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Newspaper of the
American
Psychiatric
Association

PSYCHIATRIC NEWS

inside

PERIODICALS:
TIME-SENSITIVE MATERIALS

Credit: David Hathcox

Psychiatarists Joseph Cools, M.D., and Jan Cools, M.D., along with their son, Michael, a medical student, peruse books in the APPI Bookstore during APA's 2009 annual meeting in San Francisco in May. Coverage of annual meeting sessions can be found throughout this issue.

Little Attention Paid to Effect of Parents' Depression On Their Children

The Institute of Medicine notes there are large gaps in knowledge about the effects of parental depression on children and a need for multigenerational approaches to care.

BY AARON LEVIN

Depression is too often a family affair and ought to be viewed that way, but the unsystematic nature of the U.S. health care system serves as a major block to identifying and treating millions of parents whose depression may affect their children's future, according to a report from the National Research Council and the Institute of Medicine.

"[P]arental depression is prevalent, but a comprehensive strategy to treat the depressed adults and prevent problems in the children in their care is absent," said the report from a task force chaired by Mary Jane England, M.D., president of Regis College in Weston, Mass., and a former president of APA. She spoke at a press conference in Washington, D.C., last month announcing the study's results.

The report estimates that there are 7.5 million parents with depression in the United States caring for 16 million children under age 18.

Depression is usually addressed as a disorder in individuals, but when that individual is a parent, it can affect other

please see ***Depression*** *on page 29*

FDA Advisors Back Additional Antipsychotics for Use in Teens

A multidisciplinary FDA advisory committee supports the efficacy of quetiapine, ziprasidone, and olanzapine for treating schizophrenia and bipolar disorder in children and teens but still has safety concerns.

BY JUN YAN

An 18-member advisory committee of the Food and Drug Administration (FDA) voted in June to recommend the approvals of quetiapine and olanzapine for treating schizophrenia and bipolar manic episodes in teenagers. Their opinions on whether ziprasidone should be approved to treat young patients with bipolar mania, however, were mixed.

Two other second-generation antipsychotics (SGAs), risperidone and aripiprazole, have previously been approved for treating schizophrenia in patients aged 13 to 17 and bipolar disorder in patients aged 10 to 17.

Quetiapine received the most consistent support from the committee, with a vast majority voting "yes" on the four questions pertaining to the drug's effectiveness and safety for both indications. Its manufacturer, AstraZeneca, had conducted a six-week, randomized, placebo-controlled, double-blind clinical trial of the drug in patients with schizophrenia aged 13 to 17 and a three-week trial in patients aged 10 to 17 who were experiencing a current bipolar manic episode.

The advisory committee, which met at a public hearing June 10, had a more mixed response to Pfizer's data on ziprasidone to treat bipolar mania in patients aged 10 to 17. In a four-week, randomized, placebo-controlled trial, the drug outperformed placebo in efficacy endpoints overall. However, subgroups of younger patients aged 10 to 14 and patients weigh-

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Few Employers Plan Coverage Cuts In Response to Parity Mandate

That employers say they will retain mental health coverage is crucial because the parity law requires that only those who voluntarily provide mental health coverage do so at benefit levels comparable to their other coverage.

BY RICH DALY

Three-quarters of U.S. employers do not plan to drop insurance coverage for mental health and substance use treatment when a new federal law goes into effect next year requiring them to offer such benefits at a level equal to that of other medical benefits, a recent survey indicates.

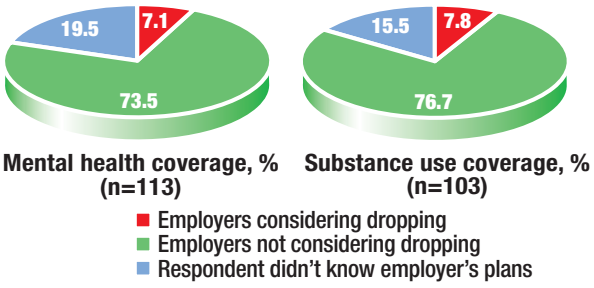
The online survey, to which more than 140 employers responded, was conducted by the Partnership for Workplace Mental Health, a program of the American Psychiatric Foundation. The survey was designed to elicit a better understanding of the extent of currently available mental health benefits and what changes employers will make to comply with the new parity law.

Among the chief results of the survey was a finding that 93 percent of respondents offer at least some mental health benefits, and among those, at least 74 percent were not considering dropping mental health coverage. In addition, at least 77 percent were not considering dropping substance use treatment coverage as a result of the law. The next-larg-

please see ***Parity*** *on page 29*

Parity Law Unlikely to Cause Dropping of MH Benefits

About three-quarters of employers will not drop coverage for mental illness or substance use treatment when the federal parity law goes into effect next year, according to a recent survey sponsored by the American Psychiatric Foundation. The law's requirements for equal coverage apply only if the insurance plan already includes coverage for mental illness.



Source: "Employer Survey Results: Mental Health Parity Law," Partnership for Workplace Mental Health, American Psychiatric Foundation, June 2009

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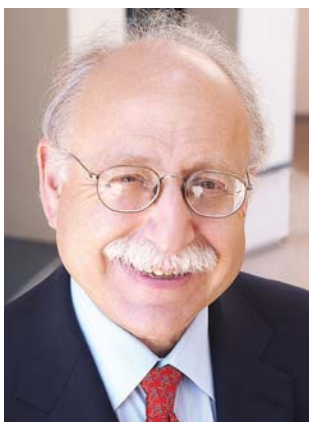
Some Thoughts on Reorganization

BY ALAN F. SCHATZBERG, M.D.



Since this is my first column as APA president, I thought it would be useful to review where we are with the reorganization of the APA governance structure. Last year, then President Nada Stotland challenged the Board of Trustees to begin to look at whether our components were efficiently discharging their assigned tasks and whether we were spending too much of our annual budget on governance. In an exercise at a Board retreat almost a year ago, it appeared that those present thought we should spend a considerably lower percentage on support of the overall governance structure to free up dollars for essential programs. The sentiments matched what APA has observed in membership surveys. Our previous president elegantly articulated that 14 councils and 93 committees were much greater numbers than are seen in our sister organizations—many of which have larger memberships than ours.

Budget problems for the Association became apparent after the 2008 annual meeting, where we observed fewer international attendees as well as reduced industry support. The medical director and the Board went into action to reduce expenses, and a number of steps were taken. The September Components Meeting was limited to components with a minimum of a half-day of work to accomplish. All other components were able to meet through conference calls or LiveMeeting. There was a freeze on staff hirings and promotions and a delay or cancellation of all nonessential spending.

One step to plan for reduced governance was to set up a task force of leaders of the Association that Dr. Stotland asked me to head. Before the group met, the Board of Trustees approved a recommendation from an earlier task force to eliminate $1 million from the governance budgets, including a large cut to the components.

Once those actions were passed in December 2008, the typical September Components Meeting became unfeasible. Thus the existing components structure was under threat. The task force met several times and recommended a number of approaches. One key recommendation was to reduce the number of committees and councils and to shift work more uniformly from the committees to councils. In March the Board approved the plan, which went into effect in May at the end of APA's 2009 annual meeting.

Under the new structure, the number of councils has been reduced from 14 to nine, with one of the councils representing a merger of two previous councils and another representing a merger of three former councils, and only core committees have been retained. Because the councils' charges have been expanded, their size and staffing have been expanded as well. The councils have the power to set up time-limited, precisely focused work groups, as needed for a particular issue.

In the end, the number of non-award committees went from 73 to 14. Corresponding committees have been eliminated. We have attempted to appoint committee chairs to the councils if their committees were eliminated and have reappointed other council members if their tenures had not expired. This will help with continuity. We can now afford to have a smaller September Components Meeting, and we plan to work with the councils to implement the new structure.

Are we finished? There has been a great deal of positive response from members in regard to our efforts to reduce costs. There are some who have been disappointed by phasing out one committee or council or another. We will formalize a process for reviewing whether we need to make further adjustments, including reinstituting some components. In addition, some functions that were part of the components would probably fit better under the Assembly, and these are being looked at as well.

In the reorganization and budget process, we have made a number of other changes. One Board of Trustees meeting has been eliminated. The Joint Reference Committee budget was decreased by 70 percent. Cuts were also made to the Assembly budget, with the structural changes to be determined by the Assembly and currently under discussion. The Board also passed a motion to have another task force look at structural changes in APA's overall governance over this coming year.

My colleagues, these are difficult economic times for all of us. We need to be as prudent as possible in our structure and work prioritization in these troubling times. We cannot afford to waste resources, and we need to be ever more focused on what the members believe we should be working on. I look forward to continuing to work with all of you on making APA an even stronger professional society. ■

Errata

• In the May 15 issue, the professional title of Fryderyka Shabry, M.D., was incorrect in the article titled "Psychiatry Resident Researchers Have Their Eyes on the Prize." Her correct title is director of child and adolescent psychiatry at Coney Island Hospital in Brooklyn, N.Y.

• In the June 5 issue, the article "FDA Reverses Earlier Decision, Approves Schizophrenia Drug" contained an error. The sentence concerning data comparing ziprasidone and risperidone should have read: "At press time, the company [Vanda Pharmaceuticals] had not released any data on how iloperidone compared with either ziprasidone or risperidone on efficacy indicators." ■

Experts Call for New Ways To Collaborate With Pharma

Psychiatric ethicist Laura Roberts, M.D., emphasizes that overlapping roles—and the potential conflicts of interest that can arise—come with the territory of being a professional, but that these can be managed.

BY MARK MORAN

Industry influence in medicine, including psychiatry, is wide, deep, and ubiquitous, and simple solutions regarding conflict-of-interest issues are not likely to be found.

That much was agreed upon by a panel of five psychiatrists—including experts in ethics, research, and medical education—at a presidential symposium at APA's 2009 annual meeting in San Francisco in May.

Outgoing APA President Nada Stotland, M.D., who served as a discussant, said that at an organizational level, realignment of APA's relationships with industry is likely to involve difficult financial trade-offs, such as when the Association opted to phase out industry-supported symposia that are known to be a popular attraction at APA's meetings; or it may involve eliminating worthy programs such as fellowships for minorities that are supported by industry.

Panel members were united in saying that pharmaceutical marketing, with demonstrable effects on physician behavior, has reached into all areas of medicine, including research, education, and clinical practice. But while APA, and individual psychiatrists, may need to terminate or realign some forms of collaboration with industry, the various academic, private, and industry stakeholders should not be singled out for scorn; rather, new ways of collaborating with industry must be devised, with appropriate safeguards in place.

"The pharmaceutical industry makes products that help people," said Jonathan Weker, M.D., a private practitioner from Montpelier, Vt., and APA Assembly member who has argued for years that the Association needs to extricate itself from the grip of industry. "Pharma is not the evil empire. We have to figure out a new relationship with industry." (See box at right for comments by Weker about the evolution of the relationship between physicians and the pharmaceutical industry.)

Credit: David Hathcox

Laura Roberts, M.D., tells attendees at a presidential symposium on psychiatrist relations with industry that education about issues of conflict of interest has been proven to work.

The five panel members were, in addition to Weker, past APA President Paul Appelbaum, M.D.; Laura Roberts, M.D., chair of a committee to revise the ethics principles for APA; Joel Yager, M.D., a professor of psychiatry at the University of Colorado; and David Baron, D.O., chair of the Department of Psychiatry at Temple University School of Medicine.

Weker's comments reflected an awareness both of the pervasive influence of industry in all areas of medicine and of the difficulty of extricating medicine from business interests that, after all, manufacture products that benefit patients. As Yager said, quoting a colleague, "If it weren't for pharma, we would still be giving people thorazine."

Nor is collaboration with industry the only, or the most pernicious, conflict of interest in medicine. Baron, who wondered about the negative consequences of cutting all ties with industry, noted that his institution monitors all physicians on their patients' length of stay in the hospital. "Length of stay has a lot to do with hospital reimbursement. . . . I would posit that that is a much greater conflict of interest. . . . This will affect my reimbursement, so I have a conflict of interest to get [a patient] out earlier. . . . Only focusing on pharma conflicts is a mistake."

Study Design Modifications Skew Results

Yet pharmaceutical-industry influence on medical education and clinical decision making has rapidly become one of the most talked-about subjects in American medicine.

While most physicians are not inclined to admit that their behavior is influenced by industry marketing, published research suggests otherwise, said Appelbaum, who presented an overview of that research.

"We know from multiple studies that meeting with pharmaceutical representatives and accepting samples and meals from industry correlate with increased requests for formulary additions of new, expensive medications; prescribing of the new medications; and decreased use of generic drugs," Appelbaum said. "Frequently these decisions fail to take into account that the newer medications are higher cost and frequently have not demonstrated higher levels of efficacy than the older medications.

"Moreover, by definition newer medications with less of a track record leave us inherently uncertain about their long-term consequences," he said. "There are those who believe the high incidence of metabolic side effects associated with second-generation antipsychotics was driven by the rapid adoption by the field of those new medications before we had a chance to learn what their longer-term consequences might be."

Published studies supported by industry need careful scrutiny. Appelbaum presented data indicating that studies showing positive results for a sponsor's product are three to four times more likely to be published than are negative ones. Negative studies are liable to go unpublished or their results may be spun by post hoc analysis highlighting positive results for a subgroup of patients, though there was no benefit shown for the sample as a whole.

Yager outlined a long list of design modifications that are sometimes employed to skew results to a positive outcome for a sponsor's product. These include using dosages of a comparator drug that are far outside the normal range, using self-serving measurement scales that lead to misleading conclusions, masking unfavorable side effects, cherry-picking subjects for certain characteristics, and touting nonsignificant but favorable differences and negating dropout differences statistically.

Conflict-of-Interest Education Possible

So what is to be done?

Roberts reminded psychiatrists that overlapping commitments are innate to being physician-leaders who must

please see ***Pharma*** *on page 26*

Adopting a 'Professional Paradigm'

At the presidential symposium "The Psychiatrist's Relationship With Industry" (see article at left), private practitioner Jonathan Weker, M.D., of Montpelier, Vt., presented a historical overview of the evolution of prescribing from its earliest days as a mercantile exercise by physicians who were essentially marketing products to the growth of the modern pharmaceutical manufacturing corporation and the contemporary regulatory structure.

"Pharmaceutical companies began to develop therapeutic agents of demonstrable utility, safety, and efficacy, which had appeal to a large market," he said. "And doctors became the portal through which access to those medicines took place. Where once patients came to doctors primarily seeking surgery or diets, now they wanted prescription drugs."

With the emergence of blockbuster drugs, pharmaceutical companies became enormously attractive to investors. "They began to experience a kind of financial success they could not have imagined before," he said. "With this, the nature of pharmaceutical companies and their relationships with doctors irrevocably changed."

Weker suggested two possibilities for how this new relationship might have evolved: a professional paradigm in which each party is principally concerned with improving the health of the populace or a mercantile model.

"In the mercantile paradigm, physicians act as surrogate consumers on behalf of their patients, and the companies court the doctors on behalf of their products." This created a situation in which clinical concerns were not ignored, but they were not alone on the table. "Both parties were not disinterested," he said. "My sense is that a de facto decision was made by both parties to adopt this mercantile paradigm."

But within the last two or three years there has been a rapid turnabout: the public and federal and state legislators are demanding accountability and transparency. "No one wants Christmas to end, but Christmas is going to end," he said.

He urged adoption of a new relationship with the pharmaceutical industry in which the professional integrity of physicians is respected, and doctors receive comprehensive, well-reasoned, unmarketed information about drug products.

"Their products make our practice look good, but at the same time our ability to diagnose and treat makes their products look good," Weker said. "If industry and the individual physician wish to coexist symbiotically in this environment, both parties would be better served by adopting the professional paradigm."

Who Will Lead APA Next?

Individual members play a key role in the nomination process for national office. That is why APA's Nominating Committee, chaired by Nada Stotland, M.D., is requesting nominations for candidates in APA's 2010 election. With six national offices up for election, every nomination counts. Please submit your nominations for president-elect, secretary, treasurer, Area 3 trustee, Area 6 trustee, and member-in-training trustee-elect (MITTE).

Nominations should be submitted via email to rjuarez@psych.org by Friday, July 24. Each nomination should include the full name of the nominated member and the office(s) that you would like him or her to be considered for in the 2010 election. All nominations will be taken into consideration by the Nominating Committee, and a final list of candidates will be announced and posted on the APA Web site in mid-September.

More information is posted on APA's Web site at <www.psych.org>.

Please note: All nominees must be currently active voting members of APA. Nominees for Area trustee must be from the respective Areas listed above. Nominees for MITTE must be classified as members-in-training and should be prepared to state their intent to continue in the position through PGY-5 if they are a PGY-3 resident. Medical-student members and international members are not eligible for nomination to national office.

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IMPORTANT SAFETY INFORMATION

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, especially during the initial few months of therapy or at times of dose changes. This risk may persist until significant remission occurs. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Lexapro is not approved for use in pediatric patients less than 12 years of age.

Lexapro is contraindicated in patients taking monoamine oxidase inhibitors (MAOIs), pimozide, or in patients with hypersensitivity to escitalopram or citalopram. As with other SSRIs, caution is indicated in the coadministration of tricyclic antidepressants (TCAs) with Lexapro. SSRIs and SNRIs (including Lexapro) may increase the risk of bleeding events. Patients should be cautioned that concomitant use of aspirin, NSAIDs, warfarin or other anticoagulants may add to the risk.

Lexapro is not approved for use in treating bipolar depression. 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. Lexapro should be used cautiously in patients with a history of mania or with a history of seizure disorder. Lexapro should be used with caution in patients with severe renal impairment or with diseases or conditions that produce altered metabolism or hemodynamic responses.

SSRIs and SNRIs have been associated with clinically significant hyponatremia. Elderly patients or patients taking diuretics or who are otherwise volume-depleted appear to be at a greater risk. Discontinuation of Lexapro should be considered in patients with symptomatic hyponatremia and appropriate medical intervention should be instituted.

The concomitant use of Lexapro with other SSRIs, SNRIs, triptans, tryptophan, antipsychotics or other dopamine antagonists is not recommended due to the potential for development of life-threatening serotonin syndrome or neuroleptic malignant syndrome (NMS)-like reactions. The management of these events should include immediate discontinuation of Lexapro and the concomitant agent and continued monitoring.

Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that Lexapro therapy does not affect their ability to engage in such activities.

For pregnant and nursing mothers, Lexapro should be used only if the potential benefit justifies the potential risk to the fetus or child.

Patients should be monitored for adverse reactions when discontinuing treatment with Lexapro. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible.

The most common adverse reactions in adults treated with Lexapro (approximately 5% or greater and at least twice the incidence of placebo) are nausea, insomnia, ejaculation disorder, fatigue and somnolence, increased sweating, decreased libido, and anorgasmia. The overall profile of adverse reactions in pediatric patients was generally similar to that seen in adult studies; however, the following additional adverse reactions were reported in adolescents at an incidence of at least 2% for Lexapro and greater than placebo: back pain, urinary tract infection, vomiting, and nasal congestion.

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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.

Task Force Finalizing New ECT Guideline

Researchers continue to seek the best recipe for ECT standards that maximize efficacy, minimize side effects, and maintain high efficacy levels over the long term.

BY JUN YAN

APA is preparing to publish a major revision of its guideline on the practice of electroconvulsive therapy (ECT) next year. The new edition will contain substantially updated recommendations, according to members of the task force in charge of revising the guideline.

Members of APA's Task Force to Revise the Practice of Electroconvulsive Therapy gave an update on the current evidence for the efficacy and safety of ECT at APA's 2009 annual meeting in San Francisco in May.

Clinical topics discussed by task force members included optimal electrode placement, informed consent and documentation, stimulus dosing, and relapse-prevention strategies.

The task force members have been reviewing the latest research evidence in weekly teleconferences and collecting feedback from clinicians for this revision, explained task force chair Sarah Lisanby, M.D., a professor of psychiatry at Columbia University and the chief of the Columbia Brain Stimulation and Therapeutic Modulation Division. The guideline will also contain proposals for training and certification for ECT practice, the task force members noted.

Charles Kellner, M.D., a professor of psychiatry at Mount Sinai School of Medicine, discussed the continuing debate over the optimal electrode placement. The current guideline recommends that practitioners "should be skilled in administering both unilateral and bilateral ECT," and the placement choice "should be based on an ongoing analysis of applicable risks and benefits" and on consultation with the psychiatrist, the person giving consent, and the attendant physician. In recent years, the use of bifrontal electrode placement has gained popularity, he noted.

In a recently completed study conducted by the Consortium for Research in ECT (CORE) and funded by the National Institute of Mental Health, 230 patients were randomized to receive right unilateral (RUL) ECT treatments at six times the seizure threshold, bifrontal (BF) ECT at 1.5 times the seizure threshold, and bilateral (BL) ECT also at 1.5 times the seizure threshold, Kellner said. The rates of remission were 55 percent for RUL, 61 percent for BF, and 64 percent for the BL treatment. The rates of response were 73 percent, 79 percent, and 82 percent, respectively. These results were not statistically significant among the treatment arms. Looking at the changes in symptoms over the treatment courses, however, "the bitemporal ECT gets patients well more quickly than the other two electrode placements," Kellner pointed out, and this difference was statistically significant.

