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American
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Association

PSYCHIATRIC NEWS

Inside

PERIODICALS:
TIME-SENSITIVE MATERIALS

Credit: Jun Yan

APA Medical Director James H. Scully Jr., M.D., testifies at a Senate hearing on industry-funded continuing medical education. At right is Murray Kopelow, M.D., head of the Accreditation Council for Continuing Medical Education. See story below.

N.J. Settlement Wins Release Of Patients to Community Care

The agreement is part of a nationwide effort to enforce provisions of a 10-year-old Supreme Court ruling that requires states to offer qualified patients the least restrictive care available.

BY RICH DALY

Mental health advocates settled a lawsuit in July with the New Jersey Department of Human Services to release by 2014 a total of nearly 300 people in the four state-run psychiatric hospitals and to provide them with housing and treatment in community settings.

The plaintiffs, which included Disability Rights New Jersey (DRNJ) and the Bazelon Center for Mental Health Law, said the transfer to the noninstitutional settings would provide healthier dwellings and independence for people who had long been kept in tightly controlled environments but were capable of living in community settings given the right treatment assistance.

The agreement settled a 2005 federal lawsuit, *DRNJ v. Velez*, brought by the mental health advocates on behalf of about 1,000 patients deemed qualified for less restrictive, supportive housing, which also provides for medical, mental health, and assisted-living services.

Under the agreement, the state will develop 1,065 new supportive housing units and similar community settings.

please see ***Settlement*** *on page 28*

Eliminating CME Conflicts Worth the Cost, Says Scully

Regulators may join the already-crowded debate over whether commercially funded CME is beneficial or detrimental to the medical profession and patients' health.

BY JUN YAN

"The fact that the relationship between the industry and the medical profession is facing increasing scrutiny is not a bad thing," James H. Scully Jr., M.D., APA's medical director and CEO, told the Senate Special Committee on Aging at a hearing in late July. He was one of the medical leaders who testified at the hearing to express their knowledge and opinions about continuing medical education (CME)—specifically, whether funding from pharmaceutical and device companies, currently accounting for half of all funding for all CME programs in the United States, leads to biased information for physicians.

The committee chair, Sen. Herb Kohl (D-Wis.), asked everyone who testified: "Are the drugs and device industries getting a return on their annual billion-dollar investment in continuing medical education?"

Several people testifying at the hearing said yes—industry-funded CME poses either a real problem or at least a serious threat to the objectivity and quality of continuing education that physicians are required to obtain and maintain. Others argued that the current system is effective and sufficient in protecting CME from the commercial interest of sponsors.

please see ***CME*** *on page 28*

Photo courtesy of CityPass

APA's 2009 Institute on Psychiatric Services will be held in New York City October 8 to 11. The Big Apple is ready to welcome you! Save on fees by registering on or before September 18. See pages 2 and 20.

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Asenapine Adds to Arsenal To Treat Psychotic Disorders

The new antipsychotic medication is formulated for sublingual administration to bypass hepatic metabolism and requires twice daily dosing, according to the product label.

BY JUN YAN

A new antipsychotic drug, asenapine, has been approved by the Food and Drug Administration (FDA) for the acute treatment of schizophrenia and manic or mixed episode in bipolar I disorder in adults.

The approval, announced on August 14, came just two weeks after an FDA advisory committee gave a favorable review to the drug at a public meeting. The advisors reviewed three phase 3, placebo-controlled trials of asenapine in patients with schizophrenia and two placebo-controlled trials in patients with a manic or mixed episode of bipolar I disorder.

The drug is expected to be available in U.S. pharmacies beginning in the fourth quarter of this year, according to an announcement by Schering-Plough.

Similar to other second-generation antipsychotics, asenapine is an antagonist of the serotonin $5HT_2$ and dopamine D_2 receptors. Schering-Plough acquired the molecule and took over its development upon the company's merger with Organon BioScience in 2007.

In two of the three phase 3 trials in schizophrenia, asenapine 5 mg twice daily showed significantly greater efficacy, measured by total score on the Positive and Negative Syndrome Scale (PANSS) than did placebo after six weeks of randomized, double-blind, acute treatment. A higher dose of 10 mg twice daily was significantly better than placebo in only one trial. Thus, the company decided to seek approval for the indication of schizophrenia treatment for the dose of 5 mg twice daily only. In a third trial, asenapine at both doses did not beat placebo in the primary endpoint.

In the two bipolar disorder trials, asenapine was given in flexible doses of between 5 mg and 10 mg twice daily for three weeks during an acute manic or mixed episode in a double-blind manner. The primary efficacy measure, improvement from baseline in the Young Mania Rating Scale (YMRS) total score, showed significant advantage for asenapine over placebo.

please see ***Asenapine*** *on page 28*

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Don't Pass Up This APA Gem!

BY ALAN F. SCHATZBERG, M.D.

APA's 2009 Institute on Psychiatric Services—which is being held October 8 to 11 in New York City—offers a great opportunity for our members to learn about a number of innovations in psychiatric treatment. The Scientific Program Committee, chaired by Dr. Stephen Goldfinger, and Dr. Debbie Hales, director of APA's Division of Education, have done a terrific job in shaping a first-rate program (see pages 2 and 20).

This year's program will expand from its more traditional community focus to include vital new information on a variety of therapeutics for other practitioners in our field. The program includes a number of special lectures, immersion courses, symposia, workshops, clinical "practical pearls," and forums, all led by experts in our field. The program can be accessed on APA's Web site at <www.psych.org/MainMenu/EducationCareerDevelopment/Meetings/InstituteonPsychiatricServices.aspx>.

In keeping with the theme of my presidency, the institute's theme is "Pride and Practice: Bringing Innovation Into Our Treatments."

For lectures, we have a series of award and invited lectures. With regard to the award lectures, Dr. Dwight Evans (APA Research in Psychiatry Award) will discuss the interface of psychiatry with other areas of medicine, with an emphasis on HIV disease progression; Dr. Victor Reus (Vestermark Award) will discuss maintaining career-long competence; Dr. Christopher McDougle (Frank J. Menolascino Award) will discuss the diagnosis and pharmacotherapy of autism; Dr. Lloyd Sederer (Administrative Psychiatry Award) will discuss public mental health; and Dr. Kenneth Pargament (Oskar Pfister Award) will discuss spirituality and mental illness.

Among the invited lectures, we have treatment-oriented lectures by Dr. Otto Kernberg on transference-focused psychotherapy, Dr. Jeffrey Lieberman on pharmacologic treatment of schizophrenia, Dr. Harold Koplewicz on treatment of adolescent depression, Dr. Linmarie Sikich on antipsychotics in children, Dr. Kim Hopper on outcomes of schizophrenia around the world, and Dr. Grayson Norquist on telepsychiatry for underserved populations. These leaders will provide their unique perspectives on obviously diverse clinical issues. I have agreed to talk on the future status of antidepressant therapy and the implications for training and practice. We have other lecturers as well, such as Dr. Paul Appelbaum on conflicts of interest in dealing with industry and Dr. Michael Hogan on mental health services in New York state.

The Scientific Program Committee has developed a series of superb half-day and full day courses—including, among others, ones on psychopharmacology, buprenorphine, and CBT for patients with psychotic disorders. These offer highly efficient opportunities to learn key, in-depth material presented by leaders in our field. The psychopharmacology course will include Dr. Charles DeBattista, Dr. Terry Ketter, and me from Stanford; Dr. Jeremy Coplan from SUNY Downstate; and Dr. Jeffrey Lieberman from Columbia. The course on CBT for psychotic disorders will be led by Dr. Michael Garrett from SUNY Downstate.

Dr. Johnny O'Reardon from the University of Pennsylvania and a leading expert in transcranial magnetic stimulation will provide a forum on the topic.

We have a number of interesting workshops including—to name but a few—one on gender and academic careers codirected by Drs. Geetha Jayaram and Leah Dickstein and one on residency issues with Drs. Sarah Johnson, Carol Bernstein, and Kayla Pope. In addition to these, we have a workshop on the pharmacotherapy of addictions with Drs. John Renner and Eric Strain and a symposium on PTSD in military psychiatry organized by Dr. Darrell Regier. There will be "practical pearl" sessions as well led by Dr. Carolyn Robinowitz and others. And there's much, much more on the scientific program, as well as the host of other social and collegiality opportunities the institute has offered over the years.

The institute is one of a number of educational opportunities that APA offers to its members. It serves an important niche not only for hospital- and community-based practitioners but all mental health clinicians. I urge you to take advantage of this opportunity, and I look forward to seeing all of you in New York City next month. ■

Sign Up Now to Vote Online

APA candidates for national office will be announced on APA's Web site by September 15. APA's Elections Committee is urging you to go green this year and take steps now to opt out of receiving a paper ballot and vote online instead. To do so, visit <www.psych.org/options>, log in as an APA member, and click "yes" beside "Electronic Ballot." Also, be sure to confirm or update your contact information.

Voting online is good for the environment by saving on paper and reduces costs associated with paper and postage. So, please, update your e-mail information now and opt to vote online (and not receive a paper ballot) by December 1. More information is available by contacting Ricardo Juarez at rjuarez@psych.org.

Clark Notes Centenary Of Historic Freud Visit

Sigmund Freud once said that America was "a gigantic mistake," but that didn't keep him from coming here and accepting an honorary degree from Clark University a century ago. The trip was his first and last to America.

BY AARON LEVIN

Once upon a time, Sigmund Freud came to America.

He walked (in Central Park), he talked (at Clark University).

Then he returned home to Vienna.

While here, he accepted the only honorary degree he would ever receive and retained his jaundiced view of the United States. His influence on the mind and its workings, however, traveled outward from that week in September a hundred years ago to rise and fall in the New World for the next half century.

To mark the centenary of Freud's visit, Clark University has planned two conferences, one from October 3 to 5 and another on November 21. Sophie Freud, granddaughter of Sigmund Freud, is one of the speakers. The New York Academy of Medicine will also commemorate the event with a conference on October 3 and 4.

Jung Helps Persuade Freud

In 1909 Freud's work was known only to a handful of scholars and clinicians on this side of the Atlantic when G. Stanley Hall, the president of Clark, wrote to invite him to join in the commemoration of the university's 20th anniversary. Hall was a major figure in American psychology and an admirer of Freud's work, especially as it applied to sexuality in early childhood.

Freud declined Hall's first invitation, saying that the original July date would interfere with seeing his patients. The Swiss psychiatrist Carl Jung wrote to tell Freud that he was missing an opportunity to draw attention to his ideas on both sides of the Atlantic. Eventually, Hall shifted the conference to early September to accommodate other speakers who had also initially begged off. He also increased Freud's honorarium from $400 to $750 (more than $18,000 in today's dollars) and offered him an honorary degree, as well. The combination was apparently enticing enough.

Credit: Courtesy Clark University Archives

Among the notable figures at Clark University's 1909 psychology conference were (front row, from left) Sigmund Freud, G. Stanley Hall (president of Clark), and Carl Jung; (back row, from left) A.A. Brill, Ernest Jones, and Sandor Ferenczi.

Freud and Clark saw mutual value in the impending conference, said Robert Tobin, Ph.D., now the Henry J. Leir Chair in Foreign Languages and Cultures at Clark, in an interview.

"Clark was new and appropriated some of the glow from its roster of distinguished speakers and honorees," said Tobin. "Even at 53, Freud was still not that eminent—*Interpretation of Dreams* had sold only 600 copies—so the degree served to validate his thinking and possibly bolster his status in Vienna."

Freud sailed from Bremen accompanied by Jung and the Hungarian psychoanalyst Sandor Ferenczi. Even this humble fact had Freudian overtones. The three had lunch while waiting to embark. When Freud fell ill during the meal, Jung paid the bill, an event that some have interpreted as an oedipal usurpation of the father of psychoanalysis by his chosen heir.

"The 1909 conference paved the way for the movement from Europe to the U.S. in the 1930s that pushed psychoanalysis to dominate psychiatry until the 1960s."

Freud Presents Five Lectures

Freud and Jung spent a few days in New York (and took that stroll through Central Park) before traveling to Worcester, Mass., home of Clark University. Freud arrived on campus on Sunday, September 5, and on Tuesday gave his first lecture, a general outline of the history of psychoanalytic research.

Freud did not read his lectures. His preparation—aside from years of thinking and writing about psychoanalysis—consisted of taking walks with Jung to discuss his intended topics.

please see ***Freud*** *on page 29*

APA, ACOG Produce Guidance on Managing Depression During Pregnancy

In addition to collaboration between obstetricians and psychiatrists, the patient's own input is "paramount" when choosing the most appropriate treatment for depression before and throughout pregnancy.

BY JUN YAN

Treating pregnant women with clinical depressive symptoms poses a difficult challenge to not only obstetricians and psychiatrists but also to the patients themselves. Specialists in both disciplines have worked together to review the literature and produce a report with practical guidance.

In a collaborative effort, APA and the American College of Obstetricians and Gynecologists (ACOG) convened a work group of psychiatrists and obstetricians/gynecologists led by Kimberly Yonkers, M.D., an associate professor of psychiatry and obstetrics, gynecology, and reproductive sciences at Yale School of Medicine. The work group examined available research and formulated recommendations on how to best manage depression during pregnancy. The report has been published simultaneously in the September *Obstetrics and Gynecology* and the September/October *General Hospital Psychiatry*.

Depressive symptoms are present in 14 percent to 23 percent of pregnant women and, if left untreated, can pose serious risks to the health and well-being of both the patient and the fetus she carries, according to the report. Although researchers have examined the risks of antidepressant exposure to birth outcomes to a certain extent, many studies have produced conflicting or inconsistent results. There are even fewer data on the effects of maternal depression on pregnancy and child developmental outcomes. Published studies are often hampered by uncontrolled confounding factors and small sample size.

"There are no clear-cut data [to quantify] the risk of antidepressant treatment independent of the underlying illness," said Yonkers in an interview with *Psychiatric News*. Although some antidepressants have been linked to a small but significant increase in adverse risks, studies have not been able to extricate the effect of medications from the effect of depression itself, she pointed out.

The work group devised antidepressant treatment algorithms and guidelines to help physicians make optimal, individualized therapeutic decisions with patients.

A thorough assessment of a patient's current symptoms and medical history is critical for determining the treatment strategy over the course of pregnancy, the group recommended. Physicians are urged to consider psychosocial treatments, especially cognitive-behavioral therapy and interpersonal psychotherapy, for patients with mild-to-moderate depression, especially for women who are planning to become pregnant or who would rather avoid antidepressant medications.

In contrast, patients with a history of severe and/or recurrent depression, psychotic symptoms, bipolar disorder, or a suicide attempt should not be discontinued from drug therapy.

Electroconvulsive therapy is an option for inducing rapid symptom relief for pregnant women who have not responded to antidepressants or other therapy or who are psychotic, suicidal, or severely disabled.

The work group strongly calls for obstetricians and psychiatrists to coordinate their care, especially for patients who require careful monitoring and evaluation as their conditions and symptoms fluctuate. Further, "respect for the patient's preferences is paramount," the report states.

The overarching message is "there isn't one simple answer," according to Yonkers. "A collaborative approach involving the psychiatrist, the obstetrician, and the patient is the best. There is no one scenario that fits every patient."

Nada Stotland, M.D., M.P.H., immediate past president of APA and an expert in reproductive psychiatry, is a coauthor of this report.

"Depression during pregnancy is a particularly common and vexing clinical problem," Stotland told *Psychiatric News*. "Untreated depression is bad for the pregnancy and a risk for postpartum depression, which is agonizing for the mother and harmful for the baby. The collaboration between APA and ACOG brought both perspectives and bases of knowledge to the work on this paper and will bring this important information to clinicians in both specialties. I hope this project will be a model for many collaborations in the future."

"The Management of Depression During Pregnancy: A Report From the American Psychiatric Association and the American College of Obstetricians and Gynecologists" can be accessed at <http://journals.lww.com/greenjournal/pages/default.aspx>. ■

RELAPSE.

Nearly 80% of patients with schizophrenia experience at least 1 relapse within 5 years of diagnosis.[1]

RELAPSE.

Patients with schizophrenia miss nearly one third of their oral antipsychotic doses every year.[2]

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References: 1. Robinson D, Woerner MG, Alvir JMJ, et al. Predictors of relapse following response from a first episode of schizophrenia or Schizoaffective Disorder. *Arch Gen Psychiatry*. 1999;56:241-247. **2.** Mahmoud RA, Engelhart LM, Janagap CC, Oster G, Ollendorf D. Risperidone versus conventional antipsychotics for schizophrenia and schizoaffective disorder: Symptoms, quality of life and resource use under customary clinical care. *Clin Drug Invest*. 2004;24:275-286.

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Psychiatrists Should Prepare For 'Swine' Flu Fallout

A massive outbreak of influenza A (H1N1) might lead to headaches for psychiatrists as well as epidemiologists.

BY AARON LEVIN

Novel influenza A (H1N1) advanced and receded in the United States this past spring, but no one in the public health community expects it to stay away. Whether the flu formerly known as swine will return this fall and winter as a mild breeze or a storm of infection is unknown at press time.

Flu is usually not the concern of psychiatrists (unless they catch it themselves), but some aspects of last spring's mini-pandemic have raised some concerns in the disaster mental health community.

These include not only neuropsychiatric effects of the disease or the medications used to treat it, but the community mental health issues that follow any major disaster (see box).

According to the Centers for Disease Control and Prevention (CDC), "seizures, encephalitis, encephalopathy, Reye's syndrome, and other neurologic disorders" and "acute cognitive and behavioral problems" have been seen in children with seasonal flu. In July the agency reported on four cases in Dallas of neurologic complications in children and adolescents with confirmed H1N1 flu. Those patients represented about 1 percent of the H1N1 cases seen at the hospitals reporting. At various times, one or more of these patients had seizures, were confused, and had difficulty responding to questions. All were hospitalized, treated, and released without long-term mental complications.

"Clinicians should consider influenza-associated encephalopathy in the differential diagnosis of children with [influenza-like illness] and seizures or mental status changes," wrote the CDC in the July 24 issue of *Morbidity and Mortality Weekly Report*. Such symptoms are manageable in normal caseloads but would presumably appear in greater absolute numbers if tens of thousands of people came down with the flu in one city.

Treatment represents another potential area of concern. The CDC recommends two neuraminidase inhibitors for the antiviral treatment and prophylaxis of H1N1 influenza: zanamivir (Relenza) and oseltamivir (Tamiflu). Recent prophylactic trials in Britain of the latter produced reports of side effects in 21 percent to 33 percent of participants, mostly gastrointestinal or headache, but the small number of participants and methodological problems limit the trials' usefulness.

Occasional reports of "bizarre behavior" after taking these drugs exist, but those effects may be attributable to the illness as much as to the medication. Early reports from Japan of increased suicides among young people taking oseltamivir were not confirmed after an FDA review, which said the events may have been related to high levels of flu-induced encephalitis there. A report last April from the drug's manufacturer (Hoffmann-La Roche) said "no increase in the incidence of claims-based neuropsychiatric events was detected" in users of the drug compared with those not taking antivirals.

Nonpharmaceutical interventions could play a role in holding down infection rates but might produce their own problems. "Social distancing"—closing schools and businesses, staying home from work when sick, and canceling concerts, sports events, and church services—has proven effective in past epidemics but might be hard to continue for more than short stretches of time.

"[M]aintaining the strict confinement of children during a pandemic would raise significant problems for many families and may cause psychosocial stress to children and adolescents," says the U.S. government flu Web site. "These considerations must be weighed against the severity of a given pandemic virus to the community at large and to children in particular."

In the worst case, if schools and child care centers were closed, workplace absenteeism could rise and incomes fall as parents stayed home to look after their children. Economic disruption could become severe. Families with members infected with the flu might be shunned by neighbors. Combined with high mortality rates, all of this would inevitably raise stress levels, or worse, as often occurs after floods and earthquakes.

Another problem might not show up for decades.

Last spring, pregnant women appeared to be at higher risk for severe complications of H1N1 flu, including death, so the CDC placed them at the top of its vaccine priority list.

Research looking at health records from the 1950s and 1960s has found that influenza infection in pregnant women is associated with increased risk of schizophrenia in their offspring. The spring 2009 outbreak struck people under the age of 25 twice as frequently as older people, reversing the seasonal flu pattern and making women of child-bearing age more vulnerable.

The H1N1 virus has some elements in its viral coat similar to that of strains circulating half a century ago, said Alan Brown of Columbia University, who has studied this question extensively. However, its viral makeup may not make much difference.

"Based on our data, the effect on the risk of schizophrenia is probably due not to the flu itself but to immune response, especially the cytokine response produced by activated T-cells," said Brown in an interview. "Infection is associated with a huge cytokine response."

Would the immune response generated by a flu vaccine cause the same problem?

"The evidence is that the cytokine response to the flu shot is far less than that from infection," said Brown. "Influenza is a greater danger when weighing the risks against the benefits."

Brown would like to see the CDC extend its vaccine recommendation to all women of childbearing age.

However, much uncertainty remains because no one has studied the effects of flu vaccine on birth outcome to see the effects of the cytokine response on the fetus, he said.

Finally, a major outbreak might also place enormous strain on health care workers and first responders, if the outbreak of severe acute respiratory syndrome (SARS) in Toronto in 2003 offers any lesson.

There, the mysteries accompanying an unknown pathogen and route of transmission, along with a high fatality rate, raised stress levels in hospital employees, reported Robert Maunder, M.D., an associate professor of psychiatry at the Mount Sinai Hospital in Toronto, in 2004 in the *Philosophical Transactions of the Royal Society of London (B)*.

"[T]he SARS outbreak turned the modern world of health care on its head in Toronto, in the sense that health care workers were seen as victims and vectors of disease rather than healers, and hospitals were seen as contaminated areas rather than places fostering health," wrote Maunder.

please see ***Flu*** *on page 29*

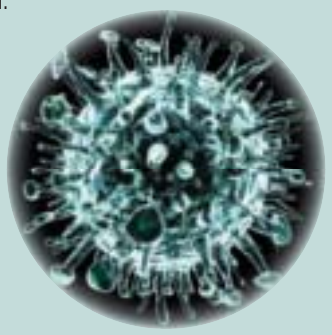
Credit: AP Photo/Yonhap, Seo Myung-gon

A thermal camera monitor is used at a South Korean airport to identify arriving passengers who may be infected with H1N1. The monitor measures body temperature.

Flu Outbreak Could Lead to Community Stress

The mental health effects of natural disasters like floods or earthquakes are fairly well documented, but there are almost no data on the mental health consequences of infectious disease outbreaks, according to the Center for the Study of Traumatic Stress. The center is part of the Department of Psychiatry at the Uniformed Services University of the Health Sciences in Bethesda, Md.

Nevertheless, from existing research and experience stemming from past disasters, the center offers a number of guidelines for clinicians and the public in preparing for the outcomes of a severe outbreak of novel influenza A (H1N1) flu.



Credit: IstockPhoto © Björn Meyer

- Public health and government officials must inform the public in advance about the science of influenza and ways to prepare for an outbreak and reduce the risk of infection.
- Public officials must understand who are the most vulnerable members of society and will need the most health services, including mental health services—people with psychiatric illness, children, the elderly, homeless people, and people who suffer losses during the pandemic.
- Community medical capacity may be overwhelmed by the sick and those who fear real or imagined exposure. Planning for such behavioral response is critical.
- Community social supports, even if hampered by the necessities of social distancing, are important. Engaging in regular activities like school or work as much as possible can lessen distress.
- Planning for mass fatalities, including stress not only on survivors, but on medical staff, funeral homes, and religious institutions, is essential.
- Good risk and safety communication must inform the public about health-protective behaviors.
- Poor material support for prevention, response, and recovery may lead to disenchantment with systems that help communities respond to disaster.
- First responders will need help assuring the safety of their families while they work and coping with the inevitable stress they will face on the job.
- Finally, mental health surveillance should track levels of PTSD, depression, and substance use, in parallel with changes in the social environment—school or work closings, housing, or transportation problems.

More information is posted at <www.centerforthestudyoftraumaticstress.org/pandemicflu.shtml>.

New Policy Helps Pediatricians Sharpen Psychiatric Skills

Expanding pediatricians' awareness and skill to assess and treat children with common mental health problems will go a long way toward improving access to care, says the chair of APA's Council on Children, Adolescents, and Their Families.

BY STEPHANIE WHYCHE

Of the estimated 13.7 million children and teens in the U.S. suffering from a mental disorder, 70 percent to 80 percent are not getting the professional treatment they need in part because there are just not enough psychiatrists—especially child psychiatrists—to help them (*Psychiatric News*, May 1). The solution, say a growing number of child health experts, is to fully harness the resources of primary care clinicians, especially pediatricians, to help tackle the problem.

Of course, that's easier said than done, considering the typical pediatrician's already tight schedule conducting routine physical exams, managing childhood immunizations, tracking developmental milestones, and attending to the daily stream of childhood illnesses and injuries.

So what's a pediatrician—poised to become a frontline warrior against mental illness—to do?

A new policy statement by the American Academy of Pediatrics (AAP) released in late June and posted online in the July *Pediatrics* offers pediatricians broad guidance from which to get started (see box). They are encouraged to read the 14-page policy statement and use it as a self-assessment tool to review their knowledge, skills, and attitudes related to child mental health. Based on the assessment, doctors can determine what "competencies" they need to acquire or enhance their clinical skills.

The statement was issued by the AAP's 2007-2008 Committee on Psychosocial Aspects of Child and Family Health and its 2007-2008 Task Force on Mental Health. The American Academy of Child and Adolescent Psychiatry and other medical and health-professional groups also provided input as the statement was being developed.

"Pediatricians have a special interest in preventing or intervening early in a condition before it rises to the level of a disorder," said Jane Foy, M.D., chair of the AAP Task Force on Mental Health, in the July *AAP News*.

The statement names the baseline "competencies" that pediatricians should have if they are to be frontline assessors of mental health in children or providers of care for patients exhibiting mental health problems. It also will help pediatricians evaluate whether they need to consult with or refer patients to psychiatrists or mental health professionals.

The statement also advocates "system enhancements" that should improve clinical practice. These include strengthening child mental health training in pediatric residency programs and continuing medical education, improving the financing/reimbursement of mental health care, and establishing collaborative relation-

please see ***Pediatricians*** *on page 29*

Mental Health Care Recognized as Integral to Primary Pediatric Care

The following is excerpted from the American Academy of Pediatrics' policy statement "The Future of Pediatrics: Mental Health Competencies for Pediatric Primary Care."

"Pediatric primary care clinicians have unique opportunities and a growing sense of responsibility to prevent and address mental health and substance abuse problems in the medical home. . . . [The AAP] proposes competencies requisite for providing mental health and substance abuse services in pediatric primary care settings and recommends steps toward achieving them. Achievement of the competencies proposed in this statement is a goal, not a current expectation. It will require innovations in residency training and continuing medical education, as well as a commitment by the individual clinician to pursue, over time, educational strategies suited to his or her learning style and skill level. System enhancements, such as collaborative relationships with mental health specialists and changes in the financing of mental health care, must precede enhancements in clinical practice. For this reason, the proposed competencies begin with knowledge and skills for system-based practice. The proposed competencies overlap those of mental health specialists in some areas; for example, they include the knowledge and skills to care for children with attention-deficit/hyperactivity disorder, anxiety, depression, and substance abuse and to recognize psychiatric and social emergencies. In other areas, the competencies reflect the uniqueness of the primary care clinician's role: building resilience in all children; promoting healthy lifestyles; preventing or mitigating mental health and substance abuse problems in children and their families; and partnering with families, schools, agencies, and mental health specialists to plan assessment and care. Proposed interpersonal and communication skills reflect the primary care clinician's critical role in overcoming barriers (perceived and/or experienced by children and families) to seeking help for mental health and substance abuse concerns."

Antidepressant Use Rises In 10-Year Period

The rate of antidepressant use doubled from 1996 to 2005, while the use of psychotherapy declined. In more recent years, other data on antidepressant use indicate that this trend has flattened or reversed.

BY JUN YAN

Antidepressant medications have gained wider acceptance and popularity, accompanied by declining use of psychotherapy, in the treatment of depression in the United States from 1996 to 2005, a study published in the August *Archives of General Psychiatry* demonstrates.

The authors, Mark Olfson, M.D., and Steven Marcus, Ph.D., compared the rates of antidepressant use in 1996 and 2005 using data collected in the Medical Expenditure Panel Survey (MEPS)–household component. The ongoing survey was first conducted by the Agency for Healthcare Research and Quality (AHRQ) in 1996.

In 2005 the annual rate of antidepressant use was estimated at 10.12 percent, nearly doubling from the 5.84 percent documented in 1996. Compared with 1996, the rates of antidepressant use in 2005 increased with statistical significance regardless of sex, age group, marital status, educational level, family income, health insurance type, and employment status. The rate of antidepressant use increased significantly among white and Hispanic, but not black, respondents.

Olfson is a professor of clinical psychiatry at Columbia University Medical School and New York State Psychiatric Institute. Marcus is a research associate professor at the University of Pennsylvania School of Social Policy and Practice. The study was supported by grants from the AHRQ and the National Alliance for Research on Schizophrenia and Depression.

During the year of MEPS, trained interviewers visited and interviewed a large sample of households throughout the United States and asked respondents to record their and their family members' health care visits, reasons for the visits, and treatments including medications throughout the year. Their diagnoses and health care visits were validated by respondents' medical records. Olfson and Marcus limited their analyses to people 6 years and older and included nearly 19,000 people from the 1996 survey and over 28,000 from the 2005 survey.

Among people who were treated with antidepressants, 5.45 percent also received antipsychotics in 1996, compared with 8.86 percent who also received antipsychotics in 2005, while the percentage of patients who also received psychotherapy declined significantly from 31.50 percent to 19.87 percent. Meanwhile, the rate of inpatient mental health service decreased significantly from 3.93 percent to 2.08 percent.

Fewer than 1 in 4 antidepressant users was being treated by a psychiatrist in 2005. This information was not collected in the 1996 survey, thus making a comparison impossible, Olfson told *Psychiatric News*. The rates of treatment by psychologists and social workers were about 9 percent and 4 percent, respectively, in 2005.

The authors suggested a number of explanations for the increase in antidepressant use, including more new drugs being approved, less stigma for mental illness, growing acceptance of psychopharmacological treatment by the public and general medical sectors, and a near fourfold increase in direct-to-consumer advertising to promote antidepressant drugs. The indications of antidepressants have expanded in the decade, which may also explain the growth of their popularity. The percentage of all antidepressant users who were being treated for depression barely changed from 1996 to 2005—from 26 percent to 27 percent. Other conditions for which they were treated included back pain, anxiety, fatigue, and sleep disorder.

The study authors offered several possible explanations for the increased antidepressant use. Two national surveys showed that the prevalence of major depression in adults rose from 3.3 percent in 1991-1992 to 7.1 percent in 2001-2002. "It is difficult to know whether depression became more common . . . or people just became more willing to disclose that they were depressed. Whatever the reason, a larger percentage of the population endorsed the symptoms of major depression in the later time period," said Olfson.

"The overall increase in the use of antidepressants since the mid-1990s is consistent with previous reports and with general clinical experience," David Fassler, M.D., commented to *Psychiatric News*. Fassler is a child psychiatrist and APA secretary-treasurer. "Physicians and the general public are more aware of the signs and symptoms of depression, and treatment with medication is more widely accepted." He found the decline in psychotherapy use unfortunate, as "research clearly demonstrates that psychotherapy is a valuable and important component of treatment for many people with depression."

Despite the increased rate of antidepressants, these data do not measure the quality of diagnosis and treatment for patients with depression and other mental illnesses, the authors acknowledged. They pointed out one disconcerting dataset: 52 percent (1996) to 65 percent (2005) of MEPS respondents with bipolar disorder were prescribed antidepressants. The effectiveness and risk of antidepressants in bipolar treatment are still controversial.

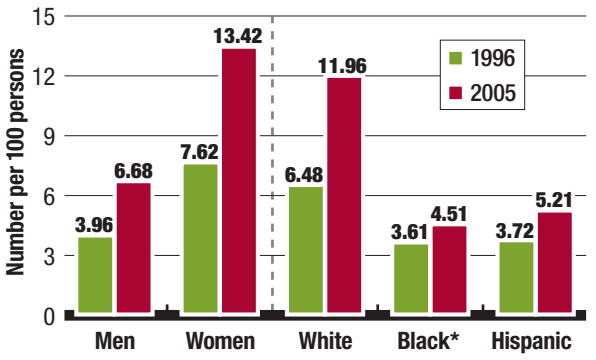
"In the long run, the real issue isn't simply how many people are taking antidepressants," said Fassler, but rather "whether or not the right people are getting the most effective and appropriate intervention possible."

