiatric Center, a fully accredited EO-AAE, seeks BC/BE Psychiatrists licensed to practice medicine in NYS (or eligible to obtain NYS license) to work in our Massena Children and Adolescent Outpatient Clinic, Children and Youth Inpatient, Ogdensburg Adult Outpatient Clinic, Gouverneur Adult Outpatient Clinic, and Adult Inpatient. We are designated by the Federal Government as MHPSA. In addition to salary ($161,750 to $174,198) and guaranteed additional compensation by voluntary participation in an on-call program, we offer an excellent benefit package including: health insurance, paid vacation, holiday and sick time, an excellent retirement plan and educational and professional leaves.

Situated on the scenic St. Lawrence Seaway in northern New York, St. Lawrence Psychiatric Center is located in Ogdensburg, an idyllic rural community offering many cultural, educational and economic opportunities. Historic and international metropolitan cultures are a reasonable driving distance away in Ottawa and Montreal, Canada, and Syracuse, NY, or travel by train from Brockville to Toronto to enjoy many multi-cultural events. Ogdensburg's location on the St. Lawrence River and close proximity to the Adirondack Mountains and Canada offers easy access to a wide variety of unspoiled natural areas and rich cultures and provides abundant recreational opportunities throughout the year.

Submit letter of interest to: Rosella Turnbull, St. Lawrence Psychiatric Center, One Chimney Point Drive, Ogdensburg, NY 13669 or at slmrrmt@omh.state.ny.us. If you have questions, please call (315) 541-2189.

NORTH CAROLINA

Medical Director - Inpatient Services
Open Rank
Department of Psychiatric Medicine
The Brody School of Medicine at East Carolina University

The Department of Psychiatric Medicine at the Brody School of Medicine at ECU is accepting applications for a full-time faculty position to serve as Medical Director for Inpatient Services, one of our major teaching sites. The position emphasizes a clinical leadership role and an active interest in educational and scholarly activities. This 52 bed service houses acute beds, combined MI-DD beds, and combined Med-Psych beds in an 800 bed tertiary care hospital serving Eastern and coastal North Carolina. The hospital provides acute, intermediate, rehabilitation, and outpatient health services to more than 1.2 million people in 29 counties. Requirements include MD or equivalent degree, completion of accredited psychiatric residency training in psychiatry, board certification in Psychiatry, and at least five years progressive experience in administrative psychiatry, with a minimum of 3years in an inpatient setting. Salary and academic rank commensurate with experience and academic background. Please send letters of interest and a CV to: John M. Diamond, M.D., Chair Search Committee, Department of Psychiatric Medicine, Brody School of Medicine at ECU, 4E-94B Brody Building, 600 Moye Blvd., Greenville, NC 27834, telephone 252-744-2673, e-mail: diamondj@ecu.edu Additionally, applicants are required to submit an on-line application to **www.jobs.ecu.edu** (position #966016) with attached cover letter, CV, and list of references. East Carolina University is an AA/EO Employer.

Fantastic Practice Opportunity in a Great Location - Live in Greensboro or Winston-Salem - Due to expansion of psychiatric services, we are seeking another psychiatrist already in practice who wants to add on some inpatient work, or we can offer an income guarantee to help a psychiatrist get their practice going. Great quality of life; great income potential. Please **call Terry B. Good at 1-804-684-5661,** Fax #: 804-684-5663; Email: terry.good@psysolutions.com.

The Department of Psychiatry and the Lineberger Comprehensive Cancer Center of the University of North Carolina (UNC) School of Medicine at Chapel Hill are seeking an early career psychiatrist to join the UNC Psycho-oncology Service. This is a full time fixed-term position at the (Clinical track) Clinical Assistant or Clinical Associate Professor level. This clinical service is a component of the UNC Comprehensive Cancer Support Program.

The major expectation for this position will be the provision of excellent psychiatric care to patients at the North Carolina Cancer Hospital and other venues served by School of Medicine and UNC Lineberger Comprehensive Cancer Center. Responsibilities will include: providing inpatient and outpatient clinical consultation and psychiatric management for cancer patients; medical leadership for a multidisciplinary psycho-oncology team; teaching medical students, residents, and other health care trainees and clinicians; and participation in the clinical research activities of the Comprehensive Cancer Support Program.

The successful candidate should have strong clinical skills, a record of scholarly achievement; evidence of effective leadership and demonstrated ability to promote a collegial environment that fosters ongoing collaboration. Candidates should have clinical experience working with cancer patients as evidenced by completion of a fellowship in psycho-oncology or psychosomatic medicine, or similar training at the interface of psychiatry and medicine. Special consideration will be given to candidates with an established record of extramural funding.

Applicants must have an M.D. and be eligible for North Carolina licensure. Rank and salary will be commensurate with experience. Applicants should forward curriculum vita and three letters of reference to Donald L. Rosenstein, M.D., Director, Comprehensive Cancer Support Program, 3134 Physicians Office Building, 170 Manning Drive, CB# 7305, The University of North Carolina at Chapel Hill, Chapel Hill, NC 27599-7305 The University of North Carolina at Chapel Hill is an Equal Opportunity employer.

The Department of Psychiatry of The University of North Carolina School of Medicine at Chapel Hill is seeking an established clinical researcher to develop and serve as Director of the Department's Center of Excellence in Anxiety and Stress Related Disorders. This is a full time tenure track/tenured position at the Associate Professor or Full Professor level. Responsibilities will include: designing and providing leadership to a multidisciplinary clinical program focusing on the treatment of Anxiety Disorders; clinical training and teaching in this area to psychiatry residents and fellows, medical students and other health care trainees and clinicians; implementation of a program of clinical research.

The successful candidate should have strong clinical skills, an established record of scholarly achievement including peer-reviewed publications, an established program of research, and a successful history of extramural grant funding; evidence of effective leadership and demonstrated ability to promote a collegial environment that fosters ongoing collaboration. Special consideration will be given to candidates with an established record of extramural funding.

Applicants must have an MD and be eligible for North Carolina licensure. Rank and salary will be commensurate with experience. Applicants should forward curriculum vita and four letters of reference to David R. Rubinow, M.D., Meymandi Distinguished Professor of Psychiatry and Chair, Department of Psychiatry, C/O Sandi Crawford, EPA Manager, Campus Box 7160, University of North Carolina, Chapel Hill, NC 27599-7160. The University of North Carolina at Chapel Hill is an Equal Opportunity Employer.

Private Practice, well est. in small southern town located near Blue Ridge Mtn. and minutes from Charlotte. Need full/part-time psychiatrist out-patient, Competitive salary. Required board certification or eligibility. Please fax or mail resume to Foothills Consulting Assoc. P.O. Box 1418 Shelby, North Carolina 28150.

Private Practice Opportunities in North Carolina

Carolina Partners in Mental HealthCare, PLLC is seeking BE/BC psychiatrists for our practices in Raleigh, Cary, and Wake Forest, NC. Child/adolescent and/or adult psychiatrists welcome. Private outpatient practices, full partnership from day one - no investment required. FT, PT flexible. Carolina Partners has ten offices in Raleigh, Durham, Cary, Chapel Hill, Pittsboro and Wake Forest, North Carolina. Good opportunity to control your life and clinical practice, while making a good income! Contact Executive Director or send CV to: Carolina Partners in Mental HealthCare, 1502 W. Hwy 54, Suite 103, Durham, NC 27707. Phone 919-967-9567; Fax 919-882-9531; Email carolinapartners@bellsouth.net. Please visit our website located at carolinapartners.com

NORTH DAKOTA

Join Prestigious Upper Midwest Medical Group

MeritCare Health System of Fargo, ND is seeking an Adult Psychiatrist to join its multi-disciplinary Psychiatry Department. Faculty appointment and teaching of psychiatry residents is available through University of North Dakota School of Medicine. MeritCare is an integrated 450-physician, multi-specialty group practice, 583-bed, Level II tertiary/trauma hospital with 27-primary care clinics in two states. Sister cities, Fargo, ND and Moorhead, MN, are a tri-college community of 190,000 located near the heart of Minnesota's lake country. Fargo-Moorhead offers excellent educational systems, recreation and sports activity as well as a variety of entertainment and cultural events. This is an excellent opportunity with a competitive compensation and benefits package being offered. This is not a designated HPSA site. To learn more about this practice opportunity visit our website at www.meritcare.com or contact:

Jean Keller, Physician Recruiter
MeritCare Health System
P O Box MC
Fargo, ND 58122-0385

Phone: 701-280-4853
Fax: 701-280-4136
Email: Jean.Keller@meritcare.com

OHIO

COLUMBUS, OHIO
Mount Carmel Health, the second largest hospital system located in Columbus, Ohio, is seeking a 5th staff psychiatrist for the hospital system. This position provides a variety of patient care opportunities, from a 20 bed adult/geriatric inpatient unit to outpatient appointments. The adult psychiatric unit in the Mount Carmel West facility houses behavioral health, extended care; and medical rehabilitation.

