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Newspaper of the
American
Psychiatric
Association

PSYCHIATRIC NEWS

Inside

PERIODICALS:
TIME-SENSITIVE MATERIALS

Credit: Maureen Keating

Col. Elspeth Cameron Ritchie, M.C., psychiatry consultant to the U.S. Army surgeon general, addresses the mental health needs of members of the military during the annual Mental Illness Awareness Week symposium sponsored by APA and NAMI last month in Washington, D.C. See article below.

Too Few Clinicians Complicate Care in VA, Military Systems

The stigma of mental illness remains a strong deterrent to treatment in the military. New efforts are under way, however, to eliminate this barrier.

BY RICH DALY

A continuing critical shortage of psychiatrists and psychologists in the armed forces and access to quality mental health care for veterans in rural areas are issues that must be addressed now, mental health leaders told members of Congress and their staffs last month.

Military and veterans officials and others identified key concerns in the treatment of mental illness during the 2007 Mental Illness Awareness Week Congressional Symposium, jointly sponsored by APA and the National Alliance on Mental Illness (NAMI). The Capitol Hill briefing described the progress made in identifying and treating mental illness among active-duty and veterans groups, as well as the significant work that remains.

"We have to be realistic that when we send men and women to war zones, we are placing them at great risk for developing psychiatric disorders," said Daniel Blazer, M.D., Ph.D., a psychiatrist and member of the Department of Defense Mental Health Task Force, which recently concluded its work with the release of a report on the need to improve mental health services for members of the military and their families (*Psychiatric News*, August 3). "If we don't pay attention to their mental health, then we are closing our eyes to the real-life cost of sending them to war."

The risk of developing mental illness as a result of combat exposure is as real as the risk of incurring physical injuries, and the government needs to be ready for that eventuality, he said. At this point the military is falling short of that commitment to provide sufficient care.

Blazer and others cited a shortage of psychiatrists and psychologists in the armed forces as the leading obstacle to effective mental illness detection and treatment for those who serve in the Iraq and Afghanistan war zones.

His conclusion echoed the leading finding in the task force's report: "The Military Health System lacks the fiscal resources and the fully-trained personnel to fulfill its mission to support psychological health in peacetime or fulfill the enhanced requirements imposed during times of conflict." The task force urged more funding to retain existing personnel and to add more, so members of the military would have greater access to care.

please see ***Military*** *on page 22*

Local Collaboration Key to Success of Health Research In Poor Countries

Conducting medical research and public health programs in underprivileged countries poses ethical and cultural challenges. An international group issues a list of key concerns.

BY JUN YAN

A summary of major ethical, social, and cultural issues in conducting scientific research and promoting technologies in developing countries provides a framework to help guide large-scale global research and health initiatives, especially those conducted in developing countries.

The Ethical, Social, and Cultural (ESC) program, a component of Grand Challenges in Global Health (GCGH), a large, nonprofit, international project aimed at "solving critical health problems in the developing world," highlights 13 major issues that can arise in conducting health research and public health initiatives in developing countries. The program, based at the University of Toronto in Canada, has gathered a group of international bioethics experts and researchers to advise and assist in GCGH's efforts throughout the world. Four articles on the ESC program, including a summary of issues, are published in the September

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Parents Can Get Expert Advice On Treatment of ADHD

A medication guide on attention-deficit/hyperactivity disorder provides the lay public with not only information regarding drug therapy but also advice on monitoring symptoms.

BY JUN YAN

The American Academy of Child and Adolescent Psychiatry (AACAP) and APA have issued a new medication guide for parents and guardians of children with attention-deficit/hyperactivity disorder (ADHD).

The guide contains an overview of the symptoms and neurological basis of the disorder and detailed explanations about the types, effectiveness, and side effects of ADHD medications. The guide also covers possible comorbidities, psychosocial and behavioral interventions for the disorder, and other resources such as readings for parents and children.

The guide's safety section addresses many parents' concerns about the side effects and risks of ADHD medications and summarizes clinical evidence in an easy-to-understand format. The guide is available in English and Spanish.

At the press conference to announce the guide's release, Adelaide Robb, M.D., a child psychiatrist at Children's National Medical Center in Washington, D.C., commented that this guide will be helpful to psychiatrists because it gives parents a better picture of ADHD symptoms and the effects of treatment, so that when children are referred to a psychiatrist, the parents can educate themselves and are better prepared to ask questions. She pointed out that the guide is also informative to adolescents and young adults who are diagnosed with ADHD and are seeing psychiatrists for the first time.

"Most ADHD patients are seen and evaluated by primary care providers," Read Sulik, M.D., medical director of the Child and Adolescent Psychiatry Department at St. Cloud Hospital's Behavioral Health Services in Minnesota, said at the press conference. An average visit is so short that most primary care providers have little time to provide adequate education and background information to parents and patients. "This guide provides a tool to assist the providers in engaging the parents and empowering [them] with consistent and sound information about ADHD and treatment options," he said.

"Millions of American children and adolescents live with ADHD," said Thomas Anders, M.D., AACAP president. "The ADHD medication guide is a user-friendly resource that will help parents make informed decisions for their children."

"Medication Guide for Treating ADHD" is posted at <www.parentsmedguide.org/pmg_adhd.html>. ■

Priority Hotel Reservations For APA Members

Beginning Tuesday, December 4, and throughout the month of December, APA members will have an exclusive opportunity to make their hotel reservations for the 2008 annual meeting in Washington, D.C. Nonmembers who plan to attend the meeting will not be able to make their hotel reservations until Wednesday, January 2, 2008.

Information on hotels and a link to reserve a room will be accessible under Members Corner on APA's Web site at <www.psych.org>. To log on, you will need your APA membership number. Traditionally, Washington, D.C., has been a popular location for the annual meeting, so you are encouraged to make your hotel reservations as soon as possible.

More information is available by calling Vernetta Copeland at (703) 907-7382.

APA RESOURCES

- ***Psychiatric News* Web Site:** pn.psychiatryonline.org/
- **APA and the APA Answer Center:** (888) 35-PSYCH in the U.S. and Canada; in other countries: (703) 907-3700. The Answer Center is open Monday through Friday, 8:30 a.m. to 6 p.m. Eastern time. All APA departments and staff may be reached through the Answer Center. Fax: (703) 907-1085 E-Mail: apa@psych.org
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Returns Are Immeasurable When You Invest in APA's Foundation

BY CAROLYN ROBINOWITZ, M.D.


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There are many ways we can put our collective voices into action for our profession and for our patients. We can contribute *work*, *wisdom*, *and wealth*. In previous columns, I have focused on advocacy—how we can *work* using our *wisdom* and experience to inform policymakers, professionals, and the public about mental illness and psychiatric care. We are seeing results in terms of greater public understanding and diminution of stigma, but there is still much to do.

The simplest contribution of wealth is paying dues—providing resources that fund APA advocacy actions and multiplying our impact. I am pleased that APA national dues have not been increased for more than a decade, thanks to superb financial planning and management from our Finance and Budget Committee, secretary-treasurer, and APA staff.

There is another important way we can contribute. The American Psychiatric Foundation (APF), the philanthropic subsidiary of APA, through its many charitable programs, promotes public awareness of mental illnesses, the importance of early intervention and access to care, and the need for high-quality services and treatment. The APF is entirely self-supporting, with all initiatives funded through contributions.

What are some APF programs? How are our contributions used?

The Typical or Troubled? School Mental Health Education Program is a school-based mental health education program that addresses the gap between recognition of mental illness and appropriate diagnosis and treatment in young adults *(Psychiatric News*, February 2). It includes school-personnel training and brochures and other educational materials that can be customized for local schools. The program has been replicated in 73 high schools nationwide through a partnership with the American School Counselors Association, School Social Workers of America, and Mental Health America, and we anticipate expanding the program to 25 additional sites in 2008.

The Helping Hands Grant program was established to encourage medical students to participate in community-service activities, particularly for underserved populations; raise awareness of mental illness including the importance of early recognition; and build students' interest in psychiatry. It provides grants of up to $5,000 to medical schools for mental health service projects that are created and managed by medical students, particularly in underserved minority communities *(Psychiatric News*, April 21, 2006).

The APF continues to be an active member of the Depression Is Real Coalition (DIR), which promotes awareness that depression is a real and treatable medical illness. APA members continue to be featured guests and hosts of the DIR weekly podcasts, which are available on the DepressionIsReal.org Web site and via iTunes. Dr. Altha Stewart, the APF president, led a panel on depression and minorities at the recent Congressional Black Caucus Foundation Braintrust.

The APF Awards for Advancing Minority Mental Health recognize psychiatrists, other health professionals, mental health programs, and other organizations that have undertaken innovative and supportive efforts to raise awareness of mental illness in underserved minority communities; address the need for early recognition, the availability of treatment, and how to access it; and cultural barriers to treatment. This recognition promotes access to quality mental health services, particularly for those with the most severe mental illness who seek care in the public health system *(Psychiatric News*, July 6).

The Partnership for Workplace Mental Health was described in detail in my column in the October 19 issue; it promotes the business case for quality mental health care and advances effective employer approaches to improving the mental health of their employees by combining the knowledge and experience of APA and its employer partners through educational materials and forums.

The High School/College Transition Program is a collaborative effort between the APF and the JED Foundation to provide education about the early warning signs of mental illness and adherence to treatment in young people transitioning from high school to college. Still in development, the program plans to target parents, school administrators, and mental health organizations located in college towns, as well as young adults.

The APF is poised for even more successes in 2008. Under the leadership of its newly appointed executive director, Paul Burke (see page 13), the APF seeks to enhance and expand the impact of existing programs and enrich partnerships to proliferate the APF mission. Former APA President Richard Harding, M.D., will also be assuming his new leadership role as APF president in January.

Donating to the APF is a wonderful way to invest in mental health education, improve public awareness, and support access to quality care. Please honor our life's work through your tax-deductible contribution.

For more information, please contact Lindsey McClenathan by e-mail at LMcClenathan@psych.org or by phone at (703) 907-8503. ■

VA Told to Establish Multiple Suicide Prevention Programs

Suicide prevention legislation advances in the Senate only after removal of a requirement that health officials track veterans identified as at risk for future mental illness.

BY RICH DALY

The Senate has approved legislation to help prevent suicide among veterans returning from war and those long retired from military service.

The bill (HR 327), titled the Joshua Omvig Veterans Suicide Prevention Act, passed the Senate unanimously in September; the House passed its version in March.

The bill requires the VA to develop and implement a comprehensive program to reduce the incidence of suicide among veterans, including the availability of 24-hour mental health care for veterans thought to be at risk for suicide. It also calls for development of an outreach and education program for veterans and their families to help them recognize readjustment problems and promote good mental health.

In addition, the legislation would provide mandatory suicide prevention training for all VA personnel involved in medical care, including how to recognize the risk factors for suicide and the best practices for suicide prevention.

The legislation also would require that each VA medical facility designate suicide prevention counselors who would work with emergency rooms, police departments, mental health organizations, and veterans service organizations on outreach to veterans and improved coordination of veterans' mental health care.

The bill is named for Joshua Omvig, an Iraq War veteran who suffered from posttraumatic stress disorder and committed suicide in 2005.

The Senate bill included amendments to address objections raised by Sen. Tom Coburn (R-Okla.), who had placed a hold on the bill over provisions that would have allowed the Department of Veterans Affairs (VA) to track veterans who have been screened and identified as mental health risks through the bill's suicide prevention system. He derided the tracking provision as a violation of veterans' civil liberties and a danger to future job prospects.

"If, in fact, you have encountered the VA and because you were screened, not of your choice and not because you had signs or symptoms, . . .that becomes a part of your record," Coburn said in a written statement. "You automatically are limited in lots of things that you cannot do in this country."

That provision and another that would have mandated a VA peer-counseling program—criticized by Coburn as ineffective—were removed by amendment. The VA can choose to offer the peer-counseling program but not mandate it.

Some of the provisions in the bill mirror initiatives undertaken administratively by the VA in recent years, including the placement of suicide prevention coordinators in every VA medical center and establishment of a veterans-focused, 24-hour, suicide prevention hotline.

APA had lobbied for a provision to require that all returnees receive a mental health screening instead of only a mental health status exam, which does little to detect mental illness or risk for suicide, said Lizbet Boroughs, deputy director of APA's Department of Government Relations. However, despite the limitations imposed by the Senate amendments, the bill's supporters recognize that overall the legislation offers tremendous benefits.

"This is bipartisan legislation that will help ensure that our veterans receive the mental health care that they need," said Jerry Reed, executive director of the Suicide Prevention Action Network (SPAN USA), in a written statement. "Research shows us that male U.S. veterans are twice as likely to die by suicide than those without military service, making passage of the Joshua Omvig Veterans Suicide Prevention Act all the more critical."

The legislation also aims to destigmatize mental health care. Many veterans have expressed fear about problems that might stem from their voicing concerns about their psychiatric problems, including whether receiving mental health care would damage future job prospects in the

*please see **VA** on page 23*

People With Psychiatric Disability Could Face Benefit Restrictions

APA joins mental health and physical therapy advocates nationwide to urge CMS to drop part of a proposed rule on Medicaid rehabilitation services, challenging the agency's claim that the proposal is beneficiary friendly.

BY RICH DALY

Medicaid beneficiaries with chronic psychiatric disorders may lose their access to rehabilitative services under a proposed rule from the Centers for Medicare and Medicaid Services (CMS).

The proposed rule is part of revisions to regulations governing Medicaid rehabilitative services, proposed in August, that CMS says will strengthen beneficiary protections through "person-centered" written rehabilitation plans and maintenance of case records. The changes also are expected to have considerable cost savings for Medicaid, estimated by CMS officials to be about $180 million in the first year and $2.2 billion over the next four years.

The tightening of rehabilitative language was meant to keep non-Medicaid programs, such as local jails, from using Medicaid funds to provide benefits to people in programs "with a focus other than that of Medicaid," according to CMS.

"These facilities are under the domain of the juvenile justice or youth systems in the state, rather than Medicaid, and there is no assurance that the claimed services reflect an independent evaluation of individual rehabilitative needs," according to a CMS statement on the need for the rules changes. "This proposed [rule] is designed to clarify the broad general language of the current regulation to ensure that rehabilitative services are provided in a coordinated manner that is in the best interest of the individuals, are limited to rehabilitative purposes, and are furnished by qualified providers."

The proposed changes also would limit Medicaid reimbursement to those whose rehabilitation care is designed to return them to a higher level of functioning, as opposed to trying to improve the functioning of those who have always been impaired.

APA and other advocates maintain, however, that those changes would cut off some beneficiaries with chronic psychiatric disorders from receiving rehabilitative services through Medicaid.

In comments submitted to the agency in response to the proposal, APA urged CMS to broaden rehabilitative services language to include rehabilitative services for beneficiaries who do not have a previous higher level of function and for those who need the services just to maintain their current level of functioning.

"This concept is essential to a broad spectrum of beneficiaries who should receive Medicaid rehabilitative services, especially those with chronic psychiatric disorders," said APA Medical Director James H. Scully Jr., M.D., in an October 12 letter to CMS. "It is not always clear in advance who may experience functional improvement through access to these services."

"Those with chronic, serious psychiatric disorders may experience benefits from rehabilitative treatments that are improvements other than restoration of pre-existing functional levels," Scully stated.

APA and other mental health groups, including the U.S. Psychiatric Rehabilitation Association (USPRA), did commend CMS for some of the proposed changes such as the requirement that those who provide rehabilitation services develop rehabilitation plans and "recovery-oriented goals" for each beneficiary.