Recent studies have suggested that the national trend of rising antidepressant prescriptions since the 1990s may have flattened or reversed since late 2004 when the Food and Drug Administration issued a series of public warnings about increased risk of suicidality in young patients associated with antidepressants (*Psychiatric News*, July 17). A boxed warning was required for all antidepressant drug labels in February 2005. This study, a cross-sectional comparison between 1996 and 2005, does not directly address this more recent trend.

An abstract of "National Patterns in Antidepressant Medication Treatment" is posted at <archpsyc.ama-assn.org/cgi/content/abstract/66/8/848>. ■

Use of Antidepressants Increased in Most Groups

The 2005 rate of antidepressant use among people 6 years and older in the United States is significantly higher than the 1996 rate in most demographic groups except blacks. Data were derived from the nationally representative Medical Expenditure Panel Surveys conducted in 1996 (n=18,993) and 2005 (n=28,445).



*Not statistically significant.

Source: Mark Olfson, M.D., M.P.H., and Steven Marcus, Ph.D., *Archives of General Psychiatry*, August 2009

Psychiatry Recruitment Formula Based on Passionate Faculty

If Bill Clinton didn't put Arkansas on the map, psychiatrists teaching at the University of Arkansas for Medical Sciences may. They are very successful at recruiting medical students into psychiatry.

BY JOAN AREHART-TREICHEL

The University of Arkansas for Medical Sciences College of Medicine has been one of the national leaders among medical schools in recruiting medical students into psychiatry during the past four years, according to APA records.

In fact, a whopping 10 percent of seniors in the school have entered a psychiatry residency program—either there or elsewhere—during the past five years, according to John Spollen, M.D., an associate professor of psychiatry and vice chair of education at the school. That compares with a national average of between 4 percent and 5 percent during the past five years, according to National Resident Matching Program figures. "So we are about double the national average over the last five years," he said.

So what's the magic?

"We hit them early and hard with our behavioral science course, which is given during the second year of medical school," Spollen told *Psychiatric News*. "We're basically using the same behavioral science course that many other medical schools have. The difference is that ours is primarily, almost solely, taught by practicing psychiatrists. The vast majority of the first two years of medical school is taught by Ph.D.s or M.D.s who usually do research, so our faculty tend to stand out as people who actually see patients for a living. And love it. We also strongly encourage the teachers of the course to weave clinical stories into their presentations. Psychiatry is about stories, and it's that fascination with the details of individual lives that makes medical students want to enter psychiatry rather than another field of medicine."

> **"Psychiatry is about stories, and it's that fascination with the details of individual lives that makes medical students want to enter psychiatry."**

Then, during their third year of medical school, Spollen continued, medical students tend to find their psychiatry rotation "interesting, fulfilling, and fun" and commit to it. And the major reason why they find the rotation captivating, he explained, is because the psychiatrists who teach it are passionate and charismatic. "We recruit faculty on the basis of whether they are great at what they do, are team players, and are fun to have dinner with."

Can psychiatry educators in other medical schools learn from their successes? "Absolutely," Spollen replied. "Pay attention to personality when recruiting faculty. Also, one way to lure psychiatrists whose passion is teaching onto your faculty is to offer them a tenure-track faculty appointment. We have a tenure track for clinician educators in our medical school, which most medical schools do not. In fact, our medical school has a long history of being a good place for teachers. Finally, make those first two years of medical school as exciting and clinically oriented as possible for students."

So will Spollen and his colleagues continue to use similar strategies over the next few years to get medical students to sign on to psychiatry? "You bet," he chuckled. "We're on quite a roll." ■

SEE ME FOR WHO I CAN BE

GREG, 35*
Diner Worker
Diagnosis: Schizophrenia

*Not an actual patient.

Do you see your patients' full potential?

GEODON is indicated for the treatment of schizophrenia.

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death compared to placebo. GEODON is not approved for the treatment of patients with dementia-related psychosis.

GEODON is contraindicated in patients with a known history of QT prolongation, recent acute myocardial infarction, or uncompensated heart failure, and should not be used with certain other QT-prolonging drugs. GEODON has a greater capacity to prolong the QT_c interval than several antipsychotics. In some drugs, QT prolongation has been associated with torsade de pointes, a potentially fatal arrhythmia. In many cases this would lead to the conclusion that other drugs should be tried first. Hypokalemia may increase the risk of QT prolongation and arrhythmia.

As with all antipsychotic medications, a rare and potentially fatal condition known as neuroleptic malignant syndrome (NMS) has been reported with GEODON. NMS can cause hyperpyrexia, muscle rigidity, diaphoresis, tachycardia, irregular pulse or blood pressure, cardiac dysrhythmia, and altered mental status. If signs and symptoms appear, immediate discontinuation, treatment, and monitoring are recommended.

Prescribing should be consistent with the need to minimize tardive dyskinesia (TD), a potentially irreversible dose- and duration-dependent syndrome. If signs and symptoms appear, discontinuation should be considered since TD may remit partially or completely.

Hyperglycemia-related adverse events, sometimes serious, have been reported in patients treated with atypical antipsychotics. There have been few reports of hyperglycemia or diabetes in patients treated with GEODON, and it is not known if GEODON is associated with these events. Patients treated with an atypical antipsychotic should be monitored for symptoms of hyperglycemia.

Precautions include the risk of rash, orthostatic hypotension, and seizures.

In short-term schizophrenia trials, the most commonly observed adverse events associated with GEODON at an incidence of ≥5% and at least twice the rate of placebo were somnolence and respiratory tract infection.

Please see brief summary of prescribing information on adjacent page.

For more information, please visit www.pfizerpro.com/GEODON

GEODON®
(ziprasidone HCl) **Capsules**

BRIEF SUMMARY. See package insert for full prescribing information.

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 seventeen 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. Geodon (ziprasidone) is not approved for the treatment of patients with Dementia-Related Psychosis (see WARNINGS).

INDICATIONS—GEODON Capsules is indicated for the treatment of schizophrenia and acute manic or mixed episodes associated with bipolar disorder with or without psychotic features. GEODON® (ziprasidone mesylate) for Injection is indicated for acute agitation in schizophrenic patients.

CONTRAINDICATIONS — *QT Prolongation:* Because of GEODON's dose-related prolongation of the QT interval and the known association of fatal arrhythmias with QT prolongation by some other drugs, GEODON is contraindicated in patients with a known history of QT prolongation (including congenital long QT syndrome), with recent acute myocardial infarction, or with uncompensated heart failure (see **WARNINGS**). Pharmacokinetic/pharmacodynamic studies between GEODON and other drugs that prolong the QT interval have not been performed. An additive effect of GEODON and other drugs that prolong the QT interval cannot be excluded. Therefore, GEODON should not be given with dofetilide, sotalol, quinidine, other Class Ia and III anti-arrhythmics, mesoridazine, thioridazine, chlorpromazine, droperidol, pimozide, sparfloxacin, gatifloxacin, moxifloxacin, halofantrine, mefloquine, pentamidine, arsenic trioxide, levomethadyl acetate, dolasetron mesylate, probucol, or tacrolimus. GEODON is also contraindicated with drugs that have demonstrated QT prolongation as one of their pharmacodynamic effects and have this effect described in the full prescribing information as a contraindication or a boxed or bolded warning (see **WARNINGS**). GEODON is contraindicated in individuals with a known hypersensitivity to the product. **WARNINGS — *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. GEODON (ziprasidone) is not approved for the treatment of patients with dementia-related psychosis (see BOXED WARNING). *QT Prolongation and Risk of Sudden Death:*** **GEODON use should be avoided in combination with other drugs that are known to prolong the QT_c interval. Additionally, clinicians should be alert to the identification of other drugs that have been consistently observed to prolong the QT_c interval. Such drugs should not be prescribed with GEODON. A study directly comparing the QT/QT_c-prolonging effect of GEODON with several other drugs effective in the treatment of schizophrenia was conducted in patient volunteers. The mean increase in QT_c from baseline for GEODON ranged from approximately 9 to 14 msec greater than for four of the comparator drugs (risperidone, olanzapine, quetiapine, and haloperidol), but was approximately 14 msec less than the prolongation observed for thioridazine. In this study, the effect of GEODON on QT_c length was not augmented by the presence of a metabolic inhibitor (ketoconazole 200 mg bid). In placebo-controlled trials, GEODON increased the QT_c interval compared to placebo by approximately 10 msec at the highest recommended daily dose of 160 mg. In clinical trials the electrocardiograms of 2/2988 (0.06%) GEODON patients and 1/440 (0.23%) placebo patients revealed QT_c intervals exceeding the potentially clinically relevant threshold of 500 msec. In the GEODON patients, neither case suggested a role of GEODON. Some drugs that prolong the QT/QT_c interval have been associated with the occurrence of torsade de pointes and with sudden unexplained death. The relationship of QT prolongation to torsade de pointes is clearest for larger increases (20 msec and greater) but it is possible that smaller QT/QT_c prolongations may also increase risk, or increase it in susceptible individuals, such as those with hypokalemia, hypomagnesemia, or genetic predisposition. Although torsade de pointes has not been observed in association with the use of GEODON at recommended doses in premarketing studies, experience is too limited to rule out an increased risk. A study evaluating the QT/QT_c prolonging effect of intramuscular GEODON, with intramuscular haloperidol as a control, was conducted in patient volunteers. In the trial, ECGs were obtained at the time of maximum plasma concentration following two injections of GEODON (20 mg then 30 mg) or haloperidol (7.5 mg then 10 mg) given four hours apart. Note that a 30 mg dose of intramuscular GEODON is 50% higher than the recommended therapeutic dose. The mean change in QT_c from baseline was calculated for each drug using a sample-based correction that removes the effect of heart rate on the QT interval. The mean increase in QT_c from baseline for GEODON was 4.6 msec following the first injection and 12.8 msec following the second injection. The mean increase in QT_c from baseline for haloperidol was 6.0 msec following the first injection and 14.7 msec following the second injection. In this study, no patient had a QT_c interval exceeding 500 msec. As with other antipsychotic drugs and placebo, sudden unexplained deaths have been reported in patients taking GEODON at recommended doses. The premarketing experience for GEODON did not reveal an excess of mortality for GEODON compared to other antipsychotic drugs or placebo, but the extent of exposure was limited, especially for the drugs used as active controls and placebo. Nevertheless, GEODON's larger prolongation of QT_c length compared to several other antipsychotic drugs raises the possibility that the risk of sudden death may be greater for GEODON than for other available drugs for treating schizophrenia. This possibility needs to be considered in deciding among alternative drug products. Certain circumstances may increase the risk of the occurrence of torsade de pointes and/or sudden death in association with the use of drugs that prolong the QT_c interval, including (1) bradycardia; (2) hypokalemia or hypomagnesemia; (3) concomitant use of other drugs that prolong the QT_c interval; and (4) presence of congenital prolongation of the QT interval. GEODON should also be avoided in patients with congenital long QT syndrome and in patients with a history of cardiac arrhythmias (see CONTRAINDICATIONS, and see *Drug Interactions* under PRECAUTIONS). It is recommended that patients being considered for GEODON treatment who are at risk for significant electrolyte disturbances, hypokalemia in particular, have baseline serum potassium and magnesium measurements. Hypokalemia (and/or hypomagnesemia) may increase the risk of QT prolongation and arrhythmia. Hypokalemia may result from diuretic therapy, diarrhea, and other causes. Patients with low serum potassium and/or magnesium should be repleted with those electrolytes before proceeding with treatment. It is essential to periodically monitor serum electrolytes in patients for whom diuretic therapy is introduced during GEODON treatment. Persistently prolonged QT_c intervals may also increase the risk of further prolongation and arrhythmia, but it is not clear that routine screening ECG measures are effective in detecting such patients. Rather, GEODON should be avoided in patients with histories of significant cardiovascular illness, eg, QT prolongation, recent acute myocardial infarction, uncompensated heart failure, or cardiac arrhythmia. GEODON should be discontinued in patients who are found to have persistent QT_c measurements >500 msec. *Neuroleptic Malignant Syndrome (NMS):*** A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with administration of antipsychotic drugs. 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. The patient should be carefully monitored, since recurrences of NMS have been reported. ***Tardive Dyskinesia (TD):*** A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients undergoing treatment with antipsychotic drugs. Although the prevalence of TD appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of antipsychotic treatment, which patients are likely to develop TD. If signs and symptoms of TD appear in a patient on GEODON, drug discontinuation should be considered. ***Hyperglycemia and Diabetes Mellitus:*** Hyperglycemia-related adverse events, sometimes serious, have been reported in patients treated with atypical antipsychotics. There have been few reports of hyperglycemia or diabetes in patients treated with GEODON, and it is not known if GEODON is associated with these events. Patients treated with an atypical antipsychotic should be monitored for symptoms of hyperglycemia. **PRECAUTIONS — *General:*** Rash: In premarketing trials, about 5% of GEODON patients developed rash and/or urticaria, with discontinuation of treatment in about one-sixth of these cases. The occurrence of rash was dose related, although the finding might also be explained by longer exposure in higher-dose patients. Several patients with rash had signs and symptoms of associated systemic illness, e.g., elevated WBCs. Most patients improved promptly upon treatment with antihistamines or steroids and/or upon discontinuation of GEODON, and all patients were reported to recover completely. Upon appearance of rash for which an alternative etiology cannot be identified, GEODON should be discontinued. Orthostatic Hypotension: GEODON may induce orthostatic hypotension associated with dizziness, tachycardia, and, in some patients, syncope, especially during the initial dose-titration period, probably reflecting its α_1-adrenergic antagonist properties. Syncope was reported in 0.6% of GEODON patients. GEODON should be used with particular caution in patients with known cardiovascular disease (history of myocardial infarction or ischemic heart disease, heart failure or conduction abnormalities), cerebrovascular disease or conditions that would predispose patients to hypotension (dehydration, hypovolemia, and treatment with antihypertensive medications). Seizures: In clinical trials, seizures occurred in 0.4% of GEODON patients. There were confounding factors that may have contributed to seizures in many of these cases. As with other antipsychotic drugs, GEODON should be used cautiously in patients with a history of seizures or with conditions that potentially lower the seizure threshold, e.g., Alzheimer's dementia. Conditions that lower the seizure threshold may be more prevalent in a population of 65 years or older. Dysphagia: Esophageal dysmotility and aspiration have been associated with antipsychotic drug use. Aspiration pneumonia is a common cause of morbidity and mortality in elderly patients, in particular those with advanced Alzheimer's dementia, and GEODON and other antipsychotic drugs should be used cautiously in patients at risk for aspiration pneumonia. **(See also Boxed WARNING, WARNINGS: Increased Mortality in Elderly Patients with Dementia-Related Psychosis).** Hyperprolactinemia: As with other drugs that antagonize dopamine D_2 receptors, GEODON elevates prolactin levels in humans. Tissue culture experiments indicate that approximately one third of human breast cancers are prolactin dependent in vitro, a factor of potential importance if the prescription of these drugs is contemplated in a patient with previously detected breast cancer. 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. Potential for Cognitive and Motor Impairment: Somnolence was a commonly reported adverse event in GEODON patients. In the 4- and 6-week placebo-controlled trials, somnolence was reported in 14% of GEODON patients vs 7% of placebo patients. Somnolence led to discontinuation in 0.3% of patients in short-term clinical trials. Since GEODON has the potential to impair judgment, thinking, or motor skills, patients should be cautioned about performing activities requiring mental alertness, such as operating a motor vehicle (including automobiles) or operating hazardous machinery until they are reasonably certain that GEODON therapy does not affect them adversely. Priapism: One case of priapism was reported in the premarketing database. Body Temperature Regulation: Although not reported with GEODON in premarketing trials, disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic agents. Suicide: The possibility of a suicide attempt is inherent in psychotic illness and close supervision of high-risk patients should accompany drug therapy. GEODON prescriptions should be written for the smallest quantity of capsules consistent with good patient management to reduce overdose risk. Use in Patients with Concomitant Illness: Clinical experience with GEODON in patients with certain concomitant systemic illnesses is limited. GEODON 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 premarketing clinical studies. Because of the risk of QT_c prolongation and orthostatic hypotension with GEODON, caution should be observed in cardiac patients (see ***QT Prolongation and Risk of Sudden Death*** in **WARNINGS** and Orthostatic Hypotension in **PRECAUTIONS**). ***Information for Patients:*** To ensure safe and effective use of GEODON, the information and instructions in the *Patient Information Section* should be discussed with patients. ***Laboratory Tests:*** Patients being considered for GEODON treatment who are at risk of significant electrolyte disturbances should have baseline serum potassium and magnesium measurements. Low serum potassium and magnesium should be repleted before treatment. Patients who are started on diuretics during GEODON therapy need periodic monitoring of serum potassium and magnesium. Discontinue GEODON in patients who are found to have persistent QT_c measurements >500 msec (see **WARNINGS**). ***Drug Interactions:*** (1) GEODON should not be used with any drug that prolongs the QT interval. (2) Given the primary CNS effects of GEODON, caution should be used when it is taken in combination with other centrally acting drugs. (3) Because of its potential for inducing hypotension, GEODON may enhance the effects of certain antihypertensive agents. (4) GEODON may antagonize the effects of levodopa and dopamine agonists. Effect of Other Drugs on GEODON: *Carbamazepine*, 200 mg bid for 21 days, resulted in a decrease of approximately 35% in the AUC of GEODON. *Ketoconazole*, a potent inhibitor of CYP3A4, 400 mg qd for 5 days, increased the AUC and C_{max} of GEODON by about 35%-40%. *Cimetidine*, 800 mg qd for 2 days, did not affect GEODON pharmacokinetics. Coadministration of 30 mL of *Maalox* did not affect GEODON pharmacokinetics. Population pharmacokinetic analysis of schizophrenic patients in controlled clinical trials has not revealed any clinically significant pharmacokinetic interactions with benztropine, propranolol, or lorazepam. Effect of GEODON on Other Drugs: In vitro studies revealed little potential for GEODON to interfere with the metabolism of drugs cleared primarily by CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A4, and little potential for drug interactions with GEODON due to displacement. GEODON 40 mg bid administered concomitantly with *lithium* 450 mg bid for 7 days did not affect the steady-state level or renal clearance of lithium. GEODON 20 mg bid did not affect the pharmacokinetics of concomitantly administered *oral contraceptives*, ethinyl estradiol (0.03 mg) and levonorgestrel (0.15 mg). Consistent with in vitro results, a study in normal healthy volunteers showed that GEODON did not alter the metabolism of *dextromethorphan*, a CYP2D6 model substrate, to its major metabolite, dextrorphan. There was no statistically significant change in the urinary dextromethorphan/dextrorphan ratio. ***Carcinogenesis, Mutagenesis, Impairment of Fertility:*** Lifetime carcinogenicity studies were conducted with GEODON in Long Evans rats and CD-1 mice. In male mice, there was no increase in incidence of tumors relative to controls. In female mice there were dose-related increases in the incidences of pituitary gland adenoma and carcinoma, and mammary gland adenocarcinoma at all doses tested. Increases in serum prolactin were observed in a 1-month dietary study in female, but not male, mice. GEODON had no effect on serum prolactin in rats in a 5-week dietary study at the doses that were used in the carcinogenicity study. The relevance for human risk of the findings of prolactin-mediated endocrine tumors in rodents is unknown (see Hyperprolactinemia). Mutagenesis: There was a reproducible mutagenic response in the Ames assay in one strain of *S. typhimurium* in the absence of metabolic activation. Positive results were obtained in both the in vitro mammalian cell gene mutation assay and the in vitro chromosomal aberration assay in human lymphocytes. Impairment of Fertility: GEODON increased time to copulation in Sprague-Dawley rats in two fertility and early embryonic development studies at doses of 10 to 160 mg/kg/day (0.5 to 8 times the MRHD of 200 mg/day on a mg/m^2 basis). Fertility rate was reduced at 160 mg/kg/day (8 times the MRHD on a mg/m^2 basis). There was no effect on fertility at 40 mg/kg/day (2 times the MRHD on a mg/m^2 basis). The fertility of female rats was reduced. ***Pregnancy—Pregnancy Category C:*** There are no adequate and well-controlled studies in pregnant women. GEODON should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. ***Labor and Delivery:*** The effect of GEODON on labor and delivery in humans is unknown. ***Nursing Mothers:*** It is not known whether, and if so in what amount, GEODON or its metabolites are excreted in human milk. It is recommended that women receiving GEODON should not breast feed. ***Pediatric Use:*** The safety and effectiveness of GEODON in pediatric patients have not been established. ***Geriatric Use:*** Of the approximately 4500 patients treated with GEODON in clinical studies, 2.4% (109) were 65 years of age or over. In general, there was no indication of any different tolerability for GEODON or of reduced clearance of GEODON in the elderly compared to younger adults. Nevertheless, the presence of multiple factors that might increase the pharmacodynamic response to GEODON, or cause poorer tolerance or orthostasis, should lead to consideration of a lower starting dose, slower titration, and careful monitoring during the initial dosing period for some elderly patients. **ADVERSE REACTIONS — *Adverse Findings Observed in Short-term, Placebo-Controlled Trials:*** The following findings are based on the short-term placebo-controlled premarketing trials for schizophrenia (a pool of two 6-week, and two 4-week fixed-dose trials) and bipolar mania (a pool of two 3-week flexible-dose trials) in which GEODON was administered in doses ranging from 10 to 200 mg/day. ***Adverse Events Associated with Discontinuation:*** Schizophrenia: Approximately 4.1% (29/702) of GEODON-treated patients in short-term, placebo-controlled studies discontinued treatment due to an adverse event, compared with about 2.2% (6/273) on placebo. The most common event associated with dropout was rash, including 7 dropouts for rash among GEODON patients (1%) compared to no placebo patients (see **PRECAUTIONS**). Bipolar Mania: Approximately 6.5% (18/279) of GEODON-treated patients in short-term, placebo-controlled studies discontinued treatment due to an adverse event, compared with about 3.7% (5/136) on placebo. The most common events associated with dropout in the GEODON-treated patients were akathisia, anxiety, depression, dizziness, dystonia, rash, and vomiting, with 2 dropouts for each of these events among GEODON patients (1%) compared to one placebo patient each for dystonia and rash (1%) and no placebo patients for the remaining adverse events. ***Adverse Events at an Incidence ≥5% and at Least Twice the Rate of Placebo:*** The most commonly observed adverse events associated with GEODON in schizophrenia trials were somnolence (14%) and respiratory tract infection (8%). The most commonly observed adverse events associated with the use of GEODON in bipolar mania trials were somnolence (31%), extrapyramidal symptoms (31%), dizziness (16%), akathisia (10%), abnormal vision (6%), asthenia (6%), and vomiting (5%). The following list enumerates the treatment-emergent adverse events that occurred during acute therapy, including only those events that occurred in 2% of GEODON patients and at a greater incidence than in placebo. Schizophrenia: Body as a Whole—asthenia, accidental injury, chest pain. Cardiovascular—tachycardia. Digestive—nausea, constipation, dyspepsia, diarrhea, dry mouth, anorexia. Nervous—extrapyramidal symptoms, somnolence, akathisia, dizziness. Respiratory—respiratory tract infection, rhinitis, cough increased. Skin and Appendages—rash, fungal dermatitis. Special Senses—abnormal vision. Bipolar Mania: Body as a Whole—headache, asthenia, accidental injury. Cardiovascular—hypertension. Digestive—nausea, diarrhea, dry mouth, vomiting, increased salivation, tongue edema, dysphagia. Musculoskeletal—myalgia. Nervous—somnolence, extrapyramidal symptoms, dizziness, akathisia, anxiety, hypesthesia, speech disorder. Respiratory—pharyngitis, dyspnea. Skin and Appendages—fungal dermatitis. Special Senses—abnormal vision. ***Dose Dependency:*** An analysis for dose response in the schizophrenia trials revealed an apparent relation of adverse event to dose for the following: asthenia, postural hypotension, anorexia, dry mouth, increased salivation, arthralgia, anxiety, dizziness, dystonia, hypertonia, somnolence, tremor, rhinitis, rash, and abnormal vision. ***Extrapyramidal Symptoms (EPS):*** The incidence of reported EPS for GEODON patients in the short-term, placebo-controlled schizophrenia trials was 14% vs 8% for placebo. Objectively collected data from those trials on the Simpson-Angus Rating Scale and the Barnes Akathisia Scale did not generally show a difference between GEODON and placebo. ***Dystonia:*** Prolonged abnormal contractions of muscle groups may occur in susceptible individuals during first few days of treatment. Dystonia may occur at any dose level but with greater frequency and severity with high potency and at higher doses of first generation antipsychotic drugs. Elevated risk is observed in males and younger age groups. ***Vital Sign Changes:*** GEODON is associated with orthostatic hypotension (see **PRECAUTIONS**). ***Weight Gain:*** In short-term schizophrenia trials, the proportions of patients meeting a weight gain criterion of ≥7% of body weight were compared, revealing a statistically significantly greater incidence of weight gain for GEODON patients (10%) vs placebo patients (4%). A median weight gain of 0.5 kg was observed in GEODON patients vs 0.0 kg in placebo patients. Weight gain was reported as an adverse event in 0.4% of both GEODON and placebo patients. During long-term therapy with GEODON, a categorization of patients at baseline on the basis of body mass index (BMI) showed the greatest mean weight gain and the highest incidence of clinically significant weight gain (>7% of body weight) in patients with a low BMI (<23) compared to normal (23-27) or overweight (>27) patients. There was a mean weight gain of 1.4 kg for patients with a "low" baseline BMI, 0.0 kg for patients with a "normal" BMI, and a 1.3 kg mean weight loss for patients with a "high" BMI. ***ECG Changes:*** GEODON is associated with an increase in the QT_c interval (see **WARNINGS**). In schizophrenia trials, GEODON was associated with a mean increase in heart rate of 1.4 beats per minute compared to a 0.2 beats per minute decrease among placebo patients. ***Other Adverse Events Observed During the Premarketing Evaluation of GEODON:*** Frequent adverse events are those occurring in at least 1/100 patients; infrequent adverse events are those occurring in 1/100 to 1/1000 patients; rare events are those occurring in fewer than 1/1000 patients. Schizophrenia: Body as a Whole — *Frequent:* abdominal pain, flu syndrome, fever, accidental fall, face edema, chills, photosensitivity reaction, flank pain, hypothermia, motor vehicle accident. Cardiovascular System — *Frequent:* tachycardia, hypertension, postural hypotension; *Infrequent:* bradycardia, angina pectoris, atrial fibrillation; *Rare:* first-degree AV block, bundle branch block, phlebitis, pulmonary embolus, cardiomegaly, cerebral infarct, cerebrovascular accident, deep thrombophlebitis, myocarditis, thrombophlebitis. Digestive System — *Frequent:* anorexia, vomiting; *Infrequent:* rectal hemorrhage, dysphagia, tongue edema; *Rare:* gum hemorrhage, jaundice, fecal impaction, gamma glutamyl transpeptidase increased, hematemesis, cholestatic jaundice, hepatitis, hepatomegaly, leukoplakia of mouth, fatty liver deposit, melena. Endocrine — *Rare:* hypothyroidism, hyperthyroidism, thyroiditis. Hemic and Lymphatic System — *Infrequent:* anemia, ecchymosis, leukocytosis, leukopenia, eosinophilia, lymphadenopathy; *Rare:* thrombocytopenia, hypochromic anemia, lymphocytosis, monocytosis, basophilia, lymphedema, polycythemia, thrombocythemia. Metabolic and Nutritional Disorders — *Infrequent:* thirst, transaminase increased, peripheral edema, hyperglycemia, creatine phosphokinase increased, alkaline phosphatase increased, hypercholesteremia, dehydration, lactic dehydrogenase increased, albuminuria, hypokalemia; *Rare:* BUN increased, creatinine increased, hyperlipemia, hypocholesteremia, hyperkalemia, hypochloremia, hypoglycemia, hyponatremia, hypoproteinemia, glucose tolerance decreased, gout, hyperchloremia, hyperuricemia, hypocalcemia, hypoglycemic reaction, hypomagnesemia, ketosis, respiratory alkalosis. Musculoskeletal System — *Frequent:* myalgia; *Infrequent:* tenosynovitis; *Rare:* myopathy. Nervous System — *Frequent:* agitation, extrapyramidal syndrome, tremor, dystonia, hypertonia, dyskinesia, hostility, twitching, paresthesia, confusion, vertigo, hypokinesia, hyperkinesia, abnormal gait, oculogyric crisis, hypesthesia, ataxia, amnesia, cogwheel rigidity, delirium, hypotonia, akinesia, dysarthria, withdrawal syndrome, buccoglossal syndrome, choreoathetosis, diplopia, incoordination, neuropathy; *Infrequent:* paralysis; *Rare:* myoclonus, nystagmus, torticollis, circumoral paresthesia, opisthotonos, reflexes increased, trismus. Respiratory System — *Frequent:* dyspnea; *Infrequent:* pneumonia, epistaxis; *Rare:* hemoptysis, laryngismus. Skin and Appendages — *Infrequent:* maculopapular rash, urticaria, alopecia, eczema, exfoliative dermatitis, contact dermatitis, vesiculobullous rash. Special Senses — *Frequent:* fungal dermatitis; *Infrequent:* conjunctivitis, dry eyes, tinnitus, blepharitis, cataract, photophobia; *Rare:* eye hemorrhage, visual field defect, keratitis, keratoconjunctivitis. Urogenital System — *Infrequent:* impotence, abnormal ejaculation, amenorrhea, hematuria, menorrhagia, female lactation, polyuria, urinary retention, metrorrhagia, male sexual dysfunction, anorgasmia, glycosuria; *Rare:* gynecomastia, vaginal hemorrhage, nocturia, oliguria, female sexual dysfunction, uterine hemorrhage. **Adverse Finding Observed in Trials of Intramuscular GEODON:** In these studies, the most commonly observed adverse events associated with the use of intramuscular GEODON (≥5%) and observed at a rate on intramuscular GEODON (in the higher dose groups) at least twice that of the lowest intramuscular GEODON group were headache (13%), nausea (12%), and somnolence (20%). **Adverse Events at an Incidence >1% in Short-Term Fixed-Dose Intramuscular Trials:** The following list enumerates the treatment-emergent adverse events that occurred in ≥1% of GEODON patients (in the higher dose groups) and at least twice that of the lowest intramuscular GEODON group. Body as a Whole — headache, injection site pain, asthenia, abdominal pain, flu syndrome, back pain. Cardiovascular — postural hypotension, hypertension, bradycardia, vasodilation. Digestive — nausea, rectal hemorrhage, diarrhea, vomiting, dyspepsia, anorexia, constipation, tooth disorder, dry mouth. Nervous — dizziness, anxiety, insomnia, somnolence, akathisia, agitation, extrapyramidal syndrome, hypertonia, cogwheel rigidity, paresthesia, personality disorder, psychosis, speech disorder. Respiratory — rhinitis. Skin and Appendages — furunculosis, sweating. Urogenital — dysmenorrhea, priapism. **DRUG ABUSE AND DEPENDENCE — *Controlled Substance Class:*** GEODON is not a controlled substance. **OVERDOSAGE** — In premarketing trials in over 5400 patients, accidental or intentional overdosage of GEODON was documented in 10 patients. All patients survived without sequelae. In the patient taking the largest confirmed amount (3240 mg), the only symptoms reported were minimal sedation, slurring of speech, and transitory hypertension (BP 200/95).

Revised August 2008

Supported Employment Helps Patients, Cuts Costs

The notion that patients with psychotic illness cannot work appears to be changing, and many patients who have gone back to work say they did so because their psychiatrist told them they could.

BY MARK MORAN

Supported employment is associated with significant reductions in mental health service utilization costs by people with serious mental illness.

The finding, reported in APA's journal *Psychiatric Services* in August, builds on a substantial literature and clinical lore testifying to the dramatic benefits of employment on functioning and outcome for people with serious mental illness. But the *Psychiatric Services* study is the first to examine long-term economic benefits of employment.

"We have known for a while that once people become steady workers, they do better in other areas of their lives," coauthor Robert Drake, M.D., told *Psychiatric News*. "They feel better about themselves and about their relationships, and they may have a little more money so they are more independent. And they control their symptoms better and stay out of the hospital. We have had so many patients over the years say that work is what really helped them recover and get out of the mental health system and have a life of their own.

"But nobody had looked at the long-term economic effects of supported employment programs," continued Drake, a professor of psychiatry and community and family medicine at Dartmouth Medical School.

In the study, Drake and colleagues calculated annual costs of outpatient services and institutional stays over a 10-year period for 187 subjects in the New Hampshire Dual-Diagnosis Program. Patients who met the following criteria were included: long-term psychotic illness (schizophrenia, schizoaffective disorder, or bipolar disorder), active substance use disorder within the past six months, and absence of mental retardation.