Meanwhile, the cognitive effects of each placement require further research. "Although it is pretty clear that bilateral electrode placements are a little bit more effective than right unilateral, and right unilateral placement causes less cognitive impairment for many patients, we're still not able to predict exactly the outcome or side effects for a particular patient," he said. Kellner and most attendees agreed that, if a patient is severely ill, suicidal, or urgently needs symptom relief, bilateral ECT is a favored placement choice.

Another controversial issue is whether the electrode placement should be explicitly mentioned in the informed consent and whether informed consent should be obtained again if the placement is changed due to treatment failure. Attendees expressed divergent opinions based on their own ECT practice.

Since patients have different seizure thresholds, a titration-based stimulus dosing strategy, in which the electric charge applied for each patient is adjusted to his or her individual seizure threshold, is better than fixed-charge dosing, in which the same electric charge is given to every patient, according to Andrew Krystal, M.D., a professor of psychiatry at Duke University School of Medicine.

please see ***ECT Guideline*** *on page 26*

Credit: David Hathcox

Charles Kellner, M.D. (left), Sarah Lisanby, M.D., and Andrew Krystal, M.D., discuss the work of the APA Task Force to Revise the Practice of Electroconvulsive Therapy.

Psychiatrists Lament Decline Of Key Treatment Modality

While the number of psychiatrists providing psychotherapy to all their patients is declining, one expert argues that routine med checks have a strong psychotherapy component.

BY MARK MORAN

Evidence of the efficacy of psychotherapy has increased dramatically in recent years even as the place of psychotherapy in the identity, practice, and training of psychiatrists is diminishing—a fact that was widely recognized and just as widely deplored during a workshop at APA's 2009 annual meeting in San Francisco in May.

It was a subject that brought out considerable passion as speakers and attendees alike insisted that psychiatry brings a unique set of skills to the biopsychosocial treatment of mental illness and that new evidence is showing that psychotherapy works not only on the mind but on the brain. At the same time, speakers acknowledged what some research evidence published last year and presented at the meeting seemed to show—that psychotherapy by psychiatrists is declining.

"There is growing evidence that psychotherapy is efficacious for a range of individual disorders and for complex comorbid disorders," said Eric Plakun, M.D., chair of APA's Committee on Psychotherapy by Psychiatrists. "We are also learning that psychotherapy is associated with brain change. Though medications seem to work from the bottom up, psychotherapy seems to work from the top down—from the cortex down to the molecular level. In at least one study, therapy responders could be distinguished from nonresponders by imaging studies.

Credit: David Hathcox

APA President Nada Stotland, M.D., served as a discussant at a workshop on psychotherapy by psychiatrists at the annual meeting. There was widespread agreement that the place of psychotherapy in the training and identity of psychiatrists has diminished.

"Yet there is also this evidence that psychotherapy is dwindling as part of the identity, skill set, and training of psychiatrists," Plakun said. "I think we can raise an interesting question of whether psychotherapy by psychiatrists is an endangered species."

Plakun said that the trend is frustratingly at odds with what would appear to be common sense. "Therapy by psychiatrists absolutely maximizes the integration of mind and body, and it certainly also maximizes the possibility of integrating prescribing of medications with psychotherapy.

'Loss to Our Patients'

"So the minimization of therapy, should it continue, is a loss to psychiatry, but above all, it's a loss to our patients," Plakun said. "Are we offering our patients all we can if we aren't thinking about biological treatments and psychosocial treatments, including psychotherapy?"

There was poignancy to the workshop in that the Committee on Psychotherapy by Psychiatrists was being "sunsetted"—it is one of a large number of committees and other components that are being terminated as part of an APA organizational restructuring to make APA more efficient (see page 3). The committee's charge will likely fall under the Council on Research and Quality Care.

Outgoing APA President Nada Stotland, M.D., who was trained analytically and has a practice devoted to psychotherapy, was a discussant at the workshop. She urged committee members and other members of APA to think about strategy going forward and to communicate ideas to leadership. "We have to think strategically and practically if we want a position that insurers should cover psychotherapy by psychiatrists," Stotland said.

"We need to think about how exactly psychotherapy by psychiatrists is going to be carried forward and to demand some accountability around this. In no way will any of your leadership want to let that go away."

The trend away from psychotherapy by psychiatrists, acknowledged by most speakers, appeared to be confirmed by research presented at the annual meeting by Ramin Mojtabai, M.D.

Mojtabai and Marc Olfson, M.D., analyzed data from the 1996-2005 cross-sectional National Ambulatory Medical Care Survey to examine trends in psychotherapy provision within nationally representative samples of visits to office-based psychiatrists. Statistical analyses examined the time trend, adjusting for patient, visit, and setting characteristics. Practice-level analyses examined time trends in the percentage of psychiatrists who provided psychotherapy to all, some, or none of their patients during a typical week.

They found that psychotherapy was provided in 5,597 of 14,108 visits sampled during the 10-year period. The percentage of visits involving psychotherapy declined from 44.4 percent in 1996-1997 to 28.9 percent in 2004-2005.

> **"The minimization of therapy . . . is a loss to psychiatry, but above all, it's a loss to our patients."**

At the practice level, the decrease in providing psychotherapy corresponded with a decline in the number of psychiatrists who provided psychotherapy to all of their patients, from 19.1 percent in 1996-1997 to 10.8 percent in 2004-2005.

"This trend is attributable to a decrease in the number of psychiatrists specializing in psychotherapy and a corresponding increase in those specializing in pharmacotherapy—changes that were likely motivated by financial incentives and growth in psychopharmacological treatments in recent years," Mojtabai said.

He is an associate professor of psychiatry at Johns Hopkins University Bloomberg School of Public Health.

Psychotherapy in a 'Med Check'?

Dissenting somewhat from the conventional wisdom was Glen Gabbard,

please see ***Modality*** *on page 25*

Youth in Comprehensive MH Programs Improve Academically, Psychiatrically

Mental health services that are tied to existing supports for young people are improving their lives, according to a federal report.

BY EVE BENDER

Young people with serious emotional problems receiving comprehensive, individualized mental health services in conjunction with schools and other community-based organizations experienced a reduction in psychiatric symptoms and an improvement in academic achievement, according to a new report from the Substance Abuse and Mental Health Services Administration (SAMHSA).

The report, "Working Together to Help Youth Thrive in Schools and Communities," was issued in May in conjunction with National Children's Mental Health Day and describes the impact that these comprehensive mental health services—also known as systems of care—have on young people with serious emotional problems.

The report found that these improvements occurred for many youth within a year of their enrollment in these programs.

According to the report, on average 11 percent of youth with mental health problems aged 14 to 18 fail to reach the next grade level, but among those involved in systems of care, only 8 percent repeated a grade.

The report also revealed that youth involved in systems of care programs for a year or more reported a 62 percent decrease in suicide attempts, and 16 percent reported lower levels of depression. Slightly more than 20 percent reported reduced levels of anxiety than when they began receiving services.

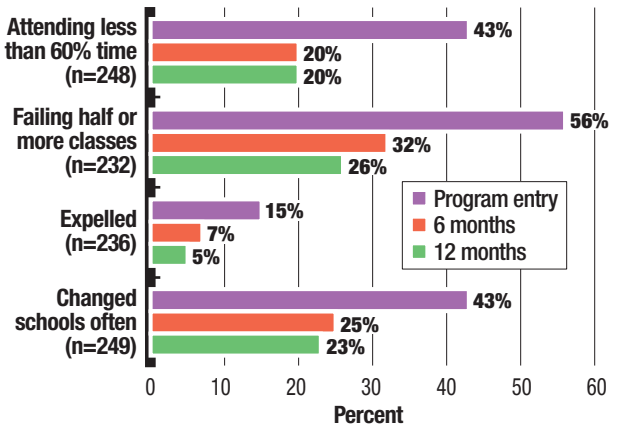
Data included in the analyses for this report represent up to 827 youth aged 14 to 18 who were assessed at intake, at six months, and at 12 months and who entered services from 2003 to 2008.

"Improving the outlook for children with mental health challenges is a critical part of improving our health and educational systems," said Eric Broderick, D.D.S., M.P.H., acting administrator of SAMHSA, in a press release. "These data show that systems of care can be an effective means of revitalizing the lives of young people and reducing long-term costly consequences of inaction."

The systems of care described in the report are designed to promote positive mental health outcomes for youth with mental health problems and their families together with schools and other community-based organizations. According to the report, about 65 percent of the young people assessed received at least some type of mental health treatment in school.

Program Helps High-Risk Youth Improve Academic Outcomes

The federal Comprehensive Community Mental Health Services for Children and Their Families Program has been found to benefit youth at highest academic risk. It is funded by the Center for Mental Health Services.



Source: Center for Mental Health Services, SAMHSA, 2009

Comprehensive mental health service plans designed for youth are highly individualized and culturally competent, according to the report.

"Working Together to Help Youth Thrive in Schools and Communities" is posted at <www.samhsa.gov/children/docs/shortReport.pdf>. ■

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).

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Unbalanced MH System Needs Major Shift in Focus

Training and continuing education of clinicians who treat mental illness must focus on evidence-based care, and licensure and credentialing must be aligned with the new learning.

BY MARK MORAN

Better but not well—that's the verdict that economist Richard Frank, Ph.D., rendered for the U.S. mental health system in a lecture at APA's 2009 annual meeting in San Francisco in May in which he provided an overview of recent trends in organization and financing of mental health services.

Though access has been expanded significantly, and treatment effectiveness has improved markedly, the financial incentives in place since the 1990s have served to "overcorrect" the system toward an overemphasis on pharmacotherapy, as opposed to psychosocial treatments, and toward primary care as opposed to specialty care.

These are the trends, Frank said, that account for most stakeholders—especially clinicians—seeing a broken and dysfunctional system even though enormous strides have been made in breaking down stigma and improving access to care.

Better But Not Well is the title of a 2006 book by Frank, published by Johns Hopkins University Press, about the evolution of the mental health system since the 1950s.

"We treat a higher percentage of people with mental disorders than at any time in U.S. history," Frank said. "Multiple effective treatments are available for most major mental disorders. And we have managed to increase access to effective offerings while claiming roughly the same share of the national income as we did in 1975. So on the face of it, there are reasons to be proud of the successes that have occurred."

But Frank presented evidence that the expansion of access to mental health care was driven by large system changes in organization and financing during the last 20 years, with strong incentives pushing care toward pharmacotherapy in the primary care setting. Reforming these imbalances will require similarly major changes; he highlighted the need to revisit the carveout model and to rethink the financial separation of specialty mental health care from the pharmacy benefit.

Credit: David Hathcox

Harvard economist Richard Frank, Ph.D., describes large system changes that have expanded access to mental health treatment, but have overemphasized pharmacotherapy in primary care settings at the expense of specialty care and psychosocial treatments.

He also called for a new emphasis in training and continuing medical education on evidence-based psychosocial treatments.

"The economic incentives in place since 1990 directed care in new directions, and the system responded," Frank told psychiatrists at the meeting. "There is now evidence emerging that care may be underemphasizing psychosocial care. Correcting the imbalance in a cost-effective way will require important and difficult institutional changes. All of them will inflict some pain, and the pain will be widely shared."

"Implementation of parity creates new opportunities to rebalance care toward psychosocial treatments."

Frank outlined the evolution of the American mental health system from its reliance in the 1960s on inpatient care and long-term psychotherapy in the outpatient setting. By the 1990s, he said, mental health financing looked more similar to that of general medical care: Medicaid and private insurance became dominant and state funds became less so, and insurance coverage for prescription drugs expanded enormously.

Especially important, managed behavioral health care companies became a dom-

please see ***MH System*** *on page 23*

Psychiatrists Help Rwandans Recover From Trauma of Brutal War

Two U.S. psychiatrists work in a clinic in Rwanda helping survivors—including rape victims and orphaned children—of that nation's 1994 genocide.

BY AARON LEVIN

The genocide in Rwanda occurred 15 years ago, but people in the African country are still coming to grips with its psychological and social aftermath in a process that is likely to continue for years, said speakers at APA's 2009 annual meeting in San Francisco in May.

During three months in 1994, between 800,000 and 1 million ethnic minority Tutsis and their moderate Hutu allies were killed by Hutus, who made up 84 percent of the population. The dead included men and women, adults and children, often cut down by neighbors with whom they had been living peacefully for many years, said Lisa Rone, M.D., an assistant professor of clinical psychiatry and behavioral sciences at Northwestern University's Feinberg School of Medicine.

Credit: Aaron Levin

Kristin Welch, M.D. (left), a psychiatrist in private practice who is affiliated with the Heartland Alliance in Chicago, and Lisa Rone, M.D., an assistant professor of clinical psychiatry and behavioral sciences at Northwestern University's Feinberg School of Medicine, reported on their psychiatric work at a clinic for survivors of Rwanda's 1994 genocide.

Following the genocide, more than 250,000 women were raped, leaving 70 percent of the victims infected with HIV and thousands of their "children of hate" left to grow up with those facts as part of their legacy. More than 90 percent of Tutsi children lost at least one family member, and 56 percent saw relatives killed.

In 2008, Rone and colleague Kristin Welch, M.D., a psychiatrist in private practice who is affiliated with the Heartland Alliance in Chicago, established a psychiatric clinic as part of the existing Women's Equity in Access to Care and Treatment (WE-ACTx) in Kigali, the capital. The clinic provides HIV testing, antiretroviral therapy, and trauma counseling.

Besides trying to help the survivors, the two Americans hoped to minimize the intergenerational transmission of trauma by people who found it "impossible to forgive and impossible to judge," said Rone.

"Traumatized parents can be a source of traumatic stress for their children," said Rone. In Rwanda, parents weren't able to protect themselves or their children during the genocide and now fear "emotional contamination" if they talk about it, she said.

The affective and cognitive consequences of parental trauma on children are ameliorated to some degree by creating safety, continuity, and predictability to their lives. Several measures have been adopted to further those outcomes.

Rwandans are beginning to recreate social bonds, often adopting orphaned children and creating new families to replace ones lost in the genocide, said Welch.

A sense of political and social safety is slowly developing through the *gacaca* system—village tribunals in which victims tell their stories, and perpetrators recount their deeds and accept some punishment.

"Hearing perpetrators' and survivors' stories in these tribunals brings some sense of justice," said Rone.

While this process sounds hopeful in theory, the reality is more complex. Some fear retraumatizing survivors. One boy, for example, wanted to testify about his mother's rape at a *gacaca* trial "to give my shame to the killers," but his mother said she would commit suicide if he did so.

Welch quoted Rwandan President Paul Kagama as saying, "It's the best we have, but nobody likes it."

At the WE-ACTx clinic Rone and Welch initiated interventions to provide simple, inexpensive ways to treat psychiatric symptoms as part of broader recovery efforts. Many patients had not slept without nightmares for 14 years but were helped by a mix of social engagement, peer support, and medications. A simple group-therapy room, consisting of a roof surrounded by curtains, allows women to tell their stories, assisted by trauma counselors.

However, nothing will be simple in helping Rwandans live with their tragedy, said Welch.

"I thought I'd heard it all after working with torture survivors, but Rwanda haunts me," she said. Victims and perpetrators still live next door to each other in a small, densely populated country.

While she believes that a psychologically healthy society is necesssary to

please see ***Rwanda*** *on page 26*

Growing Chasm Separates Parties on Health Reform

To drastically reduce the number of uninsured Americans, Democratic leaders are urging health care reform legislation that includes the creation of a controversial new public insurer to compete with private industry.

BY RICH DALY

A Republican alternative to the health care overhaul plans of congressional Democrats that is taking shape on Capitol Hill includes the use of new state-based insurance exchanges and tax subsidization of insurance premiums.

Republican leaders introduced the Patients' Choice Act (S 1099, HR 2520) to counter Democratic health care reform plans that have been widely discussed but had not yet been translated into legislative bills by mid June.

The Republican proposal would require each state to establish health insurance exchanges composed of private health insurance companies through which individuals could pick their coverage. The exchanges would serve as clearinghouses of available insurance plans through which individuals could compare features and prices of plans that meet a minimum benefit threshold. The legislation would provide $5,700 in tax credits to families and $2,200 to individuals to subsidize insurance premiums. An additional $5,000 tax credit would be given to low-income families. Funding for the credits would come from a new tax on employer-provided health benefits.

The measure "will finally enable Americans to own their health care instead of being trapped in the current system, which leaves people either uninsured, dependent on their employer, or forced into a government program," said Sen. Richard Burr (R-N.C.), who cosponsored the House bill.

The plan would allow states to shift residents covered by Medicaid into private coverage. In addition, it would establish a system to automatically enroll uninsured Americans in private insurance plans at emergency departments and motor-vehicle departments and through employers.

Sen. Tom Coburn (R-Okla.), a physician and the Senate bill's sponsor, maintained that what he described as increasing government control over health care has failed to make health care more affordable or accessible.

The Republican health reform bill would "provide every American with access to affordable health care without a tax increase, more debt, and waiting lines," Coburn said, suggesting that Democrats are working on legislation likely to produce these problems.

GOP Condemns Government Funding

The Republican plan, which supporters plan to offer as an amendment during debate on the major Democratic health care proposals planned for votes later this summer, aims to achieve universal coverage for U.S. residents while remaining budget neutral. It would not establish new government health care programs.

The Republican proposal to address rising health care costs and rates of uninsurance is in contrast to the emerging outlines of the reforms favored by Democratic leaders in Congress and by President Obama.

Senate Finance Committee Chair Max Baucus (D-Mont.) said that the GOP plan "would destroy the insurance system in America as you know it" because it would eliminate the employer-based health insurance system. Baucus and other Democrats said businesses would cease to offer their workers insurance plans if such insurance was no longer tax deductible to employers, which would be the case under the Republican plan.

The proposals by Baucus, who is leading the reform effort in the Senate, would build on the employer-based insurance system with new programs, including a publicly funded insurance option for the uninsured—similar to Medicare. The Democratic reform effort is expected to cost at least $1.2 trillion in the first 10 years, according to Democrats, although proponents maintain that the cost savings it achieves through prevention and reducing illnesses that go untreated because of lack of insurance would eventually result in overall savings.

Partisan Divide Grows

The support among many Democrats, including Obama, for the overhaul to include a publicly funded alternative for people who are unable to qualify for private insurance has become increasingly contentious. Most Democrats, including Sen. Charles Schumer of New York, have stated that a public option would end up increasing competition by breaking the "monopoly" enjoyed by private insurers.

The public option, however, has exposed health reform's political fault lines among Democrats. The so-called Blue Dog coalition, a voting block of fiscally conservative House Democrats, issued a letter in May that said it would support only a public plan that follows the same market-competition rules that private insurers must follow. Those rules would include requirements that a public plan negotiate payment rates with clinicians, allow voluntary participation in the plan by both clinicians and patients, and require its premiums and copayments to pay for all of its operations.

However, the public option has been criticized as too limited a reform by some liberal Democrats. For instance, 78 Democrats in the House have cosponsored legislation (HR 676) to expand Medicare eligibility to all Americans and replace most private insurance.

Republicans have repeatedly stressed that inclusion of a public option would likely eliminate any health care reform support from members of their party, despite the fact that Baucus and Obama have repeatedly emphasized the need for bipartisan support to ensure a reform plan's success. Republicans base their opposition to a public insurance option on their contention that private insurers could not fairly compete with a plan that did not have to make a profit, thus driving private plans out of business.

Democratic leaders in Congress have announced that they plan to work toward passage of health care reform measures in both chambers before the August recess and to pass a bill in the fall.

Congressional health reform proposals can be accessed at <http://thomas.loc.gov> by searching on the bill numbers, HR 2520, S 1099, and HR 676. ■

Some Health Reform Ideas Should Be Rejected, APA Says

Penalties for physicians who do not report quality-care indicators and cuts in specialist payments to fund increases for general practitioners are among health reform options to which APA has registered objections.

BY RICH DALY

In an effort to influence far-reaching health care reform legislation taking shape in Congress, APA has strongly urged legislators to avoid including provisions that would negatively impact psychiatrists and their patients.

APA sent its comments in May to the Senate Finance Committee, whose chair, Sen. Max Baucus (D-Mont.), has led health care overhaul efforts in that chamber. APA voiced support for enacting comprehensive health reform before the end of the current Congress, including efforts to improve accountability and quality while lowering health care costs. The comments addressed aspects of health reform in general, though these reforms are also likely to specifically affect Medicare or other government-funded health care programs.

APA found some provisions discussed for inclusion in eventual health reform bills troubling. Those provisions include penalties for physicians who do not participate in a quality-care reporting program and cuts in specialists' pay as a way to expand primary care reimbursements.

Specific concerns also were raised about a possible expanded role for the Physician Quality Reporting Initiative (PQRI), under which physicians can voluntarily report on performance measures to Medicare in exchange for a financial incentive. Some reform proposals have called for payment cuts to clinicians who do not "participate successfully" in the PQRI program. Such a provision "may have unintended consequences and should not be included in the final health reform package," APA emphasized.