"The creation of a rehabilitation plan is good practice and is necessary for shared decision making and accountability," said Marcie Granahan, CEO of USPRA, in a letter to CMS.

The most effective approach for beneficiaries with serious, chronic psychiatric disorders is acute treatment along with ongoing rehabilitative services, Scully noted.

Another change sought by APA is clarification of language in the proposed rules that critics interpret as a categorical exclusion of Medicaid payment for "personal care services, transportation, [and] vocational and prevocational services." Scully suggested that such an interpretation should not be accepted by CMS, since it would be inconsistent with CMS's stated intent to allow Medicaid coverage for at least some such services related to rehabilitation.

The CMS rules also need language to require that physicians perform the mandatory "comprehensive assessment" of beneficiaries proposed by the rules, said Scully, with psychiatrists performing the psychiatric assessments, "especially where physical comorbidities are at issue."

"The better the assessment, the more well targeted the rehabilitation plan can be for maximum outcomes," Scully wrote.

The proposed rule was open to public comments until mid-October. There is no timetable for CMS to issue final regulations.

The proposed changes can be accessed at <www.gpoaccess.gov/fr/index.html> by selecting volume 72, pages 45201-45213. ■

Grants Will Improve Services for Homeless Mentally Ill

A new SAMHSA grant program will fund outreach, mental health, substance abuse, and other community-based services.

BY DAWN DUARTE

The Substance Abuse and Mental Health Services Administration (SAMHSA) announced on September 26 that it is awarding nine grants totaling almost $17.5 million over five years to organizations working to address issues arising from homelessness in their communities.

In particular, the initiative is targeted to entities that serve chronically homeless individuals with serious psychiatric conditions and those with co-occurring disorders who live in supportive housing. The grant funds are meant to improve residential stability and reduce psychiatric symptoms.

Specifically, the grants will seek to provide community programs with resources for outreach, intensive case management, housing retention, independent-living skills, motivational interventions, and crisis care. Other aspects of the program include, but are not limited to, resources to improve mental health treatment, including treatment for posttraumatic stress, co-occurring disorders, and substance abuse, and medication management.

Each grant recipient will receive up to $450,000 a year for up to five years, with an award-continuation option subject to both the availability of funds and progress achieved by the awardees.

A list of the SAMHSA grant awardees is posted at <www.samhsa.gov/newsroom/advisories/0709262959.aspx>. ■

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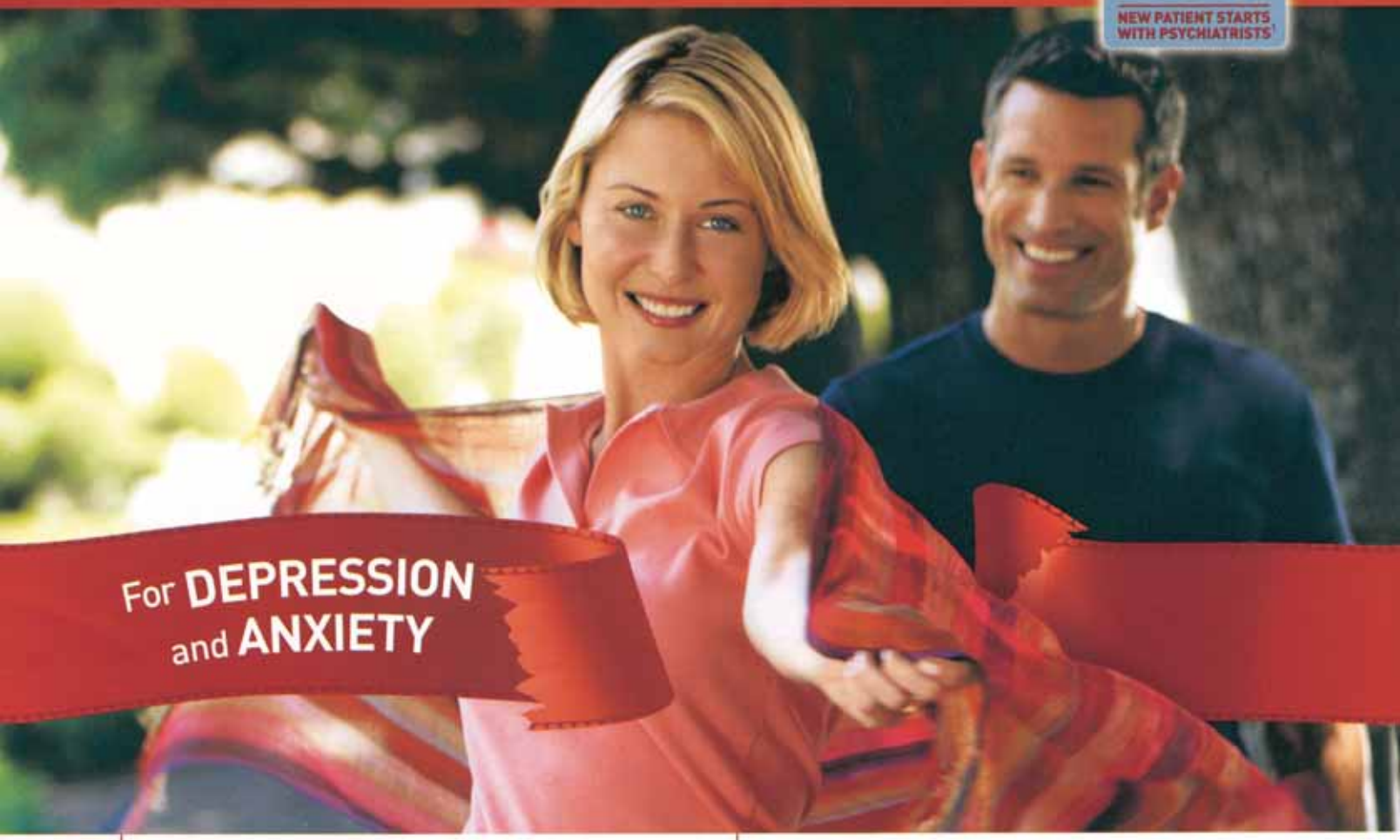

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Lexapro is contraindicated in patients taking monoamine oxidase inhibitors (MAOIs), pimozide (see DRUG INTERACTIONS – Pimozide and Celexa), or in patients with hypersensitivity to escitalopram oxalate. As with other SSRIs, caution is indicated in the coadministration of tricyclic antidepressants (TCAs) with Lexapro. As with other psychotropic drugs that interfere with serotonin reuptake, patients should be cautioned regarding the risk of bleeding associated with the concomitant use of Lexapro with NSAIDs, aspirin, or other drugs that affect coagulation. The most common adverse events with Lexapro versus placebo (approximately 5% or greater and approximately 2x placebo) were nausea, insomnia, ejaculation disorder, somnolence, increased sweating, fatigue, decreased libido, and anorgasmia.

References: 1. Verispan Weekly VONA Data (Retail Only). Twenty-four-week rolling average. September 2006. **2.** Sadock BJ, Sadock VA. *Kaplan and Sadock's Synopsis of Psychiatry: Behavioral Sciences/Clinical Psychiatry.* 9th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2003:552. **3.** LEXAPRO (package insert). St Louis, Mo: Forest Pharmaceuticals, Inc.; 2007.

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Brief Summary: For complete details, please see full prescribing information for Lexapro.