These participants were heavy service users at baseline. They were identified by their interest in co-occurring disorder services rather than in employment services; however, many were exposed to supported employment during the 10 years of follow-up, because New Hampshire implemented this service widely during the 1990s.

Group differences in utilization and cost were examined over the follow-up between two groups: a "steady-work group" (n=51) who averaged 5,060 hours per person over 10 years, and a "minimum-work group" who averaged about 45 hours per person over 10 years.

Drake and colleagues found that use of outpatient services for the steady-work group declined at a significantly greater rate than for the minimum-work group, and that the average cost for outpatient services and institutional stays for the minimum-work group exceeded that of the steady-work group by $166,350 per participant over 10 years.

Statistical controls for group differences did not make the large effects disappear, Drake told *Psychiatric News*. "We were shocked when we looked at the magnitude of the effect," he said.

More education, a bipolar disorder diagnosis (versus schizophrenia or schizoaffective disorder), work in the past year, and lower scores on the expanded Brief Psychiatric Rating Scale predicted membership in the steady-work group.

"The most parsimonious explanation for this finding, consistent with many stories of recovery, is that clients who develop independent vocational lives outside of the mental health system decrease their use of the mental health system," the researchers wrote.

"There are now five long-term follow-up studies showing that over time people who are exposed to supported employment work more hours and stay employed more of the time, over time, and consider their job a career," Drake told *Psychiatric News*. "That's interesting by itself because it's so different from everything we have found in mental health services, where treatment effects invariably tend to erode over time or go away completely. That's not so with employment—people get better and better."

The authors acknowledged in the study that they could not rule out a possibility that their findings resulted from subjects' being less ill, being better motivated, or responding better to treatments than their counterparts. However, the authors deemed these explanations unlikely for several reasons. For example, statistical controls for age, previous work, and illness severity did not strongly affect or eliminate the associations they found in the study.

Drake said that for policymakers and program administrators, the study's message is clear—supported employment works.

"In the U.S. today, we provide supported employment for about 1 percent of people with serious mental illness, and that's because there is no simple way to pay for this service," he said. "Programs are just struggling to survive financially so they are going to go on providing services paid for by Medicaid that we know are ineffective. Everyone believes we will have this gap between needs and services until we have an obvious and simple payment mechanism."

Drake added that there is also a positive message for the practicing clinician. "When we do long-term follow-up with people who have done well and become steady workers, one of the things that surprised us is that many people say they went back to work because their psychiatrist told them they could."

And changing medications or lowering doses to reduce side effects that can interfere with working has also turned out to be important, he said.

He noted that in the past the conventional wisdom was that people with psychotic illness couldn't work because employment would be too stressful.

"It turns out that it's unemployment that is stressful," Drake said.

"The Long-Term Impact of Employment on Mental Health Service Use and Costs for Persons With Severe Mental Illness" is posted at <http://ps.psychiatryonline.org/cgi/content/full/60/8/1024>. ■

More People Seeking MH Care Than Ever Before

Efforts to mainstream mental health benefits and reduce stigma appear to be encouraging more people to get needed treatment. Not surprisingly, mental health expenditures have increased as well.

BY RICH DALY

The number of people treated and the total cost of their care increased more for mental illness than for any other chronic health condition in a recent 10-year span, according to government figures.

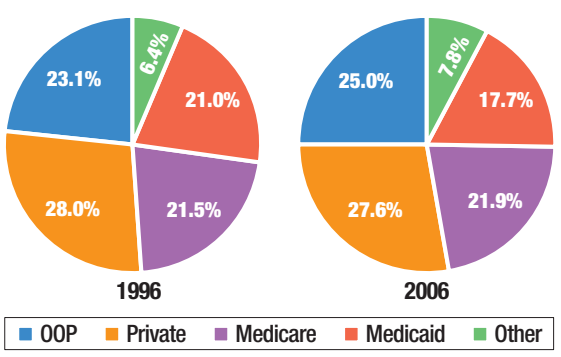
The 87 percent surge in the number of people seeking noninstitutional care for psychiatric illness from 1996 to 2006 paralleled the 63 percent increase in spending on such disorders within the same period, according to data released in July by the Agency for Healthcare Research and Quality (AHRQ).

The findings were based on an analysis of the Household Component of the Medical Expenditure Panel Survey, which identified the five most costly conditions in 1996 and 2006. Those conditions—heart conditions, cancer, trauma-related disorders, mental disorders, and asthma—were determined by totaling and ranking the expenses for the medical care delivered for the diagnosis and treatment of acute and chronic conditions.

The survey found that the number of people who sought care for psychiatric disorders nearly doubled in the 10-year period. In 1996, 19.3 million people incurred expenses for mental health care, while 36.2 million sought such care in 2006. The number seeking care for mental disorders was second only to the 48.5 million who sought asthma care in 2006.

As More Seek MH Care, More Spend Own Funds

A growing percentage of mental health costs is paid by patients out of pocket (OOP). Private insurance continues to fund the largest—although shrinking—portion of spending on psychiatric disorders.



Source: Household Component of Medical Expenditure Panel Survey, AHRQ, July 2009

The growth in the number of people receiving care for psychiatric conditions is not due to an increase in the prevalence of mental illness but rather reflects people's willingness to seek care instead of going untreated as they did in the past, said Selby Jacobs, M.D., a member of the APA Council on Healthcare Systems and Financing.

The recent AHRQ findings are "testimony to some extent on the [effectiveness of the] strategy of mainstreaming mental health benefits," Jacobs told *Psychiatric News*.

The survey found that the largest increase in spending for chronic and acute health care conditions was for the category of mental disorders. Spending related to psychiatric diagnosis and treatment rose 63 percent, while the second-largest increase in spending—47 percent—occurred for trauma-related disorders.

Jacobs credited the large jump in mental health spending to the combination of a demand for care by more people with psychiatric disorders and to the "soaring costs" of psychotropic drugs in recent years.

Other recent data also support the finding that treatment of mental illness has increased. A study in the August *Archives of General Psychiatry*, for example, concluded that antidepressant use among U.S. residents nearly doubled in a similar period, 1996 to 2005 (see page 8). The researchers, who included Eric Caine, M.D., chair of the Department of Psychiatry at the University of Rochester Medical Center, reported that the number of U.S. residents prescribed antidepressants rose from 5.84 percent, or 13.3 million people, in 1996 to 10.12 percent, or 27 million people, in 2005.

Spending on mental health care may further increase after implementation of the 2008 law that mandates parity in mental health coverage in most private insurance plans and another 2008 law that will make Medicare outpatient mental health services more affordable by phasing out the discriminatory copay.

The AHRQ data, however, indicated that the jump in mental health spending was not driven by the rising cost of an individual's treatment. In fact, the average annual per-person spending by patients, government programs, and private insurers fell in the 10-year span, from $1,825 in 1996 to $1,591 in 2006.

please see ***MH Care*** *on page 29*

Congress Readies for Fall Action On Health Care Reform

BY ROBERT CABAJ, M.D.

Overhauling America's health care system has become a leading priority of Congress this year to realize President Obama's pledge to cover millions of uninsured people while addressing rising health care costs. Since before Obama's inauguration, APA members and Department of Government Relations (DGR) staff have been working to ensure that this effort includes meaningful mental health care reform. Building on the advances of 2008 Medicare and commercial insurance parity laws, APA is fighting for timely access to appropriate psychiatric care for all Americans without payment and medical management discrimination.

In Congress, five committees hold jurisdiction over health reform legislation. Three are in the House of Representatives: Energy and Commerce, Ways and Means, and Education and Labor. They have developed a "Tri-Committee" bill introduced in July as America's Affordable Health Choices Act. Throughout July, each committee conducted a line-by-line review and amendment process called "marking up" the legislation. Three amended versions of the bill passed out of committee and will be combined into one final version of the Tri-Committee bill for a vote on the House floor this month.

The two Senate committees are the Health, Education, Labor, and Pensions (HELP) and Finance. The committees plan to mark up separate bills and merge them into one prior to consideration by the full Senate. On July 15 HELP approved its bill, the Affordable Health Choices Act, after a 13-day markup, one of the longest in the committee's history; more than 400 amendments were considered. The committee is now waiting for Finance to finish work on its bill. Sen. Max Baucus (D-Mont.), chair of the Finance Committee, set a tentative deadline of September 15 for having a bill ready for markup.

The Congressional Balancing Act

Achieving comprehensive health reform means finding a balance between competing ideological views in Congress. Even within the Democratic Party, members must work to find a compromise agreeable to both poles of the party. These competing interests can cause lockdown at any point, as seen in the House Energy and Commerce Committee; markup was stalled for weeks as conservative Blue Dog Democrats on the committee worked with Chair Henry Waxman (D-Calif.) to adjust provisions of the bill, only to be sidelined by the committee's more liberal Democrats.

The Senate Finance Committee is balancing competing interests in trying to produce a bipartisan proposal. A core group of six committee members—three Democrats and three Republicans—emerged as the lead negotiators for achieving compromise legislation. However, since Finance remains the only committee not to mark up legislation, some Democrats are pressuring Baucus to move forward in a partisan manner if the group fails to produce a bill by September 15. Challenges may also exist in reconciling the two Senate bills.

In health reform, the "balancing act" is particularly difficult when the principles of the debate are diametrically opposed by liberal and conservative members of Congress. Some of these principles include the presence of a public-plan option, increased regulation of the insurance market, and mandates, including mandated coverage and benefit mandates.

House Bill Highlights

Here's a summary of the House bill, America's Affordable Health Choices Act (HR 3200):

• Establishes a National Health Insurance Exchange so that individuals can be pooled together. The smallest employers would be allowed to participate in the exchange first; later larger employers would be eligible to join.

• Requires a basic benefit package for all qualified health benefit plans in the exchange. Mental health and substance-use disorder treatment is included in the basic benefit package, and the coverage requirement would be extended to all health insurance plans within five years.

• Includes a public option in the exchange. The original bill stated that Medicare-participating physicians would be enrolled as participating providers in the public option unless they opt out; the bill as amended by Energy and Commerce adds language that physicians can opt in or out of the public option without penalty.

• Mandates that employers must offer health insurance and that individuals must obtain a qualified health plan or face tax penalties.

• Rebases the Medicare sustainable growth rate (SGR) at 2009 levels, permanently avoiding the disastrous physician payment cut that would have been upward of 20 percent in 2010.

• Establishes two new spending targets: (1) primary and preventive care including evaluation and management services that can grow at 2 percent of GDP and (2) all other medical services, allowed to grow at 1 percent of GDP. The bill adds a five-year rolling target, with any debt accumulation falling away the sixth year.

• Includes bold steps to eliminate gaps in coverage:
  ◦ Preserves advances in the Paul Wellstone and Pete Domenici Mental Health Parity and Addiction Equity Act of 2008 for the coverage of treatment for mental health and substance abuse disorders.
  ◦ Blocks insurance discrimination based on health status and preexisting conditions.
  ◦ Extends the Medicare physician fee schedule mental health add-on as enacted in 2008.
  ◦ Phases out the Part D "donut hole" for Medicare prescription drug coverage and allows midyear changes if enrollees are adversely impacted by formulary changes.
  ◦ Addresses racial and ethnic disparities in health care through cultural competency provisions.
  ◦ Extends Medicaid eligibility to 133 percent of the federal poverty level, with federally funded affordability credits for low-income Americans to purchase health insurance.

Credit: AP Photo/Joel Page

As summer wore on, emotions ran high at the town-hall meetings held across the country on health care reform. This photo was taken last month in Portsmouth, N.H.

Senate HELP Bill Highlights

Here's a summary of the HELP bill, the Affordable Health Choices Act:

• Extends mental health parity to all plans in the Gateway (which would be similar to the "Exchange" in the House bill), as advocated by APA, but exempts small businesses.

• Requires the essential health care benefit design in the Gateway to include mental health and substance use disorder services.

• Prohibits discrimination based on a preexisting condition or medical status.

• Keeps dependents on parents' policies until age 26.

• Provides $50 million in community-based mental and behavioral health grants.

• Includes the CLASS Act—a voluntary program to help disabled Americans purchase community living assistance services.

• Includes means for future expansion of the National Health Service Corps.

• Includes mental and behavioral education and training grants for child and adolescent psychiatry, among others.

• Encourages employer-sponsored wellness programs to reward employees for positive health behaviors.

Senate Finance Committee Update

As this issue went to press, the Senate Finance Committee had not released a bill and has been tight-lipped on details. Baucus is embroiled in a working group of Democrat and Republican Finance members in an effort to craft a bipartisan bill. It is expected that they will unveil their bill and proceed to markup late this month. Then the HELP and Finance bills must be combined for a floor vote.

Stay Tuned. . .

The heat has been turned up by the masses while Congress was back home for recess, and there are still several moving targets; even the president's priority "public option" is reportedly at risk. When Congress reconvenes this month, work is expected to progress quickly to finalize the bills in the House and Senate for floor votes, and if passed, to combine the two versions into a workable compromise for the president's signature.

APA leadership and Department of Government Relations staff continue to monitor health reform legislation and advance congressional proposals that benefit APA members and their patients. By joining forces with like-minded groups, including the AMA, the Mental Health Liaison Group, and an ad-hoc coalition of medical specialty political action committees, APA expands its impact on health care decisions in Congress.

More information on the House and Senate proposals and APA's letters to Congress about them are posted at <www.psych.org/dgr>. ■

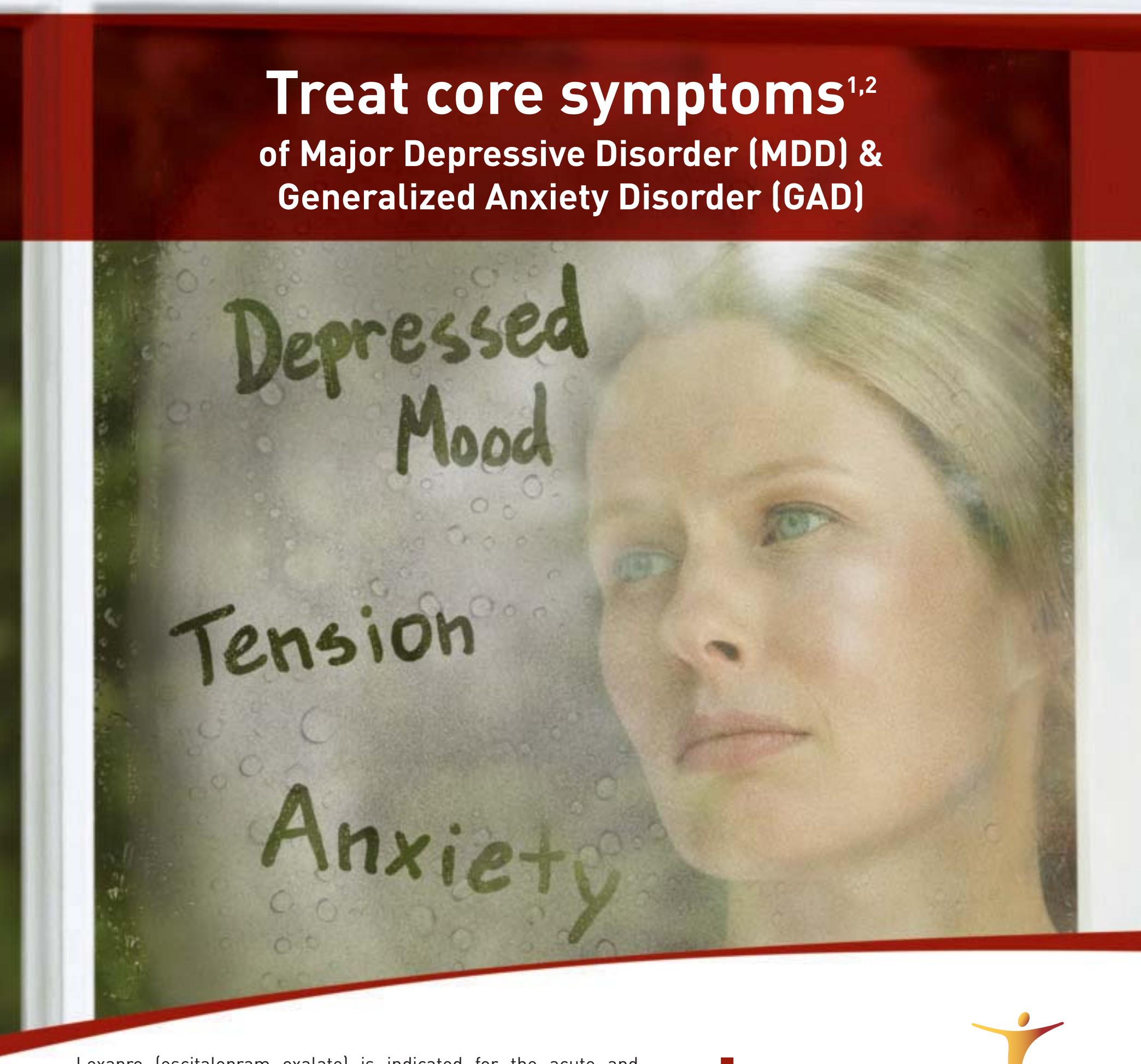
Robert Cabaj, M.D., is chair of APA's Council on Advocacy and Government Relations.

Proposals Invited

Eliot Sorel, M.D., invites colleagues from throughout the world to submit symposia, workshops, and poster presentation proposals as soon as possible for the XX World Congress of Social Psychiatry. Sorel and Tsutomu Sakuta, M.D., Ph.D., are chairing the Scientific Committee of the congress, whose theme is "Promoting the Integration of Health and Mental Health." More details are posted at <www.wasp2010.com>. ■

Treat core symptoms[1,2]

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



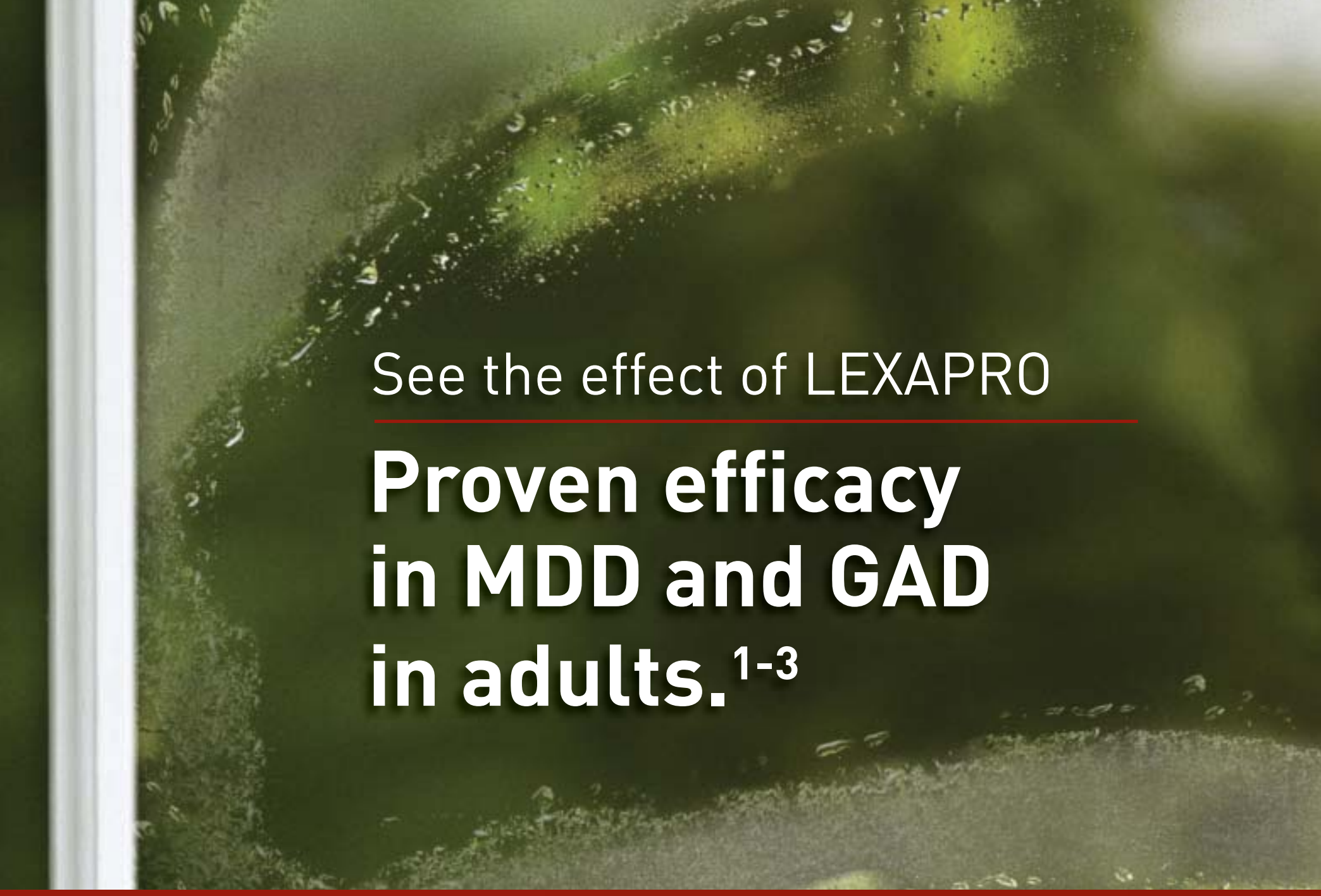
Lexapro (escitalopram oxalate) is indicated for the acute and maintenance treatment of major depressive disorder (MDD) in adults and adolescents aged 12-17 years. Lexapro is also indicated for the acute treatment of generalized anxiety disorder (GAD) in adults.

Lexapro® escitalopram oxalate

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 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 less than 12 years of age.

Please see additional Important Safety Information on following pages.



- Significantly higher rates of response and remission vs placebo in adults[2,4]
- Significantly improved quality-of-life (QOL) scores vs placebo in adults[1,2]

Lexapro (escitalopram oxalate) is indicated for the acute and maintenance treatment of major depressive disorder (MDD) in adults and adolescents aged 12-17 years. Lexapro is also indicated for the acute treatment of generalized anxiety disorder (GAD) in adults.

IMPORTANT SAFETY INFORMATION (continued)

Contraindications

- Lexapro is contraindicated in patients taking monoamine oxidase inhibitors (MAOIs). There have been reports of serious, sometimes fatal, reactions with some cases resembling neuroleptic malignant syndrome (NMS) and serotonin syndrome. Features may include 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. Serotonin syndrome was reported for two patients who were concomitantly receiving linezolid, an antibiotic which has MAOI activity. Lexapro should not be used in combination with an MAOI or within 14 days of discontinuing an MAOI. MAOIs should not be initiated within 14 days of discontinuing Lexapro.
- Lexapro is contraindicated in patients taking pimozide or with hypersensitivity to escitalopram or citalopram.

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 within the first few months of treatment or when changing the dose. Consideration should be given to changing the therapeutic regimen, including discontinuing medication, in patients whose depression is persistently worse, 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. Families and caregivers of patients treated with antidepressants should be alerted about the need to monitor patients daily for the emergence of agitation, irritability, unusual changes in behavior, or the emergence of suicidality, and report such symptoms immediately. 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.

- Prescribed to over 18 million US patients[5]
- Widely available on health plan formularies without restrictions[6]

- A major depressive episode may be the initial presentation of bipolar disorder. In patients at risk for bipolar disorder, treating such an episode with an antidepressant alone may increase the likelihood of precipitating a mixed/manic episode. Prior to initiating treatment with an antidepressant, patients should be adequately screened to determine if they are at risk for bipolar disorder. Lexapro should be used cautiously in patients with a history of mania or seizure disorder. Lexapro is not approved for use in treating bipolar depression.
- The concomitant use of Lexapro with other SSRIs, SNRIs, triptans, tryptophan, antipsychotics or other dopamine antagonists is not recommended due to potential development of life-threatening serotonin syndrome or neuroleptic malignant syndrome (NMS)-like reactions. Reactions have been reported with SNRIs and SSRIs alone, including Lexapro, but particularly with drugs that impair metabolism of serotonin (including MAOIs). Management of these events should include immediate discontinuation of Lexapro and the concomitant agent and continued monitoring.
- Patients should be monitored for adverse reactions when discontinuing treatment with Lexapro. During marketing of Lexapro and other SSRIs and SNRIs, there have been spontaneous reports of adverse events occurring upon discontinuation, including dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesias), anxiety, confusion, headache, lethargy, emotional lability, insomnia and hypomania. A gradual dose reduction rather than abrupt cessation is recommended whenever possible.

Please see additional Important Safety Information on next page.

Lexapro®
escitalopram oxalate

Visit the LEXAPRO website at www.lexapro.com

LEXAPRO: Proven efficacy in MDD and GAD in adults[1-3]

Warnings and Precautions (continued)

- SSRIs and SNRIs have been associated with clinically significant hyponatremia. Elderly patients and 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.
- SSRIs (including Lexapro) and SNRIs may increase the risk of bleeding. Patients should be cautioned that concomitant use of aspirin, NSAIDs, warfarin or other anticoagulants may add to the risk.
- Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that Lexapro does not affect their ability to engage in such activities.
- Lexapro should be used with caution in patients with severe renal impairment or with diseases or conditions that alter metabolism or hemodynamic responses. 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.
- For pregnant or nursing mothers, Lexapro should be used only if the potential benefit justifies the potential risk to the fetus or child.

Adverse Reactions

- In clinical trials of MDD, the most common adverse reactions in adults treated with Lexapro (approximately 5% or greater and at least twice the incidence of placebo) were nausea (15% vs 7%), insomnia (9% vs 4%), ejaculation disorder (9% vs <1%), fatigue (5% vs 2%), somnolence (6% vs 2%), and increased sweating (5% vs 2%). In pediatric patients, the overall profile of adverse reactions was similar to that seen in adults; however, the following additional adverse reactions were reported at an incidence of at least 2% for Lexapro and greater than placebo: back pain, urinary tract infection, vomiting, and nasal congestion.
- In clinical trials of GAD, the most common adverse reactions in adults treated with Lexapro (approximately 5% or greater and at least twice the incidence of placebo) were nausea (18% vs 8%), ejaculation disorder (14% vs 2%), insomnia (12% vs 6%), fatigue (8% vs 2%), decreased libido (7% vs 2%) and anorgasmia (6% vs <1%).

Please see accompanying brief summary of prescribing information for LEXAPRO, including Boxed Warning.

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.** Wade A, Lemming OM, Hedegaard KB. Escitalopram 10 mg/day is effective and well tolerated in a placebo-controlled study in depression in primary care. *Int Clin Psychopharmacol*. 2002;17:95-102. **5.** SDI, April 2008. Depression and Anxiety Treatment Market Overview. Based on longitudinal analysis of US electronic retail pharmacy claims submitted for third-party reimbursement. **6.** Data on file, Forest Laboratories, Inc.

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Lexapro escitalopram oxalate®

LEXAPRO® (escitalopram oxalate) TABLETS/ORAL SOLUTION **Rx Only**

Brief Summary: For complete details, please see full Prescribing Information for Lexapro.

WARNINGS: 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 less than 12 years of age. *[See Warnings and Precautions: Clinical Worsening and Suicide Risk, Patient Counseling Information: Information for Patients, and Used in Specific Populations: Pediatric Use].*

INDICATIONS AND USAGE: Major Depressive Disorder-Lexapro (escitalopram) is indicated for the acute and maintenance treatment of major depressive disorder in adults and in adolescents 12 to 17 years of age [*see Clinical tudies*]. 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. **Generalized Anxiety Disorder**-Lexapro is indicated for the acute treatment of Generalized Anxiety Disorder (GAD) in adults [*see Clinical Studies*]. 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.

CONTRAINDICATIONS: Monoamine oxidase inhibitors (MAOIs)-Concomitant use in patients taking monoamine oxidase inhibitors (MAOIs) is contraindicated [*see Warnings and Precautions*]. **Pimozide**-Concomitant use in patients taking pimozide is contraindicated [*see Drug Interactions*]. **Hypersensitivity to escitalopram or citalopram**-Lexapro is contraindicated in patients with a hypersensitivity to escitalopram or citalopram or any of the inactive ingredients in Lexapro.

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 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	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 Dosage and Administration*]. 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 [*see also Patient Counseling Information*]. 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. **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. **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*]. **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. **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. **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. **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 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 Lexapro and NSAIDs, aspirin, or other drugs that affect coagulation. **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*]. **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.

ADVERSE REACTIONS: Clinical Trials Experience-Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice. **Clinical Trial Data Sources; Pediatrics (6 -17 years)**-Adverse events were collected in 576 pediatric patients (286 Lexapro, 290 placebo) with major depressive disorder in double-blind placebo-controlled studies. Safety and effectiveness of Lexapro in pediatric patients less than 12 years of age has not been established. **Adults**-Adverse events 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 reactions 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; Pediatrics (6 -17 years)**-Adverse events were associated with discontinuation of 3.5% of 286 patients receiving Lexapro and 1% of 290 patients receiving placebo. The most common adverse event (incidence at least 1% for Lexapro and greater than placebo) associated with discontinuation was insomnia (1% Lexapro, 0% placebo). **Adults**-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; Adults**-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 Reactions in Placebo-Controlled Clinical Trials; Major Depressive Disorder; Pediatrics (6 -17 years)**-The overall profile of adverse reactions in pediatric patients was generally similar to that seen in adult studies, as shown in Table 2. However, the following adverse reactions (excluding those which appear in Table 2 and those for which the coded terms were uninformative or misleading) were reported at an incidence of at least 2% for Lexapro and greater than placebo: back pain, urinary tract infection, vomiting, and nasal congestion. **Adults**-The most commonly observed adverse reactions 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. 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.

TABLE 2
Treatment-Emergent Adverse Reactions Observed with a Frequency of ≥ 2% and Greater Than Placebo for Major Depressive Disorder

Adverse Reaction	Lexapro (N=715)	Placebo (N=592)
Autonomic Nervous System Disorders		
Dry Mouth	6%	5%
Sweating Increased	5%	2%
Central & Peripheral Nervous System Disorders		
Dizziness	5%	3%
Gastrointestinal Disorders		
Nausea	15%	7%
Diarrhea	8%	5%
Constipation	3%	1%
Indigestion	3%	1%
Abdominal Pain	2%	1%
General		
Influenza-like Symptoms	5%	4%
Fatigue	5%	2%
Psychiatric Disorders		
Insomnia	9%	4%
Somnolence	6%	2%
Appetite Decreased	3%	1%
Libido Decreased	3%	1%
Respiratory System Disorders		
Rhinitis	5%	4%
Sinusitis	3%	2%
Urogenital		
Ejaculation Disorder[1,2]	9%	<1%
Impotence[2]	3%	<1%
Anorgasmia[3]	2%	<1%

[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; Adults-The most commonly observed adverse reactions 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. 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.