Please consider these career advantages:
- Hospital employment.
- Growing base of primary care physicians.
- CNS nurses
- Call 1:5
- Medical student and resident teaching opportunities.
- Outpatient office located on the hospital campus.
- Very attractive compensation and benefit package.

Mount Carmel is a great place to expand your professional career and Columbus is an ideal place to live and raise a family. For more information, please contact:
Julie Hotchkiss, Manager Physician Recruitment; 614-546-4398 or jhotchkiss@mchs.com.

Attractive Salary with Benefits Plus Generous Sign-on Bonus - 30 minutes from Dayton suburbs - easy drive to Indianapolis - Expanded adult and geropsych services in an extremely impressive med/surg hospital (gorgeous brand new facility). Join top-notch medical staff. Services include inpatient, outpatient and IOP. Please call **Terry B. Good at 1-804-684-5661,** Fax #: 804-684-5663; Email: terry.good@psysolutions.com. EOE

OKLAHOMA

PSYCHIATRIST POSITION

Jim Taliaferro Community Mental Health Center, Oklahoma Department of Mental Health and Substance Abuse Services, is seeking a BE or BC Psychiatrist. Located in southwestern Oklahoma, Lawton is the fourth largest metropolitan area in Oklahoma with a population of 114,916 and 90 miles from Oklahoma City Metro. Area attractions include Lawton Community Theater, Lawton Philharmonic Orchestra, Cameron University, Fort Sill Army Installation, Wichita Mountain Wildlife Refuge, and numerous lakes. Excellent salary and benefits to include health, dental, and retirement plans. Base salary is $185,000 (BE) and $195,500 (BC) with additional potential income of $46, 000 per annum for on-call services. Eligible H-1B visa psychiatrist applicants welcome. Mail or fax CV to HR, ATTN: Sam Banks, Jim T aliaferro Community Mental Health Center, 602 SW 38th St. Lawton, OK 73505, (f): (580) 248-3610, (p): (580) 248-5780. EOE.

PENNSYLVANIA

Psychiatrists:

Currently we have exciting full- and part-time positions in a rapidly expanding department. Opportunities include responsibilities in and outside our five-hospital health system. There are immediate openings for child/adolescent, adult and addictions psychiatrists.

There are also practice options in a traditional psychotherapy model. Evening and weekend positions also available. Excellent salaries, no on-call nor rounding responsibilities ever and exceptional benefits package offered. Send CV to Kevin Caputo, M.D., Vice President and Chairman, Department of Psychiatry, Crozer-Keystone Health System, One Medical Center Blvd., Upland, PA 19013 or contact the department manager, Kathy Waring at 610-619-7413

Horizon Health, in partnership with **St. Vincent Health Center (Voted 5th Best Place to work in Pennsylvania!),** a 436-bed tertiary care hospital in **Erie, PA,** has an exciting opportunity for a **Medical Director** for a **32-bed** Adult and Geriatric Inpatient Psychiatric Program.
Opportunities for input and growth, tertiary care, teaching opportunities in FP residency program and LECOM medical school. Excellent compensation package with full benefits.
Located on the shores of **Lake Erie** with 7 miles of beaches, Erie is the **fourth largest city** in Pennsylvania with a metropolitan population of 280,000. For more information contact: Mark Blakeney, Voice: 972-420-7473, Fax: 972-420-8233; email: mark.blakeney@horizonhealth.com EOE.

Medical Director
Ashland, PA

Horizon Health, in partnership with **St. Catherine Medical Center** in Ashland, PA is seeking a **Medical Director** for a brand new, 14-bed Adult inpatient psychiatric unit.

Ashland is located in eastern Pennsylvania in a region that is rich with the history of America's pioneers, and is an outdoor enthusiast's playground. The world famous cheese steaks of Philadelphia and outlets of Reading are less than 90 miles away, and there is easy access to the excitement of Manhattan.

Become a pioneer and get in on this truly unique ground floor opportunity! For more information contact: Mark Blakeney, Voice: 972-420-7473, Fax: 972-420-8233; email: mark.blakeney@horizonhealth.com EOE.

Erie, Pennsylvania
Practicing Psychiatrists for the position of Psychiatry Residency Program Director. Child/Adolescent, Adult and Geriatric Psychiatrists positions are available. Fellowship Trained Geriatric Psychiatrist preferred for the Gero Unit. Millcreek Community Hospital has the region's only Adult and Child/Adolescent Behavioral Program with 62 inpatient psychiatric beds including a new geriatric unit. Interested candidates for the Residency Program Directorship must be Board Certified by the AOA in Psychiatry. Candidates for other staff psychiatry positions must be AOA or AMA Board Certified or Board Eligible. Please send CV's and information requests to: mchmeded@mch1.org or call 814/868-8217.

PITTSBURGH - Opportunities for Adult and Child Outpatient Psychiatrists at Mercy Behavioral Health. We are celebrating our 40th anniversary and continue to experience tremendous growth. Our financially solid organization offers competitive compensation and an excellent benefits package all with a flexible schedule. Contact Jim Jacobson, MD at 412-488-4927 or email JJacobson@mercybh.org.

PHILADELPHIA - Child Psychiatrist - Partial Day Program in Bucks County.
CLARION & SHIPPENSBURG - General Psychiatrists for Adult inpatient & partial program services. Fulltime positions. Salary, benefits and incentive plans. Contact Joy Lankswert @ 866-227-5415; OR email joy.lankswert@uhsinc.com

RHODE ISLAND

Outstanding opportunities offer a collegial academic environment in the major psychiatric teaching facility of the Warren Albert School of Medicine at Brown University, located in Providence, RI.

Inpatient Psychiatrist

Fulltime position available for board eligible/certified inpatient psychiatrist interested in clinical faculty position at Butler Hospital. Salary and clinical faculty appointment commensurate with experience. Apply by sending CV to Steven_Rasmussen@brown.edu .

Child and Adolescent Psychiatrist

Fulltime position available for board eligible/board certified child and adolescent psychiatrist. The position entails inpatient practice in an exciting clinical/educational/research environment. The Department of Child and Adolescent Services provides an integrated collegial staff of six other board certified child psychiatrists. Please contact: Charles E. Staunton, M.D., Associate Medical Director, e-mail: cstaunton@butler.org, (401) 455-6226, FAX: (401) 455-6604

Butler Hospital
345 Blackstone Blvd
Providence, Rhode Island 02906

Butler Hospital is an Equal Opportunity Employer
A Care New England Hospital

SOUTH CAROLINA

The South Carolina Department of Mental Health has opportunities for psychiatrists located throughout the state. For an opportunity to discuss them at the APA conference contact Dr. Brenda Ratliff at 803-215-1070, or Ed Spencer at 803-667-1016. Comparable salaries and excellent benefits. www.state.sc.us/dmh EOE