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

CONTRAINDICATIONS Concomitant use in patients taking monoamine oxidase inhibitors (MAOIs) is contraindicated (see **WARNINGS**). Concomitant use in patients taking pimozide is contraindicated (see **Drug Interactions – Pimozide and Celexa**). Lexapro is contraindicated in patients with a hypersensitivity to escitalopram or citalopram or any of the inactive ingredients in Lexapro. **WARNINGS WARNINGS-Clinical Worsening and Suicide Risk Clinical Worsening and Suicide Risk** Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. There has been a long-standing concern, however, that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients during the early phases of treatment. Pooled analyses of short-term placebo-controlled trials of antidepressant drugs (SSRIs and others) showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18-24) with major depressive disorder (MDD) and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction with antidepressants compared to placebo in adults aged 65 and older. The pooled analyses of placebo-controlled trials in children and adolescents with MDD, obsessive compulsive disorder (OCD), or other psychiatric disorders included a total of 24 short-term trials of 9 antidepressant drugs in over 4400 patients. The pooled analyses of placebo-controlled trials in adults with MDD or other psychiatric disorders included a total of 295 short-term trials (median duration of 2 months) of 11 antidepressant drugs in over 77,000 patients. There was considerable variation in risk of suicidality among drugs, but a tendency toward an increase in the younger patients for almost all drugs studied. There were differences in absolute risk of suicidality across the different indications, with the highest incidence in MDD. The risk differences (drug vs. placebo), however, were relatively stable within age strata and across indications. These risk differences (drug-placebo difference in the number of cases of suicidality per 1000 patients treated) are provided in **Table 1. TABLE 1: Age Range and Drug-Placebo Difference in Number of Cases of Suicidality per 1000 Patients Treated:** Drug-Related Increases; <18 (14 additional cases); 18-24 (5 additional cases); Drug-Related Decreases; 25-64 (1 fewer case); ≥65 (6 fewer cases). No suicides occurred in any of the pediatric trials. There were suicides in the adult trials, but the number was not sufficient to reach any conclusion about drug effect on suicide. It is unknown whether the suicidality risk extends to longer-term use, i.e., beyond several months. However, there is substantial evidence from placebo-controlled maintenance trials in adults with depression that the use of antidepressants can delay the recurrence of depression. **All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases.** The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality. Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse, or who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms. If the decision has been made to discontinue treatment, medication should be tapered, as rapidly as is feasible, but with recognition that abrupt discontinuation can be associated with certain symptoms (see PRECAUTIONS and DOSAGE AND ADMINISTRATION—Discontinuation of Treatment with Lexapro, for a description of the risks of discontinuation of Lexapro). **Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to health care providers. Such monitoring should include daily observation by families and caregivers.** Prescriptions for Lexapro should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose. **Screening Patients for Bipolar Disorder:** A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled trials) that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Whether any of the symptoms described above represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that Lexapro is not approved for use in treating bipolar depression. **Potential for Interaction with Monoamine Oxidase Inhibitors In patients receiving serotonin reuptake inhibitor drugs in combination with a monoamine oxidase inhibitor (MAOI), there have been reports of serious, sometimes fatal, reactions including hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that include extreme agitation progressing to delirium and coma. These reactions have also been reported in patients who have recently discontinued SSRI treatment and have been started on an MAOI. Some cases presented with features resembling neuroleptic malignant syndrome. Furthermore, limited animal data on the effects of combined use of SSRIs and MAOIs suggest that these drugs may act synergistically to elevate blood pressure and evoke behavioral excitation. Therefore, it is recommended that Lexapro should not be used in combination with an MAOI, or within 14 days of discontinuing treatment with an MAOI. Similarly, at least 14 days should be allowed after stopping Lexapro before starting an MAOI. Serotonin syndrome has been reported in two patients who were concomitantly receiving linezolid, an antibiotic which is a reversible non-selective MAOI.** ***Serotonin Syndrome:*** The development of a potentially life-threatening serotonin syndrome may occur with SNRIs and SSRIs, including Lexapro treatment, particularly with concomitant use of serotonergic drugs (including triptans) and with drugs which impair metabolism of serotonin (including MAOIs). Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination) and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). The concomitant use of Lexapro with MAOIs intended to treat depression is contraindicated (see **CONTRAINDICATIONS** and **WARNINGS - Potential for Interaction with Monoamine Oxidase Inhibitors.**) 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 (see **PRECAUTIONS - Drug Interactions**).The concomitant use of Lexapro with serotonin precursors (such as tryptophan) is not recommended (see **PRECAUTIONS - Drug Interactions**). **PRECAUTIONS General** Discontinuation of Treatment with Lexapro During marketing of Lexapro and other SSRIs and SNRIs (serotonin and norepinephrine reuptake inhibitors), there have been spontaneous reports of adverse events occurring upon discontinuation of these drugs, particularly when abrupt, including the following: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesias such as electric shock sensations), anxiety, confusion, headache, lethargy, emotional lability, insomnia, and hypomania. While these events are generally self-limiting, there have been reports of serious discontinuation symptoms. Patients should be monitored for these symptoms when discontinuing treatment with Lexapro. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose but at a more gradual rate (see **DOSAGE AND ADMINISTRATION**). Abnormal Bleeding Published case reports have documented the occurrence of bleeding episodes in patients treated with psychotropic drugs that interfere with serotonin reuptake. Subsequent epidemiological studies, both of the case-control and cohort design, have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. In two studies, concurrent use of a nonsteroidal anti-inflammatory drug (NSAID) or aspirin potentiated the risk of bleeding (see **Drug Interactions**). Although these studies focused on upper gastrointestinal bleeding, there is reason to believe that bleeding at other sites may be similarly potentiated. Patients should be cautioned regarding the risk of bleeding associated with the concomitant use of Lexapro with NSAIDs, aspirin, or other drugs that affect coagulation. Hyponatremia Cases of hyponatremia and SIADH (syndrome of inappropriate antidiuretic hormone secretion) have been reported in association with Lexapro treatment. All patients with these events have recovered with discontinuation of escitalopram and/or medical intervention. Hyponatremia and SIADH have also been reported in association with other marketed drugs effective in the treatment of major depressive 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. Seizures Although anticonvulsant effects of racemic citalopram have been observed in animal studies, Lexapro has not been systematically evaluated in patients with a seizure disorder. These patients were excluded from clinical studies during the product's premarketing testing. In clinical trials of Lexapro, cases of convulsion have been reported in association with Lexapro treatment. Like other drugs effective in the treatment of major depressive disorder, Lexapro should be introduced with care in patients with a history of seizure disorder. Interference with Cognitive and Motor Performance In a study in normal volunteers, Lexapro 10 mg/day did not produce impairment of intellectual function or psychomotor performance. Because any psychoactive drug may impair judgment, thinking, or motor skills, however, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that Lexapro therapy does not affect their ability to engage in such activities. Use in Patients with Concomitant Illness Clinical experience with Lexapro in patients with certain concomitant systemic illnesses is limited. Caution is advisable in using Lexapro in patients with diseases or conditions that produce altered metabolism or hemodynamic responses. Lexapro has not been systematically evaluated in patients with a recent history of myocardial infarction or unstable heart disease. Patients with these diagnoses were generally excluded from clinical studies during the product's premarketing testing. In subjects with hepatic impairment, clearance of racemic citalopram was decreased and plasma concentrations were increased. The recommended dose of Lexapro in hepatically impaired patients is 10 mg/day (see **DOSAGE AND ADMINISTRATION**). Because escitalopram is extensively metabolized, excretion of unchanged drug in urine is a minor route of elimination. Until adequate numbers of patients with severe renal impairment have been evaluated during chronic treatment with Lexapro, however, it should be used with caution in such patients (see **DOSAGE AND ADMINISTRATION**). **Information for Patients** Physicians are advised to discuss the following issues with patients for whom they prescribe Lexapro. Patients should be cautioned about the risk of serotonin syndrome with the concomitant use of Lexapro and triptans, tramadol or other serotonergic agents. In a study in normal volunteers, Lexapro 10 mg/day did not impair psychomotor performance. The effect of Lexapro on psychomotor coordination, judgment, or thinking has not been systematically examined in controlled studies. Because psychoactive drugs may impair judgment, thinking, or motor skills, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that Lexapro therapy does not affect their ability to engage in such activities. Patients should be told that, although Lexapro has not been shown in experiments with normal subjects to increase the mental and motor skill impairments caused by alcohol, the concomitant use of Lexapro and alcohol in depressed patients is not advised. Patients should be made aware that escitalopram is the active isomer of Celexa (citalopram hydrobromide) and that the two medications should not be taken concomitantly. Patients should be advised to inform their physician if they are taking, or plan to take, any prescription or over-the-counter drugs, as there is a potential for interactions. Patients should be cautioned about the concomitant use of Lexapro and NSAIDs, aspirin, or other drugs that affect coagulation since the combined use of psychotropic drugs that interfere with serotonin reuptake and these agents has been associated with an increased risk of bleeding. Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy. Patients should be advised to notify their physician if they are breastfeeding an infant. While patients may notice improvement with Lexapro therapy in 1 to 4 weeks, they should be advised to continue therapy as directed. Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with Lexapro and should counsel them in its appropriate use. A patient Medication Guide about "Antidepressant Medicines, Depression and other Serious Mental Illness, and Suicidal Thoughts or Actions" is available for Lexapro. The prescriber or health professional should instruct patients, their families, and their caregivers to read the Medication Guide and should assist them in understanding its contents. Patients should be given the opportunity to discuss the contents of the Medication Guide and to obtain answers to any questions they may have. Patients should be advised of the following issues and asked to alert their prescriber if these occur while taking Lexapro. **Clinical Worsening and Suicide Risk:** Patients, their families, and their caregivers should be encouraged to be alert to the emergence of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, mania, other unusual changes in behavior, worsening of depression, and suicidal ideation, especially early during anti-depressant treatment and when the dose is adjusted up or down. Families and caregivers of patients should be advised to look for the emergence of such symptoms on a day-to-day basis, since changes may be abrupt. Such symptoms should be reported to the patient's prescriber or health professional, especially if they are severe, abrupt in onset, or were not part of the patient's presenting symptoms. Symptoms such as these may be associated with an increased risk for suicidal thinking and behavior and indicate a need for very close monitoring and possibly changes in the medication. **Laboratory Tests** There are no specific laboratory tests recommended. **Concomitant Administration with Racemic Citalopram** Citalopram - Since escitalopram is the active isomer of racemic citalopram (Celexa), the two agents should not be coadministered. **Drug Interactions Serotonergic Drugs:** Based on the mechanism of action of SNRIs and SSRIs including Lexapro, and the potential for serotonin syndrome, caution is advised when Lexapro is coadministered with other drugs that may affect the serotonergic neurotransmitter systems, such as triptans, linezolid (an antibiotic which is a reversible non-selective MAOI), lithium, tramadol, or St. John's Wort (see **WARNINGS-Serotonin Syndrome**). The concomitant use of Lexapro with other SSRIs, SNRIs or tryptophan is not recommended (see **PRECAUTIONS - Drug Interactions**). **Triptans:** There have been rare postmarketing reports of serotonin syndrome with use of an SSRI and a triptan. If concomitant treatment of Lexapro with a triptan is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases (see **WARNINGS - Serotonin Syndrome**). CNS Drugs - Given the primary CNS effects of escitalopram, caution should be used when it is taken in combination with other centrally acting drugs. Alcohol - Although Lexapro did not potentiate the cognitive and motor effects of alcohol in a clinical trial, as with other psychotropic medications, the use of alcohol by patients taking Lexapro is not recommended. Monoamine Oxidase Inhibitors (MAOIs) - See **CONTRAINDICATIONS** and **WARNINGS**. **Drugs That Interfere With Hemostasis (NSAIDs, Aspirin, Warfarin, etc.)** Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies of the case-control and cohort design that have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding have also shown that concurrent use of an NSAID or aspirin potentiated the risk of bleeding. Thus, patients should be cautioned about the use of such drugs concurrently with Lexapro. Cimetidine - In subjects who had received 21 days of 40 mg/day racemic citalopram, combined administration of 400 mg/day cimetidine for 8 days resulted in an increase in citalopram AUC and C_{max} of 43% and 39%, respectively. The clinical significance of these findings is unknown. Digoxin - In subjects who had received 21 days of 40 mg/day racemic citalopram, combined administration of citalopram and digoxin (single dose of 1 mg) did not significantly affect the pharmacokinetics of either citalopram or digoxin. Lithium - Coadministration of racemic citalopram (40 mg/day for 10 days) and lithium (30 mmol/day for 5 days) had no significant effect on the pharmacokinetics of citalopram or lithium. Nevertheless, plasma lithium levels should be monitored with appropriate adjustment to the lithium dose in accordance with standard clinical practice. Because lithium may enhance the serotonergic effects of escitalopram, caution should be exercised when Lexapro and lithium are coadministered. Pimozide and Celexa - In a controlled study, a single dose of pimozide 2 mg co-administered with racemic citalopram 40 mg given once daily for 11 days was associated with a mean increase in QTc values of approximately 10 msec compared to pimozide given alone. Racemic citalopram did not alter the mean AUC or C_{max} of pimozide. The mechanism of this pharmacodynamic interaction is not known. Sumatriptan - There have been rare postmarketing reports describing patients with weakness, hyperreflexia, and incoordination following the use of an SSRI and sumatriptan. If concomitant treatment with sumatriptan and an SSRI (e.g., fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram, escitalopram) is clinically warranted, appropriate observation of the patient is advised. Theophylline - Combined administration of racemic citalopram (40 mg/day for 21 days) and the CYP1A2 substrate theophylline (single dose of 300 mg) did not affect the pharmacokinetics of theophylline. The effect of theophylline on the pharmacokinetics of citalopram was not evaluated. Warfarin - Administration of 40 mg/day racemic citalopram for 21 days did not affect the pharmacokinetics of warfarin, a CYP3A4 substrate. Prothrombin time was increased by 5%, the clinical significance of which is unknown. Carbamazepine - Combined administration of racemic citalopram (40 mg/day for 14 days) and carbamazepine (titrated to 400 mg/day for 35 days) did not significantly affect the pharmacokinetics of carbamazepine, a CYP3A4 substrate. Although trough citalopram plasma levels were unaffected, given the enzyme-inducing properties of carbamazepine, the possibility that carbamazepine might increase the clearance of escitalopram should be considered if the two drugs are coadministered. Triazolam - Combined administration of racemic citalopram (titrated to 40 mg/day for 28 days) and the CYP3A4 substrate triazolam (single dose of 0.25 mg) did not significantly affect the pharmacokinetics of either citalopram or triazolam. Ketoconazole - Combined administration of racemic citalopram (40 mg) and ketoconazole (200 mg), a potent CYP3A4 inhibitor, decreased the C_{max} and AUC of ketoconazole by 21% and 10%, respectively, and did not significantly affect the pharmacokinetics of citalopram. Ritonavir - Combined administration of a single dose of ritonavir (600 mg), both a CYP3A4 substrate and a potent inhibitor of CYP3A4, and escitalopram (20 mg) did not affect the pharmacokinetics of either ritonavir or escitalopram. CYP3A4 and -2C19 Inhibitors - *In vitro* studies indicated that CYP3A4 and -2C19 are the primary enzymes involved in the metabolism of escitalopram. However, coadministration of escitalopram (20 mg) and ritonavir (600 mg), a potent inhibitor of CYP3A4, did not significantly affect the pharmacokinetics of escitalopram. Because escitalopram is metabolized by multiple enzyme systems, inhibition of a single enzyme may not appreciably decrease escitalopram clearance. Drugs Metabolized by Cytochrome P4502D6 - *In vitro* studies did not reveal an inhibitory effect of escitalopram on CYP2D6. In addition, steady state levels of racemic citalopram were not significantly different in poor metabolizers and extensive CYP2D6 metabolizers after multiple-dose administration of citalopram, suggesting that coadministration, with escitalopram, of a drug that inhibits CYP2D6, is unlikely to have clinically significant effects on escitalopram metabolism. However, there are limited *in vivo* data suggesting a modest CYP2D6 inhibitory effect for escitalopram, i.e., coadministration of escitalopram (20 mg/day for 21 days) with the tricyclic antidepressant desipramine (single dose of 50 mg), a substrate for CYP2D6, resulted in a 40% increase in C_{max} and a 100% increase in AUC of desipramine. The clinical significance of this finding is unknown. Nevertheless, caution is indicated in the coadministration of escitalopram and drugs metabolized by CYP2D6. Metoprolol - Administration of 20 mg/day Lexapro for 21 days in healthy volunteers resulted in a 50% increase in C_{max} and 82% increase in AUC of the beta-adrenergic blocker metoprolol (given in a single dose of 100 mg). Increased metoprolol plasma levels have been associated with decreased cardioselectivity. Coadministration of Lexapro and metoprolol had no clinically significant effects on blood pressure or heart rate. Electroconvulsive Therapy (ECT) - There are no clinical studies of the combined use of ECT and escitalopram. **Carcinogenesis, Mutagenesis, Impairment of Fertility** Carcinogenesis Racemic citalopram was administered in the diet to NMRI/BOM strain mice and COBS WI strain rats for 18 and 24 months, respectively. There was no evidence for carcinogenicity of racemic citalopram in mice receiving up to 240 mg/kg/day. There was an increased incidence of small intestine carcinoma in rats receiving 8 or 24 mg/kg/day racemic citalopram. A no-effect dose for this finding was not established. The relevance of these findings to humans is unknown. Mutagenesis Racemic citalopram was mutagenic in the *in vitro* bacterial reverse mutation assay (Ames test) in 2 of 5 bacterial strains (Salmonella TA98 and TA1537) in the absence of metabolic activation. It was clastogenic in the *in vitro* Chinese hamster lung cell assay for chromosomal aberrations in the presence and absence of metabolic activation. Racemic citalopram was not mutagenic in the *in vitro* mammalian forward gene mutation assay (HPRT) in mouse lymphoma cells or in a coupled *in vitro*/*in vivo* unscheduled DNA synthesis (UDS) assay in rat liver. It was not clastogenic in the *in vitro* chromosomal aberration assay in human lymphocytes or in two *in vivo* mouse micronucleus assays. Impairment of Fertility When racemic citalopram was administered orally to 16 male and 24 female rats prior to and throughout mating and gestation at doses of 32, 48, and 72 mg/kg/day, mating was decreased at all doses, and fertility was decreased at doses ≥ 32 mg/kg/day. Gestation duration was increased at 48 mg/kg/day. **Pregnancy** Pregnancy Category C In a rat embryo/fetal development study, oral administration of escitalopram (56, 112, or 150 mg/kg/day) to pregnant animals during the period of organogenesis resulted in decreased fetal body weight and associated delays in ossification at the two higher doses (approximately ≥ 56 times the maximum recommended human dose [MRHD] of 20 mg/day on a body surface area [mg/m^2] basis). Maternal toxicity (clinical signs and decreased body weight gain and food consumption), mild at 56 mg/kg/day, was present at all dose levels. The developmental no-effect dose of 56 mg/kg/day is approximately 28 times the MRHD on a mg/m^2 basis. No teratogenicity was observed at any of the doses tested (as high as 75 times the MRHD on a mg/m^2 basis). When female rats were treated with escitalopram (6, 12, 24, or 48 mg/kg/day) during pregnancy and through weaning, slightly increased offspring mortality and growth retardation were noted at 48 mg/kg/day which is approximately 24 times the MRHD on a mg/m^2 basis. Slight maternal toxicity (clinical signs and decreased body weight gain and food consumption) was seen at this dose. Slightly increased offspring mortality was seen at 24 mg/kg/day. The no-effect dose was 12 mg/kg/day which is approximately 6 times the MRHD on a mg/m^2 basis. In animal reproduction studies, racemic citalopram has been shown to have adverse effects on embryo/fetal and postnatal development, including teratogenic effects, when administered at doses greater than human therapeutic doses. In two rat embryo/fetal development studies, oral administration of racemic citalopram (32, 56, or 112 mg/kg/day) to pregnant animals during the period of organogenesis resulted in decreased embryo/fetal growth and survival and an increased incidence of fetal abnormalities (including cardiovascular and skeletal defects) at the high dose. This dose was also associated with maternal toxicity (clinical signs, decreased body weight gain). The developmental no-effect dose was 56 mg/kg/day. In a rabbit study, no adverse effects on embryo/fetal development were observed at doses of racemic citalopram of up to 16 mg/kg/day. Thus, teratogenic effects of racemic citalopram were observed at a maternally toxic dose in the rat and were not observed in the rabbit. When female rats were treated with racemic citalopram (4.8, 12.8, or 32 mg/kg/day) from late gestation through weaning, increased offspring mortality during the first 4 days after birth and persistent offspring growth retardation were observed at the highest dose. The no-effect dose was 12.8 mg/kg/day. Similar effects on offspring mortality and growth were seen when dams were treated throughout gestation and early lactation at doses ≥ 24 mg/kg/day. A no-effect dose was not determined in that study. There are no adequate and well-controlled studies in pregnant women; therefore, escitalopram should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Pregnancy-Nonteratogenic Effects** Neonates exposed to Lexapro and other SSRIs or SNRIs, late in the third trimester, have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Such complications can arise immediately upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. These features are consistent with either a direct toxic effect of SSRIs and SNRIs or, possibly, a drug discontinuation syndrome. It should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome (see **WARNINGS**). Infants exposed to SSRIs in late pregnancy may have an increased risk for persistent pulmonary hypertension of the newborn (PPHN). PPHN occurs in 1–2 per 1000 live births in the general population and is associated with substantial neonatal morbidity and mortality. In a retrospective, case-control study of 377 women whose infants were born with PPHN and 836 women whose infants were born healthy, the risk for developing PPHN was approximately six-fold higher for infants exposed to SSRIs after the 20th week of gestation compared to infants who had not been exposed to antidepressants during pregnancy. There is currently no corroborative evidence regarding the risk for PPHN following exposure to SSRIs in pregnancy; this is the first study that has investigated the potential risk. The study did not include enough cases with exposure to individual SSRIs to determine if all SSRIs posed similar levels of PPHN risk. When treating a pregnant woman with Lexapro during the third trimester, the physician should carefully consider both the potential risks and benefits of treatment (see **DOSAGE AND ADMINISTRATION**). Physicians should note that in a prospective longitudinal study of 201 women with a history of major depression who were euthymic at the beginning of pregnancy, women who discontinued antidepressant medication during pregnancy were more likely to experience a relapse of major depression than women who continued antidepressant medication. **Labor and Delivery** The effect of Lexapro on labor and delivery in humans is unknown. **Nursing Mothers** Racemic citalopram, like many other drugs, is excreted in human breast milk. There have been two reports of infants experiencing excessive somnolence, decreased feeding, and weight loss in association with breastfeeding from a citalopram-treated mother; in one case, the infant was reported to recover completely upon discontinuation of citalopram by its mother and, in the second case, no follow-up information was available. The decision whether to continue or discontinue either nursing or Lexapro therapy should take into account the risks of citalopram exposure for the infant and the benefits of Lexapro treatment for the mother. **Pediatric Use** Safety and effectiveness in the pediatric population have not been established (see **BOX WARNING** and **WARNINGS—Clinical Worsening and Suicide Risk**). One placebo-controlled trial in 264 pediatric patients with MDD has been conducted with Lexapro, and the data were not sufficient to support a claim for use in pediatric patients. Anyone considering the use of Lexapro in a child or adolescent must balance the potential risks with the clinical need. **Geriatric Use** Approximately 6% of the 1144 patients receiving escitalopram in controlled trials of Lexapro in major depressive disorder and GAD were 60 years of age or older; elderly patients in these trials received daily doses of Lexapro between 10 and 20 mg. The number of elderly patients in these trials was insufficient to adequately assess for possible differential efficacy and safety measures on the basis of age. Nevertheless, greater sensitivity of some elderly individuals to effects of Lexapro cannot be ruled out. In two pharmacokinetic studies, escitalopram half-life was increased by approximately 50% in elderly subjects as compared to young subjects and C_{max} was unchanged (see **CLINICAL PHARMACOLOGY**). 10 mg/day is the recommended dose for elderly patients (see **DOSAGE AND ADMINISTRATION**). Of 4422 patients in clinical studies of racemic citalopram, 1357 were 60 and over, 1034 were 65 and over, and 457 were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but again, greater sensitivity of some elderly individuals cannot be ruled out. **ADVERSE REACTIONS** Adverse event information for Lexapro was collected from 715 patients with major depressive disorder who were exposed to escitalopram and from 592 patients who were exposed to placebo in double-blind, placebo-controlled trials. An additional 284 patients with major depressive disorder were newly exposed to escitalopram in open-label trials. The adverse event information for Lexapro in patients with GAD was collected from 429 patients exposed to escitalopram and from 427 patients exposed to placebo in double-blind, placebo-controlled trials. Adverse events during exposure were obtained primarily by general inquiry and recorded by clinical investigators using terminology of their own choosing. Consequently, it is not possible to provide a meaningful estimate of the proportion of individuals experiencing adverse events without first grouping similar types of events into a smaller number of standardized event categories. In the tables and tabulations that follow, standard World Health Organization (WHO) terminology has been used to classify reported adverse events. The stated frequencies of adverse events represent the proportion of individuals who experienced, at least once, a treatment-emergent adverse event of the type listed. An event was considered treatment-emergent if it occurred for the first time or worsened while receiving therapy following baseline evaluation. **Adverse Events Associated with Discontinuation of Treatment Major Depressive Disorder** Among the 715 depressed patients who received Lexapro in placebo-controlled trials, 6% discontinued treatment due to an adverse event, as compared to 2% of 592 patients receiving placebo. In two fixed-dose studies, the rate of discontinuation for adverse events in patients receiving 10 mg/day Lexapro was not significantly different from the rate of discontinuation for adverse events in patients receiving placebo. The rate of discontinuation for adverse events in patients assigned to a fixed dose of 20 mg/day Lexapro was 10%, which was significantly different from the rate of discontinuation for adverse events in patients receiving 10 mg/day Lexapro (4%) and placebo (3%). Adverse events that were associated with the discontinuation of at least 1% of patients treated with Lexapro, and for which the rate was at least twice that of placebo, were nausea (2%) and ejaculation disorder (2% of male patients). **Generalized Anxiety Disorder** Among the 429 GAD patients who received Lexapro 10-20 mg/day in placebo-controlled trials, 8% discontinued treatment due to an adverse event, as compared to 4% of 427 patients receiving placebo. Adverse events that were associated with the discontinuation of at least 1% of patients treated with Lexapro, and for which the rate was at least twice the placebo rate, were nausea (2%), insomnia (1%), and fatigue (1%). **Incidence of Adverse Events in Placebo-Controlled Clinical Trials Major Depressive Disorder Table 2** enumerates the incidence, rounded to the nearest percent, of treatment-emergent adverse events that occurred among 715 depressed patients who received Lexapro at doses ranging from 10 to 20 mg/day in placebo-controlled trials. Events included are those occurring in 2% or more of patients treated with Lexapro and for which the incidence in patients treated with Lexapro was greater than the incidence in placebo-treated patients. The prescriber should be aware that these figures can not be used to predict the incidence of adverse events in the course of usual medical practice where patient characteristics and other factors differ from those which prevailed in the clinical trials. Similarly, the cited frequencies cannot be compared with figures obtained from other clinical investigations involving different treatments, uses, and investigators. The cited figures, however, do provide the prescribing physician with some basis for estimating the relative contribution of drug and non-drug factors to the adverse event incidence rate in the population studied. The most commonly observed adverse events in Lexapro patients (incidence of approximately 5% or greater and approximately twice the incidence in placebo patients) were insomnia, ejaculation disorder (primarily ejaculatory delay), nausea, sweating increased, fatigue, and somnolence (see **TABLE 2**). **TABLE 2: Treatment-Emergent Adverse Events: Incidence in Placebo-Controlled Clinical Trials for Major Depressive Disorder* (Lexapro (N=715) and Placebo (N=592)): Autonomic Nervous System Disorders:** Dry Mouth (6% and 5%); Sweating Increased (5% and 2%). **Central & Peripheral Nervous System Disorders:** Dizziness (5% and 3%). **Gastrointestinal Disorders:** Nausea (15% and 7%); Diarrhea (8% and 5%); Constipation (3% and 1%); Indigestion (3% and 1%); Abdominal Pain (2% and 1%). **General:** Influenza-like Symptoms (5% and 4%); Fatigue (5% and 2%). **Psychiatric Disorders:** Insomnia (9% and 4%); Somnolence (6% and 2%); Appetite Decreased (3% and 1 %); Libido Decreased (3% and 1%). **Respiratory System Disorders:** Rhinitis (5% and 4%); Sinusitis (3% and 2%). **Urogenital:** Ejaculation Disorder[1,2] (9% and <1%); Impotence[2]