APA's letter pointed out that only three PQRI measures apply directly to the mental health field, while an additional one applies to substance use care. In addition, physician participation is undercut by the program's provision of just a 2 percent bonus to participants, which does not offset the administrative costs of reporting the data the government wants.

APA raised the possibility that any PQRI-related penalty may result in more psychiatrists opting out of Medicare.

As designed, the PQRI program does not fit the practice patterns or solo-practitioner approach of a substantial number of psychiatrists, Barry Perlman, M.D., past chair of APA's Committee on Government Relations, told *Psychiatric News*.

"We were thinking that it was very important that psychiatrists not be penalized for nonparticipation," Perlman said.

APA also is concerned that health reform legislation would be designed to increase the number of primary care and generalist physicians through a "budget-neutral" funding approach that takes funds from other specialties to reward primary care clinicians. Funding bonuses for certain clinicians by cutting payments for others "would have severe consequences for access in specialty areas, particularly for individuals seeking mental health care," according to APA.

Lizbet Boroughs, associate director of APA's Department of Government Relations, told *Psychiatric News* that by June, a month after APA sent its letter, congressional leaders were no longer openly discussing the use of payment cuts to specialists to offset increased payments to primary care physicians.

More likely, she suggested, is a short-term increase in overall physician costs to the government as the Medicare payment program is reorganized to increase primary care clinician pay, while finding cost savings that eventually would return reimbursement to physicians closer to current levels.

The APA letter also urged that any reform include psychiatrists as eligible for primary care bonuses when treating Medicare patients with a primary diagnosis of mental illness. Currently, general psychiatrists are included as primary care doctors by the government only under the National Health Service Corps, which at least one reform proposal would greatly expand.

Psychiatrists should be included under "transitional care" and "chronic care management" programs that may be created as part of national health care reform, APA said in its comments. For instance, including psychiatrists in the care of patients with mental disorders treated in primary care settings would "improve outcomes and significantly reduce costs for Medicare," stated the letter.

See above article for information on the Senate's health reform bills. Key features of a health reform draft proposal in the House of Representatives that is in line with President Obama's goals is posted at <http://waysandmeans.house.gov/media/pdf/111/tri.pdf>. ■

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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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Medicare's Condition Terminal Without Major Spending Cuts

The hospital fund is especially vulnerable, but the supplemental medical insurance fund—especially affected by physician fees—is also facing serious issues with expenditure growth.

BY MARK MORAN

The Medicare Trust Fund is expected to be exhausted in 2017—two years earlier than predicted last year, according to the 2009 annual report of the Medicare trustees.

According to the report, total Medicare outlays, less dedicated revenues, are projected to exceed 45 percent of outlays in Fiscal 2014. Since this is within the first seven fiscal years of the projection period, the trustees determined that a "Medicare funding warning" was triggered, as required by the Medicare Modernization Act.

Continuing a trend for the past several years, the report predicts a dire future for the program's Hospital Insurance (HI) fund. The Medicare program's Supplemental Medical Insurance (SMI) fund is solvent but also faces serious problems.

"The long-range financial projections for HI continue to show a substantial financial imbalance," the report stated. "Tax income is expected to be less than expenditures in all future years, and trust fund assets, which began to decline in 2008, are expected to do so continuously. Without legislation to address these deficits, HI would increasingly rely on interest income and the redemption of fund assets, thereby adding to the draw on the federal budget. . . . By the end of the 75-year period, less than one-third of HI costs could be paid from HI tax revenues. Accordingly, bringing the HI program into long-range financial balance would require very substantial increases in revenues and/or reductions in expenditures."

The financial outlook for SMI is fundamentally different from that for HI, due to the statutory differences in how these two components of Medicare are financed. Nonetheless, the report noted that rapid expenditure growth is a serious issue for SMI, as it is for HI. The SMI fund is particularly affected by the physician fee schedule. For a number of years now, the government's formula for establishing the fee schedule has called for steep cuts in physician payment, yet each year, in the face of intense lobbying by the AMA and other medical groups, Congress has stepped in to avert the pay cuts.

"[I]f Congress acts to prevent a scheduled 21.5 percent reduction in physician payment rates in 2010 and further reductions in 2011-2015, then actual Part B costs could exceed the current-law projections shown in this report by 18 percent to 21 percent in the short range and by up to 10 percent in the long range," the report stated.

Health and Human Services Secretary Kathleen Sibelius called the report a wake-up call. The report "should trouble anyone who is concerned about the future of Medicare and health care in America. Just as families, communities, and businesses are struggling under the crushing burden of skyrocketing health care costs, so too are our Medicare Trust funds. . . . And it's yet another sign that we can't wait for real, comprehensive health reform.

"I know this alarm has been sounded before. Politicians have been worrying about the growth of Medicare spending for many years. The Obama administration isn't just worrying; we're doing something about it. . . . We are working with Congress on legislation that includes and goes beyond the cost-savings policies in the president's budget. The only way to slow Medicare spending is to slow overall health system spending through comprehensive and carefully crafted legislation."

"2009 Annual Report of the Boards of Trustees of the Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Funds" is posted at <www.cms.hhs.gov/ReportsTrustFunds/downloads/tr2009.pdf>. ■

More Seniors Receive Psychotropics

A study published in the May/June *Health Affairs* finds that more health care providers are prescribing psychotropic medications to their patients, particularly to seniors.

In an analysis of U.S. mental health care trends from 1996 through 2006, Sherry Glied, Ph.D, and Richard Frank, Ph.D., found that the number of seniors receiving psychotropic drug prescriptions doubled during that time period. "Greater availability of medications to treat conditions like Alzheimer's and increased access to prescription drugs through the Medicare Modernization Act may have also played a role in doctors' prescribing drugs to seniors," said Glied, a professor and chair of health policy and management at Columbia University's Mailman School of Public Health. Frank is a professor of health economics at Harvard Medical School (see page 9).

"Trends in Mental Health Cost Growth: An Expanded Role for Management?" is posted at <http://content.healthaffairs.org/cgi/content/abstract/28/3/637>.

Congress Considers Huge Boost In Military MH Outlays

A bill before Congress would make psychiatric screenings for returning combat veterans mandatory as a way to overcome pervasive stigma that prevents them from getting diagnosed and treated.

BY RICH DALY

A bipartisan coalition in Congress has called for a $300 million boost in mental health spending by the Department of Defense (DoD) in response to a soldier's deadly rampage at one of its psychiatric treatment centers in Iraq.

In May Rep. Michael McMahon (D-N.Y.) and 50 other Republican and Democratic members of Congress formally requested a boost in spending for mental health programs and a comprehensive postdeployment psychological screening program for all service members returning from combat zones. The request was sent to Rep. John Murtha (D-Pa.), chair of the House Defense Appropriations Subcommittee, who will be writing the DoD Fiscal 2010 spending bill.

"We need to make sure the Department of Defense has the necessary resources to address this growing problem and soldiers are able to get the necessary help they deserve," said Rep. Tom Rooney (R-Fla.), who signed onto the request.

The request for additional funding was welcomed by APA and veterans groups, which have sought increased funding for several years.

Credit: Office of Rep. McMahon

Rep. Michael McMahon (D-N.Y.)

"This additional funding would be a good overall boost in the military's mental health resources," said Lizbet Boroughs, associate director of APA's Department of Government Relations.

The funding increase is identical to that requested by the Obama administration as part of its budget released earlier in May. The DoD Fiscal 2010 budget already included requests for $400 million for traumatic brain injury (TBI) research, screening, and treatment and $800 million for improving the hiring and retention of psychiatrists and mental health professionals.

The additional funding is needed, according to Rep. Dan Maffei (D-N.Y.), because long and successive combat deployments have put "a significant burden" on the mental health of soldiers and strained the ability of families to cope with the absence of the service member.

"We owe it to our brave men and women to provide assistance for all of their medical needs, physical and mental, to ensure that when they return from battle, they have a fighting chance to have a stable life again at home," Maffei said.

Rep. Bob Filner (D-Calif.), chair of the House Veterans Affairs Committee, also sought quick action on a bill—the Veterans Mental Health Screening and Assessment Act (HR 1308)—that would require mandatory mental health and TBI screenings for service members within six months of their return from a combat zone.

The mandatory-screening approach is needed, Filner said, to overcome the stigma associated with mental illness that has kept some service members who need care for posttraumatic stress disorder (PTSD) or TBI from voluntarily coming forward for testing. Many fear that seeking care for a mental disorder will have a negative impact on their military career and chances for promotion.

"Mandatory medical evaluations by competent medical personnel are vital to the health of our troops and veterans so they can access the appropriate support services," Filner said. "Our service members deserve an accurate postdeployment health assessment, and they need to know that help is available if they need it."

Legislation to mandate face-to-face screening by a licensed medical professional is one of the top priorities of the Iraq and Afghanistan Veterans of America (IAVA). The group recently launched a nationwide publicity campaign to offer support and mental health resources to new veterans and to their families and friends.

"Much more must be done to address troops' psychological injuries before they reach a crisis point," said Paul Rieckhoff, founder and executive director of IAVA, in a written statement.

Apart from the issue of mandatory screening of active-duty military, expansion of existing psychiatric screening for combat veterans also has been urged by veterans groups and APA. In addition to increases for the DoD budget, Obama's 2010 budget request would expand the mental health screening and treatment services offered by the Department of Veterans Affairs (VA). The Fiscal 2010 VA budget focuses on improving screening of veterans in rural areas, which it would achieve through an increased number of Vet Centers and mobile health clinics that provide assessment and treatment in sparsely populated areas.

More information on the Obama administration's Fiscal 2010 budget is posted at <www.whitehouse.gov/omb/fy2010_department_defense/>. The text of HR 1308 can be accessed at <www.thomas.loc.gov> by searching on the bill number. ■

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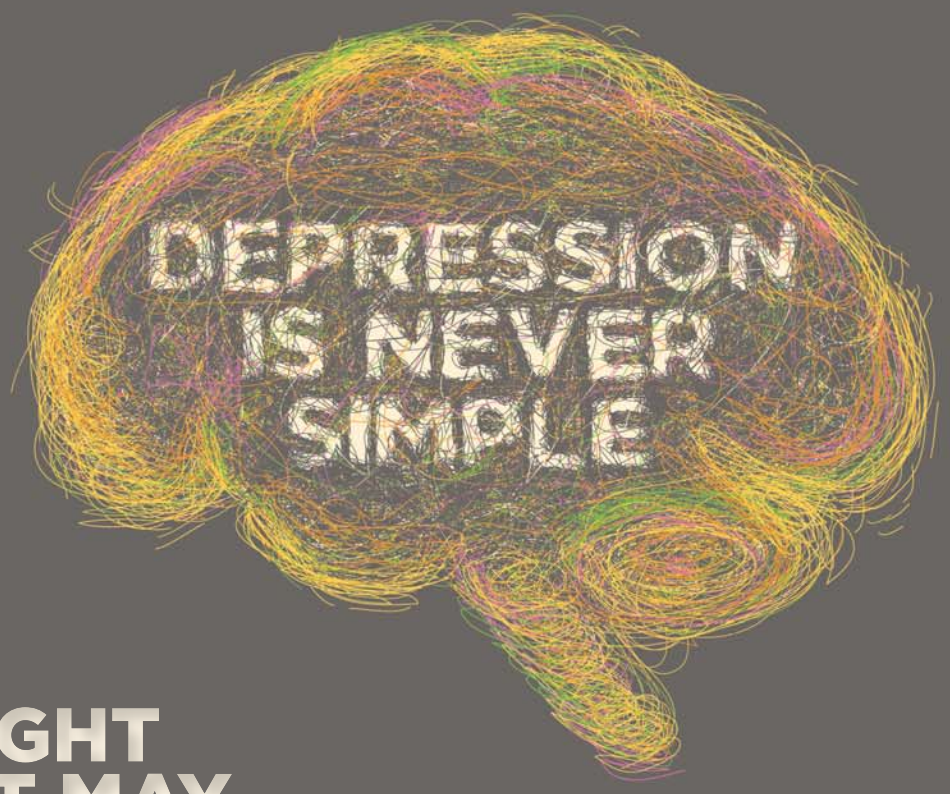

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*Venlafaxine Extended Release Tablets are not indicated for the treatment of generalized anxiety disorder or panic disorder.

INDICATIONS AND IMPORTANT SAFETY INFORMATION

WARNING: Suicidality and Antidepressants

See full Prescribing Information for complete boxed warning.

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

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

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

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

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

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

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

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

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

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

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

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

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Venlafaxine Extended Release Tablets (venlafaxine hydrochloride)

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

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

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

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

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

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

GAO Documents Misuse Of Seclusion, Restraint

Children with developmental disabilities and mental illness are often among the recipients of harsh seclusion and restraint practices by teachers and school administrators.

BY RICH DALY

The Government Accountability Office (GAO) has found that hundreds of students have been victims of abuse by teachers and school administrators through the use of seclusion and restraint and that such use has led to severe injury and even death. Although several states have enacted laws to address the issue, some in Congress think it is time for action at the federal level.

"What [the GAO] found is alarming and eye opening, and it is going to send shockwaves into every corner of this country, and it should," said Rep. George Miller (D-Calif.), who requested the GAO report. He is chair of the House Education and Labor Committee.

The GAO, which released its report in May, found that no federal law restricts the use of seclusion and restraint in public or private schools and that state laws are "widely divergent" on the matter. In fact, 19 states have no laws or regulations related to the use of seclusion or restraint in schools.

Investigators identified hundreds of cases of alleged abuse and death in the past two decades related to the seclusion and restraint of school children. Cases included a 7-year-old boy who died after he was held face down for hours by school staff and a 13-year-old who was found hanging in a seclusion room after prolonged confinement. Other incidents involved teachers and aides tying children to chairs, taping their mouths shut, using handcuffs, denying them food, fracturing bones, locking them in small dark spaces, and sitting on them until they turned blue.

The GAO also examined the details of 10 restraint and seclusion cases in which there was a criminal conviction, a finding of civil or administrative liability, or a large financial settlement.

Several common—though unrelated—themes emerged from the examination of the cases. One of them was that many of the children suffered from such disabilities as autism and mental illness, the children were not physically aggressive, and their parents had not consented to the use of restraints or seclusion.

"Though it is not limited to students with disabilities, it is happening more often to these vulnerable children," Miller said.

The GAO reported that no comprehensive, nationwide list of such incidents is maintained by any Web site, federal agency, or other entity. Some states, however, are tracking the use of seclusion and restraint. In California, for example, public schools reported 14,300 cases of seclusion, restraint, and other "emergency" interventions in the 2007-2008 school year. Texas public school officials reported restraining 4,202 students 18,741 times during the same academic year.

Whether the use of such techniques is ever necessary is a matter of debate. Bill East, executive director of the National Association of State Directors of Special Education, said that the techniques, if used properly, "can and should be used" in a few instances, such as when students are a threat to themselves or others.

Miller disagreed and called for seclusion and restraint to be replaced by techniques espoused under School Wide Positive Behavior Support programs. This approach establishes "a social culture and positive environment that uses data-driven decision making to foster appropriate behavior and improve academic achievement." Results have included fewer office discipline referrals and problematic behavior, he said.

Reece Peterson, a special education researcher who has examined educators' use of seclusion and restraint, said a possible federal role could include the establishment of nationwide guidelines that specify the situations in which seclusion and restraint are appropriate Additionally, nationwide reporting to state education departments could provide monitoring for excessive use of these tactics.

Miller said some congressional action is likely. "Congress must step in and fill the void that has resulted in scars that may never heal for these children and their families who have been victims of this abuse," Miller said. "I hope the next step will be to enact a federal policy to ensure the tragic stories we will hear today will never occur again."

"Seclusions and Restraints: Selected Cases of Death and Abuse at Public and Private Schools and Treatment Centers" is posted at <www.gao.gov/new.items/d09719t.pdf>. ■

Minority Psychiatrists Urge APA To Keep Collaborations Strong

Minority and underrepresented caucuses and allied organizations have the power to shape APA policies and represent the needs and priorities of a large, and growing, number of psychiatrists.

BY JUN YAN

Credit: David Hathcox

Outgoing APA President Nada Stotland, M.D., hosts an annual meeting discussion with psychiatrists representing APA's minority and underrepresented group caucuses and allied organizations whose members are minority psychiatrists. She emphasized that APA's commitment to including minorities in policy discussions will not wane.

Leaders of the APA Asssembly's minority and underrepresented (MUR) caucuses and allied organizations shared the history and work of their respective groups during APA's 2009 annual meeting in San Francisco and expressed concerns about their groups' future representation in and collaboration with APA. The roundtable meeting was hosted by outgoing APA President Nada Stotland, M.D., M.P.H.

Among the attendees at the meeting were Brian Benton, M.D., of the Caucus of American Indian, Alaska Native and Native Hawaiian Psychiatrists; Rahn Bailey, M.D., and Stephen McLeod-Bryant, M.D., of the Caucus of Black Psychiatrists; Gail Robinson, M.D., of the Caucus on Women; Mark Townsend, M.D., of the Caucus on Gay, Lesbian, and Bisexual Issues; and Paul Yeung, M.D., of the Caucus of Asian-American Psychiatrists.

"[APA leaders] have to pay attention to why we need these other organizations," said Stotland.

According to AMA data, women make up 34 percent of U.S. psychiatrists. Blacks make up 3 percent of the specialty, Asians 13 percent, Native-Americans 0.1 percent, and Hispanics/Latinos 5 percent. The latest APA data available in May showed that the membership was 13.6 percent Asian, 3.6 percent black, 5.2 percent Hispanic, and 0.3 percent American-Indian psychiatrists, according to APA's Office of Minority and National Affairs. Women account for 35.2 percent of APA members.

At the roundtable, most caucus representatives expressed concerns about the sunsetting of the committees under the APA Council on Minority Mental Health and Health Disparities at the end of the annual meeting and questioned whether it would result in diminished representation of MUR psychiatrists and priorities within APA.

Stotland pointed out that committees were appointed by APA presidents-elect and did not always represent their constituency's interests. Caucus leaders, however, can directly voice the concerns of the members they represent. Going forward, identity caucuses should take a much larger role in governance than before and focus on two types of activities, according to Stotland. The first would be "to produce something . . . to do tasks, which can be done without having committees." With a defined goal, a group of task-force members, and a deadline, things can be done more efficiently. The other function would be "to think of things we need to do," to help APA identify priorities for the benefit of each caucus's constituents.

Attending the roundtable were representatives from allied organizations, including the Association of Gay and Lesbian Psychiatrists, Association of Women Psychiatrists (AWP), Indo-American Psychiatric Association, Black Psychiatrists of America, Association of Korean-American Psychiatrists, American Society of Hispanic Psychiatrists, and Association of Chinese-American Psychiatrists. Each group's representatives recounted the rich history of their organization and the services provided to their members, many of whom are also APA members but often feel their interests and issues are not well represented by APA. All of the organizations work closely with APA's MUR caucuses and committees to advance the interests of their members and MUR psychiatrists in general.

"Having been part of the allied organization has focused me on Hispanic issues," said Theresa Miskimen, M.D., who represented the American Society of Hispanic Psychiatrists. In 1986, the society was formed because a group of Hispanic psychiatrists felt that "APA was big . . . [It] did not, and could not, address the issues of all the specific constituents."

Many allied organizations have a robust international membership, which brings together minority psychiatrists in the United States and practicing psychiatrists around the globe.

At the roundtable all representatives reiterated their organizations' plan to continue to collaborate with APA on matters ranging from advocacy for underrepresented populations to recruiting and retaining members. Some voiced frustration in recruiting young practitioners to join their organizations as well as APA.

"We [women psychiatrists] need as much representation as possible," said Tana Grady-Welicky, M.D., president of the AWP, which has a long tradition of working with APA caucuses and committees and strives to "enhance and promote women psychiatrists' leadership skills," she explained.

Despite financial challenges, APA will continue to support the staff and services devoted to MUR groups and issues, Stotland assured the participants. She emphasized that many of APA's priorities, such as parity, equitable Medicare reimbursement, and psychologist-prescribing legislation, are in line with the needs and concerns of MUR psychiatrists.

APA members can access the current APA component structure at <www.psych.org/Resources/Governance/Component-Restructure-Grid--April-2009.aspx>. ■

Residents, Students Network With Mentors

Some 40 psychiatrist mentors, 35 psychiatry residents, and 18 medical students gathered at the Minority Mentors Orientation Breakfast in May at APA's 2009 annual meeting in San Francisco.

The breakfast, now in its 13th year, is hosted by APA's National Minority Mentors Network. The network supports and nurtures minority psychiatrists who are in training. The network is supported by APA's Office of Minority and National Affairs (OMNA).

"This was another successful networking opportunity for our residents and students to break bread with veteran psychiatrists and alumni of the minority fellowships," Marilyn King, assistant director of OMNA's Minority Fellowships Program, said in a note of appreciation sent to all participants after the meeting.