TENNESSEE

EAST TENNESSEE STATE UNIVERSITY
JAMES H. QUILLEN COLLEGE OF MEDICINE
DEPARTMENT OF PSYCHIATRY & BEHAVIORAL SCIENCES

GENERAL PSYCHIATRIST AND CHILD PSYCHIATRIST

Full-time position available for General Psychiatrist. Additional fellowship training desired, but not required. Position may include inpatient and/or outpatient. Responsibilities include training of psychiatric residents and medical students and research activities. Salary is competitive with funding available through the Medical School, faculty private practice and extramural contracts. ETSU is located in the Tri-Cities area, rated #1 place in North America in cost-of-living, crime rate, climate and health care. **Applicants should submit a CV and two letters of reference to Merry N. Miller, M.D., Chair, Department of Psychiatry and Behavioral Sciences, ETSU, Box 70567, Johnson City TN 37614. Telephone inquiries should be made at (423)439-2235 or e-mail at lovedayc@etsu.edu. AA/EOE.**

TEXAS

SAN ANTONIO, TEXAS - Private practice opportunity to join an established outpatient practice of 3 psychiatrists and 5 therapists. Overhead covers office and staff. Ability to custom tailor practice for new or established psychiatrist. Contact: Vikki Vaiani at 210-699-8881 -Ext 19 or VikkiVaiani@hotmail.com

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AUSTIN GERIATRIC PSYCHIATRY, Thriving private practice of two Physicians, three NP's, a PA and CNS, and five CMSW's. Office, nursing and assisted living facilities, clinical research and TMS Therapy! Unique and cutting edge in beautiful Central Texas Hill Country. Great job with negotiable income, benefits and hours. CV and three references to jw@senioradults.net. Come and grow with us. www.senioradults.net

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PSYCHIATRISTS: Mental Health Mental Retardation Authority of Harris County (MHMRA) in Houston, Texas is one of the largest mental health centers in the United States. Demands have created the need for additional psychiatrists throughout the Agency.

Northwest Outpatient Clinic
Work 8 to 5 Monday through Friday
Perform psychiatric evaluations & treatment in clinic setting
No on call

Harris County Jail
Day shift or 2:00 PM to 10:00 PM
Perform psychiatric evaluations & medication management
Some on call at 24/7 facility

Texas licensure is required for all positions

MHMRA offers competitive salary plus a generous benefit package. Houston offers excellent quality of life, lower than average cost of living, no state sales tax and exciting cultural, entertainment, sporting and tourists venues.

Contact Charlotte Simmons at (713) 970-7397, or submit your C.V. to charlotte.simmons@mhmraharris.org or fax: 713-970-3386

DALLAS: In-house Night Physician. Monday - Thursday. Independent contractor position.
SHERMAN (just north of Dallas near Lake Texoma): Outstanding Private practice opportunity - inpatient & outpatient. Income guarantee & practice start-up support.
WEST TEXAS San Angelo: Private practice opportunity. Income guarantee & practice start-up support. Administrative title & duties available with additional financial stipend. Joy Lankswert @ 866-227-5415 or email joy.lankswert@uhsinc.com

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HOUSTON, TX AREA (THE WOODLANDS, TX) PSYCHIATRIST/CHILD AND ADOLESCENT PSYCHIATRIST, FT TX license required; Private practice; Mostly Child and Adolescent and Adult population, very few Geriatric Pts. Looking for partner with potential ownership in the practice. E-mail: shara@psixp.com or call 713.385.4187

UTAH

UNIVERSITY OF UTAH SCHOOL OF MEDICINE, DEPARTMENT OF PSYCHIATRY: Academic physicians are being sought for six positions at the Instructor, Assistant, Associate and Professor levels, in the clinical track. All successful applicants will be expected to participate in the teaching of psychiatric residents and medical students and contribute toward their salary through clinical activities and/or grant support. Individuals with diverse clinical and research interests will be considered. Expertise in adult inpatient and/or outpatient psychiatry, with interest in geriatric and addiction psychiatry, would present the best fit. Send CV and three professional references to William M. McMahon, M.D., Professor and Chair of Psychiatry, Univ. of Utah, Dept. of Psychiatry, 30 N. 1900 E., Suite 5R210, Salt Lake City, UT 84132. The University of Utah is an Equal Opportunity Affirmative Action employer and encourages applications from all qualified individuals- including women and minorities-and provides reasonable accommodation to the known disabilities of applicants and employees.

VIRGINIA

Inpatient/Outpatient Psychiatrist
Virginia Commonwealth University, Department of Psychiatry, School of Medicine, is recruiting a Virginia license-eligible BE/BC psychiatrist for adult attending psychiatry faculty position in the Division of Inpatient Psychiatry. Will work as inpatient/outpatient attending and will be responsible for administration and clinical care as well as teaching and supervision of medical students, residents and fellows. The selected candidate will have community outpatient clinic teaching responsibilities for medical students, psychiatric residents and other trainees. The VCU, Department of Psychiatry employs over 70 fulltime faculty and has well-funded research in genetics, addictions, child and women's mental health and psychopharmacology. VCU is a large urban university with robust health science campus and 750-bed university hospital. Richmond, the State Capital, has moderate climate and rich mix of history with modern facilities, excellent suburban housing, and top public/private schools. The internet provides comparative cost of living. J-1 applicants welcome. Send CV to Anand Pandurangi, MD, c/o Marie Baker-Roach, Human Resources, Department of Psychiatry, VCU, Box 980710, Richmond, VA 23298.
VCU is an Equal Opportunity/Affirmative Action employer. Women, minorities, and persons with disabilities are encouraged to apply.

Come Work & Play in the Mountains!

Centra Health, located in Lynchburg, Virginia, is seeking a board certified/eligible **general/adult psychiatrist** for its expanding mental health programs.

Duties include:
- seeing patients in our outpatient practice
- facilitating admissions to our acute inpatient program
- sharing call 1:7 with our psychiatric team

Centra provides the most comprehensive array of mental health programs in the Commonwealth and an unrivaled continuum of mental health and substance abuse services.

A not-for-profit healthcare system comprised of Virginia Baptist, Lynchburg General, and Southside Community Hospitals, Centra provides a guaranteed and competitive base salary and incentive bonus along with an excellent benefit package.

Located in Central Virginia on the James River, in the foothills of the Blue Ridge Mountains, the area offers a temperate climate, distinguished schools, a wide variety of activities and amenities, and a high quality of life.

For more information, contact Bill Semones, Vice President, Mental Health Services, at 434-200-4514 or bill.semones@centrahealth.com

FACILITY MEDICAL DIRECTOR

Eastern State Hospital (ESH), a Joint Commission Accredited Hospital, seeks a BC/BE psychiatrist licensed by the Virginia Board of Medicine. Our new Geriatric Center (150 beds) opened April 2008; the Adult Mental Health Center (150) beds), under construction, opens June 2010.

Candidate will provide direction, oversight and supervision of all Clinical Departments; Psychology, Social Work, Psychosocial Rehabilitation; and supervision and coordination of activities of the Medical Staff. Demonstrated knowledge and experience in administrative and clinical activities in the field of mental health required. Must be experienced and knowledgeable of joint Commission Standards and CMS Regulations. Candidate will also facilitate a broader clinical interface with other facility and community service entities. Educational affiliations include the College of William & Mary, and Eastern Virginia Medical School.

Salary range $175,000-220,000 accompanied by comprehensive state benefits package (paid malpractice, disability, and life and health insurance). ESH has been in continuous operation for 235 years!

Send CV's to:
Human Resources Department
Eastern State Hospital
4601 Ironbound Road
Williamsburg, VA 23188-2652
Tour: www.esh.dmhmrsas.virginia.gov
To apply on line:
https//jobs.agencies.virginia.gov
(757) 253-5411
(757) 253-4996 fax

EOE

PSYCHIATRIST
No Call!
Sign-On Bonus!

Catawba Hospital is accepting applications from BE/BC Psychiatrists interested in joining an outstanding medical staff in a 110-bed, Joint Commission accredited, psychiatric hospital. Academic affiliation exists with the Residency Program of the University of Virginia School of Medicine's Department of Behavioral Medicine & Psychiatry. Experience with serving adult and/or geriatric patients with severe mental illness is desired. Applicants must be licensed or eligible for licensure in Virginia. No call required.