New Award Honors Slain Schizophrenia Researcher

The *Schizophrenia Bulletin* includes manuscripts describing Wayne Fenton, M.D.'s, contributions to schizophrenia treatment and research, along with commentaries by NIMH Director Thomas Insel, M.D., and others.

BY MARK MORAN

Gerard Hogarty, M.S.W., the first awardee of the Wayne Fenton Award for Exceptional Clinical Care, died last year and received the award posthumously. He was a pioneer in psychosocial treatments for schizophrenia.

In September 2006, Wayne Fenton, M.D., who had been associate director of the National Institute of Mental Health (NIMH), was murdered by a severely mentally ill patient he had treated in his private office, leaving behind countless grieving colleagues in schizophrenia research.

To mark the occasion, *Schizophrenia Bulletin* dedicated its September issue to Fenton and inaugurated the annual Wayne Fenton Award for Exceptional Clinical Care.

Wayne Fenton, M.D.

Awardee Named

The first awardee, honored posthumously, is the late Gerard Hogarty, M.S.W., a pioneer in psychosocial treatments for schizophrenia. Hogarty, who died last year, had been a professor emeritus of psychiatry at the University of Pittsburgh School of Medicine. At last year's Institute on Psychiatric Services, he was posthumously awarded the American Psychiatric Foundation Alexander Gralnick, M.D., Award for Research in Schizophrenia *(Psychiatric News*, November 3, 2006).

In last month's *Bulletin*, former colleagues Shaun Eack, M.S.W., and Rohan Ganguli, M.D., of the University of Pittsburgh School of Medicine, and Nina Schooler, Ph.D., of Georgetown University School of Medicine, described Hogarty's contributions and the evolution of his work in psychosocial rehabilitation.

"Hogarty's art as a clinician not only ensured his personal effectiveness with patients, but also when combined with his passion for science spurred the development, refinement, and empirical validation of four major psychosocial treatments for persons with schizophrenia (major role therapy [MRT], family psychoeducation, personal therapy [PT], and cognitive enhancement therapy [CET])," they wrote. "These psychosocial treatments have expanded the treatment possibilities for this population and have significantly advanced the care that such individuals receive, not only in Pittsburgh, where he spent the last 31 years of his professional career, but also throughout the world."

Bulletin Editor William Carpenter, M.D., explained the significance of an award in Fenton's memory.

"Those of us working in the field know Wayne Fenton's very substantial vision and leadership contributions," he told *Psychiatric News*. "What was striking at his funeral and memorial service several weeks later at NIMH were the stories of Wayne's exceptional efforts and creative approaches in his care of patients. There are a number of awards to recognize research excellence. We thought it would be fitting to recognize exceptional clinical work."

Fenton's Contributions

In addition to the article on Hogarty, the *Bulletin* includes a number of manuscripts describing Fenton's contributions to schizophrenia treatment and research, along with commentaries by NIMH Director Thomas Insel, M.D., and others.

One commentary was an anonymously written firsthand account by a patient who had been treated by Fenton. "A mutual respect infused our relationship," the patient wrote, "and I believe that allowed us to fully trust one another and anticipate one another's reactions. We had an unspoken understanding between us, like a dance where the steps were seamless and carried out in unison, a dance that can only be performed with patience and genuine understanding. Sometimes he led, sometimes I did. It was a kind of collaboration and cathexis rarely witnessed or experienced, and now that it is gone, it is painfully and sorely missed."

This issue of the* Schizophrenia Bulletin *is posted at <http://schizophrenia bulletin.oxfordjournals.org> under "September 2007." ■

Guide Helps Health Care Organizations Assess Quality of Care

BY DAWN DUARTE

The Office of Inspector General (OIG) for the Department of Health and Human Services, in partnership with the American Health Lawyers Association (AHLA), released a resource guide September 13 on quality of care.

The guide is the third in a series of reports on corporate responsibility cosponsored by OIG and AHLA. The document is designed to help health care organization boards ask appropriate questions related to health care quality requirements, and includes tools to measure the quality of care and reporting requirements. Moreover, the guide is intended to assist health care organization directors in exercising their oversight responsibilities and in supporting their efforts to promote effective corporate compliance as it relates to health care quality.

The prior publications in this series addressed the oversight responsibilities of directors of health care governing boards on issues of compliance and health care law.

"These resources provide insight into the OIG's priorities and practical tools for directors to carry out their fiduciary responsibilities," said Lewis Morris, an AHLA board member, counsel to the inspector general, and co-author of the document, in a prepared statement.

AHLA joined with the OIG in publishing this document "because of the AHLA's intense commitment to the public interest [and to] act as a public resource on selected health care legal issues," Richard Shackelford, a member of the AHLA board and chair of its Public Interest Committee, said in a press statement. "I am confident that it will be an extremely valuable resource for health care boards of directors/trustees and the lawyers who advise them."

"Corporate Responsibility and Health Care Quality: A Resource for Health Care Boards of Directors" is posted at <www.oig.hhs.gov/fraud/docs/complianceguidance/CorporateResponsibilityFinal%209-4-07.pdf>. ■

Anxiety disorders often other comorbid conditions[1]

*In patients with **social anxiety disorder (SAD)** and a comorbid psychiatric disorder...*

In a study, SAD preceded the disorder in more than 75% of cases[3]

Facts about SAD

- One of the most common anxiety disorders[1]
- Affects approximately 15 million American adults—about the same amount affected by major depressive disorder[1]
- A lifetime prevalence of over 13%[4]
- Frequently not identified[5]

SAD patients have an increased risk of developing[3]*:*

- Obsessive compulsive disorder
- Major depressive disorder
- Panic disorder
- Drug and alcohol dependency

References: 1. Kessler RC, Chiu WT, Demler O, Walters EE. Prevalence, severity, and comorbidity of 12-month *DSM-IV* disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005;62:617-627. **2.** National Institute of Mental Health. The Numbers Count: Mental Disorders In America. http://www.nimh.nih.gov/publicat/numbers.cfm#MajorDepressive. Accessed August 30, 2007. **3.** Schneier FR, Johnson J, Hornig CD, Liebowitz MR, Weissman MM. Social phobia: comorbidity and morbidity in an epidemiologic sample. *Arch Gen Psychiatry*. 1992;49:282-288. **4.** Magee WJ, Eaton WW, Wittchen H-U, McGonagle KA, Kessler RC. Agoraphobia, simple phobia, and social phobia in the National Comorbidity Survey. *Arch Gen Psychiatry*. 1996;53:159-168. **5.** Connor KM, Kobak KA, Churchill LE, Katzelnick D, Davidson JRT. Mini-Spin: a brief screening assessment for generalized social anxiety disorder. *Depress Anxiety*. 2001;14:137-140. **6.** Abramowitz JS, Storch EA, Keeley M, Cordell E. Obsessive-compulsive disorder with comorbid major depression: what is the role of cognitive factors? *Behav Res Ther*. In press. **7.** Obsessive-Compulsive Disorder. In: Sadock BJ, Sadock VA, eds. *Synopsis of Psychiatry*. 9th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003:616-623. **8.** Obsessive-Compulsive Disorder. In: Hales RE, Yudofsky SC, Talbott JA, eds. *Textbook of Psychiatry*. 3rd ed. Washington, DC: American Psychiatric Press, Inc. 1999:600-610. **9.** American Psychiatric Association. Practice guideline for the treatment of patients with obsessive-compulsive disorder. http://www.psych.org/psych_pract/treatg/pg/prac_guide.cfm. Accessed August 21, 2007.

present first, before

AFFECTING MORE THAN 40 MILLION AMERICAN ADULTS EACH YEAR[2]

*In patients with **obsessive compulsive disorder (OCD)** and comorbid depression...*

OCD preceded the disorder, suggesting that mood disturbances may occur as a response to the functional impairment of OCD[6]

Facts about OCD

- Affects about 2.2 million American adults[1]
- 67% of patients will have an associated lifetime diagnosis of major depressive disorder[7]
- Can be misdiagnosed as depression, psychosis, phobias, or personality disorder[8]

OCD symptoms can be accompanied by[9]:

- Eating disorders
- Other anxiety disorders
- Major depressive disorder
- Alcohol or drug abuse

Early recognition and treatment of anxiety disorders are an important part of successful therapy

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Biostatistics a Mystery To Many Residents

Training of internal medicine residents may be inconsistent and inadequate in preparing future physicians to evaluate increasingly complex medical literature and to apply research results to their clinical practice.

BY JUN YAN

Many medical residents do not have sufficient education and training to help them fully understand and objectively evaluate the mountain of research information with which they are regularly confronted, according to a study in the September 5 *Journal of the American Medical Association (JAMA)*.

Donna Windish, M.D., M.P.H., an assistant professor of medicine at Yale University School of Medicine, and colleagues surveyed residents in 11 internal medicine residency programs in Connecticut. The survey contained questions about the residents' attitude toward statistics and their confidence in interpreting statistical concepts, as well as 20 multiple-choice questions designed to test their knowledge of statistical methods, study design, and interpretation of study results most commonly represented in recent articles in major general medical journals, such as *JAMA* and *Annals of Internal Medicine*.

The 277 residents who completed the survey did not do very well on the statistics knowledge assessment. The mean knowledge score was 41.1 percent, indicating an average of eight correct answers for the 20 test questions. While over 80 percent of the residents were able to recognize double-blind studies and interpret relative risk correctly, only about 1 in 10 interpreted the results of a Kaplan-Meier analysis correctly. Only 1 in 3 understood how to interpret an adjusted odds ratio from a multivariate regression analysis. Slightly more than half could give the meaning of a *P* value.

The lack of knowledge in statistics is consistent with the residents' self-reported lack of confidence and attitudes about interpreting medical literature. Three-quarters of the respondents said they did not understand all the statistics they encountered in the literature, and 15 percent felt they did not trust statistics "because it is easy to lie." The mean score indicating their understanding of statistical concepts was 11.4 on a scale of 0 to 20.

Several statistically significant factors were identified in the article as associated with the residents' performance on the knowledge test. Being male, having an advanced degree, having had biostatistics training, and enrollment in a university-based rather than a community-based training program were linked to higher scores. The duration since graduating from medical school was inversely associated with the score, indicating that new graduates did better on the test.

The authors urged improvements in teaching and reinforcing statistics in medical schools and residency programs, especially more advanced statistical methods beyond Student's *t* test and chi-square test, as more complex statistics such as multiple logistic regression and Kaplan-Meier analysis are used increasingly in medical research. Physicians who do not understand the statistics used in medical literature will have difficulty in critically evaluating the validity of published evidence and conclusions, which in turn will affect their ability to use the information appropriately in patient care.