The event serves as an extra orientation to the annual meeting's myriad sessions and activities for these young psychiatrists and even some medical students. They also learn much about the rewards and challenges of being a psychiatrist from a volunteer mentor network of experienced clinicians.

Toi Harris, M.D., director of the Texas Regional Psychiatry Minority Mentor Network, reformatted this year's event in which a PowerPoint presentation and a bingo game debuted. The bingo game, replete with prizes, is designed to increase interaction between mentors and mentees. Harris is an assistant professor of psychiatry and director of education and diversity in Baylor's Department of Psychiatry.

The next minority mentoring activities will be held during APA's Institute on Psychiatric Services in New York City in October and APA's 2010 annual meeting in New Orleans next May.

Credit: Marilyn King

Top, from left: APA minority fellows Vanessa Bob, M.D., Karinn Glover, M.D., and Farha Abbasi, M.D., show off their awards for identifying the most mentors during a networking bingo game, a new activity introduced at this year's Minority Mentors Orientation Breakfast.
Middle: Shirley Liu, M.D., a first-year child and adolescent psychiatry fellow at the University of Massachusetts and an APA/SAMHSA Minority Fellow, chats with mentor Russell Lim, M.D., of the University of California, Davis, School of Medicine.
Bottom: Minority mentor Petros Levounis, M.D., answers questions from medical students interested in pursuing a psychiatry career.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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APA's 2009 ANNUAL MEETING:
Golden Gate to Learning

Photos by David Hathcox

While a world-class city such as San Francisco has little to prove, one thing it did prove this spring is that it continues to be one of the most popular venues in which APA holds its annual meeting. This year more than 15,000 psychiatrists and other registrants arrived in the City by the Bay to expand their horizons with the help of a scientific program that covered every major topic in psychiatry—and a few esoteric ones as well.

Of course the prospect of endless cultural choices and cutting-edge cuisine just over the next hill added to the meeting's excitement.

APA's next scientific meeting will be held from October 8 to 11 in the most popular location for APA meetings—New York City. Register now at <www.psych.org/MainMenu/EducationCareerDevelopment/Meetings/InstituteonPsychiatricServices.aspx>.


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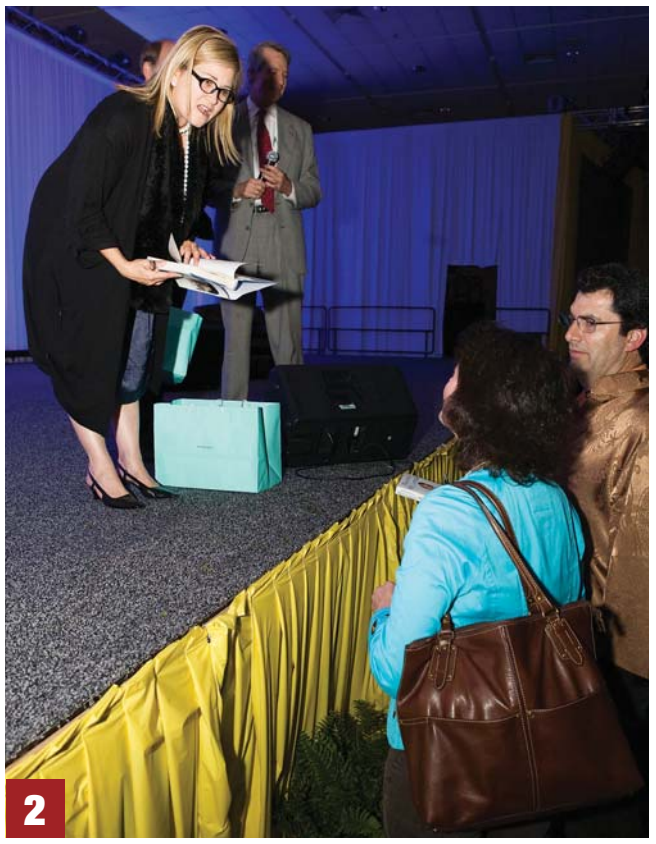
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1 Harwant Gill, M.D., and Gurnam Gill, Ph.D., discuss information with an exhibitor at a booth in the Exhibit Hall. **2** After being interviewed at the American Psychiatric Foundation's annual Conversations event about her years of struggling with, and recovery from, mental illness, actress Maureen McCormick talks to audience members. McCormick, who wrote a book on that struggle, was one of the stars of the 1970s hit TV show "The Brady Bunch." **3** Contributors to the American Psychiatric Foundation's gala fundraiser at the historic Ferry Building overlooking San Francisco Bay watch as awards are given to programs for their achievements in bringing mental health care to minority populations (see page 18). **4** Susan Kuper, director of APA's Membership Department, shows one of the many products bearing an APA logo that annual meeting attendees could purchase as souvenirs of the 2009 annual meeting. **5** Some of the more than 15,000 annual meeting attendees prepare to board one of the shuttle buses that will return them to their hotels.

Foundation Honors Programs That Target Minority MH Care

The awards were presented during the foundation's annual event, held this year at San Francisco's historic Ferry Building.

BY MARK MORAN

Credit: David Hathcox

American Psychatric Foundation President Richard Harding, M.D. (left), poses with award recipients Michael Brodsky, M.D., Hannah Wolfe, Ph.D., Andrew Michel, M.D., Alvaro Camacho, M.D., and Francis Lu, M.D. At far right is Andrei Pikalov, M.D., of Otsuka America Pharmaceutical Inc.

The American Psychiatric Foundation bestowed its Awards for Advancing Minority Mental Health on five agencies at its annual benefit event, held in May at APA's annual meeting.

The awards honor the commitments and efforts undertaken by psychiatrists and mental health professionals who have organized programs that help to provide for the mental health needs of minorities.

These are the five agencies:

• **Siloam Family Health Center of Nashville, Tenn.**, received an award for the provision of health care to low-income, uninsured people in middle Tennessee. The integration of mental health services into the primary clinic setting has provided immigrants and refugees from many countries access to affordable, culturally sensitive mental health services as well as opportunities for ongoing mental health treatment.

• **Asian Counseling and Referral Service of Seattle** received an award for the New Life program, a consumer-driven, holistic model through which individuals with a mental illness find empowerment, companionship, and skill building while enjoying the social support and network gained through participation in the program. New Life provides culturally competent and linguistically accessible prevocational and vocational rehabilitation services.

• **St. Luke's-Roosevelt Hospital Center and HIV Center for Comprehensive Care in New York City** received an award for the development, implementation, and evaluation of the Mental Health and HIV Services Collaborative. This program expands capacity and access to culturally competent and nonstigmatizing HIV-related mental health services at the center's two outpatient clinics.

• **Venice Family Clinic in Venice, Calif.,** received an award for its work providing mental health care to more than 2,100 low-income, uninsured, and homeless men, women, and children each year. Comprehensive mental and behavioral health services are given through staff, volunteers, and partnerships in the community. The clinic has a Program for Victims of Torture, which offers on-site counseling services.

• **Imperial County Behavioral Health and Sun Valley Research Center in Imperial, Calif.,** received an award for the work of Alvaro Camacho, M.D., who directs the efforts of both agencies for the underserved rural community. Home services and medical management are provided to residents in areas where there are no electricity or public utilities. Programs to improve access to care and to decrease the level of stigma have been implemented to increase the awareness to the public and private sectors about the unmet needs of individuals with mental illness among Latinos living in parts of rural Southern California.

Each organization was presented a plaque and $5,000 in honor of their work and commitment to advancing minority mental health. The awards are made possible through an unrestricted educational grant from Otsuka America Pharmaceutical Inc.

"We are proud to present these awards to these mental health professionals and organizations, which continue the strong commitment to reducing mental health disparities for racial and ethnic minorities," said Richard Harding, M.D., the foundation's president. "I congratulate all the recipients of the Awards for Advancing Minority Mental Health, and as a psychiatrist, commend their efforts to educate and raise awareness of mental health needs and services available. With education we are well on our way to a national movement to eliminate the stigma associated with mental illness."

The awards were presented at a fundraising event at San Francisco's historic Ferry Building. Beginning in the late 19th century, the Ferry Building, looking out over San Francisco Bay, was the transportation focal point for anyone arriving by train from the East or by ferry boat from surrounding bay communities.

The gala netted nearly $100,000, according to Lindsey McClenathan, the foundation's development officer. That included $2,000 from a silent auction for such items as an annual APA membership, handmade jewelry, registration for the 2009 Institute on Psychiatric Services, and tickets to see the Washington Nationals baseball team play the San Francisco Giants.

The elegance of the venue was supplemented by guest speakers who included, in addition to Harding, outgoing APA President Nada Stotland, M.D., and Gariane Gunter, M.D., a resident at the University of South Carolina where Harding is chair of the Department of Psychiatry.

As it happens, Gunter is also Mrs. United States. "This year as Mrs. United States, and daily as a psychiatrist, I am fighting to eliminate the negative stigma of mental illness," Gunter told attendees at the gala. "This title has allowed me to meet so many inspiring people and work with incredible organizations like the foundation, and for that I am forever grateful. One of my favorite sayings is, 'Be the change you want to see in this world,' and the American Psychiatric Foundation is doing just that. Through your efforts, education, and fundraising, you are making this world a more beautiful place for those suffering from a mental illness." ■

Cultural Sensitivity Hallmark Of MH Guide for Latinos

A new APA-endorsed mental health booklet and companion DVD for Latino individuals aims to improve access to care by removing the stigma surrounding mental illness.

BY STEPHANIE WHYCHE

The debut screening of a newly released, culturally sensitive DVD and a companion booklet for Latinos about mental health and illness took place in May at APA's 2009 annual meeting in San Francisco.

The 30-minute DVD and 59-page bilingual booklet are both titled "Mental Health: A Guide for Latinos and Their Families," or "Salud Mental: Una Guía para Latinos y sus Familias" in Spanish. Both the booklet and DVD are illustrated with colorful abstract images by the Ecuador-born artist Jose Ortega.

Credit: Ellen Dallager

Andres Pumariega, M.D., chair of APA's Committee of Hispanic Psychiatrists, stands before a video screen shot from the companion DVD of "Mental Health: a Guide for Latinos and Their Families."

Both the DVD and guide present the ABCs of mental health in both English and Spanish and within the context of Latino culture—from the signs and symptoms of mental illness to the importance of treatment. The overall goal of is to reduce the stigma of mental illness that can be an obstacle to getting needed care.

About 50 people attended the San Francisco screening, including Jose De La Gandara, M.D., the representative from the Assembly Hispanic Caucus; members of APA's Committee of Hispanic Psychiatrists; and interested others, including those from Spanish-speaking countries abroad.

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

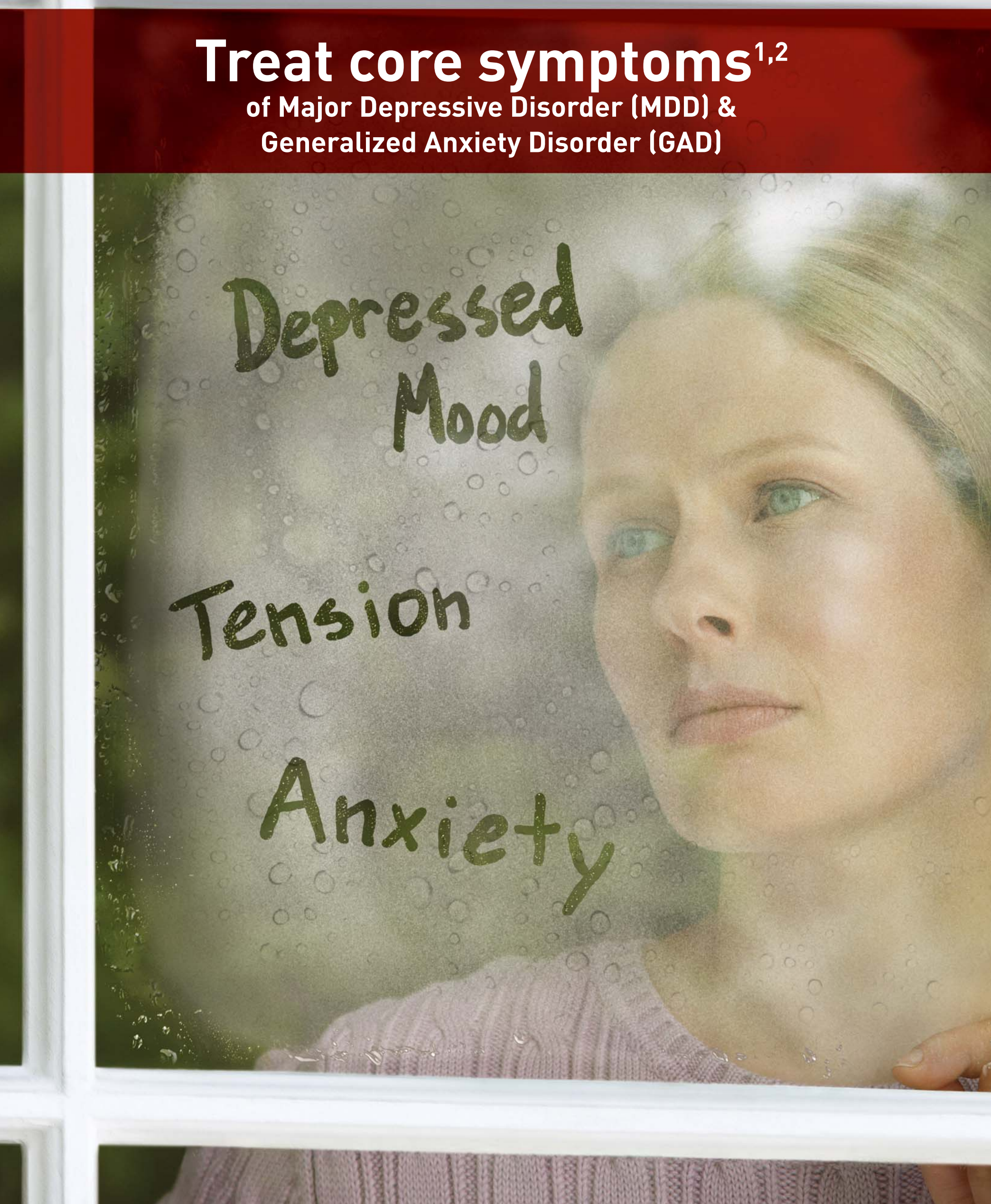
The Committee of Hispanic Psychiatrists, supported by APA's Office of Minority and National Affairs, had major involvement in this project, including the development, vetting, and editing of the guide's narrative content (including the Spanish translation) and the script featured in the DVD. The DVD features Pumariega along with Ana Campo, M.D., a former chair of APA's Committee of Hispanic Psychiatrists.

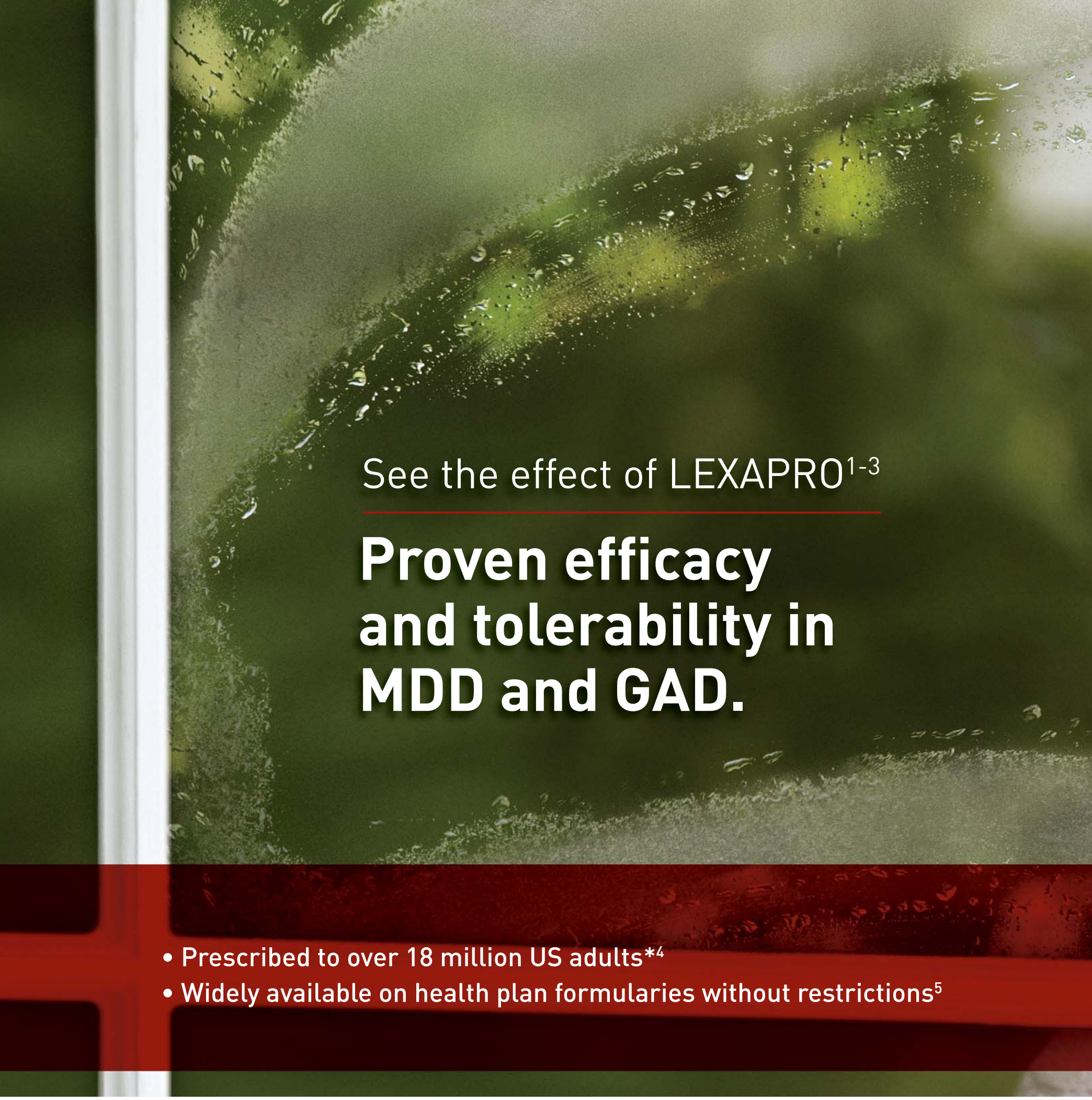
Conrad and Associates of Potomac, Md., produced the initiative and reached out to APA to provide the psychiatric content. Conrad also collaborated with the National Hispanic Medical Association and the League of United Latin American Citizens.

The guide and DVD are being distributed free of charge to Latino organizations and those who serve Latino communities. Others who would like a copy of the guide and DVD should e-mail their request to apa@psych.org. ■

Treat core symptoms[1,2]

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





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

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

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

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

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

Lexapro® escitalopram oxalate

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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/m²] 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/m² basis. No teratogenicity was observed at any of the doses tested (as high as 75 times the MRHD on a mg/m² 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/m² 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/m² 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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Social Rewards and Gray Matter: Why Are They Linked?

When people feel "all warm and fuzzy" inside, say after being praised, they should perhaps thank their orbitofrontal cortex and nucleus accumbens—two brain regions also involved in rewarding people for social interaction.

BY JOAN AREHART-TREICHEL

Whether it is savoring an ice cream cone or learning that you got a good deal on a recent purchase, two regions of your brain may move into gear.

Those regions, the nucleus accumbens and the orbitofrontal cortex, appear to process the rewarding information that comes from engaging in such pleasurable activities.

Now it looks as if these two brain regions may also be involved in processing the rewarding information that comes from engaging in social interactions. The reason? People who are emotionally warm, sentimental, and eager for people contact have been found to have significantly more gray matter in these two brain areas than do people who are more self-contained and aloof.

The study was headed by psychiatrist Graham Murray, M.D., a Medical Research Council clinician scientist at the University of Cambridge in England, and his colleagues. Results were published online on May 20 in the *European Journal of Neuroscience*.

As part of a large population study in Finland, some 2,000 young men were assessed on temperament with the Cloninger Temperament and Character Inventory, and out of these 2,000, 62 also underwent a structural MRI scan of their brains. Satisfactory MRI scan results were obtained for 41 of the 62. Murray and his team used the scan results for these 41 men, as well as the temperament information about them, for their study. Specifically, they looked to see whether there were any structural brain differences between subjects who had scored high on "reward dependence," that is, on human attachment, human dependence, openness to warm communication, and sentimentality, and subjects who had scored low on this personality trait.

Density Differs

There were differences. Gray matter was significantly denser in the orbitofrontal cortex and the nucleus accumbens in the subjects who had scored high on reward dependence than in the subjects who had scored low on it.

These findings, the researchers noted, not only "provide strong evidence for a brain structural disposition to social interaction," but suggest that the same two areas of the brain that are critical for processing reward information for some other types of activities are also critical for processing reward information for social interactions.

Still another interesting finding emerged from the study. Gray matter on the poles of the temporal lobes was significantly denser in the subjects who had scored high on reward dependence than in the subjects who had not. So these brain areas may also participate in the processing of reward information that stems from social interactions.