Located just minutes from the metropolitan community of Roanoke, VA, the area provides excellent recreational, educational, and cultural opportunities in the Blue Ridge Mountains:
- one of the ten best places to raise a family in the United States (Parenting magazine);
- ranked among the least stressful locations in the United States (Zero Population Growth, Inc.);
- 7th healthiest place to live (Kiplinger's Personal Finance Magazine);
- one of the nation's top 20 cities for quality of life (recent University of Kentucky study).

Salary up to $175,000/year based on experience and expertise.

In addition, the generous state employee benefits package brings your total compensation to the equivalent of $246,000/year.

- Malpractice covered by the Commonwealth of VA
- Financial assistance with moving expenses

No J-I positions available. Position will remain open until filled.

For telephonic/e-mail inquiries contact:

Gary Hiler, Human Resource Manager
(540) 375-4368

gary.hiler@catawba.dmhmrsas.virginia.gov

Submit CV to:

Human Resource Office
CATAWBA HOSPITAL
P.O. Box 200
Catawba, VA 24070-0200
TDD(540)375-4385
FAX(540)375-4359

EOE M/F/H/V

VIRGINIA BEACH

Board certified psychiatrist to join 1 psychiatrist and 3 therapists in well-established out-patient practice caring for children adolescents and adults. Opportunity for ownership in several years. Contact Dan Darby, MD at Tel: (757) 425-5050 Fax: (757) 425-1389.

WASHINGTON

Western Washington State: Adult/Geriatric/Forensic Psychiatrist (BE/BC with a WA state license) applications considered. Western State Hospital is a fully accredited (JCAHO) and certified (CMS) 997 bed hospital serving adult, geriatric and forensic populations. Annual salary up to $158,304 DOQ. Excellent benefits, including hospitalization/medical insurance, retirement and vacation leave, plus optional deferred income plan. Send CV to Leah Muasau, Medical Staff Coordinator; Western State Hospital; 9601 Steilacoom Blvd. SW; Lakewood, WA 98498-7213. E-Mail: MUASALL@DSHS.WA.GOV.

WEST VIRGINIA

Psychiatrist
(J-1 slot available)

Westbrook Health Services, a Comprehensive Community based, not for profit behavioral health center located in the Mid-Ohio Valley is recruiting a Psychiatrist. Outpatient and Inpatient work available.

Metro area of 150,000. A great place to raise a family. Good schools, including colleges and universities. Very low crime rate. Practice where you are wanted and appreciated. For details, call or send your CV to:

Dr. Amelia McPeak, Medical Director
Westbrook Health Services
2121 Seventh Street
Parkersburg, WV 26101
Phone: 304-485-1721 ext 273
Fax 304-422-0908
E-mail: amcpeak@westbrookhealth.com

Shenandoah Valley-3rd psychiatrist for multidisciplinary behavioral health service 90 minutes from DC/Baltimore. Experience/training in addictionology, child/adolescent psychiatry preferred. Salaried position w/incentive compensation, benefits. Community Health Center HPSA status offers potential Federal Loan Repayment. Contact Tina Burns 304 596 2610, ext 1066; tburns@svms.net FAX 304 263 0984.

WISCONSIN

Marshfield Clinic has openings for BE/BC Adult Psychiatrists to join our expanding services in Marshfield, Minocqua and Eau Claire. At our Marshfield campus, candidates with fellowship training in neuropsychiatry, geriatric or consultative psychiatry are preferred. Our regional center practices are primarily outpatient practices with a mix of C/A and adult patients. With highly skilled and dedicated allied providers and support staff, Marshfield Clinic psychiatrists employ a multidisciplinary team approach to their practice. Marshfield Clinic offers a competitive compensation package.
If you are interested in these opportunities please contact:
Beth Albee
Physician Recruitment
Marshfield Clinic
1000 N. Oak Avenue
Marshfield, WI 54449
(800) 782-8581 ext. 19775
Fax (715) 221-9779
www.marshfieldclinic.org

CHIEF PSYCHIATRIST

Waukesha County Health and Human Services is presently recruiting for an individual to join our medical staff as the Chief Psychiatrist. The Chief Psychiatrist reports to the Clinical Director and provides direction to a number of staff psychiatrists in a variety of inpatient and outpatient mental health and AODA programs. Responsibilities also include direct patient care and participation in the planning and development of the county's behavioral health system, using evidence-based practices, person-centered planning, and recovery principles.

Educational requirements are possession of a degree from a recognized medical school, completion of an approved internship, completion of three years of approved residency training in psychiatry and possession of or eligibility to obtain a license to practice medicine in the State of Wisconsin. Board certification in psychiatry or eligibility required.

The annual salary range for the Chief Psychiatrist position is $180,921 - 209,737 . Our benefit package includes vacation, holidays, sick time, health, dental and life insurance, CME time, deferred compensation program, professional liability insurance, retirement program and the opportunity for private practice on site.

Waukesha County (pop. 380,000) is located in southeastern Wisconsin, thirty minutes from downtown Milwaukee, two hours from downtown Chicago, and one hour from Madison. The city of Waukesha was named one of the 2006 Money Magazine Best Places to Live.

Interested individuals should contact Dr. Michele Cusatis at 262-548-7950 or at mcusatis@waukeshacounty.gov for more information about the position.

For information about the benefits package, contact Renee Gage, Senior Human Resources Analyst, in our Human Resources Department at 262-548-7053 or at rgage@waukeshacounty.gov.

Applicants should submit a CV to our Human Resources Division at:

Waukesha County
Administration Center
Human Resources
515 W Moreland Blvd, Rm 160
Waukesha, WI 53188
(262) 548-7044
Hearing Impaired Number (262) 548-7903
Equal Opportunity Employer
www.waukeshacounty.gov/employment

International

AUSTRALIA & NEW ZEALAND
PSYCHIATRY JOBS
Gen. Adult - Child & Adoles. - Forensics
Locum Tenens or Permanent Jobs
Salary = $250-350,000 per annum
www.IMRpsychiatry.com

Fellowships

Anxiety Disorders Fellowship at Massachusetts General Hospital

The Center for Anxiety and Traumatic Stress Disorders at the Massachusetts General Hospital is offering a 1-2 year clinical and research psychiatric fellowship in the anxiety and traumatic stress disorders. Trainees will participate in a range of research, clinical and academic activities. Interested candidates should please send a letter of interest and CV to Mark Pollack, MD at mpollack@partners.org

POSITION: Geriatric Psychiatry Fellowship
SPONSOR: University of Rochester Medical Center, Department of Psychiatry
DESCRIPTION: The University of Rochester program in Geriatrics and Neuropsychiatry offers one-year PGY-5 clinical fellowships in Geriatric Psychiatry. Ours is an ACGME accredited program, successful completion of which makes graduates eligible for the ABPN subspecialty examination in geriatric psychiatry. In addition, a two-year Interdisciplinary Geriatrics Fellowship is available that integrates the core disciplines of psychiatry, medicine, and dentistry and prepares trainees as clinical educators. Both fellowships offer training in the care of older patients in a variety of inpatient, long-term care, clinical, consultation, and palliative care services. Supervised clinical experiences are complemented by a didactic program, elective offerings, and opportunities to develop individual scholarly interests. In addition to the breadth of our clinical programs and patient populations, we have a large cadre of experienced and nationally recognized clinicians and researchers serving on our faculty. We pride ourselves on providing a stimulating, rewarding educational experience in a supportive and nurturing environment. Applications are now being accepted for the 2010/2011 academic year.
CONTACT: For more information, please contact Jeffrey M. Lyness, M.D., Director, Geriatric Psychiatry Fellowship, Department of Psychiatry, University of Rochester Medical Center, 300 Crittenden Boulevard, Rochester, NY 14642-8409 Phone: 585.275.6741; Fax: 585.273.1082; E-Mail: Jeffrey_Lyness@urmc.rochester.edu Website: www.urmc.rochester.edu/smd/psych/educ_train/fellowship/geriatrics/index.cfmThe University of Rochester is an equal opportunity/affirmative action employer.