TABLE 3
Treatment-Emergent Adverse Reactions Observed with a Frequency of ≥ 2% and Greater Than Placebo for Generalized Anxiety Disorder

Adverse Reactions	Lexapro (N=429)	Placebo (N=427)
Autonomic Nervous System Disorders		
Dry Mouth	9%	5%
Sweating Increased	4%	1%
Central & Peripheral Nervous System Disorders		
Headache	24%	17%
Paresthesia	2%	1%
Gastrointestinal Disorders		
Nausea	18%	8%
Diarrhea	8%	6%
Constipation	5%	4%
Indigestion	3%	2%
Vomiting	3%	1%
Abdominal Pain	2%	1%
Flatulence	2%	1%
Toothache	2%	0%
General		
Fatigue	8%	2%
Influenza-like Symptoms	5%	4%
Musculoskeletal System Disorder		
Neck/Shoulder Pain	3%	1%
Psychiatric Disorders		
Somnolence	13%	7%
Insomnia	12%	6%
Libido Decreased	7%	2%
Dreaming Abnormal	3%	2%
Appetite Decreased	3%	1%
Lethargy	3%	1%
Respiratory System Disorders		
Yawning	2%	1%
Urogenital		
Ejaculation Disorder[1,2]	14%	2%
Anorgasmia[3]	6%	<1%
Menstrual Disorder	2%	1%

[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 Reactions-The potential dose dependency of common adverse reactions (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 reactions 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 Reactions in Patients with Major Depressive Disorder

Adverse Reaction	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%

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
Incidence of Sexual Side Effects in Placebo-Controlled Clinical Trials

Adverse Event	Lexapro	Placebo
	In Males Only	
	(N=407)	(N=383)
Ejaculation Disorder (primarily ejaculatory delay)	12%	1%
Libido Decreased	6%	2%
Impotence	2%	<1%
	In Females Only	
	(N=737)	(N=636)
Libido Decreased	3%	1%
Anorgasmia	3%	<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 Reactions Observed During the Premarketing Evaluation of Lexapro**-Following is a list of 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. The listing does not include those events already listed in Tables 2 & 3, those events for which a drug cause was remote and at a rate less than 1% or lower than placebo, those events which were so general as to be uninformative, and those events reported only once which did not have a substantial probability of being acutely life threatening. Events are categorized by body system. Events of major clinical importance are described in the Warnings and Precautions section. Cardiovascular - hypertension, palpitation. Central and Peripheral Nervous System Disorders - light-headed feeling, migraine. Gastrointestinal Disorders - abdominal cramp, heartburn, gastroenteritis. General - allergy, chest pain, fever, hot flushes, pain in limb. Metabolic and Nutritional Disorders - increased weight. Musculoskeletal System Disorders - arthralgia, myalgia jaw stiffness. Psychiatric Disorders - appetite increased, concentration impaired, irritability. Reproductive Disorders/Female - menstrual cramps, menstrual disorder. Respiratory System Disorders - bronchitis, coughing, nasal congestion, sinus congestion, sinus headache. Skin and Appendages Disorders - rash. Special Senses - vision blurred, tinnitus. Urinary System Disorders - urinary frequency, urinary tract infection. **Post-Marketing Experience; Adverse Reactions Reported Subsequent to the Marketing of Escitalopram**-The following additional adverse reactions have been identified from spontaneous reports of escitalopram received worldwide. These adverse reactions have been chosen for inclusion because of a combination of seriousness, frequency of reporting, or potential causal connection to escitalopram and have not been listed elsewhere in labeling. However, because these adverse reactions were reported voluntarily 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 events include: Blood and Lymphatic System Disorders: anemia, agranulocytis, aplastic anemia, hemolytic anemia, idiopathic thrombocytopenia purpura, leukopenia, thrombocytopenia. Cardiac Disorders: atrial fibrillation, bradycardia, cardiac failure, myocardial infarction, tachycardia, torsade de pointes, ventricular arrhythmia, ventricular tachycardia. Ear and Labyrinth Disorders: vertigo Endocrine Disorders: diabetes mellitus, hyperprolactinemia, SIADH. Eye Disorders: diplopia, glaucoma, mydriasis, visual disturbance. Gastrointestinal Disorders: dysphagia, gastrointestinal hemorrhage, gastroesophageal reflux, pancreatitis, rectal hemorrhage. General Disorders and Administration Site Conditions: abnormal gait, asthenia, edema, fall, feeling abnormal, malaise. Hepatobiliary Disorders: fulminant hepatitis, hepatic failure, hepatic necrosis, hepatitis. Immune System Disorders: allergic reaction, anaphylaxis. Investigations: bilirubin increased, decreased weight, electrocardiogram QT prolongation, hepatic enzymes increased, hypercholesterolemia, INR increased, prothrombin decreased. Metabolism and Nutrition Disorders: hyperglycemia, hypoglycemia, hypokalemia, hyponatremia. Musculoskeletal and Connective Tissue Disorders: muscle cramp, muscle stiffness, muscle weakness, rhabdomyolysis. Nervous System Disorders: akathisia, amnesia, ataxia, choreoathetosis, cerebrovascular accident, dysarthria, dyskinesia, dystonia, extrapyramidal disorders, grand mal seizures (or convulsions), hypoaesthesia, myoclonus, nystagmus, Parkinsonism, restless legs, seizures, syncope, tardive dyskinesia, tremor. Pregnancy, Puerperium and Perinatal Conditions: spontaneous abortion. Psychiatric Disorders: acute psychosis, aggression, agitation, anger, anxiety, apathy, completed suicide, confusion, depersonalization, depression aggravated, delirium, delusion, disorientation, feeling unreal, hallucinations (visual and auditory), mood swings, nervousness, nightmare, panic reaction, paranoia, restlessness, self-harm or thoughts of self-harm, suicide attempt, suicidal ideation, suicidal tendency. Renal and Urinary Disorders: acute renal failure, dysuria, urinary retention. Reproductive System and Breast Disorders: menorrhagia, priapism. Respiratory, Thoracic and Mediastinal Disorders: dyspnea, epistaxis, pulmonary embolism, pulmonary hypertension of the newborn. Skin and Subcutaneous Tissue Disorders: alopecia, angioedema, dermatitis, ecchymosis, erythema multiforme, photosensitivity reaction, Stevens Johnson Syndrome, toxic epidermal necrolysis, urticaria. Vascular Disorders: deep vein thrombosis, flushing, hypertensive crisis, hypotension, orthostatic hypotension, phlebitis, thrombosis.

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 and Precautions*]. The concomitant use of Lexapro with other SSRIs, SNRIs or tryptophan is not recommended. **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 and Precautions*]. **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 and Precautions*]. **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.

USE IN SPECIFIC POPULATIONS: 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 also 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 and Precautions*]. 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**-Escitalopram is excreted in human breast milk. Limited data from women taking 10-20 mg escitalopram showed that exclusively breast-fed infants receive approximately 3.9% of the maternal weight-adjusted dose of escitalopram and 1.7% of the maternal weight-adjusted dose of desmethylcitalopram. There were two reports of infants experiencing excessive somnolence, decreased feeding, and weight loss in association with breastfeeding from a racemic citalopram-treated mother; in one case, the infant was reported to recover completely upon discontinuation of racemic citalopram by its mother and, in the second case, no follow-up information was available. Caution should be exercised and breastfeeding infants should be observed for adverse reactions when Lexapro is administered to a nursing woman. **Pediatric Use**-Safety and effectiveness of Lexapro has not been established in pediatric patients (less than 12 years of age) with Major Depressive Disorder. Safety and effectiveness of Lexapro has been established in adolescents (12 to 17 years of age) for the treatment of major depressive disorder [*see Clinical Studies*]. Although maintenance efficacy in adolescent patients with Major Depressive Disorder has not been systematically evaluated, maintenance efficacy can be extrapolated from adult data along with comparisons of escitalopram pharmacokinetic parameters in adults and adolescent patients. Safety and effectiveness of Lexapro has not been established in pediatric patients less than 18 years of age with Generalized Anxiety Disorder. **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 *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.

DRUG ABUSE AND DEPENDENCE: Abuse and Dependence; Physical and Psychological Dependence-Animal studies suggest that the abuse liability of racemic citalopram is low. Lexapro has not been systematically studied in humans for its potential for abuse, tolerance, or physical dependence. The premarketing clinical experience with Lexapro did not reveal any drug-seeking behavior. However, 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, physicians should carefully evaluate Lexapro patients for history of drug abuse and follow such patients closely, observing them for signs of misuse or abuse (e.g., development of tolerance, incrementations of dose, drug-seeking behavior).

OVERDOSAGE: Human Experience-In clinical trials of escitalopram, there were reports of escitalopram overdose, including overdoses of up to 600 mg, with no associated fatalities. During the postmarketing evaluation of escitalopram, Lexapro overdoses involving overdoses of over 1000 mg have been reported. As with other SSRIs, a fatal outcome in a patient who has taken an overdose of escitalopram has been rarely reported. Symptoms most often accompanying escitalopram overdose, alone or in combination with other drugs and/or alcohol, included convulsions, coma, dizziness, hypotension, insomnia, nausea, vomiting, sinus tachycardia, somnolence, and ECG changes (including QT prolongation and very rare cases of torsade de pointes). Acute renal failure has been very rarely reported accompanying overdose. **Management of Overdose**-Establish and maintain an airway to ensure adequate ventilation and oxygenation. Gastric evacuation by lavage and use of activated charcoal should be considered. Careful observation and cardiac and vital sign monitoring are recommended, along with general symptomatic and supportive care. Due to the large volume of distribution of escitalopram, forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be of benefit. There are no specific antidotes for Lexapro. 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.

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Lessons From Parity Battle Apply to Health Reform

Two experts say policymakers would do well to look ahead to the implementation phase since stakeholders will use it to lobby the government for their own interpretation of any reform.

BY MARK MORAN

The long and painful birth of mental health parity, and the story of its overdue delivery at the federal level, may hold some lessons for health system reform, now in the throes of its own painful labor.

Though the two efforts are markedly different in scope of purpose and potential impact, passage of the landmark parity bill offers some lessons for the more ambitious goal of health system reform, say psychiatrist Howard Goldman, M.D., Ph.D., and mental health policy expert Colleen Barry, Ph.D., in a commentary in the *American Journal of Psychiatry* this month.

Interviews with Congressional staffers and stakeholders involved in the parity battles led Goldman and Barry to emphasize three hard-won lessons:

- A focus on costs can create leverage with all parties that have a stake in the bottom line.
- Working out major differences behind closed doors and out of the glare of media scrutiny can help to define areas of unity when it comes time to "go public."
- Anticipation of the regulatory rule-making process that follows the passage of a law can help ensure passage of successful reform.

Goldman is editor of the APA journal *Psychiatric Services*. Barry is an associate professor of public health at Yale University School of Public Health.

The interviews are part of an effort by Goldman and Barry to write a comprehensive account of the passage of the 2008 Paul Wellstone and Pete Domenici Mental Health Parity and Addiction Equity Act.

"We were interested in doing a behind-the-scenes analysis of the passage of parity," Barry told *Psychiatric News*. "The idea was to talk to everyone who was involved, including key interest groups and congressional staffers, to understand how we were able to achieve this after so many years of trying. The interviews were quite interesting for the parallels they yielded with health system reform."

The most prominent of those is the importance of cost containment to stakeholders in both efforts. Barry and Goldman noted that opposition to parity for many years centered on the fear of "breaking the bank." But as data gathered from states where parity had been enacted and from the Federal Employees Health Benefits Program proved otherwise, that opposition was overcome.

"The market shift from indemnity insurance to managed care created a readily available method for enacting parity without driving up costs," they wrote in the commentary. "Resolving the dilemma of how to assemble a viable combination of financing and cost-containment provisions poses a more daunting challenge for health care reformers. However, the parity experience suggests that the sooner Congressional architects can agree upon a strategy for financing reform, the sooner attention will shift back to negotiating the contours of insurance expansion."

Barry told *Psychiatric News*, "From the standpoint of health care reform, costs need to be viewed as reasonable within a certain threshold. Our observation from the parity legislation is that you have to make the case that you have a viable cost-control strategy in place before you start talking about other issues."

A second lesson from parity is that bringing opponents together behind closed doors to air their differences can make it easier for them to find common ground when they have to go public.

Barry and Goldman noted that in the run-up to the passage of parity, Congress scrapped its traditional method of "shuttle diplomacy" whereby congressional committees met first with one group, then another; rather, they brought opposing stakeholders into the same room for candid discussions away from the glare of the media and public eye.

It's a lesson in "realpolitik" that runs counter to the current motif of "transparency" in all things. "I think you can differentiate transparency of process from transparency of results," Goldman told *Psychiatric News*. "A certain amount of behind-the-doors debate allows you to get to a result where people realize they have common interests."

The third piece of advice relates to what might be called "insider baseball" since it involves attention to a process largely unobserved by the general public—the regulatory rule-making process that follows formal passage of a bill.

The "implementation" phase, in which federal regulatory agencies write what sometimes amounts to pages and pages of regulatory "guidance," is where interpretive "meat" is put on the language of a bill.

With regard to parity, for instance, APA has insisted in communications with Health and Human Services Secretary Kathleen Sibelius that regulatory language should ensure that health plans and employers are prohibited from using certain indirect methods of restricting access to care—such as differential reimbursement schedules for different providers or separate-but-equal deductibles for mental health care—while still nominally complying with the law (*Psychiatric News*, June 19).

Goldman and Barry said that policymakers seeking health system reform would do well to look ahead to the implementation period since stakeholders will use it to lobby the government for their own interpretation of whatever law is passed.

"The implementation period effectively creates a second bite of the apple, whereby interest groups can fight out the smaller and sometimes not-so-small issues around interpretation of a bill, and try to argue for [an interpretation] that is most attractive to their interests," Barry said. "It is wise strategy to work out as many of the details as possible so that there will be as narrow as possible a set of issues remaining."

Several examples—the agreements the White House has reached separately with such disparate groups as the AMA and the pharmaceutical industry around cost reduction and the president's focus on reform as vital to long-term economic stability—indicate these lessons have not gone unheeded. And yet, from the vantage point of the August congressional recess and the fierce opposition to reform at town-hall meetings around the country, reform would appear to still face an uphill climb.

Goldman and Barry said that the differences between the parity and reform efforts are great—most notably in the fact that parity affects only those who already have insurance.

"It's not so easy to come up with an answer for health system reform since the basic problem is about adding people who are previously uninsured," Goldman said.

But he added that incrementalism has been the constant in American health system policy, and he expressed confidence that a major reform can be passed—even if much remains to be perfected.

"My experience is that all of health policy reform is incremental," he said. "It's just a matter of how big a bite you take each time. Just to get on the table the principle that everyone should be insured is an enormous advance. Because the president has made it a central mission of his administration and because there is a Democratic Congress, we should be able to get something."

"Lessons for Healthcare Reform From the Hard-Won Success of Behavioral Health Insurance Parity" can be accessed at <http://ajp.psychiatryonline.org> under the September issue. ■

Reform Proposals Encourage Patients To Participate in Treatment Decisions

The push for patients to play a larger role in making treatment decisions may have a big impact in the mental health area. Research indicates that mentally ill people want a more active role than those with other medical problems.

BY RICH DALY

As part of health reform under consideration by Congress, supporters of patients' playing a larger role in directing their health care have succeeded in adding measures to spur shared decision making by patients.

Advocates of shared decision making said the initiative belongs in health reform legislation because it improves patient satisfaction with outcomes. Moreover, a growing body of research has shown that patients who are educated about treatment choices and share in the decision-making process with their physicians are likely to get treatments that are less expensive than they would have otherwise received.

"The current standard of medical care in the United States fails to adequately ensure that patients are informed about all their treatment options and the risks and benefits of those options," said Sen. Ron Wyden (D-Wash.) in a Senate speech. "This leads to patients' getting medical treatments they may not have wanted had they been fully informed of their treatment options and integrated into the decision-making process."

Wyden introduced a bill (S 1133) in May to create a pilot program under Medicare on shared decision making. A similar approach was incorporated into the health reform bill approved by the Senate Health, Education, Labor, and Pensions (HELP) Committee in July. That bill would fund educational tools to help patients and caregivers understand treatment options and guide patients in choosing a treatment course with their clinician. The bill also would educate physicians on the use of decision-sharing tools, as well as tools to measure the satisfaction of patients and caregivers in the decision-making process.

A number of tools have emerged in recent years to help patients become more involved in the decision-making process, including informational videos and other materials that describe treatment options.

The proposed federal initiative builds on the efforts of several states to increase the role of patients in directing their care. A 2007 Washington state law set up a demonstration project to evaluate the cost-effectiveness of using decision aids. Similarly, legislation under consideration in Connecticut would require the state health department to develop a demonstration program on shared decision making. A bill in Vermont aims to contain health care costs through a shared decision-making demonstration program, which would include an analysis of potential barriers to clinicians' participating in shared decision making.

The increased push for patient involvement in making medical decisions follows a similar push in recent years aimed at patients with mental illness.

Mental health leaders who shaped the 2003 report by the President's New Freedom Commission on Mental Health and the authors of "Improving the 2006 Quality of Health Care for Mental and Substance-Use Conditions: Quality Chasm Series" stressed the importance of care

please see ***Decisions*** *on page 26*

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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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Disrupting Certain Neurons May Reduce Cocaine Craving

In a rat model, the memory that associates environmental cues with repeated cocaine injections is found in a "constellation of neurons" in the nucleus accumbens.

BY JUN YAN

Blocking specific neurons in the nucleus accumbens may effectively dissolve the neurological association between cocaine-related cues and cocaine's effect, a hallmark of addiction, according to a study published online in *Nature Neuroscience* on July 20.

Behavioral and brain research has shown that chronic addiction rewires certain brain circuitry, so that seeing such cues as photos of other people using drugs or drug paraphernalia can evoke strong cravings and drug-seeking behaviors. This neurological process is one of the reasons for persistently high risk of relapse even after years of abstinence.

In this study using a rat model, Eisuke Koya, Ph.D., and colleagues at the Behavioral Neuroscience Branch of the National Institute on Drug Abuse (NIDA) revealed an important mechanism with which the brain learns to associate environmental cues and the effect of cocaine.

Scientists previously established a rat model to study the effect of cocaine by quantitatively measuring rats' locomotor activity (that is, distance traveled) in a chamber (see photo below) after a cocaine injection. If cocaine injections are repeatedly paired with a specific surrounding outside of a rat's home cage, the rat will exhibit a much higher level of response after a cocaine injection in this environment than it would in a strange surrounding, even if the same dose of cocaine is given. The higher level of response is indicated by a longer cumulative distance traveled by the rat in the locomotion chamber.

The environmental cues in these experiments were chambers with varying setups, such as smooth versus woodchip-covered floors and a square cage versus a round bowl. Other cues may include odors and sounds.

Enhanced Response Is Learned Association

The phenomenon of enhanced response, or context-specific sensitization, is believed to be the result of learned association. Like Pavlov's dogs that learned to associate food with the sound of bells ringing, the sensitized rats learn to associate environmental cues with the effect of cocaine injection and have a response to cocaine beyond the cocaine's direct pharmacological effect.

"Pavlov always thought the food stimulus and the bell stimulus merged and bonded somehow in the brain, but it was all a black box," Bruce Hope, Ph.D., the senior author of the study and a senior scientist at NIDA, told *Psychiatric News*. "I was trying to find how this [type of learned association] was stored in the brain and how we could identify it, so that we can specifically find and manipulate those particular cells. That's what led up to the [current] experiment."

Researchers have known for a long time that many addiction-related behaviors have roots in neurons in the nucleus accumbens. Hope and colleagues suspected that the learned association between environmental cues and cocaine injections may lie in only 2 percent to 3 percent of the cells in the nucleus accumbens. However, finding these neurons was like looking for a few people in a country of hundreds of millions. They needed a high-resolution map.

Manipulate Neurons, Change Behavior

Previous research showed that some neurons in the nucleus accumbens are activated after the context-specific, cocaine-induced sensitization, marked by expression of the c-Fos gene in the nucleus. The difficulty was to prove a causal effect, not mere correlation, between cell activation and behavior. With conventional methods, it would be difficult to manipulate scattered neurons without damaging other neurons nearby and contaminating the experiment. The study authors found an elegant solution to this problem.

First, they took a unique breed of transgenic rats that are genetically engineered to have a beta-galactosidase gene immediately attached to the c-Fos gene. Whenever the c-Fos gene is transcribed, beta-galactosidase, a bacterial enzyme, is also produced in the cell. Meanwhile, these rats are sensitized by repeated cocaine injections in a specific environment. Next, the rats had a prodrug known as Daun02 injected directly into the nucleus accumbens. Daun02 is a prodrug of daunorubicin, which is inactive but can be converted into the active drug under certain conditions. Beta-galactosidase, however, can turn the prodrug into daunorubicin, which is a cytotoxic drug used in cancer treatment. Thus, when a neuron is activated (that is, transcribing the c-Fos gene), it begins to make daunorubicin and soon inactivates itself. Neurons that are not activated in sensitization remain intact.

Credit: Jun Yan

Bruce Hope, Ph.D., of the Behavioral Neuroscience Branch of the National Institute on Drug Abuse has been hunting for the brain cells responsible for the association between drug abuse and environmental cues.

Hope noted that it has not been proven whether daunorubicin actually kills neurons in the experiment, but it clearly inactivates them. As expected, this selective inactivation erased rats' context-specific response to cocaine. In other words, the environmental cues no longer provoked their heightened response to cocaine. In fact, the rats acted as if they had received cocaine in an unfamiliar environment.

Based on this observation, Hope and his team concluded that activation of a particular "constellation of neurons" in the nucleus accumbens is the cause of context-specific sensitization to cocaine. To make this experiment work, "it took seven years of tweaking," he said.

This model allows the researchers to pick out a few needles in a very large haystack using a magnet. Conventional methods require killing the animals and examining brain changes under a microscope. With this model researchers can manipulate selected neurons in live animals and directly observe any behavioral consequences.

Dopamine 'Stamps In' the Memory

In humans, there are addictive behaviors analogous to the animal model of context-specific sensitization. Why do certain environmental cues, such as sights, sounds, and smells associated with drug use, remain in the brain so vividly and persistently? Hope believes that a key factor is large amounts of dopamine released during drug use, which "stamps in" the memory of associated stimuli more efficiently and deeply than average learning experiences. This memory can overwhelm other memories and become long-lasting, he explained. In the rat model, the environment-cocaine association remains for at least six months after the last cocaine injection, which is a quarter of a rat's lifespan.

"On top of the pharmacological effects of cocaine itself is the effect of learning," said Hope. "In my opinion, it is the learning that leads to associating the effects of drug of abuse with stimuli in the environment . . . . Those learned associations probably play a stronger role than the pharmacological effects in the eventual addiction in humans."

If drug-related cues are coded in human brains in the same way as demonstrated in the rat model, it is theoretically possible to devise ways to find the responsible neuronal "ensembles" and inactivate them, Hope speculated. By erasing the association between cues and cue-induced memories and behaviors, abstinence may become much easier.

Credit: NIDA

A rat's response to cocaine is measured by the distance it travels inside a locomotion chamber in which its movement is recorded and quantified.

Researchers Begin to Crack Mystery

The implication of this study goes beyond addiction, Hope and colleagues pointed out. The findings open one of the doors to the mystery of memory: what it is, where it is located, how it is moved from one place to another in the brain, and how fluid it is. If learned associations can be modified or inactivated by targeting a specific "constellation of neurons," such modifications can guide treatments of trauma-related psychiatric disorders or symptoms.

Hope cautioned that despite the exciting implications of this research, a lot of empirical research must be done to understand how memory and addiction work within and beyond the nucleus accumbens, but he is optimistic that he and his colleagues are on the right track. Next, his group plans to study whether this neuronal inactivation method affects drug-seeking behaviors such as self-administration of cocaine in animals and whether these neurons can be temporarily inactivated. They also plan to test this method in the amygdala for conditioned fear responses.

An abstract of "Targeted Disruption of Cocaine-Activated Nucleus Accumbens Neurons Prevents Context-Specific Sensitization" is posted at <www.nature.com/neuro/journal/v12/n8/abs/nn.2364.html>. ■

Children With Fragile X Go Undiagnosed Too Long

Even when parents of fragile X children recognize something is wrong, getting a diagnosis may be tough. Indeed, parents may have two fragile X children before the first is diagnosed.

BY JOAN AREHART-TREICHEL

At first glance, there is no reason why children with fragile X syndrome, the most common inherited form of intellectual disability, shouldn't be diagnosed early in life.

The gene that is responsible for the syndrome has been identified (*Psychiatric News*, January 4, 2002).There is a genetic test for the syndrome (*Psychiatric News*, January 4, 2008). The American Academy of Pediatrics and the National Fragile X Foundation, among others, have been pushing to get children with the syndrome diagnosed early. Furthermore, the parents of fragile X children seem to be aware of their offspring's developmental delays earlier than they used to.

However, the average age of diagnosis today is about 3 years—the same as a few years ago, a new study has found. It was headed by Donald Bailey Jr., Ph.D., a distinguished fellow at the Research Triangle Institute (RTI) International, and reported in the August *Pediatrics*.

So, what's going on? Bailey and his colleagues suggested in their paper, "Research shows that pediatricians are aware of fragile X syndrome and support diagnostic testing for children at high risk, but would refer to a specialist instead of ordering a diagnostic test even if they suspected fragile X syndrome. The lag is probably due in part to delayed referral to specialists and in part to the time lag between referral and actual appointment."

However, not all the tardiness can be blamed on these two factors. This new study, whose subjects all had fragile X syndrome, found that the fragile X diagnostic test ordered for them was requested by pediatricians or family doctors 23 percent of the time. (The test was initiated in other instances by neurologists, geneticists, psychologists, speech-language therapists, or the families themselves.)

But why all the fuss about getting fragile X children diagnosed early? All that they need to be eligible for early-intervention programs is a diagnosis of a developmental delay, not a formal diagnosis of fragile X. There are several reasons, Bailey explained to *Psychiatric News*. It helps the parents of a fragile X child understand why he or she has developmental and behavioral problems. It also lets them know that if they have more children, those children may have fragile X as well. Indeed, a fourth of the parents who participated in this study already had a second child with the syndrome before they knew that their first child had it, Bailey said.

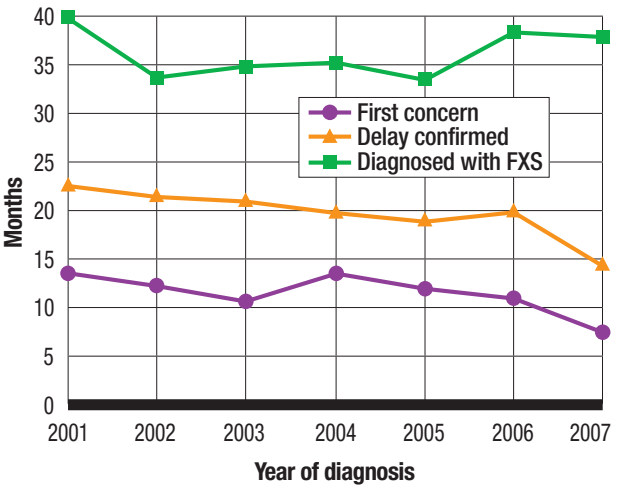
Even though nonpsychiatrist specialists are usually the ones who order fragile X diagnostic tests for developmentally delayed children, psychiatrists still have a role to play in the treatment of fragile X children. Bailey said, "Children with fragile X are often put on multiple medications to control behavior problems, attention problems, hyperactivity, aggression, seizures, anxiety, or other complications." Psychiatrists may also have a role to play in the diagnosis and treatment of depression in the mothers of fragile X children, Bailey noted, since the mothers of children with disabilities often suffer from depression, he and his colleagues found in previous research.

The study was funded by the Centers for Disease Control and Prevention and the Association for Prevention Teaching and Research.

An abstract of "No Change in the Age of Diagnosis for Fragile X Syndrome: Findings From a National Parent Survey" is posted at <http://pediatrics.aappublications.org> under the August issue. ■

Despite Parental Suspicions, Diagnoses Still Delayed

The parents of 213 boys diagnosed with fragile X syndrome between 2001 and 2007 were asked the age of their child when they first became concerned about the child's development, when a delay in development was confirmed, and when fragile X syndrome was diagnosed. The parents' responses, which were grouped according to the year their child was diagnosed, revealed that the average age of first concern and of confirmed delay decreased over the seven-year period, but that the average age of diagnosis did not.



Source: Donald Bailey, Jr., Ph.D., et al., *Pediatrics*, August 2009

Personality Disorder Prevalence Found to Vary by Country

Not all countries may be equal when it comes to disordered personalities. Colombia and the United States appear to have the most, Nigeria and Western Europe the least.

BY JOAN AREHART-TREICHEL

How many compulsive, histrionic, paranoid, or other disordered personalities are you going to encounter on your next trip to France, Ireland, or some other Western European country?

Probably fewer—if any at all—than in the United States, a study published in the July *British Journal of Psychiatry* suggests.

The interview-styled study of thousands of people the world over found the highest prevalence of personality disorders in Colombia and the United States and the lowest in Nigeria and Western Europe, with some other countries falling in-between.

Now, are there truly more disordered personalities in certain countries than others? Possibly, the study's lead investigator, Ronald Kessler, Ph.D., a professor of health care policy at Harvard Medical School and head of the National Comorbidity Survey Replication in the United States, told *Psychiatric News*. The reason to believe that this might be the case is that "we have no data that can be used . . . for making a different assumption. But caution is needed in interpreting cross-national differences . . . because clinical reappraisal studies were not done in all countries to confirm comparability of diagnostic thresholds in the instrument."

This study appears to be the first ever to estimate the prevalence of *DSM-IV* personality disorders in various countries throughout the world. If the study methodology was sound, here are other noteworthy findings:

- The prevalence estimate for any personality disorder throughout the world was 6.1 percent. The prevalence estimate of Cluster A personality disorders (paranoid, schizoid, and schizotypal) was 3.6 percent, while for Cluster B personality disorders (avoidant, dependent, and obsessive-compulsive) it was 2.7 percent, and for Cluster C personality disorders (antisocial, borderline, histrionic, and narcissistic), 1.5 percent. Some subjects had more than one disorder.
- Cluster A personality disorders were much more common in men than women. The researchers wrote that this was their strongest finding and was consistent with a statement in *DSM-IV*.
- There was a high comorbidity between personality disorders and Axis I disorders, which jibes with a lot of clinical research findings. For example, cluster B personality disorders and substance abuse disorders often went hand in hand. The reason is probably because low impulse control is a core feature of both cluster B disorders and substance abuse disorders, the researchers wrote. Cluster C personality disorders and anxiety and mood disorders often coexisted. This finding is consistent with the belief that anxiety is a hallmark of cluster C disorders, the researchers noted.
- A dose-response relationship was found between personality disorders and the number of Axis I disorders people have. For instance, the odds of having three or more Axis I disorders were 10 times greater in individuals with cluster A personality disorders than in individuals without a personality disorder, 35 times greater in individuals with cluster C personality disorders than in individuals without a personality disorder, and a whopping 49 times greater in individuals with cluster B personality disorders than in individuals without a personality disorder.

The finding that he found the most important, Kessler said, concerned personality disorders and functional impairment. "So many times people raise the question of whether our findings about impairments associated with depression, alcoholism, PTSD, and so on are really due to some unmeasured character disorder that we could assess only if we had an Axis II assessment, which we seldom have in clinical or community studies. Our finding in this paper is that it's the other way around: Axis I disorders are the ones associated with most of the impairment, and the impairments associated with Axis II disorders are largely mediated by Axis I disorders."

The study included over 21,000 subjects from 13 countries. Subjects from nine of the countries were nationally representative; those from the remaining four countries were representative of urban areas. All subjects were evaluated face to face by trained lay interviewers using the World Health Organization World Mental Health interview schedule.

The study was funded by the U.S. National Institute of Mental Health, the John D. and Catherine T. MacArthur Foundation, the U.S. Public Health Service, the Fogarty International Center, the Pan American Health Organization, and some pharmaceutical companies.

An abstract of "DSM-IV Personality Disorders in the WHO World Mental Health Surveys" is posted at <http://bjp.rcpsych.org/cgi/content/abstract/195/1/46>. ■

Comparison by Country

The study had over 21,000 subjects in 13 countries. The prevalence estimate for any *DSM-IV* personality disorder throughout the world was 6 percent.

	Any personality disorder, %	No.*
Colombia	7.9%	2381
Lebanon	6.2%	1031
Mexico	6.1%	2362
Nigeria	2.7%	2143
China	4.1%	1628
South Africa	6.8%	4315
United States	7.6%	5692
Western Europe**	2.4%	1610
Total	6.1%	21162

* Number of subjects interviewed in each category.
** Includes six countries.

Source: Ronald Kessler, Ph.D., et al., *British Journal of Psychiatry*, July 2009

APA Fellows Take Matters Into Their Own Hands

Psychiatry's future leaders apply their leadership skills by taking up the cause to preserve an important fellowship whose life is threatened by a funding cut.

BY AARON LEVIN

Credit: Ellen Dallager

Attending the annual reunion/reception for American Psychiatric Leadership fellows were (from left) Sheldon Benjamin, M.D., a professor of psychiatry at the University of Massachusetts Medical School and former fellowship committee member; fellows Stacey Burpee, D.O., of the University of Massachusetts; M. Justin Coffey, M.D., of the University of Michigan; and Mohammad Alsuwaidan, M.D., of the University of Toronto.

Graduates of the American Psychiatric Leadership Fellowship, the oldest fellowship program at APA, have set out to raise funds to continue the program's operation after pharmaceutical maker GlaxoSmithKline (GSK) withdrew its financial support two years ago.

Since 1968 the fellowship has introduced more than 500 residents to organized psychiatry and trained them in leadership skills.

"The fellowship is a priceless experience, especially early in one's career," said Leah Dickstein, M.D., a former chair of the fellowship's selection committee and a professor emerita at the University of Louisville.

The economic downturn led GSK to shift its priorities, said Alison Bondurant, associate director of APA's Office of Minority and National Affairs. "GSK moved away from funding non-CME programs like fellowships in order to focus on physician education."

Corporate support for fellowships throughout the medical world has been declining lately. However, with the help of the American Psychiatric Foundation, alumni of the fellowship have begun trying to raise the $100,000 needed each year to keep the program running.