What Do Data Mean?

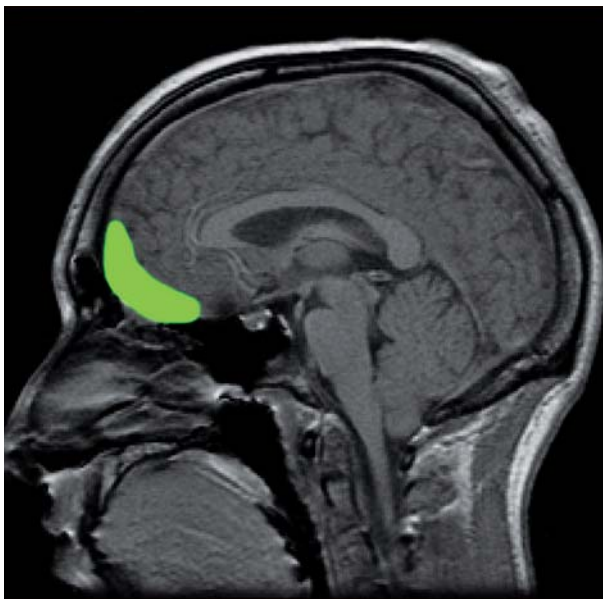
As tantalizing as such findings are, they raise provocative questions. For example, even though Murray and his colleagues found a link between a social personality and the density of gray matter in specific regions of the brain, can they really deduce from it that those particular brain areas process social rewards?

Only indirectly, he admitted to *Psychiatric News*. "It could be that social interaction itself drives brain growth in these regions rather than the other way around. Personally I think it's likely to be a two-way relationship; the more gray matter in these regions, the more pleasurable social interaction is, and the more you interact, the more growth there is in these regions. We'll need longitudinal studies of children or adolescents to confirm that."

Since the same areas of the brain seem to be involved in processing various types of rewards, could one type of reward perhaps be substituted for another and thus satisfy people's need for rewards?

"It's a nice idea!" Murray replied. "But just because the same brain circuits process information about different rewards, it doesn't mean that your brain doesn't know the difference between sex and chocolate."

Finally, what are the implications of these findings for psychiatrists? "We studied individual differences in how much pleasure people take in social interaction and related it to brain structure," Murray said. "But of course there are psychiatric disorders where the patients may take little pleasure from social interaction—autism and schizophrenia, for example. Could it be that variance in brain structure in these conditions contributes to the lack of social pleasure experienced by the patients? I'm keen to now look at this issue in patient studies. If brain structure is important for this issue in patients, how can we address it? Biological treatments could be one solution, but actually it's possible that long-term social interventions may partly work by altering brain structure."



The orbitofrontal cortex, which is known to process rewarding information accruing from various types of activities, also processes rewarding information stemming from social interactions. Along with the nucleus accumbens, it appears to be one of the brain's major reward centers.

The study was funded by the Academy of Finland, Sigrid Juselius Foundation, Stanley Medical Research Institute, Medical Research Council, and NARSAD.

An abstract of "The Brain Structural Disposition to Social Interaction" is posted at <www3.interscience.wiley.com/journal/122394540/abstract>. ■

MH System

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inant force in allocating scarce resources. This had the effect of reducing out-of-pocket costs for patients and dramatically reducing inpatient care.

But because behavioral health carve-out companies have an incentive to move care off of their budgets and into general medical care budgets, the predominance of these companies has also pushed much mental health care into the primary care setting where pharmacotherapy—rather than psychosocial treatments—is the major form of therapy.

Moreover, the very low rates of reimbursement in state Medicaid programs have discouraged the participation of specialists, while those who do participate tend to practice only pharmacotherapy rather than more time-intensive psychosocial treatments.

Treatment Shifts to Primary Care

Frank presented data showing the changes between 1990-1992 and 2000-2003 in the distribution of mental health care users by setting: while 27 percent of patients received their mental health care from a primary care physician in 1990, by 2000-2003 almost 41 percent did so. Interestingly, the distribution of people seeking care from psychiatrists also increased in that time period, from 19.6 percent to 25.8 percent.

"But there was no increase in the percentage of people treated by psychiatrists with psychotherapy," Frank emphasized. "It's all pharmacotherapy and very often pharmacotherapy alone."

Even more problematic was evidence Frank presented suggesting that early gains in quality have leveled off or dropped. Percentages of people receiving appropriate treatments for depression, schizophrenia, and bipolar disorder increased dramatically between 1975 and 1997.

But more recent quality data suggest that for depression, schizophrenia, and attention-deficit/hyperactivity disorder (ADHD), recommended psychosocial treatments have remained consistently low or have dipped somewhat. For instance, Florida Medicaid data show that the numbers of children identified as having ADHD but receiving no treatment has risen sharply.

"Quality of care is no longer increasing, and in some cases we may be giving up past gains," Frank said. "Psychosocial treatments have declined or remained flat at a very low level for most of the last 10 years. And this is true whether you look at psychosocial treatment as stand-alone psychotherapy, psychotherapy in combination with medications, or the psychosocial component of managing the pharmacotherapy."

Focusing on Evidence-Based Treatments

So, what can be done to address the imbalances in the system?

First, Frank said the passage of the parity law is an important step.

"Implementation of parity creates new opportunities to rebalance care toward psychosocial treatments," he said. "Suddenly outpatient cost-sharing will be put in line with general medical cost-sharing and with medication management and pharmacotherapy, so the consumer is going to get a price decrease for psychosocial care that will tend to drive people back in that direction.

"We eliminate the limits for outpatient care so providers have more flexibility in dealing with particular cases," Frank said.

Frank said the relegation of specialists to doing only pharmacotherapy needs to be reconsidered. "To take the people who are most focused in our system on mental health care and say 'You are only supposed to do this one little piece' makes no sense. We need to reengineer the financial incentives so we put that expertise to work improving mental health and managing the balance between psychosocial and pharmacotherapy."

But clinicians have changes to make too. In this regard Frank strongly emphasized the movement toward evidence-based care. "We need to focus on education of providers on treatments that work," he said. "Licensure and certification need to be tied to training and skill, and continuing education must be aligned with emerging evidence on what works. And clinical research needs to be focused on evidence-based psychosocial treatments that are user friendly, cost-effective, and practical to reimburse." ■

Legal Barriers, Bias Complicate Aging for Gays, Lesbians

Gays and lesbians should consider a number of psychological, social, and legal issues that may arise as they near old age—issues that heterosexuals don't face.

BY AARON LEVIN

Umee Davae, D.O. : "[Gays and lesbians] may have had to face family issues when they came out, which may strain relations as they age."

Eric Williams, M.D. : "People with a dual-minority status face a dilemma if they feel they have to choose one identity or the other."

Ellen Haller, M.D.: As they grow older, gay and lesbian individuals must consider social, legal, and financial issues that often aren't concerns of aging heterosexuals.

Credit: Aaron Levin

Having a circle of friends is a great help when you are old and gay, but you'd better also think about your Social Security and hospital-visitation rights, said several speakers at APA's annual meeting in San Francisco in May.

Social stigma and legal barriers make transitions that are difficult enough for elderly people in general even more problematic for those who are gay, lesbian, or transgendered, especially those who have come out later in life, they said.

"They may have had to face family issues when they came out, which may strain relations as they age," said Umee Davae, D.O., a staff psychiatrist at Yellowbrick, a private psychiatric facility in Evanston, Ill. And they may have to face forms of elder abuse that other seniors rarely have to deal with, she said, recounting the story of a nursing-home aide who refused to bathe a resident who was a lesbian.

Nonetheless, some gays and lesbians may adapt better because they have developed strong social circles with friends, which can provide support if their families of origin are unable or unwilling to do so. That debunks the myth of the "old, sad, lonely, aging gay person," noted Stephan Carlson, Ph.D., an assistant professor of psychiatry at Louisiana State University Health Sciences Center School of Medicine, in a paper read in his absence.

In fact, some studies show a "crisis competence" derived from considerable experience dealing with stigma and discrimination, said Carlson. "Being gay isn't a problem, but living in a homophobic society is."

Very little is known in particular about the status of older lesbian, gay, bisexual, or transgendered (LGBT) people who are members of minority groups, said Eric Williams, M.D., an assistant professor of child and adolescent psychiatry at the University of South Carolina School of Medicine. His search through the literature for the intersection of "lesbian or gay," "ethnic minority," and "elderly" yielded all of six published articles.

"People with dual-minority status face a dilemma if they feel they have to choose one identity or the other," he said. If they identify as a member of their ethnic or racial group, they may face rejection due to heterosexism or homophobia. If they choose their gay or lesbian identity, they may lose social support from their primary ethnic group and have no buffer against racism from the majority community.

Unfortunately, drawing any conclusions about the mental health needs of this population is limited by the lack of research, said Williams.

LGBT individuals have fewer legal protections, a serious problem that may come to the fore as they age, said Ellen Haller, M.D., a psychiatrist at the University of California, San Francisco. She cited, for example, the case of a 72-year-old female-to-male transsexual who was forced out of an assisted-living facility and found he had no legal recourse to challenge this action.

"Some U.S. Department of Housing and Urban Development rules prohibit discrimination, but no federal law does," said Haller. The elderly are presumed heterosexual when accessing services unless they openly acknowledge that they are not, and when they do come out, they may be taking on a whole new set of problems in receiving needed care.

LGBT individuals must also confront legal questions relating to marriage and civil unions and the legal status of their spouses or partners. And unmarried partners cannot receive the Social Security benefits derived from a deceased or disabled spouse's account.

Medical decision making may be handed over by hospitals or courts to blood relatives rather than long-time,

please see ***Barriers*** *on page 26*

Illnesses Other Than Depression Show Stronger Link to Suicide

Depression prompts people to think about suicide—anxiety, impulsivity, or substances can prompt them to act upon that impulse. Other factors that propel them from thought to action remain to be identified.

BY JOAN AREHART-TREICHEL

Mental disorders are among the strongest predictors of suicide attempts and suicide deaths. But which disorders are the culprits? Depressive disorders, right? Wrong, a new study has found. The answer is anxiety disorders, impulse control disorders, and substance use disorders.

The lead investigator was Matthew Nock, Ph.D., an associate professor of social sciences at Harvard University. The senior investigator was Ronald Kessler, Ph.D., a professor of health care policy at Harvard Medical School. Results were published online March 31 in *Molecular Psychiatry*.

Between 2001 and 2003, Kessler and colleagues undertook a formidable challenge—determining the status of Americans' mental health. Their assessment, called the National Comorbidity Survey Replication (NCS-R), was based on detailed interviews with more than 9,000 Americans representative of the American population. The first and major results from the survey were published in 2005 (*Psychiatric News*, July 15, 2005). Now Nock, Kessler, and several other Harvard colleagues have analyzed NCS-R material and determined which mental disorders are the strongest predictors of suicidal behaviors.

The researchers used responses from some 5,700 participants in the NCS-R survey for this particular study. The cohort included all NCS-R participants who had had a *DSM-IV* Axis I disorder at some point in their lives as well as a subsample of the rest of the NCS-R participants. Each participant had also reported whether he or she had ever had any suicidal ideas or had ever made any suicidal plans or attempts and, if so, when. The researchers then looked to see whether there were any links between having had a particular mental disorder and subsequently contemplating suicide or making a suicidal plan or attempt, while taking other mental disorders into consideration.

A major depression was the strongest predictor of suicidal ideation, they found. Individuals who had had a major depression were more than twice as likely to think about suicide as those who had not. But once these individuals were thinking about suicide, a major depression did not significantly predict whether they would make a suicidal plan or attempt suicide. However, anxiety disorders, impulse control disorders, and substance use disorders did.

For instance, individuals who were thinking about suicide and had had bipolar disorder were over twice as likely to make a planned suicide attempt as individuals without this illness. Those who were thinking about suicide and had posttraumatic stress disorder or a conduct disorder were more than twice as likely to make an unplanned suicide attempt as those who had not had these conditions. And individuals who were contemplating suicide and had had alcohol abuse or dependence were almost three times more likely to make an unplanned suicide attempt as were individuals who were contemplating suicide, but who did not have such a history.

"Results suggest that the onset of suicidal ideation is best predicted by depression, but depression does not predict further progression to suicide attempt," the researchers concluded. "Instead, disorders characterized by anxiety/agitation (for example, posttraumatic stress disorder) and poor impulse control (for example, bipolar disorder, conduct disorder, substance disorders) emerged as the strongest predictors of which ideators make suicide plans and attempts. . . . Future research must further delineate the mechanisms through which people come to think about suicide and progress from suicidal thoughts to attempts."

Other recent studies have produced similar results. A Finnish study found that anxiety combined with conduct disorder predicted suicidal attempts or completion (*Psychiatric News*, June 5). A study reported in the January *Journal of Nervous and Mental Disease* found a link between anxiety symptoms and suicidal thoughts or attempts even when depression was considered. That study's cohort included some 2,800 psychiatric inpatients.

The NCS-R was funded by the National Institute of Mental Health, National Institute on Drug Abuse, Substance Abuse and Mental Health Services Administration, Robert Wood Johnson Foundation, and John W. Alden Trust.

An abstract of "Mental Disorders, Comorbidity, and Suicidal Behavior: Results From the National Comorbidity Survey Replication" is posted at <www.nature.com/mp/journal/vaop/ncurrent/abs/mp200929a.html>. ■

COMPILED BY JUN YAN

This is Part 2 of a special edition of Med Check featuring summaries of new research posters presented in May at APA's 2009 annual meeting in San Francisco.

These presentations are usually preliminary in nature and often involve results that have not been peer reviewed for publication. In addition, the reports, which may involve the use of medications or procedures for indications that the FDA has not approved, are largely funded by product manufacturers.

Deep Brain Stimulation

• Researchers at the Mayo Clinic described findings from their deep brain stimulation (DBS) study in 17 patients who received stimulation in the ventral capsule/ventral striatum area, with an average follow-up of over three years. At 6 and 12 months after implantation, eight (47 percent) and nine (53 percent) patients, respectively, achieved response. Response was defined as a greater than 50 percent reduction in the Montgomery-Asberg Depression Rating Scale (MADRS) score. Five (29 percent) and seven (41 percent) of the patients achieved remission (MADRS score <10) at 6 and 12 months, respectively. These patients had had an average of six courses of antidepressants and six additional courses of drug combination/augmentation treatment. All had been refractory to ECT.

Most adverse events were minor and reversible after adjustments to the stimulation parameters. Serious adverse events included hypomania in a patient with bipolar disorder, syncope, broken leads of the device, pain at the implant site, and suicidality/increased depression. One person committed suicide after receiving the stimulation for five years. The study was supported by Medtronic Inc., which manufactures the stimulation device.

• In a study of 21 patients with refractory major depressive disorder who received DBS stimulation for at least six months, 13 patients (62 percent) achieved response at six months. Response was defined as a reduction of at least 40 percent from baseline in 17-item Hamilton Rating Scale for Depression (HRSD-17) scores. The stimulation was applied to the subgenual cingulated gyrus (SCG) and the procedure was performed at the University of British Columbia, McGill University, and the University of Toronto. Of the other eight patients, four (19 percent) had partial response, defined as 20 percent to 40 percent reduction in HRSD-17 scores, and four (19 percent) were nonresponders. Twenty of the 21 patients had been evaluated for at least one year. Among the 13 patients who achieved response at six months, all but one patient (92 percent) maintained the response at their last evaluation.

The study patients had had an average of seven depressive episodes in the past and had been in the current episode for five years. All had failed at least four courses of treatments. Eighteen (90 percent) had been treated with ECT.

Other than safety risks inherent in brain surgery and device implantation, the researchers did not see any unexpected adverse events related to the device. Two serious adverse events due to a broken extension of the device occurred. Three patients had four depression-related serious adverse events, including three suicide attempts and one suicide. One attempt was related to symptom recurrence because of treatment discontinuation; the other events were judged to be unrelated to the device. The authors pointed out that placebo-controlled studies should be conducted in future research to replicate the findings. The study was supported by St. Jude Medical Neuromodulation Division, which holds the patents for this particular DBS device.

• Canadian researchers tested the cognitive function and emotional information processing in patients receiving DBS in the SCG area and found an initial improvement in executive functions, memory, and emotional information processing tests before any significant stable mood improvement was observed. They hypothesized that cognitive symptoms in severe depression are not secondary to mood disorder but rather related to different frontal-limbic neural circuits that are modulated by the DBS.

Transcranial Magnetic Stimulation

• In a randomized, sham-controlled clinical trial, four and six weeks of daily transcranial magnetic stimulation (TMS) treatment on patients with major depressive disorder did not produce adverse effects on cognitive functioning. Patients (n=155) who received active TMS did not differ significantly from those who had sham TMS (n=146) in global cognition, as measured by the Mini Mental Status Examination; in short-term memory, as measured by the Buschke Selective Reminding test; and in long-term memory, as measured by the Autobiographical Memory Interview-Short Form. The study was sponsored by Neuronetics Inc., the maker of a TMS device recently approved by the FDA to treat adult patients with depression who have failed one adequate course of antidepressant treatment.

• Australian researchers at the Adelaide Clinic at Ramsay Health Care Mental Health Services randomized 22 referred outpatients with major depressive disorder to two TMS treatment schedules: three-days per week for six weeks (n=9) or five days per week for four weeks (n=13). Overall, the mean reduction from baseline was significant for HRSD, Hamilton Rating Scale for Anxiety (HRSA), and MADRS scores. Ten of the 22 patients (46 percent) met the criteria for response, defined as at least 50 percent improvement in HRSD score from baseline. Seven (32 percent) reached remission, or a score of 7 or less on HRSD at the end of the acute treatment course. The two TMS schedules did not differ in HRSD score reduction at the end of each course (four weeks for the five days/week schedule and six weeks for the three days/week schedule). Interestingly, the symptom reduction was not significantly different between the two schedules at four weeks. The authors concluded that three days/week TMS for four weeks was as effective as three days/week for six weeks and five days/week for four weeks as acute treatment of depression. However, whether these schedules would result in different relapse rates is unknown. The study was funded by Ramsay Health Care Mental Health Services.

• Researchers at the University of Pennsylvania have been conducting an open-label study on the feasibility and safety of low-frequency (1 Hz) TMS treatment for pregnant women with antenatal depression at 14 to 34 weeks in gestational age. The TMS was administered at a one-minute-on, one-minute-off schedule for 10 minutes per session. Each patient received a total dose of 6,000 pulses during the study. Four women had completed treatment at the time the poster was presented. No abnormality in fetal heart rate, uterine tocometry, or fetal ultrasound associated with the treatment was observed. Three of the four women achieved clinical response, defined as at least 50 percent reduction in HRSD-17. No serious adverse events were reported in the mothers or fetuses. The study was funded by Penn Comprehensive Neuroscience Center and Neuronetics Inc.

Bipolar Disorder

• Researchers at the Karolinska Institutet in Sweden reported observing micrometer-sized particles in the cerebral spinal fluid (CSF) of patients with bipolar disorder type I and type II. Fifty-nine patients treated at the bipolar outpatient unit and 21 controls with no psychiatric diagnosis consented and provided their CSF samples through lumbar puncture. The CSF was filtered and dried using vacuum suction, then examined under scanning electron microscopy. Twenty-two of the bipolar patients had thread-like structures, 42 patients had spherical particles, and six had threads with spherical particles closely attached. Some patients had more than one type of particles. Eleven of the bipolar patients had no particles at all in the CSF. None of the control subjects had any particles in their CSF. A previous study found spherical particles in the CSF of patients with schizophrenia that appeared similar to those in some of these bipolar patients. Ullvi Båve, M.D., Ph.D., the lead author of the poster presentation, and colleagues hypothesized that the particles in CSF may be related to the pathology of bipolar disorder, either as an inducer or a product of the disease process, and that this similarity provides further evidence that schizophrenia and bipolar disorder may have overlapping pathogenesis.

• Self-reported mood in patients with bipolar disorder does not appear to have a seasonal pattern, according to a study conducted by multinational researchers from Europe, North and South America, and Australia. Three hundred and sixty adult patients residing in these regions and under treatment for bipolar disorders reported their daily mood ratings using a computer software program. Climate, latitude, and seasonal variations did not have a statistically significant association with self-reported mood ratings. ■

Modality

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M.D., a renowned leader in psychoanalysis and psychodynamic therapy. He questioned what he called "the myth of the med check," saying it was not really possible to know what was happening between a therapist and patient during a visit that might be coded by the office assistant as a "medication check" and insisted that a great deal of important psychotherapy may be going on during those visits.

"We make far too much of the distinction between psychotherapy and medication," Gabbard said. "Patients don't make that distinction. They are going to see their doctor. They don't say, 'I'm in a med check, so I will only talk to you about the therapeutic effects of this medication. I think there is a lot of psychotherapy going on during so-called medication checks."

Moreover, he insisted that the principles of psychodynamic psychotherapy are applicable in every area of psychiatric practice. "There is no type of psychiatric practice that exists in a realm where psychodynamic principles—transference, countertransference, resistance, the therapeutic alliance—are irrelevant. So one of the things that I think we need to emphasize as a major public relations effort about psychiatry is that we are the integrators par excellence."