Forensic Psychiatry Fellowship

University of Massachusetts Medical School

UNEXPECTED OPENING: The University of Massachusetts Medical School (UMMS) Department of Psychiatry, Law and Psychiatry Program, has an unexpected opening in its ACGME-accredited Fellowship in Forensic Psychiatry starting 7/1/09. The one-year, full-time position involves participation in intensive academic and clinical training in issues related to forensic psychiatry and the legal regulation of mental health. Fellows conduct a wide variety of court-ordered inpatient forensic evaluations and rotate at major court clinic sites in Boston and Cambridge. Private civil and criminal forensic evaluations are conducted through the Forensic Evaluation Service. This program emphasizes intensive supervision of all work and a weekly schedule of structured didactic seminars, as well as opportunities for research. The faculty consists of a multidisciplinary team of forensic professionals who are among the national leaders in the field. Nationally recognized research programs in forensic psychiatry, psychiatric neuroscience, psychopharmacology, addiction psychiatry, child psychiatry, mental health policy, and other areas, a major commitment to community psychiatry, and over 250 faculty make UMass an exciting place to train. Interested individuals should contact: Paul Noroian, M.D., Director, Forensic Psychiatry Fellowship, Department of Psychiatry, University of Massachusetts Medical School, 55 Lake Avenue North, Worcester, MA 01655, Call (508) 856-3079 or email: Paul.Noroian@umassmed.edu. AA/EOE

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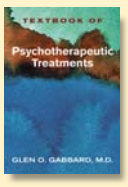

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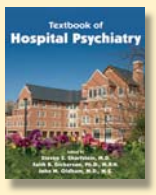

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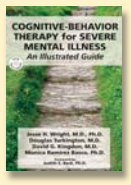

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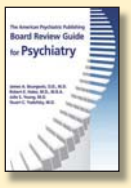

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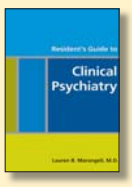

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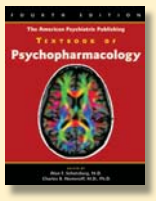

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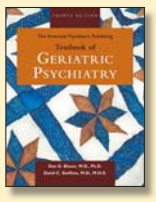

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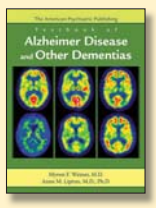

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BRIEF SUMMARY. See package insert for full Prescribing Information. For further product information and current package insert, please visit www.wyeth.com or call our medical communications department toll-free at 1-800-934-5556.

WARNING: Suicidality and Antidepressant Drugs

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of Major Depressive Disorder (MDD) and other psychiatric disorders. Anyone considering the use of Pristiq or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Pristiq is not approved for use in pediatric patients [*see Warnings and Precautions (5.1), Use in Specific Populations (8.4), and Patient Counseling Information (17.1 in the full prescribing information)*].

INDICATIONS AND USAGE: Pristiq, a selective serotonin and norepinephrine reuptake inhibitor (SNRI), is indicated for the treatment of major depressive disorder (MDD).

CONTRAINDICATIONS: Hypersensitivity- Hypersensitivity to desvenlafaxine succinate, venlafaxine hydrochloride or to any excipients in the Pristiq formulation. **Monoamine Oxidase Inhibitors-** Pristiq must not be used concomitantly in patients taking monoamine oxidase inhibitors (MAOIs) or in patients who have taken MAOIs within the preceding 14 days due to the risk of serious, sometimes fatal, drug interactions with SNRI or SSRI treatment or with other serotonergic drugs. Based on the half-life of desvenlafaxine, at least 7 days should be allowed after stopping Pristiq before starting an MAOI [*see Dosage and Administration (2.5) in the full prescribing information*].

WARNINGS AND PRECAUTIONS: Clinical Worsening and Suicide Risk- Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. There has been a long-standing concern, however, that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients during the early phases of treatment. Pooled analyses of short-term placebo-controlled studies of antidepressant drugs (SSRIs and others) showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18-24) with major depressive disorder (MDD) and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction with antidepressants compared to placebo in adults aged 65 and older. The pooled analyses of placebo-controlled studies in children and adolescents with MDD, obsessive compulsive disorder (OCD), or other psychiatric disorders included a total of 24 short-term studies of 9 antidepressant drugs in over 4,400 patients. The pooled analyses of placebo-controlled studies in adults with MDD or other psychiatric disorders included a total of 295 short-term studies (median duration of 2 months) of 11 antidepressant drugs in over 77,000 patients. There was considerable variation in risk of suicidality among drugs, but a tendency toward an increase in the younger patients for almost all drugs studied. There were differences in absolute risk of suicidality across the different indications, with the highest incidence in MDD. The risk differences (drug vs. placebo), however, were relatively stable within age strata and across indications. These risk differences (drug-placebo difference in the number of cases of suicidality per 1000 patients treated) are provided in Table 1 of the full prescribing information. No suicides occurred in any of the pediatric studies. There were suicides in the adult studies, but the number was not sufficient to reach any conclusion about drug effect on suicide. It is unknown whether the suicidality risk extends to longer-term use, i.e., beyond several months. However, there is substantial evidence from placebo-controlled maintenance studies in adults with depression that the use of antidepressants can delay the recurrence of depression. **All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases.** The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality. Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse, or who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms. If the decision has been made to discontinue treatment, medication should be tapered, as rapidly as is feasible, but with recognition that abrupt discontinuation can be associated with certain symptoms [*see Warnings and Precautions (5.9) and Dosage and Administration (2.3) in the full prescribing information for a description of the risks of discontinuation of Pristiq*]. Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to health care providers. Such monitoring should include daily observation by families and caregivers. Prescriptions for Pristiq should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose. Screening patients for bipolar disorder- A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled studies) that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Whether any of the symptoms described above represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that Pristiq is not approved for use in treating bipolar depression. **Serotonin Syndrome-** The development of a potentially life-threatening serotonin syndrome may occur with Pristiq treatment, particularly with concomitant use of other serotonergic drugs (including SSRIs, SNRIs and triptans) and with drugs that impair metabolism of serotonin (including MAOIs). The concomitant use of Pristiq and MAOIs is contraindicated [*see Contraindications (4.2)*]. If concomitant treatment with Pristiq and an SSRI, another SNRI or a 5-hydroxytryptamine receptor agonist (triptan) is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. The concomitant use of Pristiq with serotonin precursors (such as tryptophan supplements) is not recommended. **Elevated Blood Pressure-** Patients receiving Pristiq should have regular monitoring of blood pressure since dose-dependent increases were observed in clinical studies. Pre-existing hypertension should be controlled before initiating treatment with Pristiq. Caution should be exercised in treating patients with pre-existing hypertension or other underlying conditions that might be compromised by increases in blood pressure. Cases of elevated blood pressure requiring immediate treatment have been reported with Pristiq. Sustained hypertension- Sustained blood pressure increases could have adverse consequences. For patients who experience a sustained increase in blood pressure while receiving Pristiq, either dose reduction or discontinuation should be considered [*see Adverse Reactions (6.1)*]. Treatment with Pristiq in controlled studies was associated with sustained hypertension, defined as treatment-emergent supine diastolic blood pressure (SDBP) $\geq$ 90 mm Hg and $\geq$ 10 mm Hg above baseline for 3 consecutive on-therapy visits. In clinical studies, regarding the proportion of patients with sustained hypertension, the following rates were observed: placebo (0.5%), Pristiq 50 mg (1.3%), Pristiq 100 mg (0.7%), Pristiq 200 mg (1.1%), and Pristiq 400 mg (2.3%). Analyses of patients in Pristiq controlled studies who met criteria for sustained hypertension revealed a dose-dependent increase in the proportion of patients who developed sustained hypertension. **Abnormal Bleeding-** SSRIs and SNRIs can increase the risk of bleeding events. Concomitant use of aspirin, other drugs that affect platelet function, nonsteroidal anti-inflammatory drugs, warfarin, and other anticoagulants can add to this risk. Bleeding events related to SSRIs and SNRIs have ranged from ecchymosis, hematoma, epistaxis, and petechiae to life-threatening hemorrhages. Patients should be cautioned about the risk of bleeding associated with the concomitant use of Pristiq and NSAIDs, aspirin, or other drugs that affect coagulation or bleeding. **Narrow-angle Glaucoma-** Mydriasis has been reported in association with Pristiq; therefore, patients with raised intraocular pressure or those at risk of acute narrow-angle glaucoma (angle-closure glaucoma) should be monitored. **Activation of Mania/Hypomania-** During all MDD and VMS (vasomotor symptoms) phase 2 and phase 3 studies, mania was reported for approximately 0.1% of patients treated with Pristiq. Activation of mania/hypomania has also been reported in a small proportion of patients with major affective disorder who were treated with other marketed antidepressants. As with all antidepressants, Pristiq should be used cautiously in patients with a history or family history of mania or hypomania. **Cardiovascular/Cerebrovascular Disease-** Caution is advised in administering Pristiq to patients with cardiovascular, cerebrovascular, or lipid metabolism disorders [*see Adverse Reactions (6.1)*]. Increases in blood pressure and heart rate were observed in clinical studies with Pristiq. Pristiq has not been evaluated systematically in patients with a recent history of myocardial infarction, unstable heart disease, uncontrolled hypertension, or cerebrovascular disease. Patients with these diagnoses, except for cerebrovascular disease, were excluded from clinical studies. **Serum Cholesterol and Triglyceride Elevation-** Dose-related elevations in fasting serum total cholesterol, LDL (low density lipoprotein) cholesterol, and triglycerides were observed in the controlled studies. Measurement of serum lipids should be considered during treatment with Pristiq [*see Adverse Reactions (6.1)*]. **Discontinuation of Treatment with Pristiq-** Discontinuation symptoms have been systematically and prospectively evaluated in patients treated with Pristiq during clinical studies in Major Depressive Disorder. Abrupt discontinuation or dose reduction has been associated with the appearance of new symptoms that include dizziness, nausea, headache, irritability, insomnia, diarrhea, anxiety, fatigue, abnormal dreams, and hyperhidrosis. In general, discontinuation events occurred more frequently with longer duration of therapy. During marketing of SNRIs (Serotonin and Norepinephrine Reuptake Inhibitors) and SSRIs (Selective Serotonin Reuptake Inhibitors), there have been spontaneous reports of adverse events occurring upon discontinuation of these drugs, particularly when abrupt, including the following: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesia, such as electric shock sensations), anxiety, confusion, headache, lethargy, emotional lability, insomnia, hypomania, tinnitus, and seizures. While these events are generally self-limiting, there have been reports of serious discontinuation symptoms. Patients should be monitored for these symptoms when discontinuing treatment with Pristiq. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose, but at a more gradual rate [*see Dosage and Administration (2.4) and Adverse Reactions (6.1) in full prescribing information*]. **Renal Impairment-** In patients with moderate or severe renal impairment or end-stage renal disease (ESRD) the clearance of Pristiq was decreased, thus prolonging the elimination half-life of the drug. As a result, there were potentially clinically significant increases in exposures to Pristiq [*see Clinical Pharmacology (12.6) in full prescribing information*]. Dosage adjustment (50 mg every other day) is necessary in patients with severe renal impairment or ESRD. The doses should not be escalated in patients with moderate or severe renal impairment or ESRD [*see Dosage and Administration (2.2) in full prescribing information*]. **Seizure-** Cases of seizure have been reported in premarketing clinical studies with Pristiq. Pristiq should be prescribed with caution in patients with a seizure disorder. **Hyponatremia-** Hyponatremia can occur as a result of treatment with SSRIs and SNRIs, including Pristiq. In many cases, this hyponatremia appears to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Elderly patients can be at greater risk of developing hyponatremia with SSRIs and SNRIs. Also, patients taking diuretics or who are otherwise volume depleted can be at greater risk [*see Use in Specific Populations (8.5) and Clinical Pharmacology (12.6) in full prescribing information*]. Discontinuation of Pristiq should be considered in patients with symptomatic hyponatremia and appropriate medical intervention should be instituted. **Coadministration of Drugs Containing Desvenlafaxine and Venlafaxine-** Desvenlafaxine is the major active metabolite of venlafaxine. Products containing desvenlafaxine and products containing venlafaxine should not be used concomitantly with Pristiq. **Interstitial Lung Disease and Eosinophilic Pneumonia-** Interstitial lung disease and eosinophilic pneumonia associated with venlafaxine (the parent drug of Pristiq) therapy have been rarely reported. The possibility of these adverse events should be considered in patients treated with Pristiq who present with progressive dyspnea, cough, or chest discomfort. Such patients should undergo a prompt medical evaluation, and discontinuation of Pristiq should be considered.