"Understanding and being able to examine the current research is [also] critical in psychiatric practice," Molly McVoy, M.D., chair of the APA Committee of Residents and Fellows, commented to *Psychiatric News*. "There is so much to be learned in this specialty and so much new information daily that can affect our patients."

McVoy agreed that training on biostatistics and evaluation of medical literature seems to be inconsistent in programs across the country. She believes that adequate education in biostatistics should "start in medical school, where the foundation for medical practice is laid" and that "medical schools need to do a better job of helping future physicians understand and navigate current research."

She pointed out that the ability to critically evaluate research information in the literature is the key to physicians' lifelong learning once they leave residency.

An abstract of "Medicine Residents' Understanding of the Biostatistics and Results in Medical Literature" is posted at <http://jama.ama-assn.org/cgi/content/abstract/298/9/1010>. ■

Government to Spend Millions To Address Childhood Trauma

The federal government announces funding of millions of dollars for treatment centers to enhance mental health services for children who have experienced different forms of trauma.

BY EVE BENDER

An influx of funding from the federal government is intended to improve the lives of children and adolescents who are experiencing trauma, whether due to war, domestic violence, or chronic and serious illness.

The Substance Abuse and Mental Health Services Administration (SAMHSA) in September awarded $28 million to a group of programs that deal with youth being treated for the mental health sequelae of trauma exposure.

"These grants will strengthen the nation's capacity to provide help to children of all ages who experience traumatic events, such as interpersonal violence, natural disasters, or acts of terrorism," said Terry Cline, Ph.D., SAMHSA administrator, in a press release announcing the grants.

Each grant recipient will receive up to $600,000 a year for up to four years.

The following is a description of the programs that received SAMHSA grants for trauma treatment:

- **Children's Hospital Corporation, Boston:** $599,998 a year to support network centers to fund interventions for child refugees who may have been exposed to war, political oppression, torture, and/or forced displacement.
- **University of Maryland at Baltimore:** $600,000 a year to develop, implement, and evaluate family-based interventions for underserved urban and military populations.
- **The University of Montana, Missoula:** $600,000 a year to evaluate evidence-based trauma treatments for American Indian/Alaska Native children, particularly on reservations.
- **Mt. Sinai School of Medicine, New York:** $600,000 a year to fund trauma-focused interventions to serve children and families in protective-service settings.
- **Children's Hospital of Philadelphia:** $599,829 a year to address and reduce medical trauma in the lives of children and their families by promoting trauma-focused health care and integrating evidence-based tools into pediatric medical care.
- **Children's Institute, Los Angeles:** $400,000 in the first year to implement the Central Los Angeles Child Trauma Collaborative that will improve access to trauma-specific mental health treatment for high-risk urban children and adolescents, many of whom are ethnic minorities.
- **Denver Department of Human Services:** $400,000 a year to make child-parent psychotherapy available to abused and neglected children and their families within Denver's child-welfare system.
- **Children's Home Society of Florida, Pensacola:** $400,000 a year to partner with the Florida Mental Health Institute and develop a Trauma Recovery for Youth Center.
- **University of Kentucky Research Foundation, Lexington:** $400,000 a year to provide clinical training and information on evidence-based practices in four rural and urban areas in the state.
- **Mental Health Services for Homeless Persons Inc., Cleveland:** $400,000 a year to serve traumatized children aged 4 to 18 who have been referred for treatment and to provide training for employees of the Department of Children and Family Services of Cuyahoga County.
- **Latino Health Institute, Boston:** $399,999 in the first year to improve access to and quality of treatment and intervention services for Latino children and their families who have been impacted by traumatic events.
- **Kennedy Krieger Research Institute Baltimore:** $399,961 a year to provide comprehensive services for high-risk, underserved children who have experienced traumatic events.
- **Community Counseling Center, Portland, Maine:** $400,000 in the first year to implement a community-wide trauma-focused system of care for children who have witnessed violence at home.
- **Catholic Charities Inc., Jackson, Miss.:** $400,000 in the first year to implement a trauma-focused system of care to provide best practices for children and their families who have experienced trauma.
- **Aliviane Inc., El Paso, Texas:** $400,000 in the first year to create a trauma-focused initiative with an array of evidence-based services for children exposed to complex trauma to help them improve social competence and better manage their emotions. ■

IASC Releases New Guidelines

New international guidelines result from a multiagency effort to recommend steps that will protect mental health and psychosocial well-being in the midst of emergencies.

BY DAWN DUARTE

On September 14, the Inter-Agency Standing Committee (IASC)—a broad coalition of 26 United Nations (U.N.) and non-U.N. agencies—released new guidelines that identify how different approaches to mental health and psychosocial support can complement one another in the midst of emergencies.

Emergency responders sometimes view the mental health and psychosocial well-being of communities undergoing disasters or conflicts as the sole responsibility of psychiatrists and psychologists. The *IASC Guidelines on Mental Health and Psychosocial Support in Emergency Settings*, however, seeks to dispel that belief by emphasizing that protecting and promoting mental health and psychosocial well-being are the responsibilities of all humanitarian agencies and workers.

The IASC committee established the guidelines to focus on social interventions, with emphasis on the utilization of local resources, such as teachers, health workers, healers, and women's groups. Additionally, the guidelines provide direction on strengthening social networks and building on existing ways in which community members deal with distress in their lives. Such strategies include attention to protection and care of people with severe mental disorders and severe trauma-induced disorders, as well as access to "psychological first aid" for those in acute distress.

The guidelines will be available in various languages and posted at <www.humanitarianinfo.org/iasc/content/products/default.asp>. ■

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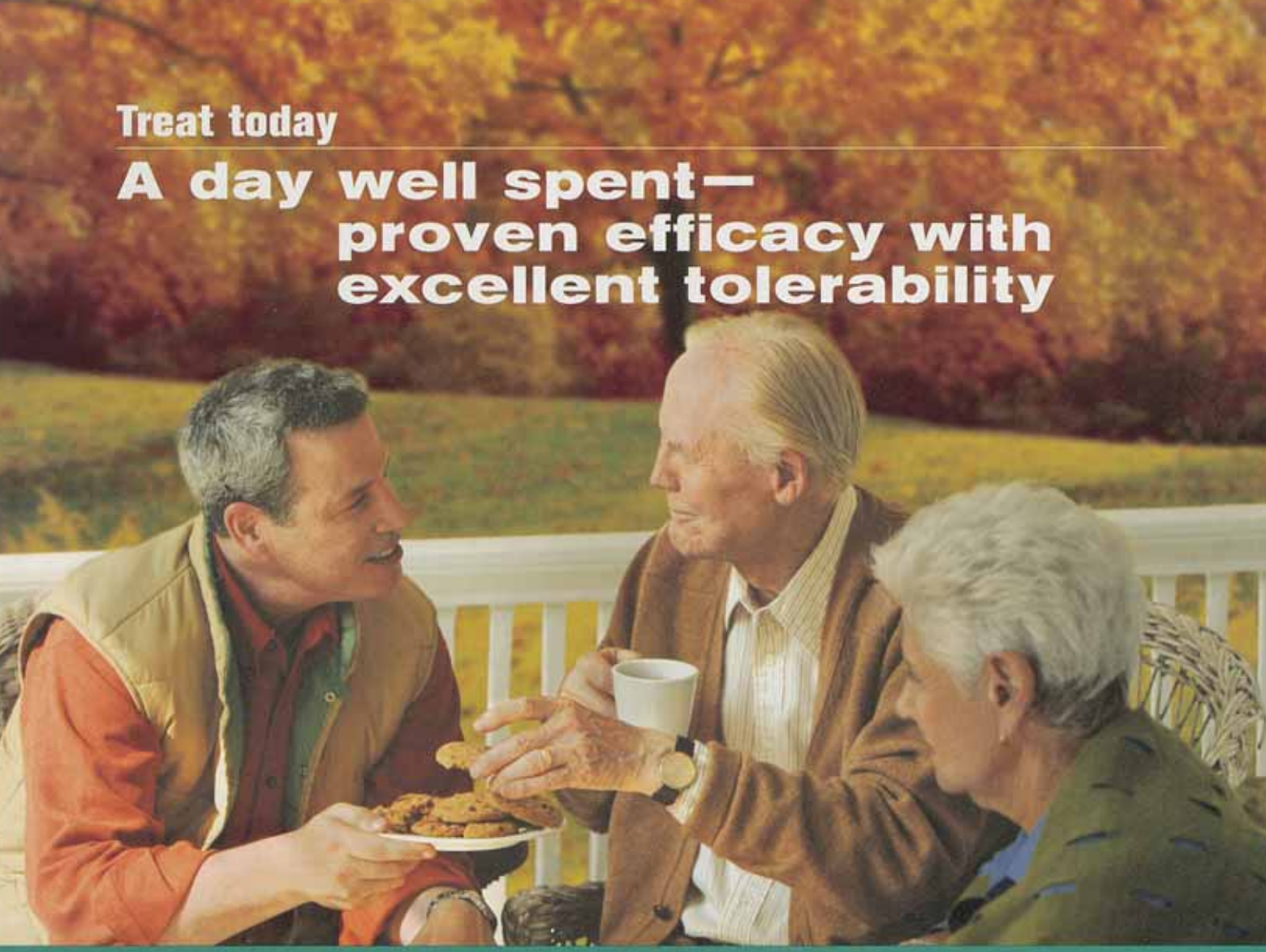

- Improves function, delays onset of behavioral symptoms, and provides benefits in cognition[1-3]
- Excellent safety and tolerability with low risk of unpleasant gastrointestinal side effects[4,5]
- May reduce care dependence and caregiver distress[3,6]
- Proven effective first-line and in combination with an acetylcholinesterase inhibitor[1,2]

Preferred status on the majority of health plan and Medicare Part D formularies[4]

Namenda
memantine HCl

Extending memory and function

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

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

References: 1. Reisberg B, Doody R, Stöffler A, Schmitt F, Ferris S, Möbius HJ, for the Memantine Study Group. Memantine in moderate-to-severe Alzheimer's disease. *N Engl J Med.* 2003;348:1333-1341. **2.** Tariot PN, Farlow MR, Grossberg GT, Graham SM, McDonald S, Gergel I, for the Memantine Study Group. Memantine treatment in patients with moderate to severe Alzheimer disease already receiving donepezil: a randomized controlled trial. *JAMA.* 2004;291:317-324. **3.** Cummings JL, Schneider E, Tariot PN, Graham SM, for the Memantine MEM-MD-02 Study Group. Behavioral effects of memantine in Alzheimer disease patients receiving donepezil treatment. *Neurology.* 2006;67:57-63. **4.** Data on file. Forest Laboratories, Inc. **5.** NAMENDA® (memantine HCl) Prescribing Information. Forest Pharmaceuticals, Inc., St Louis, Mo. **6.** Winblad B, Poritis N. Memantine in severe dementia: results of the 'M-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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For more details, please visit **www.namenda.com**.
Please see brief summary of Prescribing Information on the adjacent page.

62-1009392 11/06

Namenda
memantine HCl

Rx Only

Brief Summary of Prescribing Information.

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

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

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

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

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

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

Special Populations
Hepatic Impairment
Namenda undergoes partial hepatic metabolism, with about 48% of administered dose excreted in urine as unchanged drug or as the sum of parent drug and the N-glucuronide conjugate (74%). The pharmacokinetics of memantine in patients with hepatic impairment have not been investigated, but would be expected to be only modestly affected.

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.

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, paranoid reaction, thinking abnormal, crying abnormal, appetite increased, paroniria, delirium, depersonalization, neurosis, 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, retinal 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: atrioventricular block, bone fracture, carpal tunnel syndrome, cerebral infarction, chest pain, claudication, colitis, dyskinesia, dysphagia, gastritis, gastroesophageal reflux, grand mal convulsions, intracranial hemorrhage, hepatic failure, hyperlipidemia, hypoglycemia, ileus, impotence, malaise, neuroleptic malignant syndrome, acute pancreatitis, aspiration pneumonia, acute renal failure, prolonged QT interval, restlessness, Stevens-Johnson syndrome, sudden death, supraventricular tachycardia, tachycardia, tardive dyskinesia, and thrombocytopenia.

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
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. In a documented case of an overdosage with up to 400 mg of memantine, the patient experienced restlessness, psychosis, visual hallucinations, somnolence, stupor and loss of consciousness. The patient recovered without permanent sequelae.

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Data Refute Belief About Schizophrenia Outcomes

The assumption held by many in the mental health field that tightly knit family and social structures in developing countries lead to a better prognosis when schizophrenia develops may be a "romanticization" of poorer, rural cultures.

BY MARK MORAN

For the past 30 years, some psychiatric epidemiologists have held to a claim that has evolved into a vexing axiom: that people with schizophrenia appear to have a better outcome in developing countries than in Westernized developed countries.

It is a belief founded on three cross-cultural studies sponsored by the World Health Organization: the International Pilot Study of Schizophrenia, the Determinants of Outcome of Severe Mental Disorder (DosMed), and International Study of Schizophrenia (ISoS).

This belief has spawned a variety of seductive but largely speculative explanations about the more tightly knit family and social structures that are said to exist in developing countries and that may account for better outcomes.

But a new study in the September 28 advance online *Schizophrenia Bulletin* suggests that prognosis in the developing world is far more complicated, with a variety of outcomes—good and bad—across several domains of measurement and across, and within, countries in the developing world.

Study author Alex Cohen, Ph.D., told *Psychiatric News* that the report presents a very mixed picture for prognosis in the developing world and leaves many questions unanswered. But it should prompt a reassessment of the certainty with which assumptions have been held, as well as the implications those assumptions have for the development of services, he said.

"The development of services and policy should be based on evidence and not assumptions about the interactions of social worlds and psychiatric processes," Cohen said. "In many ways, the review points most of all to what we don't but need to know.

"But the evidence presented in the review also suggests that lack of treatment and long duration of untreated psychosis are always associated with poor clinical status and outcome, and that treatment brings improvement," Cohen said. "The notion of better outcomes also deflects attention away from the extensive human rights abuses that are well documented in much of the world."

Cohen is an assistant professor of social medicine at Harvard Medical School. His co-authors are Vikram Patel of the London School of Hygiene and Tropical Medicine; R. Thara of the Schizophrenia Research Foundation in Chennai, India; and Oye Gureje of the Department of Psychiatry at the University of Ibadan in Nigeria.

Does Abundance Cripple?

The findings from the WHO studies have prompted some to wonder if—in the words of medical anthropologist Kim Hopper, Ph.D.—"abundance cripples" and whether scarcity, and the social cohesion that is putatively a byproduct of scarcity, helps to produce better outcomes.

But the new report by Cohen and colleagues casts doubt on the representative nature of samples in those studies (given the probability of high mortality in countries where psychiatric treatment is relatively poor), the measures used to determine a good outcome, and even the theoretical foundations for distinguishing "developed" from "developing" countries.

"I've never been comfortable with the term 'developing country' because it is virtually impossible to define," said Cohen, who noted that in the ISoS study, wealthy Hong Kong was included as a "developing" site.

"In our study, we have used the terms low- and middle-income countries and have used World Bank criteria as definitions," he said. "That's not a perfect solution, but one that is consistent. The more important point is that we should be comparing sites with good outcomes with sites with poor outcomes and then investigate the factors that account for these differences."