Until GSK ended its grant, the fellowship selected 10 residents each year for a two-year program. Fellows met with the leaders of APA, took part in committee work, and visited congressional offices on trips to Washington, D.C. One fellow in each class took part in APA Board of Trustees meetings, and another worked with the APA Assembly.

"I had the chance to meet residents from other programs as well as the leadership of APA," said Keith Stowell, M.D., a 2006-2008 fellow and now a postdoctoral fellow at Western Psychiatric Institute and Clinic in Pittsburgh. Gaining professional leadership skills was not the only benefit, he said. Learning how to work in groups during his fellowship years helped Stowell deal with difficult situations that arose during his time as a chief resident.

Fellows also develop and carry out a research project. Stowell's fellowship class surveyed psychiatry residents around the country to examine how pregnancy affects both female and male psychiatrists during residency. They presented the results first at the APA annual meeting in 2007 and then to a meeting of psychiatric training directors.

The subsequent class surveyed safety training programs in psychiatric settings, said Yael Dvir, M.D., a fellow when she was a resident at the University of Massachusetts in Worcester and now an assistant professor there. Dvir said that she valued the chance to meet colleagues from around the country in her areas of interest—child psychiatry and developmental disabilities—through the fellowship program.

"Working on the class project teaches you how to get your ideas across to other people," she said. "And you learn to see the potential of good ideas in other people who may just need a little encouragement to bring them out."

Continued funding to support the fellowship was a very worthwhile investment in the future of the profession, she said.

To conserve existing funds, only five fellows were selected for the 2009-2010 class, and they will attend the annual meeting only in 2010, instead of both years.

This current class has been exploring the philanthropic interests of foundations, corporations, program alumni, and the APA Board of Trustees as part of its research project. They gave that information to the foundation, which has the authority within APA for fundraising.

"The membership should be willing to contribute in some small way to fund the program," Dickstein noted.

Contributors so far (all former fellows) are James Welton Lomax, M.D., Christine Truman, M.D., Keith Stowell, M.D., Tana Grady-Weliky, M.D., Albert John Allen, M.D., Ph.D., and Katharine Phillips, M.D.

Contributions to support the fellowship may be sent to the American Psychiatric Foundation, c/o American Psychiatric Leadership Fellowship, 1000 Wilson Boulevard, Suite 1825, Arlington, Va. 22209. ■

New Fellows Selected For APA's Minority Fellowships

APA has announced the names of the 26 new minority psychiatry residents selected to participate in the APA Minority Fellowships Program as either an APA/SAMHSA or APA/AstraZeneca fellow.

2009-2010 APA/SAMHSA Minority Fellows

Neil Aggarwal, M.D., Yale University
Randolph Baca, M.D., University of New Mexico
Marco Chavez, M.D., University of Texas, Houston
Melissa Deer, M.D., University of California, San Diego
Gina Duncan, M.D., Massachusetts General Hospital/McLean Hospital
Mandy Garber, M.D., Allegheny General Hospital
Tresha Gibbs, M.D., Columbia-New York Presbyterian Hospital
Susan Imamura, M.D., Stanford University
Kenyatta Jones, M.D., Howard University Hospital
Christian Neal, M.D., University of South Carolina, Palmetto Health
Alan Teo, M.D., University of California, San Francisco
Christopher Tjoa, M.D., University of Pennsylvania
Monique Upton, M.D., University of Louisville
Sarah Vinson, M.D., Cambridge Health Alliance

Addiction Fellows

Joseph Nissenfeld, M.D., New York University
Kimberly Roberts, M.D., Boston University Medical Center

2009-2011 AstraZeneca Fellows

Ranjan Avasthi, M.D., Morehouse School of Medicine
Deyadira Baez-Sierra, M.D., Boston University Medical Center
Juliet Glover, M.D., University of South Carolina, Palmetto Health
Steve Koh, M.D., University of California, San Diego
Timothy Liu, M.D., Yale University
Jason Mensah, M.D., Indiana University
Donna Roybal, M.D., Stanford University
Javeed Sukhera, M.D., University of Rochester
Elizabeth Tien, M.D., Temple University
Natalie Yzer, M.D., George Washington University ■

APA Announces New Member Benefits

→ Register to Receive Drug Alerts Online

APA has worked with the FDA, AMA, state medical societies, and liability carriers to bring a new service—the Health Care Notification Network (HCNN)—to APA members. The HCNN, which is a private network for physicians and health care professionals, provides secure online delivery of news about drug and medical device recalls and patient safety alerts, replacing the current paper process that is both slow and prone to error.

These are among other HCNN features:

- The HCNN is free to physicians and their staff members.
- A copy of alerts can be sent automatically to practice administrators and added to their physician account.
- Privacy is protected by the not-for-profit board that governs the HCNN.
- The HCNN does no advertising or selling.
- Recipients can opt out at any time.

Alerts sent through the HCNN are paid for by manufacturers who use the network for alert delivery.

APA members may enroll online at <www.hcnn.net/registration/apa/registration.aspx>. Additional information is available at <www.hcnn.net> or (866) 925-5155.

→ Get a Web Page on PsychSites.com

APA members are eligible for a personal Web page and directory listing on PsychSites.com. PsychSites.com is a starting place for members who have no Internet presence and provides increased visibility and links for members who already have Web sites.

Personal pages can be edited online and include online technical support. The page can include a 250-word profile, titles, office contact information, up to seven hyperlinks to other Web sites, and a photo. Participating members will be included in a database of mental health professionals that is searchable by location, specialty, and more than 150 mental health subspecialties.

To obtain more information or an access code to create a personal page, go to <www.psych.org/Resources/Membership/MemberOnlyBenefitsServices/APAMemberAffinityPrograms.aspx>.

Photo courtesy of Pete Earley

Journalist and book author Pete Earley investigated the practice of incarcerating mentally ill individuals after his son became one of the individuals caught up in the system.

Author Pete Earley Featured At Conversations Event

The 2008 winner of APA's Patient Advocacy Award and a noted author will share his insights about his son's struggle with mental illness and his own fight against the incarceration of mentally ill individuals.

BY LINDSEY MCCLENATHAN

Do I have a mental illness? Is there treatment available? Where do I go and who can I talk to? How do I live with mental illness? Reflecting on the personal struggles of living with mental illness is the aim of the interactive "Conversations" event at APA's 2009 Institute on Psychiatric Services. The host of the event is the American Psychiatric Foundation.

The institute's third annual "Conversations" event, which will be held Saturday, October 10, at 5:15 p.m., will bring the personal side of mental illness to mental health professionals as author Pete Earley shares the story of his son's struggle. This harrowing tale was the subject of his book *Crazy: A Father's Search Through America's Mental Health Madness*. It was one of two finalists for the Pulitzer Prize in 2007, and in 2008 APA presented Earley with its Patient Advocacy Award.

Lindsey McClenathan is the development officer of the American Psychiatric Foundation.

Earley is a former reporter for the *Washington Post*, hired by Bob Woodward. He went on to write nine nonfiction books and three novels. His first book, *Family of Spies: Inside the John Walker Spy Ring*, was a *New York Times* bestseller and was made into a five-hour miniseries on CBS television. For his book *The Hot House: Life Inside Leavenworth Prison*, Earley spent a year as a reporter inside a maximum security prison. His book *Circumstantial Evidence* helped lead to the release from death row of a black man who had been wrongfully convicted of murdering a white teenager in Alabama.

In *Crazy*, Earley describes his attempts to help his college-aged son Mike after he becomes ill with bipolar disorder and is arrested. It also describes a year that Earley spent at the Miami Dade County Jail in which he followed persons with mental disorders as they were released from jail into the community to see what sort of services they received.

"I had no idea," Early writes in the opening chapter of his book. "I've been a journalist for more than 30 years, a reporter for the *Washington Post*, the author of several nonfiction books about crime and punishment and society, some of them award-winning, even two bestsellers. I've interviewed murderers and spies, judges and prosecutors, always seeking the truth and attempting to convey it so that readers can see the people and the events for themselves—can understand not only what happened, but why. But I was always on the outside looking in. I had no idea what it was like to be on the inside looking out. Until my son Mike was declared mentally ill."

Earley has spoken to over 100 mental health, consumer, and law enforcement groups and is an advocate for halting the warehousing of mentally ill individuals in jails and prisons with no access to treatment. He serves on the board of directors of the Corporation for Supportive Housing, which finds innovative ways for states to finance housing projects to help eliminate homelessness.

The "Conversations" event is part of an interactive series begun at APA's annual meeting eight years ago that offers a unique opportunity for psychiatrists and others to hear the personal perspectives on mental illness and their struggles, life adjustments, and the pivotal points in life. Guests have included Maureen McCormick, Brooke Shields, George Stephanopoulos, and Carrie Fisher.

The American Psychiatric Foundation is the charitable subsidiary of the American Psychiatric Association. The mission of the foundation is to advance the public's understanding that mental illnesses are real and can be effectively treated. More information about the foundation and its programs can be found online at <www.psychfoundation.org>.

"Conversations" is sponsored by a charitable contribution from AstraZeneca to the American Psychiatric Foundation.

More information about Pete Earley is posted at <www.peteearley.com/home>. The first chapter of* Crazy: A Father's Search Through America's Mental Health Madness *also can be accessed here. ■

Register Now!

61st Institute on Psychiatric Services

APA's Institute on Psychiatric Services is being held October 8 to 11 in New York City. See page 2 for registration information. To save on fees, be sure to register before **September 18**. A discounted fee is available for residents; medical students attend free. Further savings can be obtained by making air travel reservations 30 days in advance.

Breaking News!

New sessions have just been added to the program of APA's Institute on Psychiatric Services. The New York City setting of the four-day meeting will provide that exciting spark as you reenergize your professional batteries.

THURSDAY, OCTOBER 8

8:30 a.m.-11:30 a.m.

Panel Discussion 1: "Minds on the Edge": Leveraging a PBS Program to Drive Reform of Our Fragmented Mental Health System

Thomas A. Simpatico, M.D., Jeffrey Geller, M.D., M.P.H., Tracey Skale, M.D.

"Minds on the Edge" is a one-hour television program produced for PBS by the Fred Friendly Seminars. It was created as a multiplatform video and Web media initiative to advance the public conversation about the need for systemic change in the delivery of treatment and services for people with severe mental illness. The program zeroes in on wrenching and confounding situations that Americans face as they struggle with the challenges of severe mental illness.

After watching the program, the audience will engage in a discussion with the panelists on the consequences of the fragmented mental health care system and how to bring about change.

10 a.m.-11 a.m.

Plenary Session 1: Kathryn Power, Director, Substance Abuse and Mental Health Services Administration

3:30 p.m.-5 p.m.

Discussion Group 1: Jules Ranz, M.D., on Developing Public and Community Psychiatry Fellowships

7 p.m.-9 p.m.

Town-Hall Meeting: Open Forum and Reception for MITs and ECPs With APA President-Elect Carol Bernstein, M.D.

For residents and early career psychiatrists (ECPs) only; supported by Professional Risk Management Services Inc.

In this meeting, Carol Bernstein, M.D., wants to hear ideas from psychiatry residents and ECPs about the future of American psychiatry and APA. Participants will also learn about APA and how to become involved, as well as meet and network with other residents and ECPs.

SATURDAY, OCTOBER 10

2 p.m.-5 p.m.

Forum 2: Preparing for Flu Season: Stress, Mental Health Needs, and Working With Primary Care

Craig Katz, M.D., Frederick Stoddard Jr., M.D., David Calfee, M.D., M.S., Doris Reissman, M.D., M.P.H., Anthony Ng, M.D., Charles Engel, M.D., M.P.H., Robert Ursano, M.D.

With the recent emergence of novel H1N1 influenza and declaration of an H1N1 pandemic, epidemiologic surveillance has tilted toward a dawning reality of public health alerts and crowded emergency departments. This forum will address how psychiatrists can best respond within the health care community. A historical review of the psychosocial lessons from prior flu pandemics and other infectious outbreaks will set the context for this discussion. An update on current knowledge about the behavior and pathogenicity of H1N1 and surrounding public health planning will orient the audience to the current reality. Specific consideration will be given to psychiatry's role in collaborating with primary care practitioners, including addressing medically unexplained symptoms.

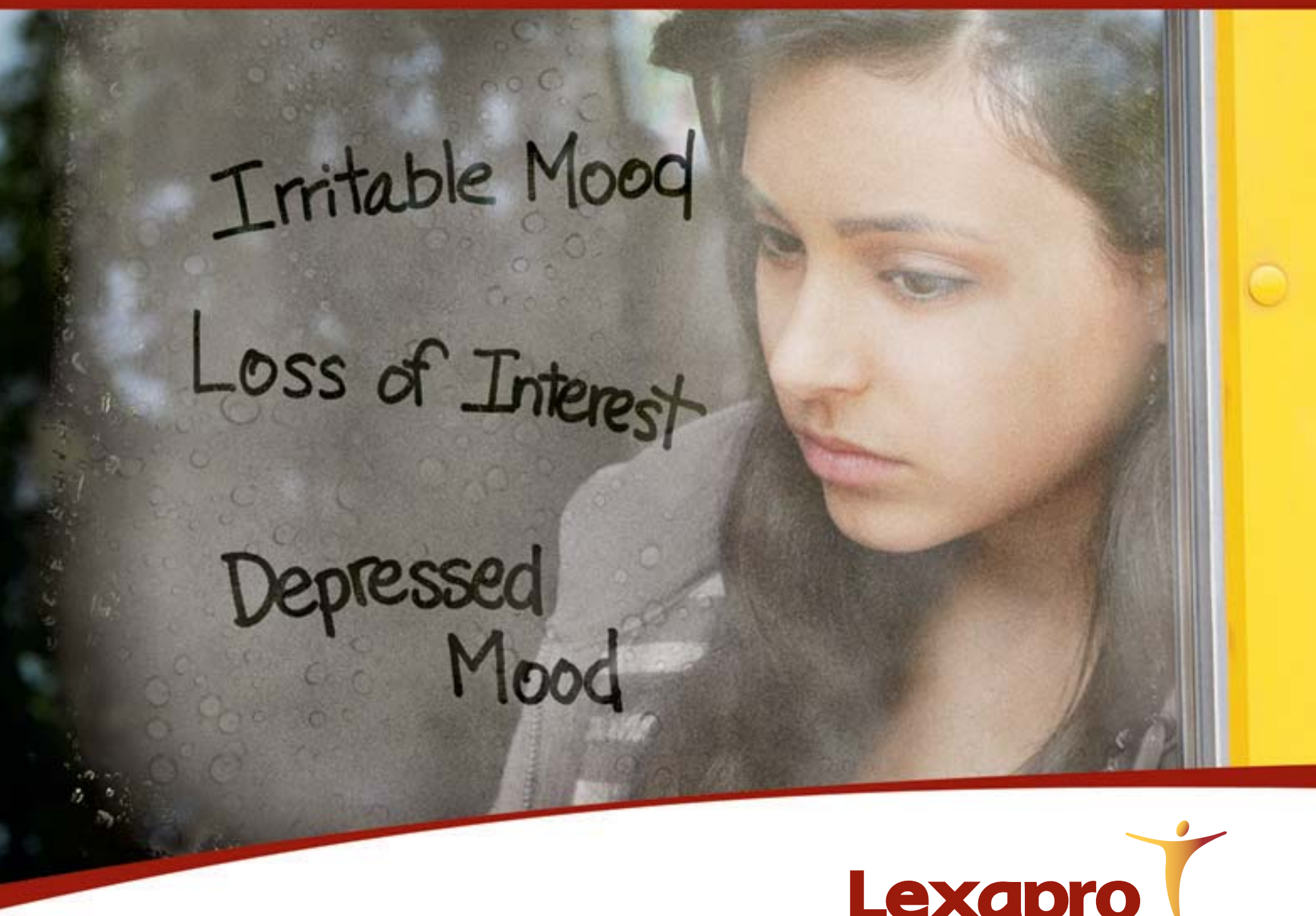
5:15 p.m.-6:15 p.m.

"Conversations" Event With Pete Earley

Sponsored by the American Psychiatric Foundation; see article at left.

For Major Depressive Disorder (MDD)...

LEXAPRO IS NOW APPROVED for adolescents aged 12 to 17[1]



Lexapro® escitalopram oxalate

DSM-IV-TR criteria for Major Depressive Episode: Five or more symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure in nearly all activities. In children and adolescents, depressed mood can be irritable mood.[2]

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 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 less than 12 years of age.

Please see additional Important Safety Information on following pages.

IMPORTANT SAFETY INFORMATION (continued)

Contraindications

- Lexapro is contraindicated in patients taking monoamine oxidase inhibitors (MAOIs). There have been reports of serious, sometimes fatal, reactions with some cases resembling neuroleptic malignant syndrome (NMS) and serotonin syndrome. Features may include 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. Serotonin syndrome was reported for two patients who were concomitantly receiving linezolid, an antibiotic which has MAOI activity. Lexapro should not be used in combination with an MAOI or within 14 days of discontinuing an MAOI. MAOIs should not be initiated within 14 days of discontinuing Lexapro.

- Lexapro is contraindicated in patients taking pimozide or with hypersensitivity to escitalopram or citalopram.

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 within the first few months of treatment or when changing the dose. Consideration should be given to changing the therapeutic regimen, including discontinuing medication, in patients whose depression is persistently worse, 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. Families and caregivers of patients treated with antidepressants should be alerted about the need to monitor patients daily for the emergence of agitation, irritability, unusual changes in behavior, or the emergence of suicidality, and report such symptoms immediately. 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.

LEXAPRO provides symptom relief for adolescents with MDD

NOW FDA APPROVED
for Major Depressive Disorder (MDD) in adolescents aged 12 to 17[1]

- **For acute and maintenance treatment[1]**
  - —Patients should be periodically reassessed to determine the need for maintenance treatment[1]
- **Significant improvement in CDRS-R scores starting at week 4[3]**
  - —Full antidepressant effect may take 4 to 6 weeks
- **Flexible dosing with a recommended dose of 10 mg/day[1]**
  - —Titration to 20 mg/day, if necessary, after a minimum of 3 weeks[1]

LEXAPRO is indicated as an integral part of a total treatment program for MDD. Drug treatment may not be indicated for all adolescents with this syndrome.

- A major depressive episode may be the initial presentation of bipolar disorder. In patients at risk for bipolar disorder, treating such an episode with an antidepressant alone may increase the likelihood of precipitating a mixed/manic episode. Prior to initiating treatment with an antidepressant, patients should be adequately screened to determine if they are at risk for bipolar disorder. Lexapro should be used cautiously in patients with a history of mania or seizure disorder. Lexapro is not approved for use in treating bipolar depression.
- The concomitant use of Lexapro with other SSRIs, SNRIs, triptans, tryptophan, antipsychotics or other dopamine antagonists is not recommended due to potential development of life-threatening serotonin syndrome or neuroleptic malignant syndrome (NMS)-like reactions. Reactions have been reported with SNRIs and SSRIs alone, including Lexapro, but particularly with drugs that impair metabolism of serotonin (including MAOIs). Management of these events should include immediate discontinuation of Lexapro and the concomitant agent and continued monitoring.
- Patients should be monitored for adverse reactions when discontinuing treatment with Lexapro. During marketing of Lexapro and other SSRIs and SNRIs, there have been spontaneous reports of adverse events occurring upon discontinuation, including dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesias), anxiety, confusion, headache, lethargy, emotional lability, insomnia and hypomania. A gradual dose reduction rather than abrupt cessation is recommended whenever possible.

Please see additional Important Safety Information on next page.

Lexapro®
escitalopram oxalate

Visit the LEXAPRO website at www.lexapro.com

References: 1. LEXAPRO [package insert]. St. Louis, Mo: Forest Pharmaceuticals, Inc.; 2009. **2.** American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.* 4th ed (Text Revision). Washington, DC: APA; 2000. **3.** Emslie GJ, Ventura D, Korotzer A, Tourkodimitris S. Escitalopram in the treatment of adolescent depression: a randomized placebo-controlled multisite trial. *J Am Acad Child Adolesc Psychiatry.* 2009;48:721-729.

LEXAPRO® (escitalopram oxalate) TABLETS/ORAL SOLUTION **Rx Only**

Brief Summary: For complete details, please see full Prescribing Information for Lexapro.

WARNINGS: 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 less than 12 years of age. *[See Warnings and Precautions: Clinical Worsening and Suicide Risk, Patient Counseling Information: Information for Patients, and Used in Specific Populations: Pediatric Use].*

INDICATIONS AND USAGE: Major Depressive Disorder-Lexapro (escitalopram) is indicated for the acute and maintenance treatment of major depressive disorder in adults and in adolescents 12 to 17 years of age [*see Clinical Studies*]. 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. **Generalized Anxiety Disorder**-Lexapro is indicated for the acute treatment of Generalized Anxiety Disorder (GAD) in adults [*see Clinical Studies*]. 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.

CONTRAINDICATIONS: Monoamine oxidase inhibitors (MAOIs)-Concomitant use in patients taking monoamine oxidase inhibitors (MAOIs) is contraindicated [*see Warnings and Precautions*]. **Pimozide**-Concomitant use in patients taking pimozide is contraindicated [*see Drug Interactions*]. **Hypersensitivity to escitalopram or citalopram**-Lexapro is contraindicated in patients with a hypersensitivity to escitalopram or citalopram or any of the inactive ingredients in Lexapro.

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 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	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 Dosage and Administration*]. 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 [*see also Patient Counseling Information*]. 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. **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. **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*]. **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. **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. **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. **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 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 Lexapro and NSAIDs, aspirin, or other drugs that affect coagulation. **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*]. **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.

ADVERSE REACTIONS: Clinical Trials Experience-Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice. **Clinical Trial Data Sources; Pediatrics (6 -17 years)**-Adverse events were collected in 576 pediatric patients (286 Lexapro, 290 placebo) with major depressive disorder in double-blind placebo-controlled studies. Safety and effectiveness of Lexapro in pediatric patients less than 12 years of age has not been established. **Adults**-Adverse events 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 reactions 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; Pediatrics (6 -17 years)**-Adverse events were associated with discontinuation of 3.5% of 286 patients receiving Lexapro and 1% of 290 patients receiving placebo. The most common adverse event (incidence at least 1% for Lexapro and greater than placebo) associated with discontinuation was insomnia (1% Lexapro, 0% placebo). **Adults**-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; Adults**-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 Reactions in Placebo-Controlled Clinical Trials; Major Depressive Disorder; Pediatrics (6 -17 years)**-The overall profile of adverse reactions in pediatric patients was generally similar to that seen in adult studies, as shown in Table 2. However, the following adverse reactions (excluding those which appear in Table 2 and those for which the coded terms were uninformative or misleading) were reported at an incidence of at least 2% for Lexapro and greater than placebo: back pain, urinary tract infection, vomiting, and nasal congestion. **Adults**-The most commonly observed adverse reactions 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. 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.

TABLE 2
Treatment-Emergent Adverse Reactions Observed with a Frequency of ≥ 2% and Greater Than Placebo for Major Depressive Disorder

Adverse Reaction	Lexapro (N=715)	Placebo (N=592)
Autonomic Nervous System Disorders		
Dry Mouth	6%	5%
Sweating Increased	5%	2%
Central & Peripheral Nervous System Disorders		
Dizziness	5%	3%
Gastrointestinal Disorders		
Nausea	15%	7%
Diarrhea	8%	5%
Constipation	3%	1%
Indigestion	3%	1%
Abdominal Pain	2%	1%
General		
Influenza-like Symptoms	5%	4%
Fatigue	5%	2%
Psychiatric Disorders		
Insomnia	9%	4%
Somnolence	6%	2%
Appetite Decreased	3%	1%
Libido Decreased	3%	1%
Respiratory System Disorders		
Rhinitis	5%	4%
Sinusitis	3%	2%
Urogenital		
Ejaculation Disorder[1,2]	9%	<1%
Impotence[2]	3%	<1%
Anorgasmia[3]	2%	<1%

[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; Adults-The most commonly observed adverse reactions 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. 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.

TABLE 3
Treatment-Emergent Adverse Reactions Observed with a Frequency of ≥ 2% and Greater Than Placebo for Generalized Anxiety Disorder

Adverse Reactions	Lexapro (N=429)	Placebo (N=427)
Autonomic Nervous System Disorders		
Dry Mouth	9%	5%
Sweating Increased	4%	1%
Central & Peripheral Nervous System Disorders		
Headache	24%	17%
Paresthesia	2%	1%
Gastrointestinal Disorders		
Nausea	18%	8%
Diarrhea	8%	6%
Constipation	5%	4%
Indigestion	3%	2%
Vomiting	3%	1%
Abdominal Pain	2%	1%
Flatulence	2%	1%
Toothache	2%	0%
General		
Fatigue	8%	2%
Influenza-like Symptoms	5%	4%
Musculoskeletal System Disorder		
Neck/Shoulder Pain	3%	1%
Psychiatric Disorders		
Somnolence	13%	7%
Insomnia	12%	6%
Libido Decreased	7%	2%
Dreaming Abnormal	3%	2%
Appetite Decreased	3%	1%
Lethargy	3%	1%
Respiratory System Disorders		
Yawning	2%	1%
Urogenital		
Ejaculation Disorder[1,2]	14%	2%
Anorgasmia[3]	6%	<1%
Menstrual Disorder	2%	1%

[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 Reactions-The potential dose dependency of common adverse reactions (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 reactions 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 Reactions in Patients with Major Depressive Disorder

Adverse Reaction	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%

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
Incidence of Sexual Side Effects in Placebo-Controlled Clinical Trials

Adverse Event	Lexapro	Placebo
	In Males Only	
	(N=407)	(N=383)
Ejaculation Disorder (primarily ejaculatory delay)	12%	1%
Libido Decreased	6%	2%
Impotence	2%	<1%
	In Females Only	
	(N=737)	(N=636)
Libido Decreased	3%	1%
Anorgasmia	3%	<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 Reactions Observed During the Premarketing Evaluation of Lexapro**-Following is a list of 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. The listing does not include those events already listed in Tables 2 & 3, those events for which a drug cause was remote and at a rate less than 1% or lower than placebo, those events which were so general as to be uninformative, and those events reported only once which did not have a substantial probability of being acutely life threatening. Events are categorized by body system. Events of major clinical importance are described in the Warnings and Precautions section. Cardiovascular - hypertension, palpitation. Central and Peripheral Nervous System Disorders - light-headed feeling, migraine. Gastrointestinal Disorders - abdominal cramp, heartburn, gastroenteritis. General - allergy, chest pain, fever, hot flushes, pain in limb. Metabolic and Nutritional Disorders - increased weight. Musculoskeletal System Disorders - arthralgia, myalgia jaw stiffness. Psychiatric Disorders - appetite increased, concentration impaired, irritability. Reproductive Disorders/Female - menstrual cramps, menstrual disorder. Respiratory System Disorders - bronchitis, coughing, nasal congestion, sinus congestion, sinus headache. Skin and Appendages Disorders - rash. Special Senses - vision blurred, tinnitus. Urinary System Disorders - urinary frequency, urinary tract infection. **Post-Marketing Experience; Adverse Reactions Reported Subsequent to the Marketing of Escitalopram**-The following additional adverse reactions have been identified from spontaneous reports of escitalopram received worldwide. These adverse reactions have been chosen for inclusion because of a combination of seriousness, frequency of reporting, or potential causal connection to escitalopram and have not been listed elsewhere in labeling. However, because these adverse reactions were reported voluntarily 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 events include: Blood and Lymphatic System Disorders: anemia, agranulocytis, aplastic anemia, hemolytic anemia, idiopathic thrombocytopenia purpura, leukopenia, thrombocytopenia. Cardiac Disorders: atrial fibrillation, bradycardia, cardiac failure, myocardial infarction, tachycardia, torsade de pointes, ventricular arrhythmia, ventricular tachycardia. Ear and Labyrinth Disorders: vertigo Endocrine Disorders: diabetes mellitus, hyperprolactinemia, SIADH. Eye Disorders: diplopia, glaucoma, mydriasis, visual disturbance. Gastrointestinal Disorders: dysphagia, gastrointestinal hemorrhage, gastroesophageal reflux, pancreatitis, rectal hemorrhage. General Disorders and Administration Site Conditions: abnormal gait, asthenia, edema, fall, feeling abnormal, malaise. Hepatobiliary Disorders: fulminant hepatitis, hepatic failure, hepatic necrosis, hepatitis. Immune System Disorders: allergic reaction, anaphylaxis. Investigations: bilirubin increased, decreased weight, electrocardiogram QT prolongation, hepatic enzymes increased, hypercholesterolemia, INR increased, prothrombin decreased. Metabolism and Nutrition Disorders: hyperglycemia, hypoglycemia, hypokalemia, hyponatremia. Musculoskeletal and Connective Tissue Disorders: muscle cramp, muscle stiffness, muscle weakness, rhabdomyolysis. Nervous System Disorders: akathisia, amnesia, ataxia, choreoathetosis, cerebrovascular accident, dysarthria, dyskinesia, dystonia, extrapyramidal disorders, grand mal seizures (or convulsions), hypoaesthesia, myoclonus, nystagmus, Parkinsonism, restless legs, seizures, syncope, tardive dyskinesia, tremor. Pregnancy, Puerperium and Perinatal Conditions: spontaneous abortion. Psychiatric Disorders: acute psychosis, aggression, agitation, anger, anxiety, apathy, completed suicide, confusion, depersonalization, depression aggravated, delirium, delusion, disorientation, feeling unreal, hallucinations (visual and auditory), mood swings, nervousness, nightmare, panic reaction, paranoia, restlessness, self-harm or thoughts of self-harm, suicide attempt, suicidal ideation, suicidal tendency. Renal and Urinary Disorders: acute renal failure, dysuria, urinary retention. Reproductive System and Breast Disorders: menorrhagia, priapism. Respiratory, Thoracic and Mediastinal Disorders: dyspnea, epistaxis, pulmonary embolism, pulmonary hypertension of the newborn. Skin and Subcutaneous Tissue Disorders: alopecia, angioedema, dermatitis, ecchymosis, erythema multiforme, photosensitivity reaction, Stevens Johnson Syndrome, toxic epidermal necrolysis, urticaria. Vascular Disorders: deep vein thrombosis, flushing, hypertensive crisis, hypotension, orthostatic hypotension, phlebitis, thrombosis.

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 and Precautions*]. The concomitant use of Lexapro with other SSRIs, SNRIs or tryptophan is not recommended. **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 and Precautions*]. **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 and Precautions*]. **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.

USE IN SPECIFIC POPULATIONS: 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 also 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 and Precautions*]. 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**-Escitalopram is excreted in human breast milk. Limited data from women taking 10-20 mg escitalopram showed that exclusively breast-fed infants receive approximately 3.9% of the maternal weight-adjusted dose of escitalopram and 1.7% of the maternal weight-adjusted dose of desmethylcitalopram. There were two reports of infants experiencing excessive somnolence, decreased feeding, and weight loss in association with breastfeeding from a racemic citalopram-treated mother; in one case, the infant was reported to recover completely upon discontinuation of racemic citalopram by its mother and, in the second case, no follow-up information was available. Caution should be exercised and breastfeeding infants should be observed for adverse reactions when Lexapro is administered to a nursing woman. **Pediatric Use**-Safety and effectiveness of Lexapro has not been established in pediatric patients (less than 12 years of age) with Major Depressive Disorder. Safety and effectiveness of Lexapro has been established in adolescents (12 to 17 years of age) for the treatment of major depressive disorder [*see Clinical Studies*]. Although maintenance efficacy in adolescent patients with Major Depressive Disorder has not been systematically evaluated, maintenance efficacy can be extrapolated from adult data along with comparisons of escitalopram pharmacokinetic parameters in adults and adolescent patients. Safety and effectiveness of Lexapro has not been established in pediatric patients less than 18 years of age with Generalized Anxiety Disorder. **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 *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.

DRUG ABUSE AND DEPENDENCE: Abuse and Dependence; Physical and Psychological Dependence-Animal studies suggest that the abuse liability of racemic citalopram is low. Lexapro has not been systematically studied in humans for its potential for abuse, tolerance, or physical dependence. The premarketing clinical experience with Lexapro did not reveal any drug-seeking behavior. However, 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, physicians should carefully evaluate Lexapro patients for history of drug abuse and follow such patients closely, observing them for signs of misuse or abuse (e.g., development of tolerance, incrementations of dose, drug-seeking behavior).