Gabbard agreed that psychiatry has "abdicated far too much ground to other mental health professions." And he wondered if the economic forces that have tended to drive the trend away from psychotherapy by psychiatrists have served as a convenient out for patients and clinicians alike who would rather avoid the difficult terrain of psychotherapy.

"As we know, the unconscious will always be resisted, and most of us would rather ignore the parts of people that are filled with pain and terror and aggression and rage," Gabbard said. "There is a powerful incentive for us to turn away from the demons that inhabit people. If we can get by on 10- or 15-minute med checks, maybe we won't have to look at that stuff."

Difficult as it may be to do psychotherapy, it is also rewarding, Gabbard said. "I train my residents that while it is true you could make money doing 15-minute medication checks, when you get to be 45 or 50, you will feel like Sisyphus pushing the boulder up the mountain, and you will have a sense of existential despair about your work," he said.

He said the satisfaction of doing psychotherapy and of getting to know people in depth "is worth taking a financial hit for." And he added, "We as psychiatrists didn't go into this for the money. We have to keep track of why we like doing this, and it is because we get to know people in depth." ■

ECT Guideline

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Some physicians use an age-based dosing algorithm to calculate the estimated seizure threshold before administering ECT rather than specifically titrating the electrical charge in each patient during the procedure. Because a higher charge above the seizure threshold is associated with a higher degree of cognitive side effects in both RUL and BL placements and people vary substantially in their individual seizure threshold, dosage titration is the more appropriate approach to optimize outcome, said Krystal.

Prior research studies have mostly used six to eight times the seizure threshold for RUL ECT. Krystal cited a 2002 study by W. Vaughn McCall, M.D., and colleagues indicating that RUL ECT given at eight times seizure threshold produced cognitive impairment and antidepressant effect similar to BL ECT at 1.5 times the seizure threshold.

Ultra-brief pulses given at 0.25 or 0.3 milliseconds are also an area of research interest, as this approach may produce efficacy similar to that achieved by conventional pulses (1.5 milliseconds) but may reduce cognitive side effects. Harold Sackeim, Ph.D., and colleagues conducted a study of 90 patients who were randomized to four groups that compared RUL with BL and ultra-brief pulse with standard pulse. Their results were published in the January 2008 *Brain Stimulation*.

The ultrabrief-pulse RUL ECT at six times the seizure threshold produced the highest remission rate (73 percent) and the least cognitive impairment compared with standard BL (2.5 times the seizure threshold), standard RUL, and ultrabrief BL. Unexpectedly, the patients on ultrabrief BL did the worst in terms of efficacy, with only 35 percent reaching remission. "It's an exciting, interesting emerging story," said Krystal, but a lot more evidence is needed to answer many questions about finding the best treatment with the lowest risk.

In addition, how to maintain the impressive response and remission rates after acute ECT and not lose ground to relapse remains an unresolved clinical question. Mustafa Husain, M.D., a professor of psychiatry and internal medicine at the University of Texas Southwestern Medical Center in Dallas, presented a 2007 study by CORE of 200 patients who had achieved remission after acute ECT. The patients were randomized to either maintenance ECT, gradually tapered to once a month, or to pharmacotherapy with lithium and nortriptyline. The six-month relapse rates did not differ significantly between the two treatments, with 32 percent on pharmacotherapy and 37 percent on maintenance ECT relapsing. Overall, 46 percent of patients on either treatment maintained their remission while the rest either relapsed or dropped out.

Other options for maintenance, such as combining maintenance ECT and pharmacotherapy and administering ECT as needed based on symptoms and algorithms, are being used in practice and need more study. Emerging neurostimulation treatments, such as transcranial magnetic stimulation, may offer additional options for relapse prevention, Husain said. ■

Rwanda

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bring about needed postconflict development in the country, Welch has found no consensus on the best practices to accomplish that.

There is general agreement that mental health care ought to be integrated into primary care in Rwanda, but that, too, is not easy. Many doctors were killed in the genocide. Psychiatry is not included in the curriculum of the nation's only medical school. Doctors and nurses are already very busy, and few resources exist for training and supervising them in psychiatric ideas and methods, said Welch. Routine psychopharmacological therapy is little used because local doctors are unfamiliar with psychotropic medications.

To help overcome stigma, the WE-ACTx Clinic hired a Rwandan psychiatric nurse who could reassure patients that it was all right to take medications or use psychotherapy.

But the steps are small, and the work is vast.

"It is not possible to forget or to get too far from the past," said Naason Munyandamutsa, M.D., a Rwandan psychiatrist, in a video presented by Rone and Welch. "We have to live together, but how do we deal with our past?" he asked. "We need justice, but we must also find a way to reconciliation. It is not easy to find that compromise." ■

Pharma

continued from page 4

play multiple roles and that the potential conflicts of interest that arise out of those overlapping commitments can be managed.

"Overlapping roles of professionals are necessary, but they always introduce ethical vulnerabilities," she said. "So instead of approaching these overlapping roles and potential conflicts of interest as something horrible that 'other people do,' I would much rather we brought this back home and acknowledge that we encounter these issues all the time. As professionals we are expected to bring expertise and sophistication to the management of these complex issues."

She urged psychiatrists to acquaint themselves with the Institute of Medicine report, "Conflicts of Interest in Medical Research, Education, and Practice." The 300-page report contains 16 recommendations addressing all areas of industry involvement in medicine (*Psychiatric News*, June 5).

Appelbaum was chair of a work group that developed guidelines that are undergoing consideration within APA addressing relationships with industry for the individual psychiatrist.

Roberts also said that education around issues related to conflict of interest is possible and proven to be effective. She presented data from her research showing that medical students can be taught, using a structured, criteria-based educational intervention, to identify ethical problems in clinical trials.

The study, "Teaching Medical Students to Discern Ethical Problems in Human Clinical Research," appeared in the October 2005 *Academic Medicine*.

Yager described efforts at a number of academic medical centers to teach students and trainees about conflict of interest. At UC Davis, for instance, pharmacy students act as drug-company representatives in role-playing exercises with medical students, and at the Mayo Clinic fourth-year students take a pharmacology course that includes critical analysis of drug advertisements.

The University of Colorado has developed an intensive four-year course in evidence-based medicine that includes critical evaluation of studies and instruction in the kind of design modifications that are used to distort findings.

"The goal is to sow thoughtful skepticism," he said. ■

Barriers

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same-sex partners. The latter may also not be covered by health insurance, except in states with domestic-partnership laws.

Tax laws prohibit a partner from automatically inheriting an individual retirement account without paying taxes. There is no protection for unmarried couples under the federal Family and Medical Leave Act. In addition, most traditional pensions continue payments to the surviving spouse of a deceased employee, but not for an unmarried partner.

"Transsexuals have even more invisibility and less legal protection" than gay men and lesbians, said Haller.

Several conventional legal documents can help LGBT individuals and couples carry out their wishes later in life. General and health-specific durable powers of attorney, along with living wills and advance directives, can guide care. A last will and testament can direct the disposition of assets. Documents that specify priority for hospital visitation may serve as a guide and may be accepted by some hospitals, but they lack full legal standing, Haller noted. Just as important, she said, is the need to train health care workers to understand and care for aging LGBT individuals and to pass antidiscrimination laws to protect sexual minorities.

The American Society for Aging has information on its "LGBT Aging Issues Network," which is posted at <www.asaging.org/lgain>. ■

Situation Worsening

While nobody can deny the success of APA in so many areas including, but not limited to, helping to achieve parity coverage of mental health care, patient care still suffers, at times even more so than it did in the early 1970s.

When I started psychiatry residency training in 1971, there were no health insurance preauthorizations and formulary restrictions and few government rules and regulations. No one other than my colleagues advised me what to do relevant to delivering high-quality care. I could prescribe any medication I thought would be serving the best interest of my patients. My patients were working in those times.

I was able to hospitalize patients whenever hospitalization was needed. No one pushed me to discharge patients prematurely because of authorization limitations. I was each patient's therapist, counselor, and spiritual consiglieri and a part of his or her family, applying different approaches based on the patient's capacity and needs.

I supervised recreational therapists, occupational therapists, and music therapists. I founded group cinema therapy sessions. Such services are not or rarely reimbursable.

Today, patients come to my office, often with no money and no insurance; many do not even meet the criteria for residency in the region or state, and thus are not eligible for assistance. How can I help these patients if all I am able to do is prescribe medications in a 15-minute appointment?

As far as drug samples are concerned, some clinics prohibit their use. Those that do use drug samples do not have any guarantee that the supply will be steady. While patient assistance programs are extremely valuable for indigent patients, some administrative and financial factors may still hinder the services.

Once the doctor-patient relationship is established, then I am responsible for the patient's well-being. What autonomy, credibility, resources, and other strengths do I have left in my medical bag in balancing this responsibility?

MEHMET FUAT ULUS, M.D.
Erie, Pa.

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In Major Depressive Disorder (MDD)...

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Lexapro (escitalopram oxalate)

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

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, especially during the initial few months of therapy or at times of dose changes. This risk may persist until significant remission occurs. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Lexapro is not approved for use in pediatric patients less than 12 years of age.

Lexapro is contraindicated in patients taking monoamine oxidase inhibitors (MAOIs), pimozide, or in patients with hypersensitivity to escitalopram or citalopram. As with other SSRIs, caution is indicated in the coadministration of tricyclic antidepressants (TCAs) with Lexapro. SSRIs and SNRIs (including Lexapro) may increase the risk of bleeding events. Patients should be cautioned that concomitant use of aspirin, NSAIDs, warfarin or other anticoagulants may add to the risk.

Lexapro is not approved for use in treating bipolar depression. 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. Lexapro should be used cautiously in patients with a history of mania or with a history of seizure disorder. Lexapro should be used with caution in patients with severe renal impairment or with diseases or conditions that produce altered metabolism or hemodynamic responses.

SSRIs and SNRIs have been associated with clinically significant hyponatremia. Elderly patients or patients taking diuretics or who are otherwise volume-depleted appear to be at a greater risk. Discontinuation of Lexapro should be considered in patients with symptomatic hyponatremia and appropriate medical intervention should be instituted.

The concomitant use of Lexapro with other SSRIs, SNRIs, triptans, tryptophan, antipsychotics or other dopamine antagonists is not recommended due to the potential for development of life-threatening serotonin syndrome or neuroleptic malignant syndrome (NMS)-like reactions. The management of these events should include immediate discontinuation of Lexapro and the concomitant agent and continued monitoring.

Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that Lexapro therapy does not affect their ability to engage in such activities.

For pregnant and nursing mothers, Lexapro should be used only if the potential benefit justifies the potential risk to the fetus or child.

Patients should be monitored for adverse reactions when discontinuing treatment with Lexapro. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible.

The most common adverse reactions in adults treated with Lexapro (approximately 5% or greater and at least twice the incidence of placebo) are nausea, insomnia, ejaculation disorder, fatigue and somnolence, increased sweating, decreased libido, and anorgasmia. The overall profile of adverse reactions in pediatric patients was generally similar to that seen in adult studies; however, the following additional adverse reactions were reported in adolescents at an incidence of at least 2% for Lexapro and greater than placebo: back pain, urinary tract infection, vomiting, and nasal congestion.

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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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Parity

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est groups of respondents did not know whether dropping either coverage was under consideration. Only about 7 percent of respondents reported they were considering dropping mental health coverage, and about 8 percent were mulling the end of substance use treatment coverage.

"The [survey] results tell us that employers understand that mental health is an essential component of health," said Alan Axelson, M.D., cochair of the partnership's Advisory Council and medical director of InterCare Psychiatric Services in Pittsburgh.

The new parity law, known as the Paul Wellstone and Pete Domenici Mental Health Parity and Addiction Equity Act, requires health plans that offer mental health coverage to have the same benefits, copayments, and treatment limits as other types of health care. The law, which potentially could give 113 million people equal access to mental health coverage if employers retain insurance plans with behavioral health features, goes into effect on January 1, 2010, for most calendar-year plans. The law exempts employers with 50 or fewer employees from its requirements. Final regulations to implement the law are expected to be issued in October.

The survey authors sent out about 1,000 questionnaires to employers of varying sizes and received 143 completed responses.

More than three-quarters of the responding companies are covered by the Employee Retirement Income Security Act (ERISA). Companies that self-insure and fall under ERISA were not subject to previous state mental health insurance parity requirements.

The survey found many employers will have to make significant changes in the health plans they offer workers to comply with the law. The law, for instance, requires employers to make several benefit design changes, including equalizing copayments and outpatient visit limits. The survey found 37 percent plan to change their copayments, 36 percent will change outpatient visit limits, and 29 percent will amend their out-of-network coverage features.

Employer responses also indicated that they plan to increase their use and promotion of wellness (35 percent) and employee-assistance (38 percent) programs.

"The current economic climate has exacerbated existing workplace mental health issues," said William Bruning, J.D., cochair of the partnership's Advisory Council and president and CEO of the Mid-America Coalition on Health Care in Kansas City. "When employees who need mental health treatment receive it, productivity increases."

The survey also found that mental health and substance abuse care were relatively inexpensive for employers. Only 9 percent of employers spent more than 5 percent of their health care budget on those two categories of care, and most did not expect that to change. Sixty-four percent of survey respondents said they expect parity implementation will reduce their costs, have no effect, or increase costs by less than 2 percent. Only 36 percent of respondents expected costs to increase by more than 2 percent.

"The business case for quality mental health care is there," Bruning said.

But even small projected increases are important, experts have said, because strong federal parity legislation was stymied for decades by business leaders' longstanding concerns that parity requirements would greatly increase their health care costs. The new law allows employers to not adhere to parity requirements if their costs increase by more than 2 percent in the first year of parity and by more than 1 percent in subsequent years.

The survey results are posted at <www.workplacementalhealth.org/pdf/EmployerParitySurveyResults20090528.pdf>. ■

Antipsychotics

continued from page 1

ing less than 45 kg did not achieve statistically significant difference between ziprasidone and placebo, and the small numbers of patients in these subgroups precluded any meaningful conclusion. The committee gave 12 votes of "yes," two votes of "no," and four abstentions on the question of ziprasidone's efficacy.

Ziprasidone's safety profile caused further concerns because of its well-established association with QTc interval prolongation in children, adolescents, and adults, which is currently described in the product label. The drug received only eight votes supporting its safety, with one vote of "no" and nine abstentions.

Olanzapine also caused much debate among committee members because of its potentially serious and long-lasting adverse effects, including weight gain, metabolic abnormalities, and prolactin increase. Eli Lilly submitted applications to the FDA seeking pediatric indications for olanzapine as early as October 2006 and has received conditional approvable letters twice since. However, the approval has remained pending as adverse-event reports increased over the past few years.

Thomas Laughren, M.D., director of the FDA's Division of Psychiatry Products, told the advisory committee that should olanzapine be approved for pediatric and adolescent indications, the agency plans to require wording on the product label recommending that physicians try other treatment options before olanzapine. A company representative also assured the committee that extensive postmarketing risk evaluation and management programs would be implemented.

Olanzapine's efficacy received support from the committee, but nearly half of the committee members expressed reservations about its safety by voting "no" or abstaining on the questions of whether olanzapine is acceptably safe for the treatment of schizophrenia and bipolar disorder in patients aged 13 to 17.

This cross-specialty advisory committee consisted of members from the FDA's psychopharmacologic drugs, pediatric, cardiovascular and renal drugs, drug safety and risk management, and endocrinologic and metabolic drugs advisory committees.

During the open public hearing, David Fassler, M.D., APA secretary-treasurer and a child and adolescent psychiatrist, urged the FDA to "consider the reality of how medications are used in the treatment of children and adolescents with complex psychiatric disorders . . . and to limit any specific indication approval to short-term, episodic use consistent with the data presented." He also recommended that the FDA require the companies that make the SGAs to conduct phase-4 trials to evaluate long-term outcomes associated with these drugs. Fassler was testifying on behalf of APA.

Laurence Greenhill, M.D., president of the American Academy of Child and Adolescent Psychiatry, also spoke at the public hearing. He urged the FDA to require a registry for the use of these antipsychotics in children and adolescents so that more long-term data on the safety and efficacy can be centrally collected and monitored. Currently, a national registry is in place for clozapine use because of its potentially fatal side effect.

While these SGAs await the FDA's decision about their use in pediatric patients, they are already often prescribed off-label for pediatric and adolescent patients with schizophrenia, bipolar disorder, and other conditions. The approvals, however, could open the door for the companies to market these indications in younger patients directly to consumers and prescribers.

Also in their testimony, both Fassler and Greenhill asked the FDA to consider ways to control direct-to-consumer (DTC) advertising, because if the SGAs do receive FDA approval, it could create a perception that these drugs are safe and effective for long-term use in children and adolescents.

"I urge you to consider recommending a moratorium on DTC advertising for a period of time following FDA approval of any specific indications currently under consideration," said Fassler. This "may be particularly appropriate for medications such as the atypical antipsychotics for which there is general agreement that we don't yet have sufficient data on long-term safety and efficacy in the pediatric population." ■

Depression

continued from page 1

family members as well. Parental depression can result in a withdrawn, detached parenting style that interferes with attachment and harms the child's physical, psychological, and social development. It can also disrupt the structure and routine that provide a framework for young lives and is associated with poorer physical health in children. Depression is often accompanied by other physical or psychological comorbidities, most prominently anxiety or substance abuse, often worsening outcomes for affected families, said England.

"We need to think about depressed parents as parents first and then as depressed people," added panel member William Beardslee, M.D., academic chair in the Department of Psychiatry at Children's Hospital Boston and the Gardner/Monks Professor of Child Psychiatry at Harvard Medical School. Current approaches to depression focus too narrowly on symptoms and diagnoses in individuals while ignoring broader effects on families. Existing screening, treatment, and research protocols, for instance, do not take into account the possibility that the patient is a parent.

The problem has received less attention than it should because it falls along the boundaries of professional and policy domains, from research to payment for services.

"There is remarkably little systematic examination of depression in parents," said the report. Research and attention usually focus on mothers, with little data available on fathers. Women are screened during pregnancy and shortly following birth, but seldom beyond that point, due to inadequate guidelines or insurance limitations involving cut-off points for reimbursing the physician. Numerous barriers to care stand in the way of screening, access, treatment, and reimbursement.

The remedy lies in comprehensive, multigenerational, family-centered care that will not only identify and treat parents with depression, help them improve their parenting skills, and provide support for their children, England said.

For a start, the U.S. Surgeon General should encourage federal health agencies to increase their recognition of depression in parents and its effects on children's development, along with collaborative research into risk and protective factors and, ultimately, demonstration projects to evaluate innovative services.

The Substance Abuse and Mental Health Services Administration and the Health Resources and Services Administration should develop collaborative training programs for primary, mental health, and substance abuse professionals to break down the silos that isolate professional groups.

Payment rules for both public and private payers should be changed to permit care in nonclinical settings (such as home visits or community centers) and eliminate current restrictions in Medicaid that prohibit same-day visits for mental health and primary care services.

"We need to think about depressed parents as parents first and then as depressed people."

Impeding use of Medicaid for this group are "low reimbursement rates, lack of benefit coverage to assess for maternal depression, prohibitions against pediatricians assess[ing] parents, and a restricted range of eligible providers . . . ."

The prospect of achieving such widespread change is daunting, even for members of the IOM committee. "We know what we should do, but we don't know how to implement it," said Beardslee in a follow-up interview. "We need a broad public-health approach. However, there will be a real payoff because medical outcomes are worse in people with depression, so there ought to be an incentive to identify and treat family members."