Outcomes in 11 Countries Studied

In their study, Cohen and colleagues reviewed literature and tabulated data from 23 longitudinal studies of schizophrenia outcomes in 11 low- and middle-income countries and examined evidence on the following domains: clinical outcomes and patterns of course; disability and social outcomes, especially focusing on marital and occupational status; and untreated samples and duration of untreated psychosis.

The 11 countries are Brazil, Bulgaria, China, Colombia, Ethiopia, India, Indonesia, Jamaica, Nigeria, South Africa, and Trinidad. The identified studies were prospective and retrospective, had follow-up periods ranging from one to 20 years, included prevalent and first-episode cases, and drew samples from a variety of settings (outpatient clinics, hospitals, and communities). Twelve of the studies followed 100 or more subjects.

To provide a basis for comparison, the investigators included data from the following ISoS sites—Bulgaria, China, India (Agra, urban Chandigarh, and rural Chandigarh), and Colombia—and Nigeria from the DosMed study.

In general, and most strikingly, they found wide variation in outcomes from study to study and within countries. For instance, clinical outcomes and patterns of the course of illness were generally good in India, but not nearly so positive in Brazil, Nigeria, and China.

A 10-year longitudinal study in Madras, India, found that 74 percent of patients had little or no difficulty in social and occupational domains; in the Chandigarh, India, site in the ISoS study, 63 percent to 71 percent of patients had good to excellent social functioning.

In contrast, the study site in rural China found that 68 percent had "seriously impaired" social functioning; in Nigeria 56.6 percent had moderate to severe social disability.

But even within India, outcomes varied depending on the measure. For instance, in one study in rural Karnataka, only 13 percent of patients had regular employment. In the multisite study, 82 percent were reported working with no or only some impairment.

Cohen said that apart from refuting the blanket assumption of better outcomes in developing countries, the findings raise the larger question of why outcomes vary, not only in low- and middle-income countries, but in high-income countries as well.

"The short answer is, we have no idea," he said. "People speculate about variations in tolerance, family support, and social integration, but there is little direct evidence linking these factors to outcomes, at least in low- and middle-income countries. And our review suggests the presence, at times, of social rejection, high levels of stigma, and breakdowns in family support."

Cohen and colleagues also found the same level of variability across the developing countries on measures of disability and social outcome, employment, and marital status as was found with regard to clinical status.

Also revealing was the lack of biomedical treatment and associated duration of psychosis in the developing countries (see box).

Egocentric vs. Sociocentric Societies

Schizophrenia Bulletin Editor William Carpenter, M.D., a principal investigator in the International Pilot Study on Schizophrenia, told *Psychiatric News* that as one of those

please see ***Outcomes*** *on page 23*

Many Untreated in Developing Countries

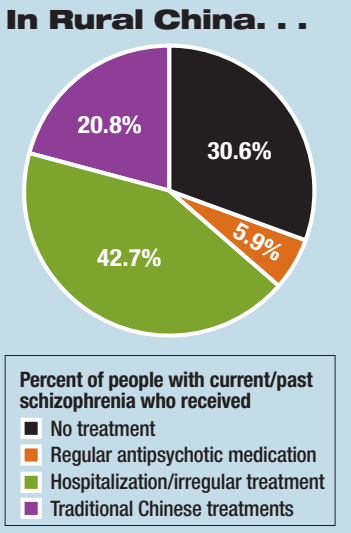
In rural China, rural Ethiopia, and Chennai, India, community surveys found large numbers of patients who received little or no treatment for schizophrenia or were receiving traditional remedies.

The survey in Chennai identified a cohort of 261 persons with a diagnosis of schizophrenia, of whom 28.7 percent had never received treatment even though they lived in close proximity to public general hospitals with psychiatric units and to a large mental hospital. Compared with those who had received treatment, those in the untreated group were, on average, older and more likely to be unemployed, illiterate, and living in an extended family. Clinically, the untreated group was more likely to be symptomatic and suffering from severe global disability.

In rural China a survey identified 510 persons who had a current diagnosis or history of schizophrenia. Of these, 30.6 percent had never received any treatment (see chart).

In rural Ethiopia a community survey identified 321 persons with schizophrenia of whom 88.8 percent had never received treatment with antipsychotic medications. At one- to four-year follow-ups, these individuals displayed a significant improvement in positive symptoms, a result attributed to the antipsychotic medication that was offered free to all of them.

"These findings suggest that good outcomes cannot be assumed for untreated schizophrenia in low- and middle-income countries and that treatment does make a significant difference," Alex Cohen, Ph.D., and colleagues stated in their report in *Schizophrenia Bulletin* (see article at left).



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Many Westerners have long believed that individuals with schizophrenia in developing countries fare better than those in developed countries, but Alex Cohen, Ph.D., and his team have found otherwise. Above: Patients in the Kandahar Insane Asylum in Afghanistan are locked inside the courtyard in the city center. Because of two decades of war and lack of funding for medical care, people in state-run facilities do not get proper care.

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What Can Neuroscience Teach the Legal System?

The legal system assumes that people make totally conscious choices, but neuroscience indicates that their choices do not always reflect that level of awareness. Can the contradiction be resolved?

BY JOAN AREHART-TREICHEL

On October 9, American neuroscientists and legal experts came together in the Daniel Patrick Moynihan United States Court House in New York City to launch the Law and Neuroscience Project.

The project constitutes one of the first systematic efforts in the United States to bring the worlds of neuroscience and law together in an effort to determine where neuroscience informs the legal process and where it probably doesn't have anything to say.

The project will be financed by an initial three-year, $10 million grant from the John D. and Catherine T. MacArthur Foundation. It will be headed by Michael Gazzaniga, Ph.D., director for the SAGE Center for Study of Mind at the University of California, Santa Barbara. Former Supreme Court Justice Sandra Day O'Connor is honorary chair of the project. One of the members of the project's governing board is Stephen Hyman, M.D., a former director of the National Institute of Mental Health and now a professor of neurobiology at Harvard University.

Not long ago, "we did a search to find out how often neuroscience is used in current court cases," Gazzaniga told *Psychiatric News*. She and her colleagues identified 916 cases on dockets throughout the country. The cases concern questions such as whether brain scans can divulge culpability, whether psychological pain can be measured objectively, what is the impact of punishment severity, and what kind of culpability should be applied to people who are addicted. During the project's first year, its members will focus on such questions, and during the second and third years they will conduct research to answer some of them.

Moreover, they plan on developing guidelines for the legal profession on subjects such as the determination of competency and culpability and treatment for psychopaths or persons determined to be criminally insane. They also aim to develop a primer for judges and lawyers that will give a quick reference to neuroscience subjects that might arise in court proceedings—for example, addiction, impulsivity, lies, memory, prejudice, psychopathy, and the use and limits of different kinds of brain scans.

What are several of the major challenges that the project members will face? "I think nailing down the specifics on all of these issues and determining which questions can be answered with current technology and which cannot," Gazzaniga stated. For example, she noted, can lies be detected with brain scans or electrophysiological methods, and can people really make deliberate, totally conscious choices?

"The legal system assumes that people make deliberate choices and what we choose determines what we do," Walter Sinnott-Armstrong, Ph.D., a professor of legal studies at Dartmouth College and a project member, said in a prepared statement issued in conjunction with the October 9 conference. "However, neuroscience indicates that our choices sometimes are based upon electrical impulses and neuron activity that are not part of conscious behavior." If this contradiction can be resolved, it would impact not just criminal guilt, but also decisions made by police, prosecutors, or jurors to arrest, prosecute, or convict, Sinnott-Armstrong suggested.

"Neuroscience could have an impact on the legal system that is as dramatic as DNA testing," MacArthur Foundation President Jonathan Fanton predicted.

As information is collected and analyzed, it will be posted on the project's Web site and reported at public conferences. The project will also arrange several weekend retreats each year so that judges, lawyers, legislators, and opinion leaders can learn the basics of neuroscience and its application to the law.

More information about the Law and Neuroscience Project is posted at <www.lawandneuroscienceproject.org>. ■

APA Wants To Help!

If any of your patients are being denied access to their appropriate drugs under the Medicare Part D prescription drug program, call (800) 343-4671. More information is available from Ellen Jaffe of APA's Office of Health Care Systems and Financing at (703) 907-8591 or ejaffe@psych.org.

New CME Program Coming to Your Inbox

An interactive, Web-based program will supplement one of APA's journals in order to help psychiatrists hone their clinical decision-making skills.

BY EVE BENDER

A new, interactive clinical decision-making program will soon arrive by e-mail to APA members and subscribers of *Focus: The Journal of Lifelong Learning*, APA's clinical CME journal. Clinical eFocus is a brief e-mail and Web-based educational activity developed to help psychiatrists review their clinical decision-making skills.

Clinical eFocus features a clinical vignette in the form of an interactive e-mail that will enable recipients to choose what they believe is the best treatment for the patient in the vignette and also to see what treatments have been endorsed by other psychiatrists responding to the vignette.

"Clinical eFocus is an exciting, new opportunity for APA to offer its members continuing education that is easy to use during their busy days," Deborah Hales, M.D., told *Psychiatric News*. Hales is director of APA's Division of Education and a co-editor of *Focus*.

The patient vignettes appearing in each Clinical eFocus will address a clinical theme featured in the previous issue of *Focus*, which is published on a quarterly basis to help psychiatrists stay abreast of advances in the field.

Each interactive e-mail will provide a link to a corresponding *Focus* article pertaining to the clinical topic.

"We hope that eFocus will provide us an opportunity to use the enormous power of the Internet to both collect and disseminate information," Thomas Kramer, M.D., an associate editor of Clinical eFocus told *Psychiatric News*.

He explained that developing a way to enable practicing psychiatrists to see what their peers would do in the management of a particular case will give them "a sense of how their thinking compares to that of other practitioners."

Kramer, who wrote a Clinical eFocus vignette about a patient with symptoms of obsessive-compulsive disorder experiencing adverse side effects from his current treatment, noted that there are no wrong answers among the multiple-choice selections provided below the vignette.

The first Clinical eFocus arrived in APA members' and *Focus* subscribers' inboxes last month.

After the dissemination of the interactive case presentation, there will be a subsequent e-mail featuring clinical commentary from an expert in the field and discussing the merits of the treatment options provided in the case presentation.

Focus co-editor Mark Rapaport, M.D., who is also chair of APA's Committee on CME and Lifelong Learning, called Clinical eFocus "an extension of APA's efforts to enhance learning for practicing psychiatrists." ■

Apply Now for Administrative Certification

The Certification in Psychiatric Administration and Management is offered yearly in conjunction with APA's annual meeting. The application deadline for certification candidates (including letters of reference) is January 31, 2008. Early applications are encouraged to allow candidates adequate preparation time.

More information is available from Crystal Garner at cgarner@psych.org or online at <www.psych.org/edu/cert-psych.cfm>. ■

Mentors Sought for Minority Members

APA members are encouraged to join the National Minority Mentors Network and become mentors to APA's younger minority colleagues.

Mentors play an important role in the professional growth and development of beginning psychiatrists and receive great satisfaction from sharing their hard-earned wisdom and experience. Moreover, mentoring is critical to fostering successful careers in psychiatry and ensuring the field's future success.

APA members who are interested in joining or obtaining additional information about the network should contact Marilyn King at (703) 907-8653 or mking@psych.org. ■

Vergare Appointed

Michael Vergare, M.D., professor and chair of the Department of Psychiatry and Human Behavior at Jefferson Medical College of Thomas Jefferson University in Philadelphia, has been named interim dean of the medical school effective December 12. He has also been named interim senior vice president for academic affairs at Thomas Jefferson University. ■

APA's 100% Club Picks Up Another Member Program

The psychiatry residency training program at St. Louis University School of Medicine is the latest residency program to have all of its psychiatry residents become members of APA.

It joins the ranks of an exclusive organization within APA: the 100% Club**.** This club was established to encourage residents throughout the United States and Canada to join APA and to do so with other trainees in their programs, according to Deborah Hales, M.D., director of APA's Division of Education.

A photo of each program that joins the 100% Club is turned into a poster and mailed to every medical school in the United States and Canada to encourage medical students to join APA. In addition, programs in the 100% Club receive a major textbook from American Psychiatric Publishing Inc. and a free online subscription to *Focus: The Journal of Lifelong Learning* for each year that all of their residents are APA members.

Said training director Miggie Greenberg, M.D., "We are delighted that all our residents are all APA members. APA provides valuable information and opportunities for residents during residency training and throughout their careers."

More information about the 100% Club is available from Nancy Delanoche of APA's Division of Education at (703) 907-8635. Programs that are interested in signing up all their residents should also contact Delanoche. ■

Front row: Lauren Flynn, M.D., Elena Luchanok, M.D., Rachel Morel, D.O., Anna Jurec, M.D., Stacy Neff, D.O., Rachel Brown, M.D., Harmeeta Singh, M.D., Rangsun Sitthichai, M.D., and Pamela Whisenhunt (coordinator). Back row: Miggie Greenberg, M.D. (program director), Jennifer Chaffin, M.D., Deepali Chand, M.D., Roomana Arain, M.D., Sundeep Jayaprabhu, M.D., Mehret Gebretsadik, M.D., Sekhar Vangala, M.D., Arshad Bhatt, M.D., Jeffery Kao, M.D., and Marlon Mangahas, M.D. The psychiatry residency training program at St. Louis University School of Medicine is the latest residency program to have all of its psychiatry residents become members of APA.

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IN SCHIZOPHRENIA

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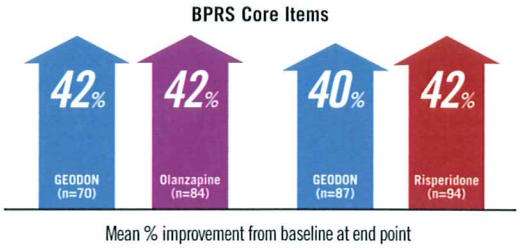
Consistent results in acute head-to-head studies[1-3]



A 6-week, double-blind, randomized study of GEODON vs olanzapine and an 8-week, double-blind, randomized study of GEODON vs risperidone.

- BPRS core items include hallucinatory behavior, unusual thought content, conceptual disorganization, and suspiciousness
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  —up to 1 year vs risperidone[1]
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In the acute head-to-head studies...

- In the GEODON vs olanzapine study, olanzapine significantly increased body weight (8 lb vs 2 lb for GEODON, $P<0.0001$)[1,2]
- In the GEODON vs risperidone study, risperidone increased body weight (2 lb vs 0 lb for GEODON, $P<0.01$)[1,3]

CHOOSE GEODON® (ziprasidone HCl) Oral Capsules

GEODON is indicated for the treatment of acute manic or mixed episodes associated with bipolar disorder and for the treatment of schizophrenia.

Elderly patients with dementia-related psychosis treated with atypical 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 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.

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.

The most common adverse events associated with GEODON in bipolar mania were somnolence, extrapyramidal symptoms, dizziness, akathisia, and abnormal vision.

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.

In short-term schizophrenia clinical trials, 10% of GEODON-treated patients experienced a weight gain of ≥7% of body weight vs 4% for placebo.

Pfizer

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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 atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of seventeen placebo controlled trials (modal duration of 10 weeks) in these patients revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times that seen 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. GEODON (ziprasidone) is not approved for the treatment of patients with Dementia-Related Psychosis.

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 atypical antipsychotic drugs are at an increased risk of death compared to placebo. 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 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. ***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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Revised November 2006

American Psychiatric Foundation Names New Director

Paul Burke brings many years of work in the nonprofit sector to his new appointment as executive director of the American Psychiatric Foundation.