OVERDOSAGE: Human Experience-In clinical trials of escitalopram, there were reports of escitalopram overdose, including overdoses of up to 600 mg, with no associated fatalities. During the postmarketing evaluation of escitalopram, Lexapro overdoses involving overdoses of over 1000 mg have been reported. As with other SSRIs, a fatal outcome in a patient who has taken an overdose of escitalopram has been rarely reported. Symptoms most often accompanying escitalopram overdose, alone or in combination with other drugs and/or alcohol, included convulsions, coma, dizziness, hypotension, insomnia, nausea, vomiting, sinus tachycardia, somnolence, and ECG changes (including QT prolongation and very rare cases of torsade de pointes). Acute renal failure has been very rarely reported accompanying overdose. **Management of Overdose**-Establish and maintain an airway to ensure adequate ventilation and oxygenation. Gastric evacuation by lavage and use of activated charcoal should be considered. Careful observation and cardiac and vital sign monitoring are recommended, along with general symptomatic and supportive care. Due to the large volume of distribution of escitalopram, forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be of benefit. There are no specific antidotes for Lexapro. 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.

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Industry Briefs

• In a phase 3 trial involving schizophrenia patients with predominant, persistent negative symptoms, one-year treatment with the antipsychotic medication ***asenapine*** produced a statistically significantly larger reduction in negative symptoms than did olanzapine, Schering-Plough announced on July 24. Negative symptoms were measured by the total score on the 16-item Negative Symptom Assessment scale (NSA-16). A total of 468 patients were first randomized to either olanzapine or asenapine in a 26-week, double-blind study, and 195 of them continued for another 26 weeks of an extension study. The extension study was also double-blind. At the end of the first 26 weeks, the negative symptom reduction did not differ significantly between the two groups. After one year, however, the patients who participated in the extension study had 15.8 point and 11.0 point reductions from baseline, respectively, for the asenapine and olanzapine groups on the NSA-16 score. More information about asepanine appears on page 2.

• A phase 2 trial of an investigational antidepressant yielded positive results, according to H. Lundbeck A/S, a Denmark-based pharmaceutical company, in a July 2 announcement. The drug, known as ***Lu AA24530***, has been shown to modulate a number of serotonin receptors and, in animal studies, increase acetylcholine, norepinephrine, dopamine, and serotonin levels in certain brain regions. In the double-blind, phase 2 trial, placebo and duloxetine (as an active control) were compared with three dosage levels of Lu AA24530 for efficacy and safety in 652 patients with major depression during six weeks of treatment. The drug beat placebo and met the primary and secondary efficacy endpoints for depression symptoms, measured by standard scales, and had tolerability similar to that for duloxetine, the company said. Lu AA24530 is being developed by Lundbeck and Takeda Pharmaceuticals for treatment of depression and anxiety disorders.

• An investigational drug being developed by Sepracor Inc. for treating major depressive disorder failed to meet its primary efficacy endpoint, the company announced on July 1. The drug ***SEP-225289*** was tested in a phase 2, double-blind study of 514 patients for eight weeks and compared with placebo and venlafaxine extended-release. The company said the findings were inconclusive, because the study drug's serum concentrations were unexpectedly low, which could indicate that patients did not get enough active drug. Pharmacologically, SEP-225289 inhibits serotonin, norepinephrine, and dopamine reuptake transporters. The company has not announced whether it will proceed with the drug's development.

• Targacept Inc. released some results of a phase 2b trial of its investigational drug ***TC-5214***, which was tested as an augmentation treatment for major depression. In the trial, 579 patients with major depression were first given citalopram for eight weeks. The 265 patients who were nonresponders at the end of eight weeks were then randomized to receive an add-on treatment of either TC-5214 or placebo along with citalopram for another eight weeks in a double-blind phase. The group receiving TC-5214 and citalopram had significantly greater improvement in the primary endpoint, reduction of the score on the 17-item Hamilton Rating Scale for Depression, than did the group receiving citalopram and placebo. The groups also differed significantly in the secondary efficacy endpoints that measured depressive and cognitive symptoms. The trial drug is an antagonist of neuronal nicotinic receptors (NNRs) and modulates the alpha4beta2 NNR subtype. One patient in the citalopram/TC-5214 group had a seizure that was deemed to be related to the study treatment.

Regulatory Briefs

• The National Institute for Health and Clinical Excellence (NICE) announced in June that it would not change its guidelines on the use of ***donepezil, galantamine, rivastigmine, and memantine.*** NICE is an independent organization that advises the National Health Service of England, and its therapeutic guidelines are adopted by many other countries' governments to set reimbursement criteria. NICE guidelines, originally issued in 2006, recommended that donepezil, galantamine, rivastigmine, and memantine be used in treating moderate Alzheimer's disease only.

Japan-based Eisai and U.S.-based Pfizer, which comarket donepezil, fought NICE in court in the United Kingdom over its recommendation that donepezil should be used for treating moderate Alzheimer's disease only, arguing that the drug is also effective in treating mild Alzheimer's disease and that NICE's pharmacoeconomic model was flawed. The court then ruled that NICE should have made the economic model used in the decision making available for the manufacturers to review and voice their objections. After the economic model was reviewed and commented on by the manufacturers, NICE concluded that "although a number of technical inaccuracies were highlighted, and amendments were made to the economic model, these were not sufficient to change the original conclusion that these treatments are not cost-effective in the mild stages of the disease." In an announcement released on July 1, the companies repeated their criticism of NICE's economic model but said they would not appeal the institute's decision.

• In June, the FDA requested a safety-related labeling change for ***atomoxetine***, a nonstimulant treatment for attention-deficit/hyperactivity disorder (ADHD). The "Warnings and Precautions" section of the drug label was expanded to include reported cases of severe liver injury that occurred mostly within 120 days of starting atomoxetine. A warning about orthostatic hypotension and syncope was also added. ***Details about the labeling changes are posted at <www.fda.gov/Safety/MedWatch/SafetyInformation/ucm169981.htm>.***

• At its July meeting, the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) issued an opinion against an application for marketing ***milnacipran*** as a treatment for fibromyalgia. Milnacipran is a selective serotonin and norepinephrine reuptake inhibitor. The committee reviewers decided that the efficacy of milnacipran in short-term clinical trials in fibromyalgia was marginal and were concerned that long-term data in a European population were lacking. Milnacipran is approved in the United States to treat fibromyalgia.

• The CHMP turned down a previous appeal by Pfizer at the July meeting and again refused to approve ***pregabalin*** for treatment of fibromyalgia. The committee initially issued a negative opinion in April in response to the company's application. Pregabalin has already been authorized for the treatment of neuropathic pain, partial seizures, and generalized anxiety disorder in Europe. In the United States the drug is approved for fibromyalgia, neuropathic pain associated with diabetic peripheral neuropathy, postherpetic neuralgia, and partial seizures. The CHMP cited its concerns that the drug's benefits in clinical trials had not been shown consistently in either the short term or long term.

Research Brief

The National Institute of Mental Health announced on July 21 that it would fund a large research project to investigate early and aggressive treatment for schizophrenia. The project, named the Recovery After an Initial Schizophrenia Episode (RAISE) study, will compare different interventions such as medication therapies and psychosocial treatment immediately after first-episode schizophrenia is diagnosed. These treatments will be tested in real-world clinical settings for their effectiveness in reducing symptoms, preserving cognitive function, and preventing disability.

Two research groups have been selected to lead the project: the Research Foundation for Mental Hygiene in New York City, led by Jeffrey Lieberman, M.D.; and Zucker Hillside Hospital at Feinstein Institute for Medical Research in Manhasset, N.Y., led by John Kane, M.D. Lieberman is the chair of APA's Council on Research and Quality Care, chair of the Department of Psychiatry at Columbia University College of Physicians and Surgeons, and director of the New York State Psychiatric Institute. Kane is chair of the Department of Psychiatry at Zucker Hillside Hospital and a professor of both psychiatry and neurology at Albert Einstein College of Medicine. The research will be conducted at multiple clinical sites across the United States. ■

government news

Decisions

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that is guided by patients' preferences and by shared knowledge that stems from the free flow of information.

The push for greater patient involvement in mental health care was driven in part by earlier studies indicating that many people with mental disorders have no decision-making impairment. Mental health advocates have noted that because most patients ultimately decide for themselves what they will or will not do in regard to treatment, clinicians should embrace a more formalized role for patients in deciding a treatment course.

Recent research found that even for patients with serious and persistent mental illness, shared decision making offers benefits. A study published in the August *Psychiatric Services* found that a decision-sharing approach between psychiatrists and schizophrenia patients was useful for well-informed and compliant patients and for those who disliked their current antipsychotic medication. It was not useful for patients who may have a reduced ability to make decisions.

Similarly, a September 2007 report in *Psychiatric Services* found that many patients with severe mental illness preferred "active and collaborative roles, similar to those [patients] with other medical conditions." The study found that patients preferred greater participation in mental health treatment decisions than they were generally allowed and that they were particularly interested in having an active role in decisions involving the use of psychotropic medications.

Helping patients to play a larger role in their medical decision making has been limited by the need for more detailed research on effective approaches and its limitations. In recent years research in this area has become a priority for the National Institute of Mental Health (NIMH) because patient involvement in treatment decisions is seen as critical to an individual's quality of life and autonomy and can help improve health outcomes.

To date NIMH-supported research has focused on understanding how patients with psychiatric disorders make decisions, testing interventions to support effective decision making, and measuring the outcomes of patients sharing in decision making.

As the research is completed, policymakers need to ensure that the findings are made available to patients and caregivers so individuals can educate themselves about their conditions or the conditions of their loved ones, said Tony Coelho. Coelho, chair of the Partnership to Improve Patient Care, spoke in June at a briefing sponsored by the Alliance for Health Reform.

"There is no way that providers and patients get the information today that they need," he said. "Somebody in the ivory tower knows and people write books and do all kinds of things based on this information, but it doesn't get to patients and to providers."

The Empowering Medicare Patient Choices Act is posted at <http://thomas.loc.gov> by searching on the bill number, S 1133. ■

Doing Double Duty for Patients

BY MELINDA FIERROS, M.D.

Earlier this year I participated in APA's National Advocacy Day, and I learned much about my profession, my legislature, and how to communicate my profession's needs to my legislators. I arrived an intimidated resident and left transformed into an empowered constituent.

My experience at Advocacy Day inspired me to get my colleagues involved in advocacy at the state level. To do this, I knew I would have to anticipate potential roadblocks and see if I could devise workable detours around any obstacles that might limit residents' participation (such as leave and clinic obligations). So I decided to approach my program director about getting residents involved in advocacy. I told him about my experience on Capitol Hill and how all residents should know how to advocate for their profession. Now came the hard part. I asked if he would allow residents to participate in the Ohio Psychiatric Physicians Association's (OPPA) Advocacy Day *and* count it as a work day. He said yes, with the following conditions:

- There would have to be a system of accountability (a sign-in sheet).
- We would have to arrange coverage at our clinical sites and get permission from our attending physicians.
- We would have to write about our experience and turn it in to him.

Melinda Fierros, M.D., is a PGY-5 child and adolescent psychiatry fellow at Wright State University.

What follows are my experiences at OPPA's Advocacy Day.

Two colleagues and I met at 8 a.m., got into one of our vehicles, and began the drive to Columbus, where we would soon be rubbing elbows with our elected officials. There was an air of excitement in the car, less about what would happen later in the day and more about getting this hour and a half to sit and catch up with each other. We laughed and gossiped, and I became sentimental as the realization sank in that my fellow fourth-year residents would soon be leaving me behind to finish out my child fellowship.

We parked close to a Doubletree Hotel, and id-laden dreams of yummy cookies entered my consciousness (the Doubletree makes heavenly chocolate-chip pecan cookies). My colleagues and I made a plan (OK, I made the plan for them) to return to the Doubletree after our hard work with the politicians, in search of said cookies.

OPPA had arranged for a few members of Ohio's state legislature to address the participating advocates, and they thanked us for being there, emphasized the importance of what we were doing, and noted the impact we would have on legislative decision making. The OPPA staff also gave us a review of the Ohio legislative system and the many legislative proposals that were likely to have a direct impact on our lives, including scope-of-practice and insurance-parity issues. I was struck by the enormity of it all and by how empowered and important I felt.

We had faxed letters to our state representatives in advance and requested appointments on Advocacy Day. My two colleagues and I devised an action plan before we headed to our first scheduled meeting, which was with Rep. Jarrod Martin. He was held up in session, and so we met with his aide, who was profusely apologetic. Among other topics, we discussed the importance of mental health parity and ensuring that the intent of a bill on parity was translated into practice in its implementation. He listened to us intently and took notes, asking questions and thanking us for our visit.

We headed to our next meeting with Sen. Chris Widener, who met with us for some time. We discussed the importance of providing mental health care to military members and veterans. He asked us about our own military experiences with mental health care. We discussed the scope-of-practice issues, and he made it clear that he understood, noting that he is a licensed architect and such issues arise in his profession. He thanked us and then graciously posed for a picture.

We had done it! Our plan of action was successful! We headed back to the parking garage, feeling an enhanced sense of not only accomplishment, but camaraderie as well. I looked forward to the long drive home with my colleagues, but first, cookies!

Having seen the impact that meeting with legislators can have, I now believe that all residents should be required to participate in some form of advocacy before they graduate. I encourage all of you to broach the subject of resident advocacy with your program director and see if you can devise creative ways to get you and your colleagues involved. ■

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.

On the Decline Of Psychotherapy

In the July 3 issue, *Psychiatric News* published yet another article lamenting the decline of psychotherapy in the practice of psychiatry ("Psychiatrists Lament Decline of Key Treatment Modality"). It seems this "tragedy" has been gradually occurring in the field over a number of years. In multiple articles and lectures, it's referred to as "losing the mind." Supposedly, psychiatry is in danger of becoming less of what it is, and the rest of medicine will be worse off because of it. Psychoanalytic/psychodynamic psychiatric practitioners regard themselves as the last bastion against the creep of a non-feeling, coldhearted, high-tech medical world. To these psychiatrists, they are the guardians of humanity in medicine; only a psychiatrist trained in psychodynamic psychotherapy knows how to talk and empathize with patients.

All of this is not only false, but insulting to many nonpsychiatric physicians, who provide respectful listening to their patients.

The diminishing role of psychotherapy in the psychiatrist's tool bag isn't a loss to be mourned and resisted, but progress to be praised and encouraged. It reflects a move toward the medical identity of psychiatry. The psychotherapy-oriented psychiatrists would like to blame their demise on HMOs, but the truth of the matter is, the decline of psychotherapy by psychiatrists parallels the growth of psychopharmacology. It is also representative of the free-choice and preference of our patients. The value of psychotherapy and how much to pay for it are determined by the mutual agreement of physician and patient. Let's be honest: a person can receive quality psychotherapy from a nonphysician. If psychiatrists want to provide traditional psychotherapy, they either have to charge a competitive fee or convince the patient that the extra expense is worth it. If our leaders were smart, they would recognize the absurdity of emphasizing a skill that a social worker can provide adequately at a much lower fee. In general terms, there have always been two types of physicians: those who are innovative and open to new modalities of care, and those who resist change and stick to roles that are neither economically sound nor therapeutically advantageous.

In truth, the only damage done with the decline of psychodynamic psychotherapy by psychiatrists is to the pocketbooks of the practitioners, not to the patients themselves.

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Recently I had two referral experiences that I would like to share. The circumstances of both were identical. An insurance company had given two patients my name—however, the company had given out two names: that of a mental health therapist who it said would perform the evaluation and provide treatment and that of "a psychiatrist for your medications." It does indeed appear that psychiatry has traded off the "50-minute hour" for the "15-minute med-check visit." Perhaps the time has come to change the official definition of what a psychiatrist does.

I began to wonder about this "sea change"—not just in psychiatry but in medicine in general—and the proverbial swinging pendulum between mind and body. Clearly one cannot have a psychogenic illness without a brain, and as such, the neurosciences and medications are a realistic consideration. However, it does appear that we have taken the psychotherapy out of psychiatry.

I began to wonder how this has come about; it has been a slow and progressive process. Periodically we read about circuit-riding psychiatrists being subsidized liberally by pharmaceutical companies. We read about large pharmaceutical studies. Rarely do we read about psychotherapy studies—an exception being the article in the October 1, 2008, *Journal of the American Medical Association*, titled "Effectiveness of Long-Term Psychodynamic Psychotherapy: A Meta-Analysis."

We see pharmaceutical ads saturating the airwaves, magazines, and all manner of reading material. We now have conflict-of-interest disclosures. One must begin to wonder by whom and how is psychiatry being defined. Or perhaps we should remember the Watergate metaphor and "follow the money." I began to wonder about how our psychiatrists are being trained and what are the philosophies that are defining their training—is it perhaps an amalgam of big pharma, insurance companies, and who knows what else?

Progress is inevitable and realistic. I am not suggesting a return to the past—that also had its limitations, biases, and omissions. But, to repeat myself, we cannot have a psychogenic illness without a brain. We have established the appropriate need to examine the pivotal role of the brain. However, perhaps it is time for psychiatry to reintroduce the 50-minute hour and develop an equal interest in examining the human side of that mind/body equation.

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Conference on Learning Disorders

The Interdisciplinary Council on Developmental and Learning Disorders will hold its 2009 annual conference from November 6 to 8 in Bethesda, Md.

The goal of the conference is to help psychiatrists and professionals from related fields and parents integrate knowledge and competencies from different disciplines that will improve prevention, assessment, diagnosis, and treatment of emotional and developmental disorders in infancy and childhood. Speakers will include Stanley Greenspan, M.D., Ricki Robinson, M.D., Sally Rogers, M.D., and Nancy Minshew, M.D.

More information is posted at <www.icdl.com>. ■

CME

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APA and the American Medical Student Association were the only medical associations testifying at the hearing.

As a CME provider for tens of thousands of psychiatrist members, APA has been closely examining the potential conflict of interest in the education it provides, Scully testified. "We've taken considerable pains to implement policies to reduce the conflict of interest in the provision of continuing medical education," he told the senators.

In March APA's Board of Trustees voted to phase out all industry-supported symposia at APA's scientific meetings, the first medical professional society to implement this policy, Scully told the committee.

"This action is not without real cost. . . . For example, this year we'll lose a million and a half dollars in revenue that we would have had," said Scully. However, he noted that "in the long run, we believe the elimination of even the perception of undue influence and maintaining or regaining the public's trust is well worth the cost."

In March 2008 the AMA rejected a proposal to ban commercial support for CME presented by its Council on Ethical and Judicial Affairs (CEJA). CEJA softened its stance in its 2009 report and suggested guidelines for "ethically permissible" commercially supported CME. In June AMA delegates again declined to adopt the recommendations.

At the hearing, Sen. Kohl expressed his disappointment about the AMA's continued lack of policy on the acceptance and management of industry funding.

Credibility of Accrediting Body Questioned

From 1998 to 2007, industry-funded CME activities that were accredited by the Accreditation Council for Continuing Medical Education (ACCME) increased by more than 300 percent. The industry funding reversed this upward trend in 2008, when it declined by $200 million, to total approximately $1 billion.

The independent ACCME is the primary overseer of CME providers, and its accreditation is recognized by medical boards throughout the country. However, its effectiveness in safeguarding the quality and objectivity of CME content was questioned by several panelists at the hearing. Lewis Morris, chief counsel of the Office of Inspector General (OIG) at the Department of Health and Human Services, told the committee that the "ACCME's role in mitigating commercial bias is limited. Oversight is complaint driven and occurs after the fact." He cited federal lawsuits in which pharmaceutical companies were accused of promoting off-label use of prescription drugs that is disguised as independently provided CME. Several such lawsuits filed by the OIG and the Justice Department in the past decade have been settled for hundreds of millions of dollars.

"The current environment tolerates industry sponsors' preferential funding of programs that serve the business needs of the funders," Morris said.

Steven Nissen, M.D., chair of the Department of Cardiovascular Medicine at the Cleveland Clinic, told the committee that the current oversight by the ACCME is "largely ineffective" and that the organization "appears uninterested or incapable of enforcing [its rules]." He recommended that the medical profession needs an independent board to replace the ACCME.

Murray Kopelow, M.D., M.S., chief executive of the ACCME, vehemently disputed the criticism at the hearing. He told the committee that in 2007 the ACCME began a public discussion on whether commercial support for CME should continue or be eliminated. In March 2009, the ACCME board decided that it would not be taking any action to end commercial support for accredited CME at this time. Kopelow noted that the ACCME has been tightening its standards for CME providers in the past few years to ensure their independence from commercial interest.

In 2008 and 2009, the ACCME investigated and closed 17 inquiries of CME providers, 12 of which related to commercial support. Of the 12 inquiries, five were found noncompliant and seven compliant with the ACCME standards. Kopelow also pointed out that the number of CME providers put on probation by the ACCME increased from 1 percent before 2008 to the current rate of 10 percent.

Kopelow insisted that the current oversight works: "The ACCME *is* the firewall between promotion and education. Accredited CME *is* independent from commercial interests."

Benefits of Industry Funding Argued

Thomas Stossel, M.D., director of the Translational Medicine Division and senior physician of the Hematology Division at Brigham and Women's Hospital, Harvard Medical School, testified to the committee that modern medical advances owe much to the close relationship between industry and physicians.

"Of course companies are trying to sell products," Stossel acknowledged, but that is not a bad thing. He believes that the industry's interest is consistent, not in conflict, with patients' own. He urged the committee to examine "the quality of the product, not . . . the motive of the producer." Industry involvement in CME is beneficial to physicians and patients, he maintained, as nonprofit organizations cannot rapidly disseminate the latest research and information about new drugs and technologies to clinical practice.

At the hearing, the committee's ranking member, Mel Martinez (R-Fla.), asked why physicians cannot all be required to pay for their continuing medical education, thus eliminating the need for industry subsidies.

Eliminating industry funding would negatively affect physicians with limited resources such as rural physicians and residents, Stossel and Kopelow argued. These physicians would have less access to information on the newest products and research.

An independent grant organization that pools and distributes industry funding may serve as a firewall between commercial interests and CME content, but this mechanism seems to have little prospect, Morris told the committee. He gave an example of such a grant recently established by the American Academy of Orthopaedic Surgeons. The organization's board members who distribute the grants are prohibited from relationships with device or pharmaceutical companies. So far, major device manufacturers in the field have declined to contribute to this organization and elected to make grants directly to CME providers. ■

Asenapine

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In these short-term trials, common adverse reactions to asenapine included somnolence, extrapyramidal symptoms, akathisia, oral hypoesthesia, and dizziness.

In a long-term schizophrenia trial, in which asenapine was compared with olanzapine, the mean body weight gain from baseline was 1.6 kg after one year; patients who took olanzapine for one year had a gain of 5.6 kg. Clinically meaningful weight gain (at least 7 percent increase from baseline) occurred in 14.7 percent of patients on asenapine and 36.1 percent on olanzapine.

In the short-term trials, these metabolic indicators, including glucose and cholesterol levels, appeared to be less affected by asenapine than by olanzapine.

In the long-term schizophrenia trial, three of the 908 patients (0.3 percent) treated with asenapine had a QTc interval increase from baseline of greater than 60 msec. None had a QTc interval increase of 500 msec or more.

Ten of the 12 advisory committee members voted to indicate that asenapine has been shown to be effective and acceptably safe as an acute treatment for schizophrenia. Nine agreed that the balance of its effectiveness and safety is acceptable for approval. Three advisors were troubled by the one trial in which asenapine did not beat placebo and were reluctant to support its approval for this indication.

The two positive studies in bipolar I disorder convinced the committee to vote unanimously in favor of the efficacy and safety of asenapine to treat that disorder.

Asenapine is formulated as sublingual tablets to optimize its bioavailability upon absorption, since the drug is extensively metabolized in the liver. The tablet should not be swallowed. The approved dosage for acute schizophrenia treatment is 5 mg twice daily. The dosage for bipolar I disorder is to start with 10 mg twice daily with the option of decreasing to 5 mg twice daily if the patient experiences adverse effects.

At the advisory meeting, the company said it plans to study the drug in pediatric and adolescent populations as well as for long-term maintenance treatment for the two disorders in adults.

Prescribing information for asenapine is posted at <www.spfiles.com/pisaphrisv1.pdf>. ■

Settlement

continued from page 1

The agreement could provide significant savings for the state. In research on the New Jersey mental health system, plaintiffs found that the annual cost for each resident at a state psychiatric hospital was about $220,000, while the annual cost for treatment and housing support for the same type of patient in a community setting was less than $40,000 a year.

Most important, of course, are the patients themselves, said Joe Young, executive director of DRNJ; the community services treatment approach is highly preferred by people with mental disabilities.

The settlement is similar to one Bazelon reached last year with San Francisco over its institutionalization of people deemed capable of living in supportive housing. At least four similar lawsuits are pending in other states.

All of the suits alleged that the state or local government's failure to provide community services for the patients violated their legal duty under the Americans With Disabilities Act and the U.S. Supreme Court's *Olmstead* decision to care for people with disabilities in the most integrated setting appropriate to their needs.

"I hope it affects every community's policies over access to care with its emphasis on community housing as a much more effective remedy for people with mental illness," Andrew Penn told *Psychiatric News*. He is a senior staff attorney for Bazelon and worked on the case.

Further information on the settlement is posted at <www.bazelon.org/newsroom/2009/7-29-07NJPAsettles.htm#work>. ■

Applications Invited for APA/Shire Fellowship

Applications are invited for the 2010-2011 APA/Shire Child and Adolescent Psychiatry Fellowship Program. Fellowships will be awarded to five residents to travel to APA's 2010 and 2011 annual meetings and to work with mentors on issues in child and adolescent psychiatry.

The fellowship was established in 2002 to interest general psychiatry residents in considering careers in child and adolescent psychiatry through specific educational opportunities unavailable to them otherwise.

The fellowship is open to PGY-1 through PGY-3 residents. Applicants must be APA members and have approval from their training director or department chair.

The deadline for applications is November 20. They must include a completed application form; a 500-word letter of interest detailing the applicant's experience, knowledge, and career path; curriculum vitae; and a letter of support from a residency training director or department chair including the applicant's potential contribution to child and adolescent psychiatry.

The fellowship is supported by an unrestricted educational grant from Shire Pharmaceuticals.

Application materials are posted at <www.psych.org/share/OMNA/APAShireChildAdolescentPsychiatryFellowship.aspx>. More information is available by contacting Alison Bondurant at abondurant@psych.org or (703) 907-8639. ■

Freud

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He spoke in German. That may not have been an impediment to much of his audience. Clark, Johns Hopkins University, and the University of Chicago were founded around the same time as graduate research institutions based on the German model. Many of those who attended the lectures, including Stanley Hall, had studied in Germany, and German was the primary language of research at the time. Reports of Freud's lectures also appeared in English the next day in the Worcester *Telegram*.

Freud continued his discussion of the history of psychoanalysis on Wednesday morning. On Thursday morning he addressed the psychopathology of everyday life, as expressed in the slips of tongue and pen. He talked about infant sexuality on Friday and transference and wish fulfillment on Saturday.

He seemed to appreciate the moment, despite his earlier reticence.

"[A]s I stepped out to the platform at Worcester to deliver my Five Lectures upon Psycho-Analysis, it seemed like the realization of some incredible day-dream," he wrote in 1925. "Psychoanalysis was no longer a product of delusion; it had become a valuable part of reality."

The talks were ultimately compiled and published as *Five Lectures on Psycho-Analysis*.

Freud wasn't the only significant figure in town that week. Hall used Clark's 20th anniversary as the focus for several conferences intended to celebrate the university as a major research center. (Clark didn't admit undergraduates until 1902, and then only under pressure from its eponymous patron, Jonas Clark.) Hall organized sessions on biology, chemistry, physics, mathematics, and China and the Far East. A conference on child welfare was held in July.

Physicist Albert Michelson, the first American to win a Nobel Prize in science for his work on measuring the speed of light, British physics Nobelist Ernest Rutherford, and astronomer Percival Lowell were honored with degrees. Leo Baekeland, inventor of the first fully synthetic plastic, attended. Robert Goddard, who later became known as the father of American rocketry, was a grad student at Clark and appears in photographs of the distinguished attendees.

Besides Jung and Ferenczi, other speakers or attendees from the realms of psychiatry and psychology included anthropologist Franz Boas; psychiatrists Adolph Meyer and William Alanson White; neuropathologist James J. Putnam, founder of the American Neurology Association; and Mary Whiton Calkins, the first woman president of the American Psychological Association. The philosopher and psychologist William James came up from Harvard to listen to one of Freud's lectures.

Solomon Carter Fuller, recognized today as the first African-American psychiatrist, attended, too, at the invitation of Clark's biology department. Fuller was a neuropathologist at Westborough State Hospital and was Hall's personal physician for a time. He, too, had spent several years studying in Germany, working part of the time in Alois Alzheimer's lab.

One nonscientist, Emma Goldman, the well-known and widely feared anarchist, a former resident of Worcester, was back in town to speak, although not at Clark. Goldman agreed with Freud that sexuality was central to human development, but thought that sexual expression, not repression, was the source of human creativity, according to Candace Falk, Ph.D., editor and director of the Emma Goldman Papers at the University of California, Berkeley.

"The most important event of our Worcester visit was an address given by Sigmund Freud," wrote Goldman in her autobiography. "I was deeply impressed by the lucidity of his mind and the simplicity of his delivery. Among the array of professors, looking stiff and important in their university caps and gowns, Sigmund Freud, in ordinary attire, unassuming, almost shrinking, stood out like a giant among pygmies.

"He had aged somewhat since I had heard him in Vienna in 1896. He had been reviled then as a Jew and irresponsible innovator; now he was a world figure; but neither obloquy nor fame had influenced the great man."

Before returning to Europe, Freud spent a few days after the conference with Putnam at the latter's camp in the Adirondacks. Their interchanges strengthened Putnam's enthusiasm for psychoanalysis, according to articles he wrote in the *Journal of Abnormal Psychology*.

Ripples from the Clark conference spread, slowly at first, but then became a tidal wave.

"The U.S. was already fertile ground for Freud's ideas," said Robert Paul, Ph.D., a professor of anthropology and dean of the College of Arts and Sciences at Emory University, in an interview. "The 1909 conference paved the way for the movement from Europe to the U.S. in the 1930s that pushed psychoanalysis to dominate psychiatry until the 1960s."

Freud's ideas also would change the cultural world, as well, especially following the horrors of World War I, added Tobin. "In the 1920s, intellectuals and artists who wanted to be modern latched onto his ideas, not only about sexuality but also regarding the notion that the mind worked on many different layers."

Today, we might look back at the conferences with some degree of ambivalence, but they played an important role at the turn of the century in placing Clark on the map in the emerging science of psychology, said Mark Freeman, Ph.D., a professor of psychology at Holy Cross College in Worcester, in an interview. "In addition to the familiar clinical and experimental approaches to psychology, Clark had—and has—an interest in the conceptual, philosophical, and theoretical bases of the field, especially in relationship to developmental psychology."

"The real value of the 1909 conference was Hall's interest in drawing on a variety of intellectual traditions and disciplines to inspire his campus," Michael Bamberg, Ph.D., a professor of psychology at Clark, told *Psychiatric News*. "In selecting his speakers, he was trying things out, looking at innovative trends in emerging disciplines that hadn't made it into the mainstream but were knocking on the door."

An agenda for Clark University's commemoration of the centennial of Sigmund Freud's lectures is posted at <www.clarku.edu/micro/freudcentennial/conferences/index.cfm>. The New York Academy of Medicine's program is posted at <www.nyam.org/events/?id=448&click=>. ■

Pediatricians

continued from page 7

ships with psychiatrists and mental health providers. The latter is reflected in the AAP's collaborating with psychiatrists on the development of the statement, said Michael Houston, M.D., chair of APA's Council on Children, Adolescents, and Their Families.

"This new policy is welcome and an important step forward," Houston told *Psychiatric News*. "Due to workforce shortages, ignorance, and stigma, only 1 in 5 of the children and adolescents who need mental health care receives it."

He added that the policy statement fits in well with the work of APA's Ad Hoc Work Group on the Integration of Psychiatry and Primary Care, which is discussing ways to improve access to mental health services for both children and adults.

"The Future of Pediatrics: Mental Health Competencies for Pediatric Primary Care" is posted at <http://pediatrics.aappublications.org/cgi/content/full/124/1/410>. ■

Flu

continued from page 6

Besides worrying about infection risk to themselves, their families, and coworkers, health workers had to deal with the isolation enforced by quarantine procedures. Access to hospitals was restricted, handshaking was forbidden, and protective gear made everyone anonymous without repeated introductions. Staff who followed orders and avoided colleagues reported greater stress, according to a post-outbreak survey. Collectively, this social isolation took its toll on workers, said Maunder.

Novel influenza A (H1N1) may return as a modest surge in the winter's usual flu cases or it may roar back like wildfire across a dry prairie, but anyone involved in caring for patients must be prepared for any of its eventualities.