ADVERSE REACTIONS: Clinical Studies Experience: The most commonly observed adverse reactions in Pristiq-treated MDD patients in short-term fixed-dose studies (incidence ≥5% and at least twice the rate of placebo in the 50- or 100-mg dose groups) were nausea, dizziness, insomnia, hyperhidrosis, constipation, somnolence, decreased appetite, anxiety, and specific male sexual function disorders. Adverse reactions reported as reasons for discontinuation of treatment- The most common adverse reactions leading to discontinuation in at least 2% of the Pristiq-treated patients in the short-term studies, up to 8 weeks, were nausea (4%); dizziness, headache and vomiting (2% each); in the long-term study, up to 9 months, the most common was vomiting (2%). Common adverse reactions in placebo-controlled MDD studies- Table 3 in full PI shows the incidence of common adverse reactions that occurred in ≥2% of Pristiq-treated MDD patients at any dose in the 8-week, placebo-controlled, fixed-dose, premarketing clinical studies. In general, the adverse reactions were most frequent in the first week of treatment. Cardiac disorders: Palpitations, Tachycardia, Blood pressure increased; Gastrointestinal disorders: Nausea, Dry mouth, Diarrhea, Constipation, Vomiting; General disorders and administration site conditions: Fatigue, Chills, Feeling jittery, Asthenia; Metabolism and nutrition disorders: Decreased appetite, weight decreased; Nervous system disorders: Dizziness, Somnolence, Headache, Tremor, Paraesthesia, Disturbance in attention; Psychiatric Disorders: Insomnia, Anxiety, Nervousness, Irritability, Abnormal dreams; Renal and urinary disorders: Urinary hesitation; Respiratory, thoracic, and mediastinal disorders: Yawning; Skin and subcutaneous tissue disorders: Hyperhidrosis, Rash; Special Senses: Vision blurred; Mydriasis, Tinnitus, Dysgeusia; Vascular Disorders: Hot flush. Sexual function adverse reactions-Table 4 shows the incidence of sexual function adverse reactions that occurred in ≥2% of Pristiq-treated MDD patients in any fixed-dose group (8-week, placebo-controlled, fixed and flexible-dose, premarketing clinical studies). Men Only: Anorgasmia, Libido decreased, Orgasm abnormal, Ejaculation delayed, Erectile dysfunction, Ejaculation disorder, Ejaculation failure, Sexual dysfunction; Women Only: Anorgasmia Other adverse reactions observed in premarketing clinical studies: Other infrequent adverse reactions occurring at an incidence of <2% in MDD patients treated with Pristiq were: *Immune system disorders* – Hypersensitivity. *Investigations* – Liver function test abnormal, blood prolactin increased. *Nervous system disorders* – Convulsion, syncope, extrapyramidal disorder. *Psychiatric disorders* – Depersonalization, hypomania. *Respiratory, thoracic and mediastinal disorders* – Epistaxis. *Vascular disorders* – Orthostatic hypotension. In clinical studies, there were uncommon reports of ischemic cardiac adverse events, including myocardial ischemia, myocardial infarction, and coronary occlusion requiring revascularization; these patients had multiple underlying cardiac risk factors. More patients experienced these events during Pristiq treatment as compared to placebo *[see Warnings and Precautions (5.7)*]. Discontinuation events-Adverse events reported in association with abrupt discontinuation, dose reduction or tapering of treatment in MDD clinical studies at a rate of ≥5% include dizziness, nausea, headache, irritability, insomnia, diarrhea, anxiety, abnormal dreams, fatigue, and hyperhidrosis. In general, discontinuation events occurred more frequently with longer duration of therapy [*see Dosage and Administration (2.4) and Warnings and Precautions (5.9) in full prescribing information*]. Laboratory, ECG and vital sign changes observed in MDD clinical studies- The following changes were observed in placebo-controlled, short-term, premarketing MDD studies with Pristiq. *Lipids*-Elevations in fasting serum total cholesterol, LDL (low density lipoproteins) cholesterol, and triglycerides occurred in the controlled studies. Some of these abnormalities were considered potentially clinically significant [*see Warnings and Precautions (5.8)*]. *Proteinuria*-Proteinuria, greater than or equal to trace, was observed in the fixed-dose controlled studies (see Table 6 in full prescribing information). This proteinuria was not associated with increases in BUN or creatinine and was generally transient. *ECG changes*-Electrocardiograms were obtained from 1,492 Pristiq-treated patients with major depressive disorder and 984 placebo-treated patients in clinical studies lasting up to 8 weeks. No clinically relevant differences were observed between Pristiq-treated and placebo-treated patients for QT, QTc, PR, and QRS intervals. In a thorough QTc study with prospectively determined criteria, desvenlafaxine did not cause QT prolongation. No difference was observed between placebo and desvenlafaxine treatments for the QRS interval. *Vital sign changes*-Table 7 summarizes the changes that were observed in placebo-controlled, short-term, premarketing studies with Pristiq in patients with MDD (doses 50 to 400 mg). Relative to placebo, Pristiq was associated with mean increase of up to 2.1 mm Hg in systolic blood pressure, 2.3 mm Hg in diastolic blood pressure, and 4.1 bpm with supine pulse. At the final on-therapy assessment in the 6-month, double-blind, placebo-controlled phase of a long-term study in patients who had responded to Pristiq during the initial 12-week, open-label phase, there was no statistical difference in mean weight gain between Pristiq- and placebo-treated patients. **DRUG INTERACTIONS: Central Nervous System (CNS)-Active Agents-** The risk of using Pristiq in combination with other CNS-active drugs has not been systematically evaluated. Consequently, caution is advised when Pristiq is taken in combination with other CNS-active drugs [*see Warnings and Precautions (5.13)*]. **Monoamine Oxidase Inhibitors (MAOIs)-** Adverse reactions, some of which were serious, have been reported in patients who have recently been discontinued from a monoamine oxidase inhibitor (MAOI) and started on antidepressants with pharmacological properties similar to Pristiq (SNRIs or SSRIs), or who have recently had SNRI or SSRI therapy discontinued prior to initiation of an MAOI [*see Contraindications (4.2)*]. **Serotonergic Drugs-** Based on the mechanism of action of Pristiq and the potential for serotonin syndrome, caution is advised when Pristiq is coadministered with other drugs that may affect the serotonergic neurotransmitter systems [*see Warnings and Precautions (5.2)*]. **Drugs that Interfere with Hemostasis (e.g., NSAIDs, Aspirin, and Warfarin)-** Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies of case-control and cohort design have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. These studies have also shown that concurrent use of an NSAID or aspirin may potentiate this risk of bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when SSRIs and SNRIs are coadministered with warfarin. Patients receiving warfarin therapy should be carefully monitored when Pristiq is initiated or discontinued. **Ethanol-** A clinical study has shown that desvenlafaxine does not increase the impairment of mental and motor skills caused by ethanol. However, as with all CNS-active drugs, patients should be advised to avoid alcohol consumption while taking Pristiq. **Potential for Other Drugs to Affect Desvenlafaxine-** Inhibitors of CYP3A4 (ketoconazole)- CYP3A4 is a minor pathway for the metabolism of Pristiq. Concomitant use of Pristiq with potent inhibitors of CYP3A4 may result in higher concentrations of Pristiq. Inhibitors of other CYP enzymes- Based on *in vitro* data, drugs that inhibit CYP isozymes 1A1, 1A2, 2A6, 2D6, 2C8, 2C9, 2C19, and 2E1 are not expected to have significant impact on the pharmacokinetic profile of Pristiq. **Potential for Desvenlafaxine to Affect Other Drugs-** Drugs metabolized by CYP2D6 (desipramine)- *In vitro* studies showed minimal inhibitory effect of desvenlafaxine on CYP2D6. Clinical studies have shown that desvenlafaxine does not have a clinically relevant effect on CYP2D6 metabolism at the dose of 100 mg daily. Concomitant use of desvenlafaxine with a drug metabolized by CYP2D6 can result in higher concentrations of that drug. Drugs metabolized by CYP3A4 (midazolam)- *In vitro*, desvenlafaxine does not inhibit or induce the CYP3A4 isozyme. Concomitant use of Pristiq with a drug metabolized by CYP3A4 can result in lower exposures to that drug. Drugs metabolized by CYP1A2, 2A6, 2C8, 2C9 and 2C19- *In vitro*, desvenlafaxine does not inhibit CYP1A2, 2A6, 2C8, 2C9, and 2C19 isozymes and would not be expected to affect the pharmacokinetics of drugs that are metabolized by these CYP isozymes. **P-glycoprotein Transporter-** *In vitro*, desvenlafaxine is not a substrate or an inhibitor for the P-glycoprotein transporter. The pharmacokinetics of Pristiq are unlikely to be affected by drugs that inhibit the P-glycoprotein transporter, and desvenlafaxine is not likely to affect the pharmacokinetics of drugs that are substrates of the P-glycoprotein transporter. **Electroconvulsive Therapy-** There are no clinical data establishing the risks and/or benefits of electroconvulsive therapy combined with Pristiq treatment. **USE IN SPECIFIC POPULATIONS: Pregnancy-** Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy. Teratogenic effects – Pregnancy Category C- There are no adequate and well-controlled studies of Pristiq in pregnant women. Therefore, Pristiq should be used during pregnancy only if the potential benefits justify the potential risks. Non-teratogenic effects- Neonates exposed to SNRIs (Serotonin and Norepinephrine Reuptake Inhibitors), or SSRIs (Selective Serotonin Reuptake Inhibitors), late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Such complications can arise immediately upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. These features are consistent with either a direct toxic effect of SSRIs and SNRIs or, possibly, a drug discontinuation syndrome. It should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome [*see Warnings and Precautions (5.2)*]. When treating a pregnant woman with Pristiq during the third trimester, the physician should carefully consider the potential risks and benefits of treatment [*see Dosage and Administration (2.2)*]. **Labor and Delivery-** The effect of Pristiq on labor and delivery in humans is unknown. Pristiq should be used during labor and delivery only if the potential benefits justify the potential risks. **Nursing Mothers-** Desvenlafaxine (O-desmethylvenlafaxine) is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from Pristiq, a decision should be made whether or not to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. Only administer Pristiq to breastfeeding women if the expected benefits outweigh any possible risk. **Pediatric Use-** Safety and effectiveness in the pediatric population have not been established [*see Box Warning and Warnings and Precautions (5.1)*]. Anyone considering the use of Pristiq in a child or adolescent must balance the potential risks with the clinical need. **Geriatric Use-** Of the 3,292 patients in clinical studies with Pristiq, 5% were 65 years of age or older. No overall differences in safety or efficacy were observed between these patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out. For elderly patients, possible reduced renal clearance of desvenlafaxine should be considered when determining dose [*see Dosage and Administration (2.2) and Clinical Pharmacology (12.6) in the full prescribing information*]. **Renal Impairment-** In subjects with renal impairment the clearance of Pristiq was decreased. In subjects with severe renal impairment (24-hr CrCl < 30 mL/min) and end-stage renal disease, elimination half-lives were significantly prolonged, increasing exposures to Pristiq; therefore, dosage adjustment is recommended in these patients [*see Dosage and Administration (2.2) and Clinical Pharmacology (12.6) in the full prescribing information*]. **Hepatic Impairment-** The mean $t_{1/2}$ changed from approximately 10 hours in healthy subjects and subjects with mild hepatic impairment to 13 and 14 hours in moderate and severe hepatic impairment, respectively. No adjustment in starting dosage is necessary for patients with hepatic impairment.