BY DAWN DUARTE

The American Psychiatric Foundation (APF) has announced the appointment of Paul Burke as the foundation's new executive director. Burke brings many years of distinguished experience in the nonprofit sector to APF. Most recently, he served as the president and CEO of CureSearch National Childhood Cancer Foundation, and previous to that he was the national director of marketing and communications for the disability organization United Cerebral Palsy.

Under Burke's leadership, CureSearch completely rebranded itself and created a National Advertising Council campaign to increase public awareness of childhood cancer. Largely as a result of Burke's leadership, CureSearch received the leading international honor for Web sites, the Webby Award of the International Academy of Digital Arts and Sciences. He was also the architect and leader of a legislative advocacy network responsible for gaining more than $8 million in supplemental funding for childhood cancer research through congressional appropriations.

During his time with CureSearch, Burke and his team significantly increased private funding for CureSearch through the development of relationships with Major League Baseball, the National Hockey League, the Merrill Lynch Shootout, and Hyundai. In 2006 Burke received the prestigious Golden Halo Award from the Cause Marketing Forum.

Burke has an impressive record in business and government. He was director of Texaco's legislative affairs in alternate energy and served as the first chair of the Renewable Fuels Association.

His public service includes tenure as an assistant administrator in the U.S. Department of Energy, a staff position in the White House Special Action Office for Drug Abuse Prevention, and decorated service in Vietnam as an officer in the U.S. Army. He earned a master's degree in government from George Washington University.

Burke is a member of the National Board of Directors of America's Charities. He is also an adjunct professor of marketing and communications at George Mason University.

Credit: Aaron Levin

Paul Burke

"We are fortunate to have someone who has a demonstrated ability to lead and build relationships joining the foundation as we plan for the next steps in our development," said Altha Stewart, M.D., APF president. "Burke possesses a clear understanding of the current issues facing the foundation. He also shares the vision of the board and staff to increase awareness and support of the foundation among APA members and other individual donor groups in order to expand our ability to fund public education and outreach grant programs."

"It is an honor and privilege to have the opportunity to serve as executive director for the American Psychiatric Foundation," stated Burke. "I look forward to working with the APA leadership and staff to expand and enhance the foundation's important mission." ■

They Died With No Fanfare, But That May Change

Buried and for too long forgotten, deceased residents of America's state mental hospitals are being remembered at last.

BY AARON LEVIN

Across the United States, the graves of tens of thousands of people who once lived in state mental hospitals lie almost forgotten.

In Oregon, 5,000 copper urns hold the cremated remains of patients who died at Oregon State Hospital in Salem. Perhaps 25,000 patients lie buried at the former Georgia State Lunatic Asylum in Milledgeville, their graves indicated only by small, rusted iron markers. Groundskeepers in the 1960s uprooted even those tokens to make mowing the lawn easier.

"No names, just numbers," recalled a former hospital employee. "Unknown humans, shunned when living, deprived of their very names in death."

Now, even if all those names cannot be retrieved, the long-forgotten patients will have some remembrance of their existence in the nation's capital.

Advocates, led by Larry Fricks, vice president for peer services at the Depression and Bipolar Support Alliance, are planning a national consumer memorial on the grounds of St. Elizabeths Hospital in Washington, D.C. Fricks helped restore the Milledgeville cemetery and is spearheading the project on behalf of the National Association of Consumer/Survivor Administrators.

The memorial will "honor those who were segregated, died, and buried on the grounds of state hospitals nationwide," said Fricks in an interview. "Every state probably has a cemetery like Milledgeville's."

For the moment, Fricks is concentrating on building support among a number of consumer and professional groups. Mental Health America has established a tax-exempt account to accept donations, and the University of Georgia School of Environmental Design has volunteered consulting services.

The leading suggestion for the proposed memorial is a collection of large rocks, one from each state, with the names of institutions and the numbers buried at each. A winding path would guide visitors through the rock garden and back out to the community—a symbolic journey as well as a physical one.

The garden would reflect therapeutic ideas that first informed the design of mental hospitals in early 19th-century America. Called "moral treatment," that model embraced an enlightened medical view of mental illness, emphasizing recovery and a belief that patients could be treated with some hope of success, rather than casting them into jails or worse (*Psychiatric News*, September 2, 2005).

Credit: Georgia Consumer Council

Hundreds of numbered iron markers once topped the graves of patients who died at the former Georgia State Lunatic Asylum in Milledgeville, Ga. Members of the Georgia Consumer Council organized the restoration of the cemetery and replanted the markers.

"This is a new way to honor people and the institutions that served them, for good or ill," said Steven Baron, L.C.S.W.-C., director of Washington, D.C.'s Department of Mental Health, which oversees St. Elizabeths. "I'm really excited about this idea and hope we can make it happen. Anything that draws attention to the role of public psychiatry is a good thing."

As of press time, however, there was no formal agreement with Baron's department or the city.

Baron, Fricks, and others have even begun thinking about ideas for an adjacent museum to explain the mixed history of the state hospitals and the people who spent their lives in them, although such a museum is probably several more long steps down the road, said Baron.

(The rumored location of the St. Elizabeths' grounds as the new headquarters of the Department of Homeland Security will not affect the location of the memorial, said Baron. The federal government owns only the old West Campus of the hospital, not the East Campus, which belongs to Washington, D.C.)

The memorial will not only remember the departed, but will also provide hope for the living, said spokesperson Jim McNulty of the National Alliance on Mental Illness. "You put your past in a place where you honor it and—hopefully—learn from it," he said.

More information on the memorial appeared in the September* Psychiatric Services *and is posted at <http://ps.psychiatryonline.org/cgi/content/full/58/9/1236>. Donations may be sent to Consumer Memorial Fund, c/o Mental Health America, 2000 North Beauregard Street, 6th Floor, Alexandria, Va. 22311, or made online at <www.uspra.org/i4a/pages/Index.cfm?pageID=4050>. ■

Depressed Youth Respond Best to Combination Therapy

Adding CBT to fluoxetine treatment appears to provide depressed adolescents with the benefits of both quick-acting and longer-duration treatments.

BY DAWN DUARTE
AARON LEVIN

Combining medication and psychotherapy provides adolescents with depression the treatment advantages of both a sprint and a marathon.

The combination of the antidepressant medication fluoxetine (Prozac) and cognitive-behavioral therapy (CBT) appears more effective than either strategy alone for the long-term treatment of adolescents with depression, according to the latest report from the Treatment for Adolescents With Depression Study (TADS) in the October *Archives of General Psychiatry*.

The report lengthens observations in the TADS from the 12 weeks reported earlier this year (*Psychiatric News*, March 2) to 36 weeks.

The benefit of combination therapy derives from the swifter initial action of the drug linked with the longer term effects of CBT, said lead author John March, M.D., M.P.H., professor and chief of child and adolescent psychiatry in the Department of Psychiatry and Behavioral Science at Duke University.

All three treatments proved equally successful at the end of the trial, but the response rate at that point is not the only standard to use, said March in an interview with *Psychiatric News*.

"There are a lot of things we can do to get a patient better, but faster is important too," he said. "Three months in the life of a depressed kid is a long time."

The longer trial period is a more clinically relevant time frame, said Stan Kutcher, M.D., the Sun Life Financial Chair in Adolescent Mental Health in the Department of Psychiatry at Dalhousie University in Halifax, Nova Scotia.

"Nobody treats depression for just 12 weeks," Kutcher told *Psychiatric News*. "This is the best information we have to date about treating this disorder in young people."

The TADS study, funded by the National Institute of Mental Health (NIMH) in 1999, is part of ongoing research seeking to improve the treatment of depression in youth. According to the researchers, major depressive disorder affects approximately 5 percent of adolescents.

The researchers randomly assigned 327 patients aged 12 to 17 with a *DSM-IV* diagnosis of major depression to one of the three treatment conditions: combination therapy (n=107), fluoxetine therapy (n=109), or CBT (n=111).

Fluoxetine was initially prescribed at a dosage of 10 mgs a day and then titrated in response to whether patients experienced positive reactions to treatment or underwent adverse effects. Patients receiving CBT had 15 one-hour sessions during the first 12 weeks; thereafter, therapy was usually less frequent, dependent on how the patients responded to treatment.

Positive responders were those who showed as "very much improved" or "much improved" on the Clinical Global Impressions–Improvement scale (CGI-I), which requires the clinician to rate how much the patient's illness has improved or worsened relative to baseline.

According to the researchers, 73 percent of patients receiving combination therapy, 62 percent of those receiving fluoxetine only, and 48 percent of those receiving CBT only responded to treatment after the initial 12 weeks. At the end of 36 weeks, 243 (74 percent) of the patients remained in the study. Positive response rates at that time were 86 percent for combination therapy, 81 percent for fluoxetine, and 81 percent for CBT.

CBT Response Increased Dramatically

However, the response to CBT alone increased from 48 percent to 65 percent by week 18, while fluoxetine therapy response increased only from 65 percent to 69 percent over the same period.

"The data show that CBT caught up with fluoxetine therapy by weeks 18 to 24 and to combination therapy by weeks 30 to 36," the researchers said.

"Starting patients on fluoxetine improved functioning and lowered illness burden quickly, while adding CBT seems to have had an additional effect on modulating suicide," said Kutcher, who was not involved in the trial.

The TADS findings were broadly generalizable, said the authors, because the study population included both sexes, older and younger adolescents, minority representation proportionate to the U.S. population, and those from varied socioeconomic backgrounds.

"We designed the trial to represent what you'd want in clinical practice," said March. "Patients were treated by real psychiatrists and psychologists who paid attention to the details of clinical practice, not just the protocols."

Kutcher, who has also conducted clinical trials related to adolescent depression, was impressed by the study's ability to retain patients. Patient retention is often difficult in clinical trials, especially in those in which psychotropics are being used.

That retention, said March, was due to the effects of therapy as well as having plans in place for expectable contingencies.

Many Had Suicidal Ideation

About 30 percent of study patients met criteria for clinically significant suicidal ideation at baseline, based on the Suicidal Ideation Questionnaire-Junior High School Version (SIQ-Jr). Despite "aggressive" treatment over 36 weeks, there were suicidal events (ideation, an attempt, or preparatory action) in 10 percent of patients, nearly 70 percent of them occurring in the first 12 weeks—although not evenly distributed across trial arms.

"There was twice the risk of suicidal events in the fluoxetine-only group (16 patients), compared with the CBT (seven patients) or combination (nine patients) groups," said March. There were no completed suicides in the TADS.

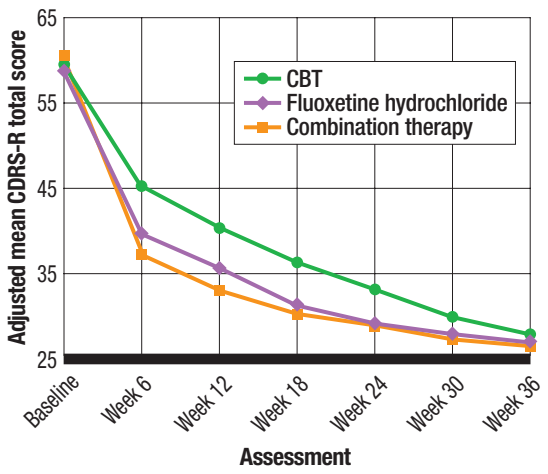
"TADS replicated the Food and Drug Administration (FDA) findings on the suicidal-event rate using fluoxetine alone," said March. An FDA meta-analysis was used as the basis for the initial black-box label warning regarding possible suicidality in youngsters taking antidepressants.

After considering the benefits and risks of the two treatments as monotherapies, the authors concluded that fluoxetine alone or in combination with CBT accelerated improvement of depression compared with CBT alone

please see ***Youth*** *on page 28*

Combined Treatment Found Superior

The graph shows the observed cases (OCs) trajectories using the scalar Children's Depression Rating Scale–Revised (CDRS-R) for the three active treatments—fluoxetine, CBT, and combination therapy—across 36 weeks. All three treatments converged at week 36. Weighing benefits against risks, researchers concluded that combined treatment appears superior to either monotherapy to treat major depression in adolescents.



The OC analyses included only data for patients who were still in their assigned treatment arm at the time of assessment.

Source: John S. March, M.D., *Archives of General Psychiatry*, October 2007

FDA Warns of Serious Side Effects From I.V. Haloperidol

Reported cases of potentially fatal arrhythmias associated with haloperidol, especially when injected intravenously, prompt a labeling change and FDA warnings to health care professionals.

BY JUN YAN

The Food and Drug Administration (FDA) issued a safety alert to health care professionals regarding the risk of arrhythmias and sudden death associated with haloperidol administered intravenously or at a higher-than-recommended dose.

Haloperidol injection, available as a decanoate salt and a lactate salt, is approved for intramuscular administration only, but intravenous use is a "relatively common off-label" use to treat severe agitation in intensive care units, according to the FDA.

The agency cited at least 28 cases of torsades de pointes and prolongation of the QT interval, some resulting in death, associated with intravenous use of haloperidol in the medical literature. In postmarketing analyses conducted by Johnson and Johnson, the manufacturer of the brand-name product Haldol, 229 reports of adverse events related to QT prolongation were identified with all formulations and uses of the drug in their worldwide safety database up to June 2005, including cases that the company described as "confounded by concomitant QT-prolonging drugs or medical conditions."

The analyses and reports had been requested by the Italian equivalent of the FDA. The reports included 73 cases of torsades de pointes, 11 of which resulted in death. Eight of these 11 deaths involved intravenously administered haloperidol. A second postmarketing safety analysis, which the company also conducted for the Italian agency and submitted to the FDA in March, included 13 cases involving torsades de pointes, QT prolongation, ventricular arrhythmias, and/or sudden death, according to the FDA. The FDA alert states that the frequency of these adverse effects cannot be estimated based on these case reports.

In September, the FDA approved labeling revisions to include an additional warning about the risks of sudden death, QT prolongation, and torsades de pointes. The updated warning advises caution in using any formulation of haloperidol in patients who "have other QT-prolonging conditions, including electrolyte imbalance; have underlying cardiac abnormalities, hypothyroidism, or familial long QT syndrome"; or are taking concomitant drugs with QT-prolonging effects. The new label also recommends ECG monitoring if haloperidol is given intravenously.

The prescribing information for haloperidol recommends an intramuscular dosage of 2 to 5 mg for acutely agitated schizophrenia patients with moderately severe to very severe symptoms. "Depending on the response of the patient, subsequent doses may be given, administered as often as every hour, although 4- to 8-hour intervals may be satisfactory," according to the package insert. No definition of high dose for intravenous haloperidol is given in the FDA alert.

The updated prescribing information had not been posted on the FDA's Web site by press time.

The FDA alert for haloperidol is posted at <www.fda.gov/cder/drug/InfoSheets/HCP/haloperidol.htm>. ■

TREAT ME LIKE ME...
so I can be who I want to be

Important Safety Information

- Daytrana should not be used in patients with allergy to methylphenidate or patch components; marked anxiety, tension and agitation; glaucoma; tics, diagnosis or a family history of Tourette's syndrome; seizures; or during or within 14 days after treatment with monoamine oxidase inhibitors (MAOIs).
- Sudden death has been reported in association with CNS stimulant treatment at usual doses in children and adolescents with structural cardiac abnormalities or other serious heart problems. Sudden deaths, stroke, and myocardial infarction have been reported in adults taking stimulant drugs at usual doses in ADHD. Physicians should take a careful patient history, including family history, and physical exam to assess the presence of cardiac disease. Patients who report symptoms of cardiac disease such as exertional chest pain and unexplained syncope should be promptly evaluated. Use with caution in patients whose underlying medical condition might be affected by increases in blood pressure or heart rate.
- New psychosis, mania, aggression, growth suppression, and visual disturbances have been associated with the use of stimulants. Use with caution in patients with a history of: psychosis; EEG abnormalities; bipolar disorder; depression. Growth and hematologic monitoring is advised during prolonged treatment. Patients should avoid applying external heat to the Daytrana patch. Skin irritation or contact sensitization may occur.
- **Daytrana should be given cautiously to patients with a history of drug dependence and alcoholism. Chronic abuse can lead to marked tolerance and psychological dependence. Frank psychotic episodes can occur, especially with parenteral abuse. Careful supervision is required during withdrawal from abusive use, since severe depression may occur. Withdrawal following chronic therapeutic use may unmask symptoms of the underlying disorder.**
- Common adverse events reported by patients who received Daytrana in clinical trials were decreased appetite, insomnia, nausea, vomiting, decreased weight, tics, affect lability, and anorexia, consistent with adverse events commonly associated with the use of methylphenidate.