More information is posted at the CDC's flu Web site at <www.flu.gov/plan/community/commitigation.html#I>. ■

MH Care

continued from page 9

Despite the drop in the overall cost of mental health care, out-of-pocket costs have risen for patients. Out-of-pocket payments for the treatment of psychiatric disorders were among the highest for all disorders in both 1996 and 2006 (see chart on page 9). These payments rose from 23.1 percent of the average amount individuals spent on mental health care in 1996 to 25 percent in 2006.

That patient spending increase is consistent with the fact that many solo mental health clinicians, including psychiatrists, practice outside of managed care systems and are thus less likely to accept a managed care benefit, Jacobs said.

A summary of the "Five Most Costly Conditions, 1996 and 2006: Estimates for the U.S. Civilian Noninstitutionalized Population" is posted at <www.meps.ahrq.gov/mepsweb/data_files/publications/st248/stat248.pdf>. ■

Shah Wins Award

Parind Shah, M.D., a psychiatry resident at Griffin Memorial Hospital in Norman, Okla., has won the 2008 Hamilton Clinic Award, which honors outstanding writing in the mental health field. He was awarded for his paper "Referral of a Psychiatric Patient: More Than Routine Patient Care." The award comes with a $1,000 check and was established in 2007 by Oklahoma psychiatrist William Hamilton, M.D.

Another Oklahoma psychiatrist, James Boger, M.D., a resident at the University of Oklahoma Health Sciences Center, won honorable mention for his paper "Behavioral Improvement and Decreased Parental Stress Associated With Vagus Nerve Stimulation in a 6-Year-Old Child."

Information about this year's competition is available by phone at (580) 765-3900. ■

Blumenthal Named Health Leader

The Commissioned Officers Association of the U.S. Public Health Service has announced that Susan J. Blumenthal, M.D., is the recipient of its 2009 Health Leader of the Year Award. She is a retired rear admiral and assistant surgeon general in the U.S. Public Health Service Commissioned Corps.

Blumenthal is being recognized for her lifetime achievements and leadership in raising national awareness and scientific attention to women's health issues, as well as a range of other critical public health concerns. Among her numerous accomplishments, she was the first deputy assistant secretary of women's health in the Department of Health and Human Services and served as a White House advisor on health issues. She is a recipient of the Distinguished Service Medal of the U.S. Public Health Service.

Blumenthal is now director of the Health and Medicine Program at the Center for the Study of the Presidency and Congress, where she leads its Commission on Charting New Directions in the field. ■

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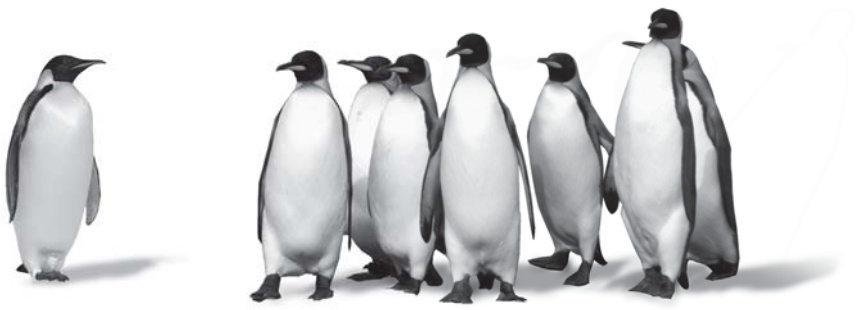

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Department of Psychiatry Harvard Medical School
&
The VA Boston Healthcare System

Harvard Medical School and the VA Boston Healthcare System are recruiting a Training Director for the Harvard South Shore Psychiatry Residency Training Program (HSS). The Harvard Department of Psychiatry at the VA Boston Healthcare System has undergone a major expansion of teaching, research, and academic clinical programming over the past two years. The current Training Director is assuming the duties of Departmental Chair for Academic Development, which will include ongoing support to HSS including teaching, supervision, and consultative support to the incoming Training Director.

HSS is a consortium program affiliated with Harvard Medical School and sponsored by the VA Boston Healthcare System. Residents rotate among three Boston VA campuses, other Harvard-affiliated training hospitals, and Massachusetts Department of Mental Health facilities. HSS receives stable funding for 32 PGY I-IV resident positions plus ample administrative support, not dependent on GME pass-through funding. Major foci of program excellence include biopsychosocial assessment and interviewing skills, academic development in research, teaching and leadership, evidence-based pharmacotherapy, and manual-guided psychotherapies. Comprehensive program description can be found at **www.harvardsouthshorepsychiatry.org.**

The competitive Training Director candidate will have strong academic credentials, residency administration experience at the site or program level, and demonstrated scholarly ability in a relevant field. The applicant must be board-certified in psychiatry with a minimum of 5 years of post-residency experience, and is expected to qualify for a Harvard Medical School appointment at the Assistant or Associate Professor level.

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Drs. Mark Bauer & Gary Kaplan, Search Committee Co-Chairs
940 Belmont Street, Brockton, MA 02301; or email materials to:
Eugene.Francois@va.gov with a copy to vhabhsjobs@med.va.gov

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For additional information and/or to apply visit www.uacareertrack.com and reference specific job # from above. If you have questions, please contact: Ashley Lott, Human Resources, Dept. of Psychiatry, 1501 N. Campbell Avenue, P.O. Box 245002, Tucson, AZ 85724-5002; (520) 626-3819; or aelott@email.arizona.edu. Review of applications is ongoing until positions are filled. The University of Arizona is an EEO/AA Employer-M/W/D/V

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UC DAVIS SCHOOL OF MEDICINE DEPARTMENT OF PSYCHIATRY AND BEHAVIORAL SCIENCES

Health Sciences Assistant/Associate Clinical Professor. The University of California, Davis, Department of Psychiatry and Behavioral Sciences is recruiting for a Health Sciences Assistant/Associate Clinical Professor in the clinician/teaching series to serve as a teaching attending on the Psychosomatic Medicine Service located at the UC Davis Medical Center in Sacramento. The Unit is staffed with three UC Davis faculty, general psychiatry residents, and UC Davis medical students. Experience in teaching and supervision of medical students, residents, and other mental health professionals is highly desirable. The successful candidate should be board eligible or certified in general psychiatry, be in possession of, or eligible for, a California Medical license, and have an interest in psychiatric education and training. Completion of a fellowship in Psychosomatic Medicine is highly desirable but not required. The successful candidate will lecture in seminars and case conferences, and provide group and individual supervision of clinical cases. The candidate will also provide clinical teaching for general psychiatry residents, psychology fellows, medical students and other mental health professionals including timely and appropriate evaluation of trainee performance.

For full consideration, applications must be received by November 30, 2009. Position is open until filled, but no later than February 28, 2010. Interested candidates should email a curriculum vitae and letter of interest in response to Position #PY-07R-09 to Juli Koeberlein at juli.koeberlein@ucdmc.ucdavis.edu. In conformance with applicable law and University policy, the University of California, Davis, is an equal opportunity/affirmative action employer.

http://www.ucdmc.ucdavis.edu/psychiatry/

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

CALIFORNIA
BC/BE STAFF PSYCHIATRIST

Patton State Hospital is recruiting board certified/eligible psychiatrists. Patton is a Joint Commission accredited, 1500 bed, adult forensic 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 confidential consideration, send CV to George Christison, M.D., (A) Medical Director, 3102 East Highland Avenue, Patton, California 92369, (909) 425-7326 or Fax (909) 425-6635.

UC DAVIS SCHOOL OF MEDICINE
DEPARTMENT OF PSYCHIATRY AND BEHAVIORAL SCIENCES

Health Sciences Assistant/Associate Clinical Professor - APSS Clinic. The University of California, Davis, Department of Psychiatry and Behavioral Sciences is recruiting for a Health Sciences Assistant/Associate Clinical Professor in the clinician/teaching series to serve as teaching attending at the Adult Psychiatry Support Services Clinic located next to the UC Davis Medical Center in Sacramento. The Clinic is staffed with four UC Davis faculty, two general psychiatry residents, and two medical students. Experience in teaching and supervision of medical students, residents, and other mental health professional is highly desirable. The successful candidate should be board eligible or certified in general psychiatry, be in possession of or eligible for a California Medical license, and have an interest in psychiatric education and training. The successful candidate will lecture in seminars and case conferences, and provide group and individual supervision of clinical cases. The incumbent will provide clinical teaching for general psychiatry residents, psychology fellows, medical students and other mental health professionals including timely and appropriate evaluation of trainee performance.

For full consideration, applications must be received by November 30, 2009. Position is open until filled, but no later than February 28, 2010. Interested candidates should email a curriculum vitae and letter of interest in response to Position #PY-06R-09 to juli.koeberlein@ucdmc.ucdavis.edu. In conformance with applicable law and University policy, the University of California, Davis, is an equal opportunity/affirmative action employer.

http://www.ucdmc.ucdavis.edu/psychiatry/

PSYCHIATRIST

Immediate opening for Gero-Psychiatrist with progressive medical group in Los Angeles area. Psychiatrist duties include the development of Telemental Health programs. 200K salary and benefit package, and will pay for relocation.

Email: jminor@asanamg.com or pbennett@asanamg.com
Fax: (818) 907-1482. For more information call Janet Minor or Peter Bennett: (818) 907-1480.

Psychiatrist Opening at the County of Santa Barbara. Our Lompoc Clinic ACT Program is actively recruiting for an ADULT BOARD CERTIFIED OUTPATIENT PSYCHIATRIST. Call ratio is one weekend out of every 2 months. Salary will pay up to $210,761 plus $5,927.74 cash benefit allowance. We also offer the opportunity for relocation assistance and other incentives. For a more detailed job description and to apply for the position please visit www.sbcountyjobs.com. You may also contact Tarah Cronquist at tcronquist@sbcountyjobs.com, or by calling at 805-884-8098. Job will be open until filled. The County of Santa Barbara strongly promotes diversity and equality in the workforce.

COLORADO

Horizon Health, the nation's leader in Psychiatric Contract Management seeks a **Psychiatrist** for a **10-bed Gero-psych** unit less than one hour from **Denver International Airport.** Attractive salary and benefits accompany this exciting new opportunity. Contact: Mark Blakeney, Horizon Health, 972-420-7473, fax CV: 972-420-8233, or email mark.blakeney@horizonhealth.com. EOE.

BOULDER: General or Child Psychiatrist. Staff and Admin/Clinical positions. Inpatient & Partial programs. Fulltime positions offering salary, benefits and incentive plan. Newly acquired UHS hospital. Contact: Joy Lankswert, In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com

CONNECTICUT

CONSULTATION-LIAISON PSYCHIATRIST

The Yale University School of Medicine, Department of Psychiatry, is seeking a full time consultation liaison psychiatrist. Candidates must be licensed (or license eligible) to practice in the state of Connecticut, eligible for medical staff privileges at Yale-New Haven Hospital, and board eligible in psychiatry. Added qualifications in psychosomatic medicine highly desirable. This is an exciting academic opportunity in a behavioral medicine program involving both outpatient and inpatient work, with opportunities for teaching and research. The position carries academic appointment commensurate with experience.

Available fall, 2009. To apply please contact Paul Desan, MD, PhD, 20 York St CB2039, New Haven, CT 06504, paul.desan@yale.edu. Yale University is an affirmative action, equal opportunity employer. Applications from women and minority group members are encouraged.

INPATIENT ADULT PSYCHIATRIST-CENTRAL CT

FT/PT opportunity for BC/BE adult psychiatrist in 16-bed inpatient service with a community hospital offering a comprehensive mental health continuum. Enjoy working with an established team bringing a multidisciplinary approach to patient care. Crisis Center located in emergency department. This position offers a competitive salary and benefits and adaptable hours for the right individual. Call 1:5.

The practice is located in a family-oriented city located approximately two hours from NYC and Boston and 20 minutes to the capitol city of Hartford. Enjoy the charm of four seasons with a choice of attractive communities with Connecticut's best rated schools, shopping, award-winning restaurants, and regional theatre and easy access to skiing and the coast.

For more information about this opportunity, please contact Carolyn Doughtie of Physician Recruitment at 800.892.3846 or fax/email your CV to 860.585.3133. EOE

Email address: cdoughti@bristolhospital.org

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

DELAWARE

WILMINGTON / NEWARK & DOVER: Child Psychiatrist. Inpatient/partial programs. Very competitive salary, benefits & incentive plans. Will sponsor visa candidates. Contact Joy Lankswert @ 866-227-5415; OR email joy.lankswert@uhsinc.com

DISTRICT OF COLUMBIA

Medical Director Position - Adult Unit - Seeking Psychiatrist who likes working with the CPEP patients & likes Psych ER work for directorship position on adult inpatient unit. Can offer a **very** attractive compensation package; or can contract with physician already in practice. Please **call Terry B. Good at 1-804-684-5661,** Fax #: 804-684-5663; Email: terry.good@horizonhealth.com.

Washington, DC
George Washington University Medical Center

Founded in 1977, this ACGME-accredited fellowship in Psychosomatic Medicine is currently accepting applications for three PGY-V positions starting July 1, 2010. Under the guidance of **Thomas N. Wise, M.D.** and **Catherine C. Crone, M.D.,** the fellowship offers training in both inpatient and outpatient settings at a large tertiary care teaching facility that provides care to a diverse socioeconomic and cross-cultural patient population. This includes extensive experience in oncology, Ob-Gyn, HIV, pulmonary, cardiology, and organ transplantation. Emphasis is placed on a balance of clinical experience and didactic teaching addressing the biopsychosocial approach to understanding the medically ill patient. The experience is enhanced further by constant mentoring throughout the academic year along with efforts to tailor the training experience according to the individual fellow's interests and career goals. Opportunities in teaching, research, and outpatient psychotherapy are readily available and strongly encouraged. The program is based at Inova Fairfax Hospital, an 833-bed hospital located near Washington, D.C.

Interested individuals should contact
Catherine C. Crone MD, Fellowship Director
George Washington University Medical Center
c/o Inova Fairfax Hospital
3300 Gallows Rd, Falls Church, VA 22042
(703) 776-3380 Fax: (703) 776-3029
cathy.crone@inova.org

FLORIDA

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.

PSYCHIATRIST

Board certified (or eligible) Adult and/or 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

Psychiatrists (2)
Tampa Area

Excellent opportunity to join our psychiatric team in the further development and enhancement of hospital based psychiatric services. Located 30 minutes from Tampa, Florida Hospital Zephyrhills is committed to the continued enhancement and expansion of its psychiatric services throughout its service delivery system. Successful candidates will enjoy a professional environment and collegial support. Current services include adult/geriatric inpatient, intensive outpatient services, and general outpatient.

Florida Hospital Zephyrhills has partnered with Diamond Healthcare Corporation, a national provider of behavioral health management services, to assist it in furthering developing and expanding services and in the planning for new facilities. Board Eligibility required, Board Certification with an interest in geriatric psychiatry preferred.

An excellent compensation package is offered and both income guaranty and full time salaried opportunities are available. **CONTACT:** Lindsay Shuff, VP Development, Diamond Healthcare, email lshuff@diamondhealth.com (Fax) 804.228.4997 (phone) 800.443.9346

GEORGIA

Hospitalist Psychiatrist position and an Office-Based 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.

ATLANTA: Adult and Child Psychiatrists - Inpatient & partial programs. Fulltime or Part-time positions (Mon-Fri) offering salary, benefits & bonus plans. Admin/clinical opportunity for qualified/interested candidates. Weekend moonlighting also available for day shifts only at several UHS hospitals - no overnight call.

MOULTRIE - South GA: General Psychiatrist - partial hospital and outpatient services. Contact Joy Lankswert, In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com

KENTUCKY

COMMUNICARE

A progressive community mental health organization has the following position available in Elizabethtown, KY.

Psychiatrist

This full time position is responsible for directing and providing general psychiatric services at Hardin Memorial Hospital/14 bed Inpatient Psychiatric Unit. Qualifications include: Active Kentucky medical licensure, active DEA licensure, and Board eligible in psychiatry. Ability to work closely and congenially with interdisciplinary professional staff in a team management atmosphere. Must provide own transportation.

Communicare offers a lucrative salary, flexible scheduling and an exceptional benefit plan to include: Medical, Dental, Vision, and Life Insurance, 401(k), KY Retirement, and other exceptional benefits. For consideration please e-mail, fax, or mail resumes to:

Communicare, Inc.
Attn: Human Resources/Job Opportunities
107 Cranes Roost Court
Elizabethtown, KY 42701
(270) 765-2605 phone
(270) 763-9554 fax
hr@communicare.org
"Equal Opportunity Employer"

Radcliff - easy commute from LOUISVILLE: Child or General Psychiatrist for inpatient & outpatient services. Highly competitive salary, benefits, & bonus. Will sponsor visa candidates. Contact Joy Lankswert, In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com

LOUISIANA

DEPARTMENT OF PSYCHIATRY AND NEUROLOGY, TULANE UNIVERSITY SCHOOL OF MEDICINE in New Orleans, LA, is recruiting for several general and forensic psychiatrists (clinical track) for our growing department, at the Assistant/Associate Professor level. Candidates must have completed an approved general psychiatry residency and be board certified/eligible in general psychiatry and forensic psychiatry, respectively. Responsibilities will include direct patient care, teaching of medical students and house officers, and research (clinical and basic science) at various state hospitals, state correctional institutions, and at Tulane University Health Sciences Center. Time allocations will be based upon individual situations. Applicants must be eligible to obtain a Louisiana medical license. In addition, candidates must be eligible for clinical privileges at Tulane University Hospital and Clinic under the appropriate staff category and must agree to abide by those privileges as outlined by the current bylaws of the institution. Applications will be accepted until suitable qualified candidates are found. Send CV and list of references to Daniel K. Winstead, MD, Heath Professor and Chair, Department of Psychiatry and Neurology, Tulane University School of Medicine, 1440 Canal Street TB48, New Orleans, LA 70112. For further information, you may contact Dr. Winstead, at 504-988-5246 or winstead@tulane.edu. Tulane is strongly committed to policies of non-discrimination and affirmative action in student admission and in employment.

The Southeast Louisiana Veterans Health Care System (SLVHCS), formerly the New Orleans Veterans Affairs Medical Center and the Department of Psychiatry and Neurology at Tulane University School of Medicine seek a candidate to fill the position of Chief, Mental Health Service at SLVHCS. All candidates will have clinical, administrative, teaching and research responsibilities and must be board eligible/certified and have academic credentials to be qualified for a faculty appointment at Tulane University School of Medicine

Applicants should have both clinical and administrative experience, and may be psychiatrists, psychologists, nurses, or social workers. A doctoral degree is required. Applicants must possess a knowledge and understanding of health care policies, missions, and operating programs, and be knowledgeable about mental health care delivery and about mental health information management. He/she will be involved in the design of the Mental Health areas of the new VA hospital planned for Southeast Louisiana. United States citizenship or permanent residency is required. Salary and academic rank will be commensurate with qualifications and experience of the applicant.

We will continue to accept applications until a suitable qualified candidate is found. Interested applicants should mail a curriculum vitae with a list of 7 references to Daniel K. Winstead MD, Tulane Dept. of Psychiatry and Neurology, 1440 Canal Street TB48, New Orleans, LA 70112 or e-mail CV and references to winstead@tulane.edu. Tulane is strongly committed to policies of non-discrimination and affirmative action in student admissions and in employment.

CHILD PSYCHIATRISTS - DEPARTMENT OF PSYCHIATRY AND NEUROLOGY, TULANE UNIVERSITY SCHOOL OF MEDICINE in New Orleans, LA, is recruiting for BE/BC child psychiatrists at the instructor or assistant professor level, salary commensurate with experience. Clinical responsibilities available in the areas of inpatient psychiatry, community based child and adolescent psychiatry, and early childhood mental health. Teaching responsibilities include the supervision of residents, clinical psychology fellows and interns, and medical students rotating through the clinical facilities serviced by this position as well as the presentation of grand rounds and participation in the didactic series in child psychiatry. Clinical research is strongly encouraged. The persons selected must be professionally competent and be board eligible/certified in general psychiatry. She/he must be eligible for medical licensure in the State of Louisiana and have a current state and federal narcotics number. In addition, candidates must be eligible for clinical privileges at Tulane University Hospital and Clinic under the appropriate staff category and must agree to abide by those privileges as outlined by the current bylaws of the institution. Applications will be accepted until a suitable qualified candidate is found. Send CV and list of professional/academic references to Charley Zeanah, Jr, MD, Professor and Vice Chair, Child and Adolescent Psychiatry, Tulane University School of Medicine, Department of Psychiatry and Neurology, 1440 Canal Street TB52, New Orleans, LA 70112 (czeanah@tulane.edu). Tulane is strongly committed to policies of non-discrimination and affirmative action in student admission and in employment.

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 35 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.

The Department of Psychiatry and Neurology at Tulane University School of Medicine is recruiting a geriatric psychiatrist for a full-time faculty position. The candidate will spend part of their time at the Southeast Louisiana Veterans Health Care System (SLVHCS) and will also be involved in the new initiatives in both clinical geriatric care and special geriatric education programs at Tulane. Responsibilities include patient care as well as contributing to the various teaching and training programs of Tulane University's Department of Psychiatry and Neurology at the SLVHCS. He/she will be provided the opportunity to pursue their research interests. The person selected for this position must be professionally competent and be board eligible/certified in general psychiatry and in geriatric psychiatry. She/he must be eligible for medical licensure in the State of Louisiana and have a current state and federal narcotics number. In addition, candidates must be eligible for clinical privileges at Tulane University Hospital and Clinic under the appropriate staff category and must agree to abide by those privileges as outlined by the current bylaws of the institution. Salary will be competitive and commensurate with the level of the candidate's academic appointment. Applications will be accepted until a suitable qualified candidate is found. Applicants should send letter of interest, updated CV and list of references to Daniel K. Winstead, MD, Heath Professor and Chair, Department of Psychiatry and Neurology, Tulane University School of Medicine, 1440 Canal Street TB48, New Orleans, LA 70112. Interested and eligible candidates may obtain further information by contacting Daniel K. Winstead, MD at 504-988-5246 or winstead@tulane.edu. Tulane is strongly committed to policies of non-discrimination and affirmative action in student admissions and in employment.

MAINE

Make a difference as the Psychiatric Medical Director of our innovative Portland, Maine community mental health agency. You'll direct a small team of psychiatrists, nurse practitioners, and therapists serving the mental health needs of adults, children, and families. Your primary responsibilities involve supervision, team leadership, supporting clinical integrity, and provision of direct service, with limited after-hours on-call responsibility. This is an excellent opportunity to work with a team to provide innovative client-centered service.

Our location in Greater Portland provides a robust network of professional colleagues, and the cultural amenities of a vibrant small city on the ocean. Portland, listed in two dozen surveys as one of the top 10 most desirable places to live in the US, is connected by Amtrak to Boston (two hours away), and is just an hour from a variety of mountains, lakes and rivers.

Send resume and cover letter to Kristen O'Gara, HR Office, Youth Alternatives Ingraham, 50 Lydia Lane, So. Portland, Me. 04106.

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

Springfield Hospital Center is seeking Board-certified or Board-eligible **general psychiatrists** for our 350-bed MHA adult inpatient facility. Salary is negotiable, within MHA guidelines. Our rural, tobacco-free campus is 22 miles west of Baltimore, convenient to the Chesapeake Bay, Washington, and a variety of cultural, historic, sports, and recreational venues. Benefits include 27 paid days off in the first year, subsidized health insurance, free parking, a generous retirement program, and a truly pleasant workplace. A Medical Services physician is always on campus to attend to patients' somatic needs. Staff psychiatrists are not expected to work after hours, but some choose to supplement their salary by providing evening and weekend/holiday coverage under contract. In addition, we offer after-hours coverage contracts to psychiatrists who are not full-time staff members. Please send CV to **Jonathan Book, M.D., Clinical Director, SHC, 6655 Sykesville Road, Sykesville, MD 21784. For questions, call (410)970-7006 or e-mail JBook@dhmh.state.md.us.** EOE

MASSACHUSETTS

Consult-Liaison Transplant Psychiatrist

Half-time position for transplant psychiatrist to join multi-disciplinary medical team. Psychiatrist will conduct outpatient pre-screening psychiatric evaluations for potential organ recipient and donor patients. May provide short term medication management. Participates in selection committee. Person should enjoy being part of a multi-disciplinary team and have consult liaison experience.

Our Department of Psychiatry has a large clinical faculty with clinical, teaching, and academic opportunities in a wide variety of inpatient and outpatient settings. We have faculty development programs, and are committed to care, training, and research missions, as well as 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

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 area (Lynn) BayRidge Hospital, a non-profit psychiatric facility on Boston's North Shore, a teaching site for Boston University Medical School, will have a position for an inpatient/partial hospital psychiatrist in January, 2010. This is an opportunity to work in a collegial atmosphere with strong support. No required night call, but participation in a lucrative call system is optional. Full benefit package includes generous time off as well as reimbursement for malpractice insurance and CME.. Contact Barry Ginsberg, M.D., Medical Director, 60 Granite Street, Lynn MA 01904. Phone (781) 477-6964, Fax (781) 477-6967, email bginsber@nhs-healthlink.org

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High Point Treatment Center is seeking a 40 hr week psychiatrist to allocate 20 hrs managing 8-beds Inpatient Psychiatric Unit and 20 hrs allocated to outpatient services 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.

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.

Child and/or Adult Psychiatrist to join, busy, large, established private psychiatric group practice. Work consists of outpatient psychiatric treatment, both psychotherapy and psychopharmacology, and some hospital consultations. A lot of flexibility in terms of job and schedule. Please send C.V. to Paul Menitoff, M.D. Greater Lowell Psychiatric Associates, LLC 9 Acton Road Suite 25 Chelmsford, MA 01824.

BOSTON areas - Brookline, Jamaica Plain, Pembroke, Lowell and Westwood: Child & General Psychiatrists. Inpatient/partial programs. Staff & Medical Director Positions depending on location. Very competitive salaries, benefits & incentive plans. **NO CALL.** Contact Joy Lankswert, In-house recruiter @ 866-227-5415; OR email joy.lankswert@uhsinc.com

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Vinfen, www.vinfen.org, one of Massachusetts largest human services agencies dedicated to transforming the lives of people facing the challenges of psychiatric and developmental disabilities is seeking a PT or FT psychiatrist to support our PACT teams in the North Shore area. As a team member, the psychiatrist prescribes medication to all PACT clients and has clinical supervisory responsibilities for clients and staff. The psychiatrist provides training to the team members in the use of evidence-based practices in the delivery of services to persons with serious mental illness. Requirements: MD degree from an accredited medical school with completed internship and adult psychiatry residency experience. American Board of Psychiatric and Neurology (ABPN) board certification in Adult Psychiatry preferred; eligibility for Board certification mandatory. Experience working with people with psychiatric disability, co-occurring disorders including substance abuse and/or medical conditions preferred. Preference given to bi-lingual/bi-cultural applicants and applicants with lived experience of psychiatric conditions.
To apply, please forward CV with letter of interest to teneroa@vinfen.org.

MICHIGAN

Medical Director - An Easy Income Potential of $220k to $240k (Or More) - No long workdays necessary to make a great income. Seeking Psychiatrist for clinical and part-time administrative responsibilities on Psychiatric Services in a hospital in Saginaw, MI. Adult and C/A psychiatric services. Salary w/benefits is also an option. Very close to Bay City on Lake Huron and Flint. Only an hour and a half to Detroit and Ann Arbor. Please call **Terry B. Good at 1-804-684-5661,** Fax #: 804-684-5663; Email: terry.good@horizonhealth.com.

GRAND RAPIDS - Staff Psychiatrist. Inpatient and Outpatient practice position. Collegial clinical care & work environment. Very competitive salary & benefits. Contact Joy Lankswert @ 866-227-5415 or email joy.lankswert@uhsinc.com

MINNESOTA

Outpatient Psychiatrist: Seeking board eligible/board certified psychiatrist with unrestricted license to practice in Minnesota and Iowa. General multifaceted outpatient practice with geriatric (nursing home), general adult and chemical dependency patients. Hospital consultations to medical and surgical patients also provided and ability to expand to child/adolescent available if candidate is interested. Albert Lea Medical Center - Mayo Health System is located in Albert Lea, MN a scenic community of 18,000 just 90 minutes south of Minneapolis, MN and 150 miles north of Des Moines, IA. Please contact Diane Clark, RN, Physician Services Administrator, 507-377-4707 or e-mail clark.diane@mayo.edu.

MISSOURI

Weekend Call Opportunity - Seeking a Psychiatrist to provide one weekend of on-call coverage every third weekend on adult inpatient psychiatric unit in St. Joseph, MO-one hour north of Kansas City. Please **call Terry B. Good, Horizon Health, at 1-804-684-5661,** Fax #: 804-684-5663; email: terry.good@horizonhealth.com.

Outstanding Financial Opportunity - Close to Springfield - Inpatient and/or outpatient work in southwest MO. Strong hospital support for behavioral health. Unit is a 10-bed geropsychiatric program. Medical Director position available. Can offer salary w/benefits, or income guarantee, or contract with local physician's practice. Psychiatrists with National Health Service Corp. obligation welcome. Please **call Terry B. Good at 1-804-684-5661,** Fax #: 804-684-5663; Email: terry.good@horizonhealth.com.

KANSAS CITY - Medical Director & Staff Psychiatrist - Two Rivers Hospital. Medical Director will have clinical/administrative duties and Staff Physician will be all clinical. General and specialty inpatient and Partial programs. Fulltime position s offering salary, benefits and incentive plan. Contact Joy Lankswert, In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com

MONTANA

PSYCHIATRIST-Seeking full-time board certified psychiatrists to fill positions in VA Montana Healthcare System. Responsibilities include adult outpatient treatment with urgent care/walk-in service and inpatient consultation service in a facility where state-of-the-art medicine is practiced. Positions are located at Fort Harrison (Helena), MT; Billings, MT and Kalispell, MT. Competitive salary, benefits and liability included. Information available at www.vacareers.va.gov or Fax curriculum vitae to Chief of Staff, VA Montana Healthcare System, fax 406-447-7900 or 406-447-7965 or call Psychiatry Service at 406-447-7595, 406-461-4083 or Human Resources at 406-447-7566.

Rocky Mountain Paradise! 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

AtlantiCare
BEHAVIORAL HEALTH

AtlantiCare Behavioral Health (ABH), the leading outpatient behavioral health organization located just minutes away from Atlantic City, is seeking a full time psychiatrist. We offer competitive salaries & benefits, relocation assistance & pension plans.

Visit our website to see the full job description and to apply for the position at www.atlanticare.org

Interested individuals may send their resume to:
AtlantiCare Behavioral Health
Christine Loper
Phone: 609-645-7601 x106 Fax: 609-646-5725
Email: Christine.loper@atlanticare.org

EOE/AA

CHILD & ADOLESCENT PSYCHIATRIST

Child psychiatrist to join unique, private, fee for service, child, adolescent & adult therapy Center in New Jersey. Center provides wide array of services, provides high quality care, is successful and continues to grow. Locations in Cedar Knolls, Westfield, Ridgewood and Princeton. Openings currently available in each location. Compensation is generous. Hours are flexible. Collegial atmosphere is quite pleasant. E-mail CV to abbaznr@aol.com.

Westampton Township - Just East of Philadelphia. Addiction Psychiatrist or General Psychiatrist with interest in dual diagnoses. Dual Diagnoses Unit. Very competitive compensation and benefits. No on site weekend call required. Contact Joy Lankswert, In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com

NEW YORK CITY & AREA

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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Outpatient Psychiatrists

The Department of Psychiatry at The Mount Sinai Medical Center in Manhattan has an opening for a General Adult Psychiatrist. The FT/PT position includes outpatient work at the World Trade Center Mental Health Program with 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 additional experience in treating mood and anxiety disorders. Spanish and/or Polish speaking physicians are strongly encouraged to apply. 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 Fatih Ozbay, MD, Associate Medical Director of the WTC Mental Health Program at (212) 241 8462 or email fatih.ozbay@mssm.edu

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On Call Psychiatrists: Psychiatrists, Fellows and Senior Residents to cover days, nights, weekends and Holidays in the Psychiatric Emergency Department at the Long Island College Hospital. Please fax resume to: THE LONG ISLAND COLLEGE HOSPITAL, DEPARTMENT OF PSYCHIATRY, 339 Hicks Street, FAX: (718) 780-1827 Attn: Judith Velez or call 718-780-1065.