"Depression in Parents, Parenting, and Children: Opportunities to Improve Identification, Treatment, and Prevention" is posted at <www.bocyf.org/parental_depression_brief.pdf>. ■

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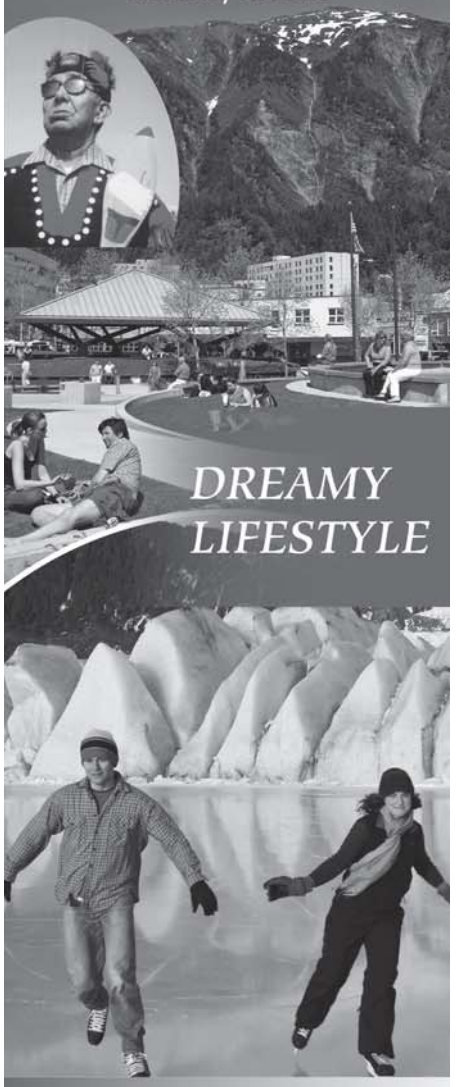

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kcallahan@bartletthospital.org
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Providence Behavioral Health Hospital

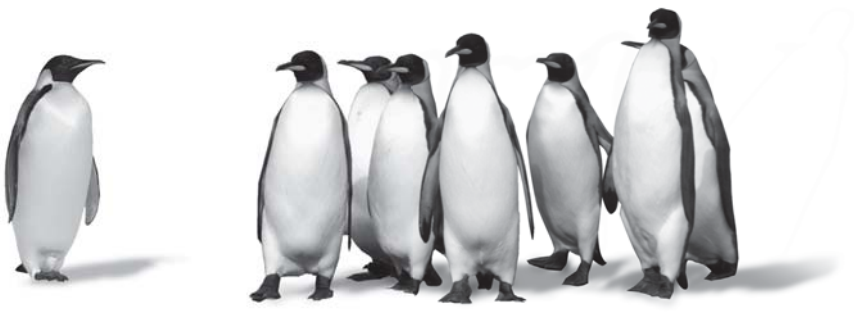
Providence Behavioral Health Hospital, of The Sisters of Providence Healthcare System, is seeking an experienced, Board Certified psychiatrist to join its leadership team as the Chief Medical Officer.

The successful candidate shall be board certified in Psychiatry with an additional qualification of an MBA or similar leadership experience desirable. Knowledge and experience with quality measures, regulatory compliance, and hospital reimbursement is essential.

The facility has 124 inpatient beds and is comprised of 3 psychiatric units treating Adults, Older Adults, Child and Adolescents; an inpatient Detoxification unit, and an Acute Residential Treatment program for children and adolescents. PBHH, with its related clinics and residential facilities, is the largest provider of integrated and comprehensive behavioral health services west of Boston.

We are located in the Pioneer Valley in Western Massachusetts. The Pioneer Valley region encompasses 43 cities and towns in the Connecticut River Valley. Please contact Mr. Gene Corbett for more information about our practice. You may reach him direct at 800-229-9759 or recruiting@mercymedicalrecruiting.com.

EOE.



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Issue	Deadline (Friday, 2 p.m. E.T.)
August 7	July 24
August 21	August 7

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ARIZONA

University of Arizona

The University of Arizona's **Psychiatry Department** is recruiting adult and child psychiatrists to join a progressive and growing academic department located in the beautiful Southwest. Candidates must have current credentials to practice medicine in the United States and be Board-certified or -eligible in Psychiatry.

Assistant/Associate Professor, Clinical Psychiatry (NTE) - Inpatient & Women's Mental Health, Job #42184 - The successful candidate will assist in caring for inpatients in an 8 bed unit at the University Medical Center (UMC), and coordinate activities and direct all efforts of the Women's Mental Health program. The Women's Mental Health program is dedicated to improving detection of mental health issues and providing expert care to women across the lifespan. Ongoing responsibilities include the diagnosis and treatment of mental disorders common in women, participation in community forums/presentations to provide education to the community regarding mental health issues in women, supervision of resident care, and performing attending psychiatric evaluations and the care of up to eight inpatients. Other duties may include participation in committees and department services as directed by the Department Head, assistance in reviews and audits of the inpatient unit, and other clinical duties as assigned.

Child Psychiatrist / Assistant or Associate Professor or Professor, Clinical Psychiatry Job # 39689 - Responsibilities include child and adolescent services for outpatient care and in a correction/residential treatment setting. Other duties include providing a significant contribution to the didactic and supervisory component for training programs. Individuals must be Board-certified or -eligible in Child and Adolescent Psychiatry. Salary: DOE

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

ARKANSAS

LITTLE ROCK & FAYETTEVILLE-General & Child Psychiatrists. Admin/Clinical & Staff positions. Inpatient & partial programs. Fulltime or part-time positions offering very competitive salary & benefits. Contact Joy Lankswert @ 866-227-5415 or email joy.lankswert@uhsinc.com

CALIFORNIA

San Diego County needs psychiatrist for hospital, possible ER and telepsychiatry. Salary extremely competitive for San Diego - up to 170K plus 10% Boards and extra 5% second Boards. CV to Marshall Lewis, MD, Clinical Dir, County Behavioral Health Div, Marshall.Lewis@sdcounty.ca.gov. Apply now at www.sdcounty.ca.gov/hr.

Mental Health

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 Wadsworth Murad, D.O., (A) Medical Director, 3102 East Highland Avenue, Patton, California 92369, (909) 425-7326 or Fax (909) 425-6635.

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

Contract psychiatrists are needed to work 10 hours, 4 days wkly at Coalinga State Hospital, CA, at hrly rate of $180. Call 800-758-7012 or fax CV to 800-758-7013 or e-mail hahacorp@gmail.com if interested. CA license, and insurance needed. We will work with recruiter for a fee.

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. **J-1 Visa waiver available.** Contact: Mark Blakeney, Horizon Health, 972-420-7473, fax CV: 972-420-8233, or email mark.blakeney@horizonhealth.com. EOE.

CONNECTICUT

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

STAFF PSYCHIATRIST, FULL-TIME - At the Hospital of Saint Raphael, a 511-bed community teaching hospital in New Haven, CT, our vision is to provide the highest quality care and the most balanced, caring and professional environment possible to each face that walks through our doors. Full-time staff psychiatrist will provide services on our Adult Inpatient Unit as well as in the PHP/IOP. One out of four weekends call schedule. Board Certified or eligible in Psychiatry required. We offer a competitive salary and a supportive, friendly environment. Please call Travis Taigen to learn more about these opportunities at **1-800-322-2380** or contact at **ttaigen@srhs.org.** For consideration, please apply online at: www.srhs.org/career. Committed to equal opportunity and an environment that celebrates diversity.

GENERAL PSYCHIATRY-CT
Busy two-person provider of behavioral healthcare services seeks a BE/BC psychiatrist to join their private practice providing adult psychiatric services. Practice is affiliated with a suburban community hospital offering a full continuum of mental health services. The practice is offering a competitive salary and benefits package and partnership potential.

ATTRACTIVE SOUTHERN NEW ENGLAND LIVING

Our central CT location offers a choice of upscale suburban communities with first-rate schools and is a short distance from professional sporting events, concerts, ballet, gourmet dining, and theatre. The coastal beaches of Long Island Sound are within easy reach and in just two hours, you can enjoy Boston, New York and the ski slopes of Vermont.

To learn more about this opportunity, call toll-free, Christine Bourbeau, Director of Physician Recruitment at 800.892.3846/860.714.1090 or fax/email your resume to 860.714.8894. EOE.

Email address: cbourbeau@brishosp.chime.org

DELAWARE

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

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.

GEORGIA

BEAUTIFUL AREA - VERY CLOSE TO TALLAHASSEE, FL - Seeking another Psychiatrist to work on adult and gero psychiatric services (inpatient, PHP & outpatient) in an impressive hospital in Thomasville, GA. Offering attractive salary w/benefits. Great quality of life: great climate; great opportunity- have it all. Please **call Terry B. Good at 1-804-684-5661,** Fax #: 804-684-5663; Email: terry.good@psysolutions.com.

ATLANTA: General, Geriatric or Addiction Psychiatrist - Inpatient & partial programs. Fulltime positions offering salary, benefits & bonus plans. Weekend moonlighting is also available for day shifts only at several hospitals - no overnight call. Joy Lankswert @ 866-227-5415 or email joy.lankswert@uhsinc.com

ILLINOIS

MEDICAL DIRECTOR OF OUTPATIENT SERVICES

Edward Hines VA Medical Center, located near Chicago, is seeking a full-time Medical Director of our outpatient Mental Health Clinic. Hines is a nationally recognized leader in patient care and, as one of the country's largest VAs, offers considerable breadth of opportunity both clinically and academically. This key Board Certified position includes an academic appointment with the Department of Psychiatry and Behavioral Neurosciences at Loyola University Medical Center. A minimum of 4 years of post-residency/fellowship experience in mental health are required. Proven administrative/clinical productivity in a VA medical center and in an academic environment are highly desirable. Salary is commensurate with qualifications and experience and includes an excellent benefits package. Submit letter of interest and CV to Edward Hines, Jr. VA Hospital, ATTN: Marilyn Boughton; PO Box 5000 South 5th Avenue; Hines, Illinois 60141. Inquires contact Thomas Nutter, MD, Assistant Chief of the Mental Health Service Line, 708 202 8387 extension 27826.

KANSAS

Supervisory Psychiatrist (Chief of Psychiatry) - Topeka, KS
The VA Eastern Kansas Health Care System is seeking a Chief of Psychiatry to serve as an executive supervisor of behavioral health prescription providers. The manager will demonstrate leadership and direction for effective, uniform and economical accomplishment of Behavioral Health Service Line functions within Eastern Kansas Health Care System at both Topeka and Leavenworth sites. This position is responsible for all aspects of administrative and clinical duties relating to prescription providers located within EKHCS. The manager will work with the Quality Management Coordinator, manage quality assurance and improvement activities for all programs and ensure compliance with all applicable JCAHO standards. Additionally, the manager will participate fully in management discussions, decisions, policymaking and shares in the responsibility to top management actions covering activities related to the Behavioral Health Service Line. English language proficiency and US citizenship required, BC/BE in Psychiatry, possess a valid, unrestricted license, have training or experience in psychopharmacology, and be eligible for academic appointment. VA Healthcare providers are entitled to immunity from medical malpractice claims as provided by the Federal Tort Claims Act. In addition to an attractive salary, we offer vacation/sick leave, health/life insurance coverage and a retirement package including a tax-deferred savings plan. Interested candidates should send current CV and references to James Marfield at james.marfield@va.gov. EOE.

KENTUCKY

Radcliff - easy commute from LOUISVILLE: Child or General Psychiatrist for inpatient & outpatient programs. Great salary, benefits, & bonus plans. **Will sponsor J1 or H1.** Contact Joy Lankswert @ 866-227-5415 or email joy.lankswert@uhsinc.com

LOUISIANA

BC/BE Psychiatrist

OCHSNER ST. ANNE GENERAL HOSPITAL is seeking:

- A BC/BE Psychiatrist for an employed position in Raceland, Louisiana
- Located 40 miles from New Orleans with a population of approximately 40,000
- Not-for-profit critical access hospital providing inpatient & outpatient services with high quality, cost-effective emergency, medical & surgical care
- Part of nationally renowned health system of 7 hospitals, 700+ member physician group, and 40 health centers
- Very competitive salary and benefits
- Family-oriented community with year-round outdoor activities
- Favorable malpractice environment in Louisiana
- Ochsner Health System is an equal opportunity employer.

Please email CVs to: profrecruiting@ochsner.org or call (800) 488-2240. Ref# APSTA09. EOE.

MAINE

Adult and Child/Adolescent Psychiatrists
Nation's 1st Psychiatric Magnet Hospital seeking BC/BE psychiatrists for both our adult and child/adolescent inpatient and outpatient programs. We are a thriving, non-profit, private community-based hospital offering acute psychiatric care for adults and children, as well as chemical dependency programs. One of only two private psychiatric hospitals in Maine. We offer physicians clinical practice in a highly collaborative, multi-disciplinary setting. Competitive salary/benefit package. Send CV to: VP of Medical Affairs, The Acadia Hospital, P.O. Box 422, Bangor, ME 04402-0422. **www.acadiahospital.org**

MARYLAND

"THE MARYLAND PLAN" is a nationally acclaimed program in public psychiatry. Positions are available for child and adult psychiatrists. Academic involvement with med. schools in your area of interest is encouraged. Please e-mail CV with area of interest and geographic preference to: GJordanRandolph@dhmh.state.md.us or mail to: Gayle Jordan-Randolph, M.D., Mental Hygiene Administration, Spring Grove Hospital, Dix Building, 55 Wade Avenue, Catonsville, MD 21228.

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

CAMBRIDGE: Adult Psychiatry

Positions available at Cambridge Health Alliance. The Department of Psychiatry at Cambridge Health Alliance is an appointing department at Harvard Medical School with excellent residencies in adult and child psychiatry. Our public health commitment to improving the health of our communities, coupled with a strong academic tradition, make this an ideal opportunity for candidates interested in caring for underserved populations in a rich clinical environment.

Adult Inpatient Psychiatrist - We are seeking a psychiatrist to join a collegial team and become an active member of a rich clinical department. This opportunity is a full-time inpatient psychiatrist position with clinical and teaching responsibilities for an inpatient team on an active community training service. Clinical care is provided through a multidisciplinary team approach with psychiatrist leadership. Academic appointment, as determined by the criteria of Harvard Medical School, is available for qualified candidates.

Weekend Moonlighting Psychiatrists: Lucrative and flexible opportunities available for attending psychiatrists to provide weekend/holiday coverage of inpatient units.

Qualifications: BE/BC, demonstrated commitment to public sector populations, strong clinical skills, team oriented, problem solver. Interest and/or experience with dual diagnosis patients a plus. Cambridge Health Alliance is an Equal Employment Opportunity employer, and women and minority candidates are strongly encouraged to apply. CV & letter to Susan Lewis, Department of Psychiatry, 1493 Cambridge Street, Cambridge, MA; Fax: 617-665-1204. **Email preferred: SLewis@challiance.org.**

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

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Starr Psychiatric Center seeks a 20-30 hr psychiatrist for dynamic established psychiatric practice On Boston's South Shore. Medical model, multi-disciplinary staff. Stimulating environment, good pay. Clinic has a reputation for successful care, where others have failed. Email davidzstarr@juno.com or call 508.580.2211.

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 lymouth, 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.

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 or 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.

Associate Director, Division of Child and Adolescent Psychiatry
University of Massachusetts Medical School
UMass Memorial Health Care
Worcester, MA

The University of Massachusetts Medical School and UMass Memorial Health Care are recruiting for an Associate Director of the Division of Child and Adolescent Psychiatry due to an expansion of clinical, training, and research activities and goals. Candidates must be Board Certified in Child and Adolescent Psychiatry and have strong administrative and research experience. The Division has 20 Child and Adolescent Psychiatrists and 16 faculty from a range of other disciplines. Faculty work in a variety of settings, including Worcester State Hospital, Westborough State Hospital, Community Healthlink, Inc., E.K. Shriver Center (MR/DD), UMass Memorial Health Care, the Center for Mental Health Services Research (CMHSR), and the Brudnick Neuropsychiatric Research Institute. Areas of academic strength of the division include mental health services research, public sector, adolescent inpatient, continuing care, primary care integration, systems of care and intensive home and community-based services, addiction, psychopharmacology, mental retardation and developmental disabilities, juvenile justice/law and psychiatry, preclinical imaging and molecular research, trauma, and sexual abuse. The Division of Child Psychiatry oversees a large network of clinical services in Central MA, and is active in the Department's Mental Health Research Network throughout the State. There is a fully accredited child psychiatry residency, including an innovative combined adult/child psychiatry track.

The Associate Director position is supported by a competitive salary and excellent benefits. To apply, please send CV and letter of interest to Jean A. Frazier, MD, Vice Chair and Director, Division of Child and Adolescent Psychiatry, University of Massachusetts Medical School and UMass Memorial Health Care, 55 Lake Avenue N., Worcester, MA 01655 or e-mail: Jean.Frazier@umassmed.edu. AA/EOE

Central Massachusetts - The University of Massachusetts Department of Psychiatry is seeking BC/BE psychiatrists for part-time to full-time positions in our community mental health centers in Worcester and Leominster. Community HealthLink (CHL) is a dynamic organization providing services to those with mental illness, developmental disabilities and substance abuse (see www.communityhealthlink.org). Work with a dedicated multidisciplinary staff. CHL psychiatrists are part of our UMass faculty with opportunities for teaching and research. Please email psychiatryrecruitment@umassmemorial.org or fax to 508-856-5990. AA/EOE

Berkshire Health Systems: Seeks BE/BC Adult Psychiatrist with interest in inpatient and/or community mental health for an integrated mental health and substance abuse treatment network.

- Approved psychiatry residency program for 16 residents
- Hospital Employed position
- Excellent Compensation & Benefits, including relocation
- Support of a full spectrum of Behavioral Health Providers including a staff of 15 psychiatrists
- Academic appointment possible through teaching affiliation with UMASS medical school

Berkshire Medical Center, an affiliate of BHS, is located in the Berkshires of Western Massachusetts and is the region's leading provider of comprehensive healthcare services. A 302-bed community teaching hospital and Level II Trauma Center, BMC is a Major teaching affiliate of the University of Massachusetts Medical School, offering residency programs in Internal Medicine, Surgery, Pathology, Dentistry, and Psychiatry.

Berkshire Medical Center is ranked among the Top 5% in the nation and is a recipient of the 2009 Distinguished Hospital Award for Clinical Excellence from Health Grades.

The Berkshires are located just 2 ½ hours from Boston & New York City. Berkshire County is one of the most picturesque regions in the nation and is known for its cultural and recreational; opportunities. For more information, please contact: Catherine Sommers, (413)395-7673, csommers@bhs1.org. www.berkshirehealthsystems.org

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CAMBRIDGE: Outpatient Psychiatry

OUTPATIENT PSYCHIATRIST: Cambridge Health Alliance is seeking a half-to-full-time psychiatrist, preferably with added qualifications in addictions, to join our outpatient service with integrated addictions and dual diagnosis programs serving a multi-ethnic and diverse patient population. The Department of Psychiatry at Cambridge Health Alliance is an appointing department at Harvard Medical School. Our public health commitment to improving the health of our communities, coupled with a strong academic tradition, make this an ideal opportunity for candidates interested in caring for underserved populations in a rich clinical environment. We have strong adult and child residency training programs which provide opportunities for teaching. Academic appointment, as determined by the criteria of Harvard Medical School, is anticipated.

Qualifications: BE/BC, demonstrated commitment to public sector populations, strong clinical skills, strong leadership and management skills, team oriented, problem solver. Bilingual and/or bicultural abilities are desirable. Experience with dual diagnosis and substance use disorders, and Suboxone certification. We offer competitive compensation and excellent benefits package. Cambridge Health Alliance is an Equal Employment Opportunity employer, and women and minority candidates are strongly encouraged to apply. CV & letter to Susan Lewis, Department of Psychiatry, 1493 Cambridge Street, Cambridge, MA; Fax: 617-665-1204. Email preferred: SLewis@challiance.org.

MICHIGAN

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

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Medical Director - Seeking Psychiatrist for clinical and part-time administrative responsibilities on adult psychiatric unit in a medical facility that houses behavioral health, extended care, and medical rehabilitation in Saginaw, MI. 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@psysolutions.com.

ADDICTION PSYCHIATRIST NEEDED

The **University of Michigan Department Of Psychiatry** is seeking a full-time, board-certified or board-eligible addiction psychiatrist for a tenure stream, academic track appointment in its Substance Abuse Section. Although the position is currently listed at the assistant professor level, applicants at all ranks will be considered. Candidates with a strong background in either neurobiology of addiction or in clinical trials research are especially encouraged to apply. Applicants should have a record of peer-reviewed publication and early programmatic research activity that indicates promise for research funding at the national level. In addition to the research involvement, professional activity will include direct outpatient care with the University of Michigan Addiction Treatment Services (UMATS), the Section's clinical treatment facility, as well as teaching psychiatry residents, medical students, and addiction psychiatry fellows. This position provides an outstanding research environment for an academic track career with a highly productive and collaborative faculty. The Section is home to more than a dozen faculty and research scientists. Its Addiction Research Center is currently the base for over 20 projects focused on the etiology, course, treatment, and outcome of substance abuse disorders; moreover, substance abuse research accounts for more than 40 percent of the department's total research activity. The Section has two NIH post-doctoral/post-residency research training programs, an ACGME certified Addiction Psychiatry Training program, and exceptionally strong collaborative relationships both within the Medical School and with other segments the University community. The University of Michigan is an equal opportunity employer.

Please send letter of interest and C.V. to:
Robert A Zucker, PhD
Director, Substance Abuse Section and
Addiction Research Center
Department of Psychiatry
University of Michigan
Rachel Upjohn Bldg, Campus Zip: 5740
4250 Plymouth Rd
Ann Arbor, MI 48109-2700
734-232-0280

Email: shauncie@med.umich.edu

A Non-Discriminatory, Affirmative action Employer

Horizon Health seeks an **Associate Medical Director** for a 15-bed Adult Inpatient Psychiatric Program in **Alpena, MI.** Enjoy your practice in a state-of-the-art, 146-bed acute care facility with nearly 100 physicians, over 900 employees and approximately 300 volunteers. Federally-designated as a rural Regional Referral Center for all of Northeastern Michigan.

Practice opportunity includes easily attainable income of up to **$240-265K,** inclusive of salary and call reimbursement. In addition, **Productivity Bonus, Sign-On Bonus** and **Loan Repayment** included!