OVERDOSAGE: Human Experience with Overdosage- There is limited clinical experience with desvenlafaxine succinate overdosage in humans. In premarketing clinical studies, no cases of fatal acute overdose of desvenlafaxine were reported. The adverse reactions reported within 5 days of an overdose > 600 mg that were possibly related to Pristiq included headache, vomiting, agitation, dizziness, nausea, constipation, diarrhea, dry mouth, paresthesia, and tachycardia. Desvenlafaxine (Pristiq) is the major active metabolite of venlafaxine. Overdose experience reported with venlafaxine (the parent drug of Pristiq) is presented below; the identical information can be found in the *Overdosage* section of the venlafaxine package insert. In postmarketing experience, overdose with venlafaxine (the parent drug of Pristiq) has occurred predominantly in combination with alcohol and/or other drugs. The most commonly reported events in overdosage include tachycardia, changes in level of consciousness (ranging from somnolence to coma), mydriasis, seizures, and vomiting. Electrocardiogram changes (e.g., prolongation of QT interval, bundle branch block, QRS prolongation), sinus and ventricular tachycardia, bradycardia, hypotension, rhabdomyolysis, vertigo, liver necrosis, serotonin syndrome, and death have been reported. Published retrospective studies report that venlafaxine overdosage may be associated with an increased risk of fatal outcomes compared to that observed with SSRI antidepressant products, but lower than that for tricyclic antidepressants. Epidemiological studies have shown that venlafaxine-treated patients have a higher pre-existing burden of suicide risk factors than SSRI-treated patients. The extent to which the finding of an increased risk of fatal outcomes can be attributed to the toxicity of venlafaxine in overdosage, as opposed to some characteristic(s) of venlafaxine-treated patients, is not clear. Prescriptions for Pristiq should be written for the smallest quantity of capsules consistent with good patient management, in order to reduce the risk of overdose. **Management of Overdosage-** Treatment should consist of those general measures employed in the management of overdosage with any SSRI/SNRI. Ensure an adequate airway, oxygenation, and ventilation. Monitor cardiac rhythm and vital signs. General supportive and symptomatic measures are also recommended. Gastric lavage with a large-bore orogastric tube with appropriate airway protection, if needed, may be indicated if performed soon after ingestion or in symptomatic patients. Activated charcoal should be administered. Induction of emesis is not recommended. Because of the moderate volume of distribution of this drug, forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be of benefit. No specific antidotes for desvenlafaxine are known. In managing an overdose, consider the possibility of multiple drug involvement. The physician should consider contacting a poison control center for additional information on the treatment of any overdose. Telephone numbers for certified poison control centers are listed in the Physicians Desk Reference (PDR®).