Upper Manhattan or Westchester
Child/Adol Assoc Clin Dir. 1 FT or 2 PT pos
Inpt academic clin care with leadership, admin & teaching duties. Daytime hrs- no call, wknds or ev's. 25 day LOS, little mg'd care. AdolMD@gmail.com or 917-710-2456

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

Western New York-Chautauqua Region: Jamestown Psychiatric PC is seeking a Psychiatrist to join our rapidly growing Adult and Child Psychiatric team. Competitive salary and flexible growth opportunities are offered. We will offer a starting bonus to eligible candidates. Loan repayment, J1 or H1 assistance available. Please contact Mrs. Linda Jones, office manager @ lj@psychwebmd.com or Phone 716-483-2603. Fax CV and qualifications to 716-483-2828.

Central New York Psychiatric Center, a state-operated, JCAHO Accredited facility, is seeking Psychiatrists for full-time positions at its main Inpatient Facility in Marcy, NY, and at its Forensic Outpatient Units throughout New York State, including: Albion, Auburn, Elmira, 5 Points (Romulus) and the Regional Mental Health Unit (Marcy). A position is also anticipated in the Hudson River Area.

- Comprehensive NY State Benefits package available
- Outstanding NY State Pension Plan
- Opportunity for Loan Forgiveness Program
- Opportunities exist for additional compensation

Assistant Psychiatrist: $104,192-$115,970 (general salary increases of 3% in 2009 and 4% in 2010 are scheduled)
Qualifications: Possession of a NY State Limited Permit AND completion of a training program in psychiatry approved by the American Board of Psychiatry and Neurology for entrance into their certifying examination AND eligibility for full and unconditional participation in Medicaid and Medicare programs.
Psychiatrist 1: $161,751 (general salary increase of 4% in 2010 is scheduled)
Qualifications: Possession of a License to practice medicine in NY State OR possession of a Limited Permit and licensure in another state or by written examination in Canada; AND completion of a training program in psychiatry approved by the American Board of Psychiatry and Neurology for entrance into their certifying examination; AND eligibility for full and unconditional participation in Medicaid and Medicare programs.
Psychiatrist 2: $169,707 (general salary increase of 3% in 2009 and 4% in 2010 are scheduled)
Qualifications: Possession of a license to practice medicine in NY State OR possession of a Limited Permit and licensure in another state or by written examination in Canada; AND certified in psychiatry by the American Board of Psychiatry and Neurology; AND eligibility for full and unconditional participation in Medicaid and Medicare programs.

Dr. Jonathan Kaplan, Clinical Director
Central New York Psychiatric Center
Box 300 Marcy, NY 13403
Phone: (315) 765-3624 Fax: (315) 765-3629
E-Mail CN00025@OMH.STATE.NY.US

Ulster County Mental Health, an outpatient clinic with a wide range of services, has a potential opening for Staff Psychiatrist. Position requires a recovery-oriented board certified or board-eligible community psychiatrist to treat adult patients. AOT interest is a bonus. UCMH is located in the beautiful Hudson Valley, two hours north of NYC. Competitive salary, on-site psychopharmacology supervision and collegial atmosphere. No on-call or weekends. Hours and benefits to be determined. FAX CV to JuLita Adamczak, MD, Medical Director, FAX #845-340-4094.

NORTH CAROLINA

Great Opportunity for Psychiatrist Already in Practice in Greensboro/Winston-Salem/ High Point Area - Increase income/Capture new market. Seeking a 3rd psychiatrist to do inpatient work on expanding geropsych unit as part of their private practice in the area. Please **call Terry B. Good at 1-804-684-5661,** Fax #: 804-684-5663; Email: terry.good@horizonhealth.com.

OHIO

Attractive Salary with Benefits Plus Generous Sign-on Bonus - One position filled; one more opening. 30 minutes from Dayton suburbs - easy drive to Indianapolis - Expanded adult and geropsych services in an extremely impressive med/surg hospital (gorgeous 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@horizonhealth.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 Taliaferro Community Mental Health Center, 602 SW 38th St. Lawton, OK 73505, (f): (580) 248-3610, (p): (580) 248-5780. EOE.

PENNSYLVANIA

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.

One Hour From Downtown Philadelphia; One and a Half Hours to Baltimore - Seeking a Psychiatrist to work on new 10-bed inpatient geropsychiatric unit in an impressive med/surg hospital in a beautiful Lancaster—close to Harrisburg. Have adult unit as well. Offering attractive salary/benefits, relo pkg, and bonus plan. Great quality of life in a great location. Please call **Terry B. Good at 1-804-684-5661,** Fax #: 804-684-5663; Email: terry.good@horizonhealth.com.

Director of Adult Inpatient Psychiatry Unit and Adult Psychiatrist

Pennsylvania-72 miles east of Pittsburgh - Memorial Medical Center, affiliated with Conemaugh Health System is seeking a BC/BE Adult psychiatrist and a Director for the 29-bed Adult Psychiatry inpatient unit. Position will have Administrative and clinical responsibilities.

Conemaugh Health System (CHS) is the largest healthcare provider in West Central Pennsylvania. With 4,500+ employees and 350 physicians, CHS offers a continuum of care and highly specialized services Serving over a half-million patients annually through its network of hospitals, physician offices, specialty clinics and other patient-focused programs.

This practice opportunity offers a generous salary ($200K+, based on experience), with full benefits including insurance, vacation, CME, relocation, and incentive compensation. For more information contact: Mark Blakeney, Horizon Health, 972-420-7473, fax CV: 972-420-8233, or email mark.blakeney@horizonhealth.com.

PHILADELPHIA - Child Psychiatrist - Residential, Inpatient and/or Partial Programs. **CLARION (Western PA) and SHIPPENSBURG (near Harrisburg) - J1 & H1 Eligible.** General or Child Psychiatrists for inpatient & partial program services. Very competitive salary, benefits and incentive plans. Contact Joy Lankswert @ 866-227-5415; OR email joy.lankswert@uhsinc.com

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Outpatient Clinical Director

The Philadelphia VA Medical Center (PVAMC) seeks candidates for the full-time Director of the Behavioral Health Outpatient Program who will be responsible for the administration of the Mental Health Clinics which provide treatment to approximately 7000 veterans in the Philadelphia area. The PVAMC Behavioral Healthcare Service provides a full range of high quality, restorative and preventative behavioral health services to the veteran population including evidence based psychotherapies. The Philadelphia VAMC is affiliated with the University of Pennsylvania and a faculty appointment may be available in the university's department of Psychiatry. Full federal benefits; including tuition reimbursement under the Education Debt Reduction Program. Salary is commensurate with experience.

Applicants must have U.S. citizenship; M.D. or equivalent degree; an unrestricted license and proficiency in spoken and written English. Demonstrated excellent qualifications in Clinical Care, Education, and Research; ABPN certification or eligibility in Psychiatry are required.

The PVAMC is an equal opportunity, affirmative action employer.

Please submit curriculum vitae, a cover letter, and references to: Philadelphia VA Medical Center, 3900 Woodland Avenue, Philadelphia, PA 19104, Attn: Announcement #297-09

Great Opportunity for Psychiatrist in Practice in or near Montgomery County, PA - Increase income/Capture new market. Geropsychiatric Unit in general hospital. Associate Medical Director position with annual stipend. Position nicely compliments already existing private practice and we'll market your practice as well. Please **call Terry B. Good at 1-804-684-5661,** Fax #: 804-684-5663; Email: terry.good@horizonhealth.com.

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

SOUTH CAROLINA

CHIEF of MENTAL HEALTH SERVICE

The WJB Dorn Veterans Affairs Medical Center (VAMC) is seeking an individual with clinical leadership and managerial skills to direct our Mental Health Service. Dorn VA Medical Center, part of the VA Southeast Network (VISN 7), is a 216-bed facility, encompassing medical, surgical, psychiatric, and geriatric care. The medical center provides care to approximately 67,000 veterans in the midlands and upstate South Carolina. Community Based Outpatient Clinics (CBOCs) are located in Anderson, Greenville, Spartanburg, Florence, Orangeburg, Sumter, and Rock Hill, SC, and provide primary care, mental health, and telemedicine services. Dorn VAMC is affiliated with the University of South Carolina (USC) School of Medicine and provides teaching services for students and residents. USC is the state's flagship research university, with Schools of Public Health, Nursing, Pharmacy, and an active Graduate School.

The Chief of Mental Health will assist in planning and development of our long-term strategic initiative to create a "Mental Health Center of Excellence." Applicants should be from one of the four core mental health professional disciplines: Nursing, Psychiatry, Psychology, and Social Work and should have experience and expertise in research, administering programs, clinics, staff, and trainees. This individual will be responsible for oversight, direction, and development of outpatient, inpatient, and tele-mental health services at the Medical Center and its CBOCs and joint program development with the USC School of Medicine. The successful candidate will qualify for a faculty appointment at University of South Carolina commensurate with training and experience.

Columbia's variety in cultural and recreational activities, its location (2 hours from the ocean and 2 hours from the mountains), and weather (mild winters), make it a pleasant place to live. Columbia has an excellent airport, a thriving arts and cultural community, fine restaurants, an abundance of golf courses and mountain-biking trails, and whitewater and trout fishing within the city limits. Large lakes which offer world-class fishing, sailing, water-skiing, and waterfront camping are a short drive away.

Interested individuals should send their CV and 3 professional references to:

Human Resources (05M)
WJB Dorn VA Medical Center
6439 Garners Ferry Road
Columbia, SC 29209-1639
Fax: 803-695-6702
Phone: 803-776-4000, extension 6264
Also refer to: http://www.usajobs.opm.gov #09-188-COS for more information
For specific information concerning the position, contact:
Dr. Stephen Hawes
Chair, Search Committee
Director of Mental Health Service
803-776-4000, extension 7143

TENNESSEE

Board-certified/eligible psychiatrists needed for full time and part time positions in a large Psychiatry Service at Mountain Home VAMC in Johnson City, Tennessee. Primary responsibility will be managing outpatients with a variety of psychiatric disorders. Join staff of 30 prescribers, including 18 psychiatrists at ETSU-affiliated residency training program with medical students, adult and med-psych residencies. Clinical appointment potential and some teaching expected. Research a plus. On-call (full time positions only) is backup to residents and shared amongst staff psychiatrists. NO STATE INCOME TAX, LOW COST OF LIVING, BEAUTIFUL MOUNTAINOUS REGION, LOTS OF PARKS, GOLF COURSES, LAKES, NATIONAL FOREST.
Inquiries:
Deborah Burchfield, (423) 979-3465, or Deborah.Burchfield@va.gov and George.brown@va.gov. Applications and/or CVs to: James H. Quillen VA Medical Center P.O. Box 4000 (05), Mountain Home, TN 37684 or Fax: (423) 979-3443 or Email: mtnhomehrmservice@med.va.gov

TEXAS

Associate Professor

The Department of Psychiatry at the University of Texas Medical Branch in Galveston is seeking an Associate Professor for our Adult division.

Responsibilities include direct patient care, resident supervision and teaching. Research opportunities are available. The position can be required to work in any of our three locations one of which is located in Webster; the other two are on Galveston Island. The position reports directly to the Chair of the Department. Minimum qualifications are medical doctor with a Texas medical license and must have graduated from an accredited Psychiatry Residency Program. Board certified in Psychiatry and Neurology with experience in clinical psychiatry is preferred.

Candidates with interest and skills in this area should send a curriculum vitae and cover letter to: Robert M.A. Hirschfeld, M.D., The University of Texas Medical Branch, Department of Psychiatry, 301 University, Galveston, TX 77555-0188.

The University of Texas Medical Branch at Galveston is an equal opportunity, affirmative action institution which proudly values diversity. Candidates of all backgrounds are encouraged to apply.

Vericare is currently seeking TeleMed Board Certified Psychiatrists in Texas with Geriatric experience.

Does spending less time in your car and more time seeing patients appeal to you? Or spending more time at home and less time at the office? Do you want to directly impact a population in desperate need of quality care? If yes, then join us at Vericare. Work with our team of dynamic professionals who are breaking through conventional methods of care! Our Telemed service line enables you to provide care to a population who previously had little hope of receiving the care they deserve.

If you are interested in learning how you can join our dynamic Vericare team, **please contact me at 800-257-8715 x1166, slekic@vericare.com or visit us at www.vericare.com.** To be eligible, you must have a medical degree and have completed your residency in psychiatry from an accredited institution, state licensure in good standing, and board certification in adult and/or geriatric psychiatry.

Interested in loving where you live and work? Then consider- Lufkin

Lufkin State Supported Living Center is looking for a psychiatrist. We are located in beautiful deep east Texas near two national forests, boasting of great lakes, parks and one of the best golf courses in Texas. According to the Chamber of Commerce- Lufkin is the #1 Micropolitan community in Texas and has many dining and shopping opportunities. Lufkin State Supported Living Center is a developmental facility for people with mental retardation and physical disabilities as well as persons with dual diagnosis which includes mental illness. A typical work schedule is Monday - Friday 8 a.m. to 5 p.m. The work environment is casual and the medical problems are challenging. We have a strong support system and offer excellent benefits (competitive salary, retirement, health/dental insurance, paid vacation and sick days, life insurance, longevity pay, up to 15 paid holidays per year, and more). A three bedroom, home with a formal dining/living room and den is available on campus with all bills paid and a modest rent.

For more information, call 936-853-8350, or e-mail: gale.wasson@dads.state.tx.us

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Corpus Christi, TX - Psychiatrist Retiring from a stable, thriving practice of 20+ yrs. Excellent income potential with a variety of practice options and call groups. Relocation assistance available. Oceanside community with beautiful beaches and sunsets - with an array of outdoor activities including sailing, fishing, and Wind-surfing. Call or email Lynda DePanicis at 361-986-1801 - lynda.depanicis@padrehospital.com to inquire.

Texas Gulf Coast Medical Group

Psychiatrist to join a respected and well established large family and multi-specialty practice in Webster, Texas, a Houston suburb. The patients are waiting for you! Brand new officebuilding with EMR and state of the art equipment. Lakes, the ocean, fishing, golfing, excellent schools, and warm temperatures year round. See our website at www.txgulfcoastmed.com or fax your CV to (281) 724-0210

The Department of Psychiatry and Behavioral Sciences of the University of Texas Medical School at Houston has an extraordinary opportunity for psychiatrists seeking to develop and implement new inpatient and outpatient clinical and research initiatives. Under new leadership, the Department is looking to expand clinical and research areas and is seeking general psychiatrists, child and adolescent psychiatrists and geriatric psychiatrists to join a growing academic department dedicated to excellence in clinical care, research and education. The Medical School is part of the University of Texas Health Science Center Houston, located in the Texas Medical Center - the largest medical center in the world. The Department of Psychiatry will shortly be moving into a brand-new building that will house the new Institute of Psychiatry. Individuals applying for these positions must be Board Certified in general psychiatry, child & adolescent psychiatry and geriatric psychiatry or have completed an accredited training in these specialty and subspecialty areas in the United States. Additionally, they must be licensed or be eligible for licensing in the State of Texas. Depending upon the applicant's qualification and credentials, faculty appointments at the level of Assistant Professor, Associate Professor or Professor will be offered. Salary levels are very competitive and also carry excellent fringe benefit packages. To find out more information about these unique academically-driven positions or to apply for them, please write to Jair C. Soares, M.D., Professor and Chair, and include a copy of your curriculum vitae and a letter of interest to 1300 Moursund Street, Houston, Texas 77030, e-mail: Jair.C.Soares@uth.tmc.edu phone 713-500-2507; fax 713-500-2553. The University of Texas Health Science Center at Houston is an EO/AA employer. M/F/D/V

Central West Texas. BC/BE Psychiatrist in an in/outpatient setting.
- 22 bed unit - adult/geriatrics only
- Call 10 nights a month - alternate weekends
- Employee of Shannon Clinic
- 3 yr contract, with 1st year guarantee, $200,000+
- Production and Quality incentives
- Sign on bonus
- Relocation allowance
- 35 days vacation
- Annual CME allowances
- Health/dental/disability/life
- Retirement

San Angelo is a city of 100,000
- Service area of 250,000
- NO TRAFFIC
- Pleasant climate
- Affordable housing
- Exemplary schools
- State University
- Regional airport

Shannon Clinic
Carrie Hallman - 325/481-6390
carriehallman@shannonhealth.org
www.shannonhealth.com

AUSTIN: Child Psychiatrist - Residential Treatment Center. **Employment - salary & full benefits.**
DALLAS area - SHERMAN. General Psychiatrist - Private practice of inpatient and outpatient.
WEST TEXAS San Angelo: Child Psychiatrist. Great private practice opportunity. Busy practice from start.
Contact: Joy Lankswert @ 866-227-5415 or email joy.lankswert@uhsinc.com

VIRGINIA

VIRGINIA BEACH

Outstanding private practice opportunity for board certified psychiatrist to join 1 psychiatrist and 3 therapists in well-established (25 year) out-patient practice caring for children, adolescents and adults. Partnership plan with opportunity to own. Guarantee $120,000 plus monthly bonus. Contact Dan Darby, MD at Tel: (757) 425-5050 Fax: (757) 425-1389.

Virginia Commonwealth University, School of Medicine, Department of Psychiatry, is recruiting a BE/BC Psychiatrist with academic career interest of residents/medical students and to provide outpatient and/or inpatient clinical care. The Divisions of Ambulatory Care Psychiatry and Inpatient Services are leaders in clinical education and growing in research capabilities. VCU's Department of Psychiatry employs over 75 fulltime faculty and has well-funded research in genetics, addictions, child and women's mental health and psychopharmacology. VCU is the largest university in Virginia 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, public/private schools. Internet provides comparative cost of living. Send CV to Dr. Joel Silverman, c/o Marie Roach, Human Resources, Department of Psychiatry, VCU, Box 980710, Richmond, VA 23298 (Fax 804-828-1472). VCU is an Equal Opportunity, Affirmative Action employer. Women, minorities, and persons with disabilities are encouraged to apply.

Horizon Health, the nation's largest provider of psychiatric contract management services, is seeking a Psychiatrist for a 20-bed Adult, and 8-bed Geriatric, psychiatric inpatient programs located just 30 minutes west of **Charlottesville, VA.** Salaried position, plus productivity bonus, and full benefits. For more information, please contact: Mark Blakeney, Horizon Health. Voice: 972-420-7473; Fax: 972-420-8233; or email: mark.blakeney@horizonhealth.com

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ADDICTIONS PSYCHIATRY, FACULTY CHAIR

The Department of Psychiatry, Medical College of Virginia at Virginia Commonwealth University, in collaboration with the Hunter Holmes McGuire Veterans Administration Medical Center, and VCU Institute for Drug and Alcohol Studies, is recruiting an academic physician Chair for the Division of Addiction Psychiatry. Chair is responsible for developing research, teaching and clinical programs. Funded ACGME accredited Addictions Fellowship. Strong programs in psychiatric genetics, epidemiology, pharmacology, toxicology, and women's health. Emerging School of Public Health. State funded health practitioner impairment program, laboratory and community based research are active areas for collaboration. Department of Psychiatry has over 75 full-time faculty, 39 residents, multiple fellowships and research centers including an addiction genetics research center. The Veterans Administration Medical Center has robust residential and outpatient addictions programming, and an outstanding program in Psychiatry and Primary Care. VCU is Virginia's largest university with robust health science campus and 750-bed university hospital. Richmond, the State Capital, has moderate climate, a rich history, cultural activities, excellent choices for urban, suburban, or country living, outstanding public/private schools. See comparative cost of living via Internet at www.coli.org/. Virginia Commonwealth University is an Equal Opportunity/Affirmative Action employer. Women, persons with disabilities, and minorities are encouraged to apply. Send applications to Joel J. Silverman, M.D., Chairman, c/o Marie Baker-Roach, Department of Psychiatry, MCV/VCU Box 980710, Richmond, VA 23298. Please contact Dr. Joel Silverman at 804/828-9156 or email jsilverman@mcvh-vcu.edu

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VIRGINIA COMMONWEALTH UNIVERSITY, Department of Psychiatry, School of Medicine, is recruiting a BE/BC Psychiatrist to serve as **Chair, Division of Ambulatory Psychiatry, position available as of July 1, 2008.** Duties include development of new programs, ambulatory care research, ambulatory resident and student education, and direction of general and specialty clinics and staff supervision. Significant experience in academic ambulatory care, teaching, administration and clinical research required. Faculty with funded research preferred. Ambulatory Care Clinics are located at the VCU Medical Campus, and have an estimated 16,000 patient visits/year. Department of Psychiatry employs over 80 fulltime faculty and is nationally ranked in federally funded research. Richmond, the State Capital, has moderate climate and rich mix of history, a diverse multicultural community, excellent housing and public/private schools. Internet provides comparative cost of living. Send CV to Search Committee, c/o Marie Roach, VCU, Box 980710, Richmond VA 23298. Virginia Commonwealth University is an Equal Opportunity/Affirmative Action employer. Women, persons with disabilities, and minorities are encouraged to apply.

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

VIRGINIA COMMONWEALTH UNIVERSITY: The Department of Psychiatry, School of Medicine, is recruiting a BE/BC Psychiatrist to serve as Outpatient Director of the Virginia Treatment Center for Children (VTCC), Ambulatory Care Psychiatry, at the VCU Medical Center. Duties include development of new programs, outpatient clinical care, ambulatory resident and student education, and direction of medical clinics and staff supervision. The VTCC is a leader in clinical education and is growing in research capabilities. Academic experience, including clinical education, research and scholarly endeavors, preferred. VCU Department of Psychiatry employs over 80-fulltime faculty and is nationally ranked in federally funded research. Richmond, the State Capitol, has moderate climate and rich mix of history, a diverse multicultural community, excellent housing, and public/private schools. Internet provides comparative cost of living. Send CV to Marie Roach, Human Resources, Department of Psychiatry, VCU, Box 980710, Richmond, VA 23298 (Fax 804-828-1472). VCU is an Equal Opportunity/Affirmative Action employer. Women, minorities, and persons with disabilities are encouraged to apply.

WASHINGTON

CHIEF, BEHAVIORAL HEALTH SERVICE STAFF PSYCHIATRIST

The Veterans Affairs Medical Center in Spokane, WA, is seeking a Board Certified Psychiatrist to fill the position of **Chief, Behavioral Health Service.** This physician administrator manages the mental health service line. 10% of the time is performing clinical duties, which may include covering the 8-bed inpatient psychiatric ward, or working in one of the outpatient clinics.

We are also seeking a **Staff Psychiatrist** to provide assessment and management of psychiatric care for veterans, including traumatic brain injury, and Operation Enduring Freedom/Operation Iraqi Freedom evaluations and treatment.

Located in the heart of the Pacific Northwest, Spokane is a vibrant community with a population of approximately 300,000. Spokane offers exceptional recreational, educational and cultural opportunities in a four-season climate.

Our physicians enjoy a unique quality mix of career and leisure time. Benefits include:
- Salaried position
- Malpractice coverage
- Excellent retirement program
- Generous paid vacation/sick/CME days
- 10 paid holidays

Call or send resume in confidence to:
Donna Dehart-Ray, RN, MS, MD/
Nurse Recruiter
4815 N. Assembly
Spokane, WA 99205-6197
Telephone: (509) 434-7657
Fax: (509) 434-7134

An Equal Opportunity Employer

WEST VIRGINIA

West Virginia School of Osteopathic Medicine, Lewisburg, WV is seeking a fulltime, tenure, faculty in Psychiatry. Duties include teaching medical students, interns, residents; developing psychiatric curriculum for students years 1-2; developing curriculum, rotational components and evaluation instruments for students years 3-4; maintaining a clinical practice. Research supported but not required. D.O. or M.D. degree, completed residency, board certification or eligibility in Psychiatry and clinical experience in general psychiatry. Must be able to be licensed in WV, which requires a rotating osteopathic internship for osteopathic physicians.

Excellent benefit package including the availability of fully paid malpractice insurance, educational loan repayment. Salary and faculty rank based on experience and training. Information at WWW.WVSOM.EDU . Apply by contacting Leslie Bicksler, Director HR at lbicksler@wvsom.edu , 304/647-6279. AA/EOE.

PSYCHIATRIST-West Virginia University School of Medicine, The Department of Behavioral Medicine and Psychiatry, has ongoing opportunities and faculty positions for full-time, part-time or per diem BE/BC psychiatrists in various locations throughout the state of West Virginia, including its primary clinical, educational and research location in Morgantown, WV, as well as William R. Sharpe Jr. Hospital, a 150-bed, JCAHO-accredited, state psychiatric hospital in Weston, WV. Responsibilities include patient care and teaching, with opportunities for research. Positions will remain open until filled. Contact Susan Clayton at sclayton@hsc.wvu.edu. WVU is an AA/EO employer.

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Fellowships

PSYCHOSOMATIC MEDICINE FELLOWSHIP

One year exciting, well-established, fellowship program, one of the first accredited by the ACGME, in a 750-bed university hospital, accepting applications for July 1, 2010. Advanced training offered to psychiatrists who have completed residency. Please write or call: James L. Levenson, M.D., Chairman, C-L Division, VCU Health System, Department of Psychiatry, Box 980268, Richmond, VA. 23298-0268, jlevenson@mcvh-vcu.edu (804) 828-0762 or Sherif Meguid, M.D. aabdel-meguid@mcvh-vcu.edu

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FELLOWSHIP PUBLIC PSYCHIATRY at YALE

The Connecticut Mental Health Center - Yale University School of Medicine is accepting applications for a one-year Fellowship in Public Psychiatry for July 2010. CMHC is a major site for training, research and clinical service within the Yale and State systems. As a state-funded, academic, urban mental health center it provides a unique setting for psychiatrists to obtain advanced training as they pursue careers as leaders in the field. Fellows spend 50% time in seminars, supervision, and administrative/policy meetings of CMHC and the CT Dept. of Mental Health and Addiction Services; and up to 50% effort providing direct clinical service and/or consultation within public mental health settings in New Haven. Candidates must be eligible for board certification and CT licensure. Minority applicants are encouraged to apply. For further information contact Jeanne Steiner, D.O. Medical Director, CMHC - Yale Univ., 34 Park St New Haven, CT 06519 or Jeanne.Steiner@yale.edu.

PSYCHOSOMATIC MEDICINE FELLOWSHIP BETH ISRAEL MEDICAL CENTER, NEW YORK CITY

Available full-time position for July 2010 at Beth Israel Medical Center, a major teaching affiliate of the Albert Einstein College of Medicine, located in beautiful Gramercy Park, Manhattan. This ACGME accredited program provides a broad training experience working with patients and staff in a variety of med-surg settings including oncology, HIV-AIDS, intensive care, ob-gyn, cardiology, and ambulatory primary care. Educational activities include a weekly didactic course in Psychosomatic Medicine (C-L Psychiatry), fellow's journal club, and extensive individual supervision. Teaching/supervision of psychiatry residents and medical students is emphasized and independent academic projects/ research are encouraged. Interested applicants should contact Nancy Maruyama, MD: NMaruyam@CHPNET.org -or phone (212) 420-4094

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 Lisa Boyle, M.D., Director, Geriatric Psychiatry Fellowship, Department of Psychiatry, University of Rochester Medical Center, 300 Crittenden Boulevard, Rochester, NY 14642-8409 Phone: 585.275.2824; Fax: 585.273.1082; E-Mail: Lisa_Boyle@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.

UCSD DEPARTMENT OF PSYCHIATRY - FORENSIC FELLOWSHIP

The University of California, San Diego is recruiting Fellows for our new Forensic Fellowship beginning July 1, 2010. For detailed description please go to: http://www.aapl.org/fellow.php#UN_UCSD
For an application and additional information, please send your email indicating interest to: kstuart@ucsd.edu

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Mount Sinai School of Medicine Department of Psychiatry Psychiatry Hospitalist Fellowship

Mount Sinai School of Medicine Department of Psychiatry offers a one-year fellowship in Hospitalist Psychiatry. This unique fellowship extends to psychiatry the established training for hospitalist physicians in internal medicine. The goal of the training is to prepare graduate psychiatrists for hospital positions with administrative roles, including Medical Directors of psychiatric services. Fellows will work under the direct supervision of the fellowship director, Vansh Sharma, MD, Vice Chair of Clinical Affairs.

The fellowship provides: 1) clinical and administrative training in the acute care of patients in inpatient, ER and C-L settings, plus 2) training in budgetary and administrative issues relating to hospital psychiatric services, including billing, reimbursement, and technical aspects of hospital-based budgeting. See further description at http://www.hospitalmedicine.org. Under Education and Hospital Medicine Fellowships.

Stipend for the fellowship is projected to be $70,000 for the period 7/1/2010- 6/30/2011. Interested applicants should contact Dr. Sharma, sending CV to: vansh.sharma@mssm.edu. EOE.

PSYCHOSOMATIC MEDICINE FELLOWSHIPS AND CHIEF RESIDENCY POSITIONS AT YALE UNIVERSITY

This ACGME-accredited one-year fellowship has five Psychosomatic Medicine Fellowship positions available at the PGY-V level or above, starting July 1, 2010. Applications for Chief Resident positions are also welcome (PGY IV year training does not provide eligibility for subspecialty board certification). The program offers training in inpatient and outpatient consultation-liaison psychiatry at Yale New Haven Hospital and at the VA Connecticut Healthcare System, with multiple specialty electives. An Equal Opportunity employer. Please contact Paul Desan, MD, PhD, Yale New Haven Hospital, 20 York St CB2039, New Haven, CT 06504, paul.desan@yale.edu, (203) 785-2618.

PSYCHOSOMATIC MEDICINE/ CONSULTATION-LIAISON PSYCHIATRY COLUMBIA UNIVERSITY COLLEGE OF PHYSICIANS AND SURGEONS

The Department of Psychiatry at Columbia University College of Physicians and Surgeons offers a one-year fellowship in Psychosomatic Medicine at New York Presbyterian Hospital-Columbia University Medical Center for board eligible/board certified graduates of approved psychiatric residency programs. The fellowship seeks psychiatrists with outstanding clinical and academic records as evidenced by publications, presentations, teaching experience, and exceptional letters of recommendation, who are interested in an academic career in Psychosomatic Medicine (consultation-liaison psychiatry). Spanish speaking a plus. This is a full-time, ACGME-approved program with clinical, research, and teaching experience at a major tertiary care center. Some call is required. Applicants are sought for the 2010-2011 academic year. To apply, please submit a personal statement, three letters of recommendation, and a C.V., no later than October 15, 2009. For further information applicants should contact Dr. Peter A. Shapiro at Columbia University, College of Physicians and Surgeons, 622 West 168th Street, Box 427, New York, NY 10032; (212) 305-9985, or by email at mf251@columbia.edu. Columbia University is an AAEOE.

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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, ie, 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 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 Pristiq treatment, but particularly with concomitant use of serotonergic drugs (including triptans), with drugs that impair metabolism of serotonin (including MAOIs), or with antipsychotics or other dopamine antagonists. Serotonin syndrome symptoms may include mental status changes (eg, agitation, hallucinations, coma), autonomic instability (eg, tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (eg, hyperreflexia, incoordination) and/or gastrointestinal symptoms (eg, 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 Pristiq with MAOIs intended to treat depression is contraindicated [see Contraindications (4.2)]. If concomitant treatment of Pristiq 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 Pristiq with serotonin precursors (such as tryptophan) is not recommended. Treatment with Pristiq 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. **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) ≥90 mm Hg and ≥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 (eg, 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 lipoprotein) 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. Orthostatic hypotension- In the short-term, placebo-controlled clinical studies with doses of 50-400 mg, systolic orthostatic hypotension (decrease ≥30 mm Hg from supine to standing position) occurred more frequently in patients ≥65 years of age receiving Pristiq (8.0%, 7/87) versus placebo (2.5%, 1/40), compared to patients <65 years of age receiving Pristiq (0.9%, 18/1,937) versus placebo (0.7%, 8/1,218). **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 (eg, 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; however, in the short-term, placebo-controlled studies, there was a higher incidence of systolic orthostatic hypotension in patients ≥65 years of age compared to patients <65 years of age treated with Pristiq [see Adverse Reactions (6)]. 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)]. If Pristiq is poorly tolerated, every other day dosing can be considered. SSRIs and SNRIs, including Pristiq, have been associated with cases of clinically significant hyponatremia in elderly patients, who may be at greater risk for this adverse event [see Warnings and Precautions (5.12)]. Greater sensitivity of some older individuals cannot be ruled out. **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 (eg, 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 tablets 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 W10529C004, revised February 2009.

 254124-01

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 or Neuroleptic Malignant Syndrome-like reactions have been reported with SNRIs and SSRIs alone, including PRISTIQ treatment, but particularly with concomitant use of serotonergic drugs, including triptans, with drugs that impair the metabolism of serotonin (including MAOIs), or with antipsychotics or other dopamine antagonists. If concomitant use with a triptan 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.

For more information on PRISTIQ, please visit **www.PristiqHCP.com**.

Pristiq® desvenlafaxine EXTENDED-RELEASE TABLETS

Wyeth®

Philadelphia, PA 19101 254124-01