Alpena overlooks Lake Huron's picturesque Thunder Bay in northern Michigan, and is located on the Sunrise Side Coastal Highway, a 200-mile stretch of US 23 graced with scenic views, undeveloped wild areas, roomy beaches and recreational areas for hiking, biking, cross-country skiing and snowmobiling. Great place to raise a family and excellent quality of life! Contact: Mark Blakeney, Horizon Health, 972-420-7473, fax CV: 972-420-8233, or email mark.blakeney@horizonhealth.com. EOE.

MINNESOTA

Improve the quality of life for everyone, including yourself!

Brainerd Lakes Health is currently seeking a **BE/BC General Psychiatrist** to see patients in both our 22 bed inpatient unit as well as our outpatient clinic. Our facility is located in the beautiful northern woods of Brainerd Minnesota, just 2 hours north of the Twin Cities! Enjoy excellent outdoor recreation year round and the conveniences of a big city with none of the traffic. For more information or to apply please forward CV to Ryan.berreth@brainerdclinic.com or call 218-454-5800.

MISSOURI

KANSAS CITY, MISSOURI...FT BC/BE psychiatrist needed in prominent, established private practice in North KC. Large referral base of 10-15 new patients daily. Combined office and hospital consult-liaison duties. Shared call, 1 wk out of 4, with our experienced and professional team of 3 psychiatrists. Salary, bonuses and benefits are offered. Interested parties fax cover letter and CV to 816-454-3601, e-mail to thill@kcnps.com, or call Todd Hill, DO at 816-453-6777.

Close to Springfield - Inpatient and outpatient work in a very impressive general hospital in southwest MO. Strong hospital support for behavioral health. Unit is a 10-bed geropsychiatric program. Can offer salary w/benefits, or income guarantee, or contract with local physician's practice. Please **call Terry B. Good at 1-804-684-5661,** Fax #: 804-684-5663; Email: terry.good@psysolutions.com.

MONTANA

Horizon Health invites you to consider an exciting new practice opportunity for two NEW distinct **Adult** and **Geriatric** Inpatient Psychiatric Units, comprised of **26** total beds in **Helena, MT.** Nestled beneath the foothills of the Montana Rockies, **Helena,** the Capital of Montana, is alive with history and culture. This charming and beautiful Victorian city of 70,000 people provides a diverse attraction with many street festivals, theater, museums, symphonies, fairs and rodeos. There is truly something for everyone here! Excellent practice opportunity with great income ($200K+) and unparalleled quality of life! For more information contact: Mark Blakeney, Voice: 972-420-7473, Fax: 972-420-8233; email: mark.blakeney@horizonhealth.com EOE.

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.

NEW JERSEY

P/T Adolescent/Adult Psychiatrist for small non-profit counseling center-6 hours per week - providing psychiatric evaluations and medication monitoring. Please send CV to: Irvcounseling@aol.com or Irvington Counseling Ctr, 21-29 Wagner Pl, Irv, NJ 07111 or fax to 973-399-7552

NEW MEXICO

Presbyterian Healthcare Services (PHS) in New Mexico has openings in general adult and child/adolescent psychiatry. PHS is New Mexico's largest private, non-profit integrated healthcare system. The Behavioral Medicine Program is a full-service psychiatry department covering inpatient and outpatient care, intensive outpatient treatment, emergency and consultative psychiatry and mental health services embedded in primary care. These are full-time employed positions with the 500+ provider Presbyterian Medical Group. PHS provides competitive salary and benefits including malpractice insurance and relocation allowance. Additional information about PHS can be found at www.phs.org.

Contact: Susan Camenisch, Physician Recruiter, PHS
E-mail: scamenisc@phs.org
Phone: 1-866-742-7053

NEW YORK CITY & AREA

Geriatric Psychiatrist

The Department of Psychiatry at The Mount Sinai Medical Center in the heart of NYC, has an opening for a Geriatric Psychiatrist beginning July 1, 2009. The position includes patient care on our 21-bed inpatient geriatric psychiatry unit and our ECT service, supervision of residents and fellows and opportunities for teaching and clinical research. The position will include an academic appointment commensurate with experience. Qualified candidates will possess an MD or DO degree, be board-eligible or certified in General Adult Psychiatry and preferably have advanced training in geriatric psychiatry. The Mount Sinai Medical Center is a premier 1,171-bed tertiary-care facility internationally acclaimed for excellence in clinical care, education and scientific research in nearly every aspect of medicine.

Interested applicants should contact Dr. Charles Kellner, Chief of the Division of Geriatric Psychiatry and Director of the Electroconvulsive Therapy Clinical Service at 212-659-8285 or email charles.kellner@mssm.edu.

FULL-TIME PSYCHIATRIST: EXCELLENT OPPORTUNITY for a general or geriatric psychiatrist available at The Long Island College Hospital in brownstone Brooklyn, one step from Manhattan over the Brooklyn Bridge. This BC/BE psychiatrist will be a member of an active inpatient 39 bed unit. We offer a competitive salary/benefit package. We're looking for highly motivated and committed physician. 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.

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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Consult Liaison Psychiatrist

The Department of Psychiatry at The Mount Sinai Medical Center in the heart of NYC, has an opening for a CL Psychiatrist beginning July 1, 2009. The position includes both inpatient and outpatient consultation liaison work, supervision of residents and fellows and opportunities for teaching and clinical research. The position will include an academic appointment commensurate with experience. Qualified candidates will possess an MD or DO degree, be board eligible or certified in General Adult Psychiatry and preferably have advanced training in Psychosomatic Medicine. The Mount Sinai Medical Center is a premier 1,171 bed tertiary-care facility internationally acclaimed for excellence in clinical care, education and scientific research in nearly every aspect of medicine.

Interested applicants should contact Dr. Kim Klipstein, Director of Behavioral Medicine and Consultation Psychiatry at 212-659-8712 or email kim.klipstein@mssm.edu.

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.

The Brookdale University Hospital and Medical Center

Major teaching hospital in Brooklyn is looking for BE/BC Adult psychiatrists to work in their inpatient, outpatient and CPEP areas. Also looking for a nurse practitioner for their outpatient and CPEP. Excellent salary and benefit package recently upgraded. Academic involvement with adult residency program. Faculty appointment with affiliated medical schools depending on qualifications. Forward CV to Dinshaw Bamji MD, Associate Chair, Department of Psychiatry to fax number (718) 240-5986 or e-mail dbamji@brookdale.edu

NEW YORK STATE

PSYCHIATRIST

An established and progressive private practice located in Albany, NY is seeking a N.Y.S. Certified Psychiatrist for an adolescent and adult outpatient program with flexible hours available. Excellent weekly salary and full administrative services included, in a warm and pleasant ambience. Insurance panel a plus. Please forward your C.V. to: pinbill@nycap.rr.com

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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

NORTH CAROLINA

Private Practice Opportunities in North Carolina

Carolina Partners in Mental HealthCare, PLLC is seeking BE/BC psychiatrists for our practices in Raleigh, Cary, and Wake Forest, NC. Child/adolescent and/or adult psychiatrists welcome. Private outpatient practices, full partnership from day one - no investment required. FT, PT flexible. Carolina Partners has ten offices in Raleigh, Durham, Cary, Chapel Hill, Pittsboro and Wake Forest, North Carolina. Good opportunity to control your life and clinical practice, while making a good income! Contact Executive Director or send CV to: Carolina Partners in Mental HealthCare, 1502 W. Hwy 54, Suite 103, Durham, NC 27707. Phone 919-967-9567; Fax 919-882-9531; Email carolinapartners@bellsouth.net. Please visit our website located at carolinapartners.com

OHIO

Attractive Salary with Benefits Plus Generous Sign-on Bonus - 30 minutes from Dayton suburbs - easy drive to Indianapolis - Expanded adult and geropsych services in an extremely impressive med/surg hospital (gorgeous new facility). Join top-notch medical staff. Services include inpatient, outpatient and IOP. Please call **Terry B. Good at 1-804-684-5661,** Fax #: 804-684-5663; Email: terry.good@psysolutions.com. EOE

COLUMBUS, OHIO
Mount Carmel Health, the second largest hospital system located in Columbus, Ohio, is seeking a 5th staff psychiatrist for the hospital system. This position provides a variety of patient care opportunities, from a 20 bed adult/geriatric inpatient unit to outpatient appointments. The adult psychiatric unit in the Mount Carmel West facility houses behavioral health, extended care; and medical rehabilitation.

Please consider these career advantages:
- Hospital employment.
- Growing base of primary care physicians.
- CNS nurses
- Call 1:5
- Medical student and resident teaching opportunities.
- Outpatient office located on the hospital campus.
- Very attractive compensation and benefit package.

Mount Carmel is a great place to expand your professional career and Columbus is an ideal place to live and raise a family. For more information, please contact:
Julie Hotchkiss, Manager Physician Recruitment; 614-546-4398 or jhotchkiss@mchs.com.

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

Ohio Valley General Hospital is seeking an experienced psychiatrist on a casual basis to work with top regional physicians to prevent, diagnose, and treat mental disorders.

Under direction of hospital physicians, but with independent responsibility for professional results, the selected candidate will provide psychiatric, diagnostic and therapeutic services to hospital patients and also perform related duties as required. The selected candidate will be required to skillfully diagnose and treat severely and persistently mentally ill patients, analyze situations and adopt an effective course of action, establish and maintain effective working relationships with others and maintain objectivity and confidentiality.

The position will additionally require individual and group psychotherapy, administration and interpretation of projective tests, participation in staff conferences and assisting in developing and organizing a program of clinical treatment. The selected candidate should also have experience with direct case conferences and may serve as a consultant to other clinical staff. The candidate may also be expected to confer with patients' relatives regarding illness and treatment.

About Ohio Valley

Ohio Valley General Hospital has been proving the Pittsburgh area with high quality care for more than 100 years and has recently been voted the best hospital in the western Pittsburgh suburbs by the readers of the Pittsburgh Tribune Review. Ohio Valley was also awarded the Exceeding Patient Expectations Award from Avatar International for the seventh consecutive year. For more information, visit www.ohiovalleyhospital.org.

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 - Bucks County. Also weeknight & weekend moonlighting shifts available on inpatient services.
CLARION (Western PA) and SHIPPENSBURG (near Harrisburg) - General Psychiatrists for Adult inpatient & partial program services. Salary, benefits and incentive plans. Contact Joy Lankswert @ 866-227-5415; OR email joy.lankswert@uhsinc.com

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Board certified/eligible general psychiatrist sought for immediate opening in private practice. Located in Pocono Resort area of N.E. PA-fast access to NYC & Phila. Excellent starting salary & benefits. Email CV: ISL6187@PTN.net or fax to 570-424-6271. Attn: Kathie Walsh, Practice Administrator.

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.

Erie, Pennsylvania
Practicing Psychiatrists for the position of Psychiatry Residency Program Director. Child/Adolescent, Adult and Geriatric Psychiatrists positions are available. Fellowship Trained Geriatric Psychiatrist preferred for the Gero Unit. Millcreek Community Hospital has the region's only Adult and Child/Adolescent Behavioral Program with 62 inpatient psychiatric beds including a new geriatric unit. Interested candidates for the Residency Program Directorship must be Board Certified by the AOA in Psychiatry. Candidates for other staff psychiatry positions must be AOA or AMA Board Certified or Board Eligible. Please send CV's and information requests to: mchmeded@mch1.org or call 814/868-8217.

Great Opportunities!! Outpatient, Telepsychiatry, Inpatient Gero-psychiatric unit, Child/Adolescent and Adult Psychiatrists: Positions available in the scenic Laurel Highlands of Southwestern Pennsylvania (60 minutes SE of Pittsburgh/3 hours NW of D.C.). Join team of 11 psychiatrists in a progressive community-based behavioral health program. Full time and part time positions. Treatment provided in concert with a team of PA's, CRNP's, certified psychiatric nurses and professional counselors. Crisis intervention team provides 24/7 on-call coverage. Competitive salary and excellent benefit package. J-1/H-1 positions available. Please forward CV to: Mike Quinn, CEO, Chestnut Ridge Counseling Service, Inc., 100 New Salem Rd, Uniontown, PA 15401 Fax:724-439-2779. Email: mquinn@crcsi.org. To learn more about Chestnut Ridge Counseling please visit our website at www.crcsi.org.

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

AIKEN near Augusta, GA: General Psychiatrist. **Predominant outpatient** with small inpatient caseload. Fulltime position - salary, benefits & incentive plan. Contact Joy Lankswert @ 866-227-5415 or email joy.lankswert@uhsinc.com

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

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EAST TENNESSEE STATE UNIVERSITY
JAMES H. QUILLEN COLLEGE OF MEDICINE
DEPARTMENT OF PSYCHIATRY & BEHAVIORAL SCIENCES

GENERAL PSYCHIATRIST AND CHILD PSYCHIATRIST

Full-time position available for General Psychiatrist. Additional fellowship training desired, but not required. Position may include inpatient and/or outpatient. Responsibilities include training of psychiatric residents and medical students and research activities. Salary is competitive with funding available through the Medical School, faculty private practice and extramural contracts. ETSU is located in the Tri-Cities area, rated #1 place in North America in cost-of-living, crime rate, climate and health care. **Applicants should submit a CV and two letters of reference to Merry N. Miller, M.D., Chair, Department of Psychiatry and Behavioral Sciences, ETSU, Box 70567, Johnson City TN 37614. Telephone inquiries should be made at (423)439-2235 or e-mail at lovedayc@etsu.edu. AA/EOE.**

TEXAS

AUSTIN: Child Psychiatrist - Residential Treatment Center. **Employment - salary & full benefits.**
DALLAS: In-house Night Physician. Monday - Thursday or will consider individual nights. Independent contractor compensation. Physician suite for accommodations.
WEST TEXAS San Angelo: Great private practice opportunity. Income guarantee & practice overhead support. Busy practice from start. Contact: Joy Lankswert @ 866-227-5415 or email joy.lankswert@uhsinc.com

VIRGINIA

MEDICAL DIRECTOR

The **Northern Virginia Mental Health Institute,** a 129-bed Joint Commission accredited facility located in Fairfax County, is seeking a Board Certified **Medical Director** to provide leadership to a dedicated group of psychiatrists who lead interdisciplinary treatment teams. Our inpatient facility offers the highest quality behavioral healthcare for adults requiring acute, forensic and psychosocial rehabilitative services. As a leader and innovator in the delivery of mental health services, we are seeking an individual interested in collaborating with a cohesive leadership team to implement and contribute to evidence based practice. The position offers diverse clinical and administrative opportunities to influence the quality of care including medical staff committee chairmanships, performance improvement initiatives, teaching affiliations with medical education institutions and participation in regional planning partnerships. We are located minutes from Washington, DC and close to Virginia beaches. Virginia licensure to practice medicine as well as a federal license to prescribe medications required. Certification in psychiatry by the American Board of Psychiatry and Neurology required. Clinical experience in hospital psychiatry strongly preferred with some familiarity with forensic psychiatry. Past administrative experience in hospital psychiatry preferred. Experience supervising clinical and non-clinical departments preferred. Position is open until filled.

We offer a competitive salary, a state benefits package which includes health insurance, life insurance, malpractice insurance, a generous leave package and a retirement program along with other outstanding benefits. For consideration, please submit a completed Commonwealth of Virginia application (http://jobs.agencies.virginia.gov). Please visit the Career Opportunities page on our website at www.nvmhi.dmhmrsas.virginia.gov for more information. EOE

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 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. Contact Dan Darby, MD at Tel: (757) 425-5050 Fax: (757) 425-1389.

BON SECOURS MEDICAL GROUP
Bon Secours Richmond Health System

Good People
Are Called to Serve

General Psychiatrist - Hospitalist
Richmond, Virginia

Bon Secours Richmond Health System, located in historic Richmond, Virginia is growing its Behavior Health service line and seeking to add a Psychiatric Hospitalist position with Medical Director and/or Associate Medical Director responsibilities to our world class health system.

The position will be located at Richmond Community Hospital and will have primary responsibility for the expansion and development of the product line as well as psychiatric consultative service throughout the system. Call is currently shared with community psychiatric colleagues.

Bon Secours Richmond Health System is a member of Bon Secours Health System, Inc., a national Catholic health care system with a healing ministry that serves 15 communities in nine states throughout the United States. Bon Secours Richmond operates four award-winning hospitals in Central Virginia - Richmond Community Hospital, St. Mary's Hospital, Memorial Regional Medical Center, and St. Francis Medical Center - two of which provide acute inpatient psychiatric services. Bon Secours Richmond is one of metropolitan Richmond's largest employers with more than 6000 employees.

In return for your compassionate character and commitment to providing the best care possible, we'll reward you with a generous compensation package, including competitive salary, pension, excellent medical insurance, dental coverage, life insurance, relocation assistance and allowances for professional membership dues and CME reimbursements.

To submit CV on-line, please visit www.bonsecoursmedicalgroup.com/careers, or for more information, please contact:

David C. Coon
Physician Recruiter
Bon Secours Richmond Health System
(Office) 804.281.0294
David_Coon@bshsi.org

WASHINGTON

University of Washington Dept of Psychiatry & Beh. Sciences and Harborview Medical Center are seeking a part-time psychiatrist to work in the Psychiatric Emergency Services (PES). The coverage is shared among several psychiatrists who work under the supervision of the PES Medical Director. The position will receive a UW clinical faculty appointment. The PES attending psychiatrists provide direct evaluation, triage and acute treatment to patients, and overall supervision of the clinical team, including residents. The highly competitive pay scale due to shift work and off-hours schedule has recently been increased further. HMC has a nationally recognized psychiatric emergency service and strives to deliver state of the art care in an academic medical setting. Please forward your letter and CV to: Peter Roy-Byrne, MD, Box 359911 Psychiatry HMC 325 9th Avenue, Seattle 98104 or email to lsd1@u.washington.edu. The UW is building a culturally diverse faculty and strongly encourages applications from females and minority candidates. The UW is and EOE/AA employer. University of Washington faculty engage in teaching, research, and service.

WEST VIRGINIA

PSYCHIATRIST-West Virginia University School of Medicine, The Department of Behavioral Medicine and Psychiatry, has ongoing opportunities and faculty positions for full-time 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.

WISCONSIN

Psychiatrist Supervisor
Taycheedah Correctional Institution
Fond du Lac, Wisconsin

Up to $226,000
Outstanding Benefits, No Call, No Weekends

Taycheedah Correctional institution is the primary facility for incarcerating female offenders in the state of Wisconsin. This newly-created position will split time between supervision of 5 part-time psychiatrists and provision of clinical services to female offenders. Desirable qualities include board certification, correctional and supervisory experience. This position provides the opportunity for program development and participation in quality improvement activities.

As a full time state employee this position has an outstanding benefits package. Benefits include paid vacation, 36 hours personal holiday, 16 sick days per year, health insurance ($78/month in most cases for family plan), ability to convert sick leave to pay for health insurance on retirement, retirement plan currently at 11.2% annually, medical liability covered by the state, moving and relocation expenses available, and optional deferred compensation program available.

Fond du Lac is a lakeside community located about 70 miles from downtown Milwaukee and 75 miles from Madison Wisconsin.

For further information, contact Dr. Molli Rolli at Martha.rolli@wisconsin.gov

For a detailed job description and application information, please see: http://www.wi-doc.com/index_employment.htm

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Fellowships

University of Michigan Addiction Psychiatry Fellowship

The Addiction Psychiatry Fellowship Program is a one-year, post-residency, clinical training program for psychiatrists interested in addiction psychiatry. The program is accredited by the Accreditation Council for Graduate Medical Education, and successful completion of the 1-year clinical track qualifies psychiatrists to apply for subspecialty certification in addiction psychiatry from the American Board of Psychiatry and Neurology. Qualified applicants will have completed (before starting the fellowship) an accredited psychiatry residency in the U.S. and have passed all necessary examinations to obtain a physician's license in the State of Michigan. Training licenses will not be accepted. Applicants with J1 visas will be considered. Information: http://www.med.umich.edu/psych/education/addiction/, or Carol Skala, Program Coordinator, 734-232-0294.

Boston University Medical Center Fellowship Program in Psychosomatic Medicine

Boston University Medical Center is seeking applicants for its **ACGME-accredited Fellowship Program in Psychosomatic Medicine** for July 1, 2010. All participating fellowship programs are Equal Opportunity Employers.

Fellowship Program in Psychosomatic Medicine: This is a 12-month program, which provides extensive training in Psychosomatic Medicine at both Boston Medical Center and the VA Boston Healthcare System. Fellows will have the opportunity to work with a diverse patient population in both acute medical/surgical inpatient and outpatient settings. In addition to providing consultation and teaching to the medical staff, fellows are involved in a variety of educational experiences and have the opportunity to pursue research interests. This one-year program meets all requirements for Board Examination eligibility for Added Qualifications in Psychosomatic Medicine. Interested applicants should send CVs to: Dr. Isidore Berenbaum, M.D., Boston Medical Center, Suite B-410, 88 East Newton St., Boston, MA 02118 **Tel: 617-638-8670 Fax: 617-638-8724 Email: bbq@bu.edu**

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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

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