This brief summary is based on Pristiq Prescribing Information W10529C002, revised April 2008.

Wyeth®

244265-01

For the treatment of adults with major depressive disorder

The start is just the beginning

It's not just about starting your adult patients with MDD on therapy; it's about helping them toward their treatment goals. Patients should be periodically reassessed to determine the need for continued treatment.[1]

PRISTIQ 50 mg:

- **SNRI therapy with efficacy proven in 8-week clinical studies**
- **One recommended therapeutic dose from the start**
- **Discontinuation rate due to adverse events comparable to placebo in 8-week clinical studies[1]**

Pristiq® desvenlafaxine 50 mg

think beyond start™

IMPORTANT TREATMENT CONSIDERATIONS

PRISTIQ 50-mg Extended-Release Tablets are indicated for the treatment of major depressive disorder in adults.

WARNING: SUICIDALITY AND ANTIDEPRESSANT DRUGS

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of Major Depressive Disorder (MDD) and other psychiatric disorders. Anyone considering the use of PRISTIQ or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. PRISTIQ is not approved for use in pediatric patients.

Contraindications

- PRISTIQ is contraindicated in patients with a known hypersensitivity to PRISTIQ or venlafaxine.
- PRISTIQ must not be used concomitantly with an MAOI or within 14 days of stopping an MAOI. Allow 7 days after stopping PRISTIQ before starting an MAOI.

Warnings and Precautions

- **All patients treated with antidepressants should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the first few months of treatment and when changing the dose.** Consider changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse or includes symptoms of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia, hypomania, mania, or suicidality that are severe, abrupt in onset, or were not part of the patient's presenting symptoms. **Families and caregivers of patients being treated with antidepressants should be alerted about the need to monitor patients.**
- Development of a potentially life-threatening serotonin syndrome may occur with SNRIs and SSRIs, including PRISTIQ, particularly with concomitant use of serotonergic drugs, including triptans, and with drugs that impair the metabolism of serotonin (including MAOIs). If concomitant use is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. Concomitant use of PRISTIQ with serotonin precursors is not recommended.
- Patients receiving PRISTIQ should have regular monitoring of blood pressure since sustained increases in blood pressure were observed in clinical studies. Pre-existing hypertension should be controlled before starting PRISTIQ. Caution should be exercised in treating patients with pre-existing hypertension or other underlying conditions that might be compromised by increases in blood pressure. Cases of elevated blood pressure requiring immediate treatment have been reported. For patients who experience a sustained increase in blood pressure, either dose reduction or discontinuation should be considered.
- SSRIs and SNRIs, including PRISTIQ, may increase the risk of bleeding events. Concomitant use of aspirin, NSAIDs, warfarin, and other anticoagulants may add to this risk.
- Mydriasis has been reported in association with PRISTIQ; therefore, patients with raised intraocular pressure or those at risk of acute narrow-angle glaucoma (angle-closure glaucoma) should be monitored.
- PRISTIQ is not approved for use in bipolar depression. Prior to initiating treatment with an antidepressant, patients should be adequately screened to determine the risk of bipolar disorder.
- As with all antidepressants, PRISTIQ should be used cautiously in patients with a history or family history of mania or hypomania, or with a history of seizure disorder.
- Caution is advised in administering PRISTIQ to patients with cardiovascular, cerebrovascular, or lipid metabolism disorders. Increases in blood pressure and small increases in heart rate were observed in clinical studies with PRISTIQ. PRISTIQ has not been evaluated systematically in patients with a recent history of myocardial infarction, unstable heart disease, uncontrolled hypertension, or cerebrovascular disease.
- Dose-related elevations in fasting serum total cholesterol, LDL (low density lipoprotein) cholesterol, and triglycerides were observed in clinical studies. Measurement of serum lipids should be considered during PRISTIQ treatment.
- On discontinuation, adverse events, some of which may be serious, have been reported with PRISTIQ and other SSRIs and SNRIs. Abrupt discontinuation of PRISTIQ has been associated with the appearance of new symptoms. Patients should be monitored for symptoms when discontinuing treatment. A gradual reduction in dose (by giving 50 mg of PRISTIQ less frequently) rather than abrupt cessation is recommended whenever possible.
- Dosage adjustment (50 mg every other day) is necessary in patients with severe renal impairment or end-stage renal disease (ESRD). The dose should not be escalated in patients with moderate or severe renal impairment or ESRD.
- Products containing desvenlafaxine and products containing venlafaxine should not be used concomitantly with PRISTIQ.
- Hyponatremia may occur as a result of treatment with SSRIs and SNRIs, including PRISTIQ. Discontinuation of PRISTIQ should be considered in patients with symptomatic hyponatremia.
- Interstitial lung disease and eosinophilic pneumonia associated with venlafaxine (the parent drug of PRISTIQ) therapy have been rarely reported.

Adverse Reactions

- The most commonly observed adverse reactions in patients taking PRISTIQ vs placebo for MDD in short-term fixed-dose premarketing studies (incidence ≥5% and twice the rate of placebo in the 50-mg dose group) were nausea (22% vs 10%), dizziness (13% vs 5%), hyperhidrosis (10% vs 4%), constipation (9% vs 4%), and decreased appetite (5% vs 2%).

Reference: 1. Pristiq® (desvenlafaxine) Prescribing Information, Wyeth Pharmaceuticals Inc.

Please see brief summary of Prescribing Information on adjacent page.

Pristiq® desvenlafaxine EXTENDED-RELEASE TABLETS

Wyeth®