Please see accompanying Brief Summary of Prescribing Information on adjacent page, including Boxed Warning.

References: 1. Daytrana [package insert]. Wayne, Pa: Shire US Inc; 03/07. **2.** McGough JJ, Wigal SB, Abikoff H, et al. A randomized, double-blind, placebo-controlled, laboratory classroom assessment of methylphenidate transdermal system in children with ADHD. *J Atten Disord.* 2006;9:476-485.

Shire US Inc.
...your ADHD Support Company™ 1-800-828-2088

www.Daytrana.com
Shire

With Daytrana™ the methylphenidate patch

Every child is unique. And so are their schedules. Daytrana provides a novel way to treat ADHD on all their different days.

INDIVIDUALIZATION...

- The ability to personalize ADHD treatment according to daily needs by adding flexible wear time to dose titration[1]
- A way to treat from weekday to weekend

THE BENEFITS OF INDIVIDUALIZATION...

- Control through the 12-hour time point with the recommended 9-hour wear time,[1] to take them through school, homework, and family time
- Option of shorter wear time for parents who are concerned about the potential for late-day side effects[1]

Daytrana is indicated as an integral part of a comprehensive ADHD treatment program that may include other measures (psychological, educational, social). The efficacy of Daytrana was established in clinical trials in children aged 6 to 12 years.[1]

Daytrana™ (methylphenidate transdermal system)

ADHD Treatment That Sticks[2]

Natural Selection May Have Purpose for Schizophrenia

"The mechanisms connecting schizotypal cognition and creativity with [natural selection] are unclear, but may include . . . creative and artistic skills or general benefits from insight problem solving."

BY MARK MORAN

"One thing about diversity in natural species that is well understood by evolutionary biologists," said Nobel Prize–winning mathematician John Nash, "is that the natural phenomenon of mutations serves to prepare a species for adaptation to changing conditions or for improved adaptation to an existing level of environmental circumstances.

"So a possible, but perhaps questionable, inference is that humans are notably subject to mental illness because there was a need for diversity in the patterns of human mental functions."

Nash, who has schizophrenia, was speaking at APA's 2007 annual meeting in San Diego, where he presented the William C. Menninger Memorial Lecture. The speech, delivered to a packed auditorium at the Convocation of Fellows, was a theoretical meditation on a paradox that has long intrigued schizophrenia researchers: though the disease negatively impacts reproductive capacity, it persists at a prevalence of about 1 percent in all human cultures.

Compounding the curiosity is the occasional nexus—of which Nash himself is a prime example—between psychosis and genius.

Applying his specialized understanding of "game theory" to an analysis of mental illness and his own experience with psychosis, Nash suggested during his address that severe mental illness exists in nature as a consequence of the diversification of species and that it may serve the needs of adaptation by its not infrequent association with genius.

Now, genetic researchers have published evidence that Nash's theory may be on the money. A study in the *Proceedings of the Royal Society of Biological Sciences* reports the results of two separate tests looking at the likelihood of evolutionary selection for 76 genes believed to be linked to schizophrenia. The study is currently posted online and will appear in print in the November 22 issue.

The researchers found that both tests showed that positive selection was evident using one or both methods for 28 of the 76 genes, including DISC1, DTNBP1, and NRG1, which exhibit especially strong and well-replicated functional and genetic links to schizophrenia.

The lead author of the study was Bernard Crespi, Ph.D., of Simon Fraser University in British Columbia.

Exactly why these genes—which carry a high risk for such a deleterious and maladaptive disease—should be naturally selected over generations is unclear. But Crespi and colleagues suggested that cognitive creativity—of the sort exhibited by John Nash—may be part of it.

"The mechanisms connecting schizotypal cognition and creativity with [natural selection] are unclear, but may include sexual selection, creative and artistic skills, or general benefits from insight problem solving," they wrote. "These processes could potentially help to explain the paradoxical high heritability and persistence of schizophrenia. . . ."

Ping-I Lin, M.D., Ph.D., a professor of genetics and genomic medicine at the Maryland Psychiatric Research Center, and Gunvant Thaker, M.D., chief of the Schizophrenia Related Disorders Program there, reviewed the report for *Psychiatric News* and said the authors have found evidence of positive selection for many of the genes that are thought to be associated with schizophrenia liability.

Lin explained that one of the tests involved examining relatively large blocks of DNA containing schizophrenia-associated genes in recent human evolution. Using this test, the researchers found that the schizophrenia genes are conserved and more frequently transmitted to succeeding generations than expected.

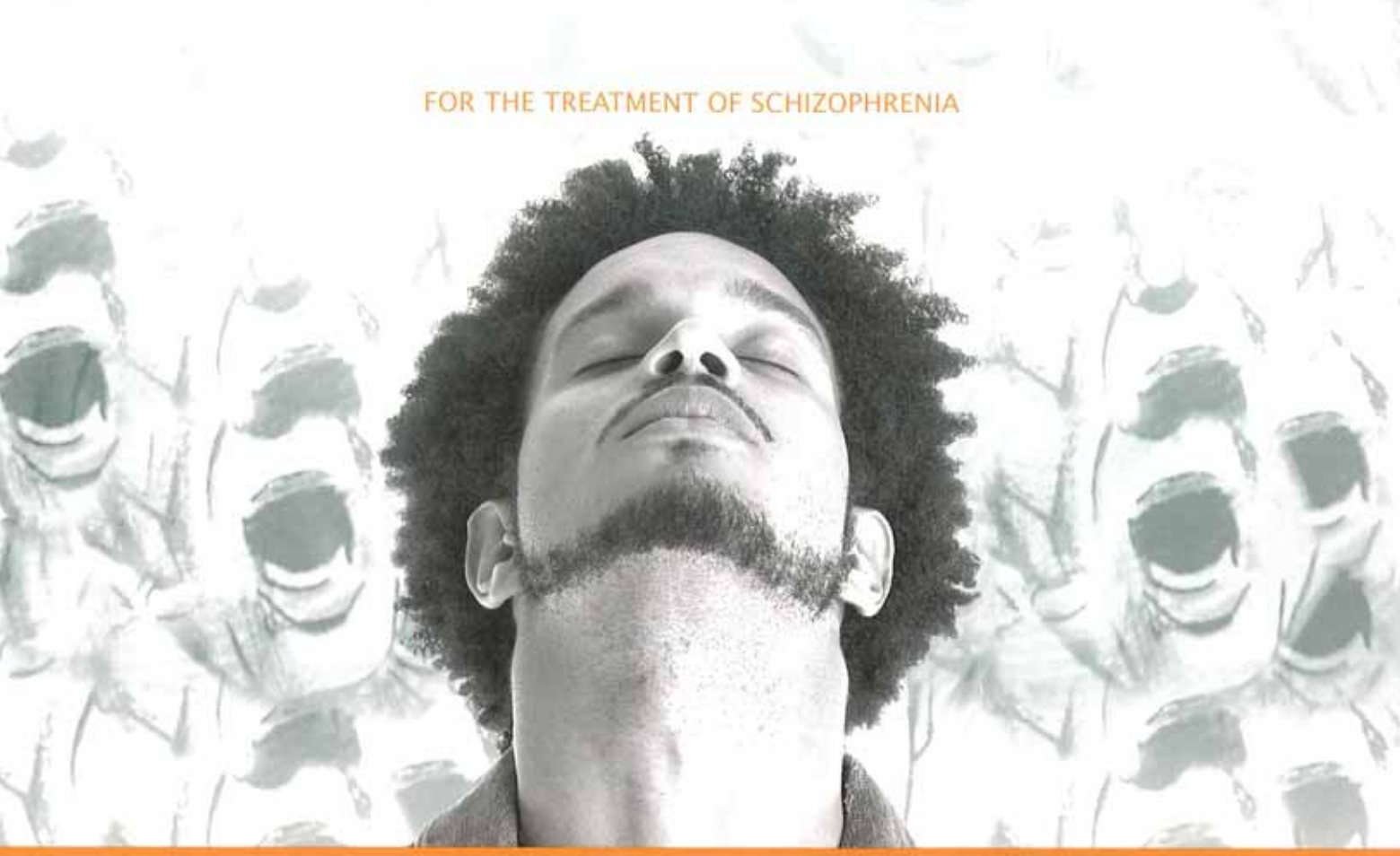
A second analysis was aimed at inferring the evidence for positive selection by comparing, in a human lineage, the ratio of DNA sequence changes that cause protein structural changes with DNA sequence changes that do not affect the protein structure.

"The higher the ratio is, the more likely that positive selection for protein-coding sequence changes may have occurred," Lin explained.

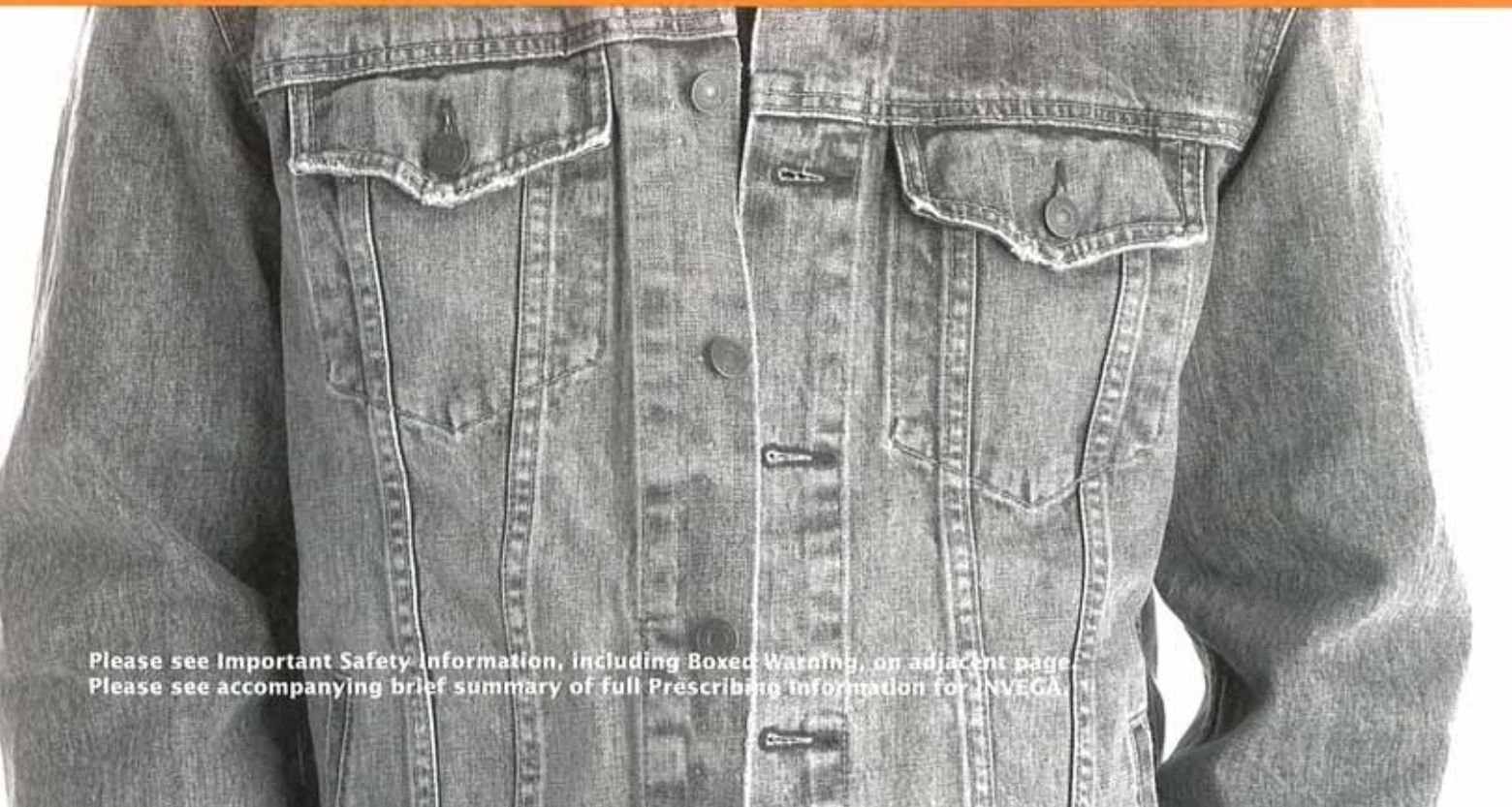
The positive selection for DNA sequence changes causing protein structural changes

please see ***Selection*** *on page 28*

FOR THE TREATMENT OF SCHIZOPHRENIA



He Needs Powerful Efficacy for His Mind
But What Will It Do to His Body?



Please see Important Safety Information, including Boxed Warning, on adjacent page.
Please see accompanying brief summary of full Prescribing Information for INVEGA.

IN THE TREATMENT OF SCHIZOPHRENIA

Powerful Efficacy for the Mind

- Every dose proven to effectively control symptoms in every acute pivotal trial (6 weeks)[1]
- Demonstrated efficacy over the longer term by delaying time to relapse[2]
- The first antipsychotic to measure efficacy by improvements in personal and social performance[3]

EXPERIENCE THE

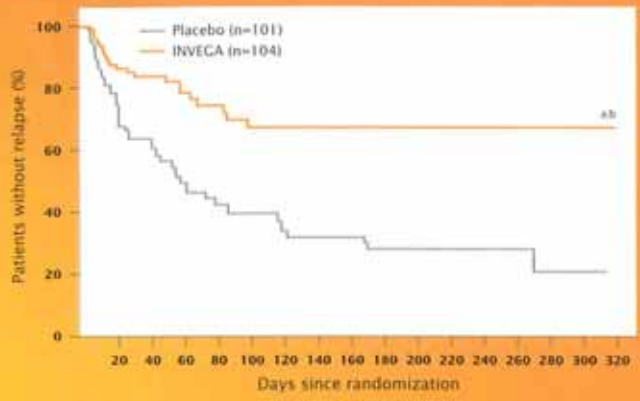
Proven Safety and Tolerability for the Body

- Weight gain comparable with placebo in 6-week clinical trials
- EPS rates comparable with placebo in 6-week trials with the recommended 6-mg dose*
- Adverse event type and severity in a longer-term trial were similar to those seen in 6-week pivotal trials

*Total EPS-related adverse events at the 9-mg and 12-mg doses were 25% and 26%, respectively, versus 11% for placebo.

Janssen L.P.

TIME TO RELAPSE[2]
(KAPLAN-MEIER PLOT OF TIME)



[a]$P<0.001$ vs placebo.
[b]Percentage of patients without recurrence at 11 months is projected.

From Kramer et al.[2]
Results from a placebo-controlled study that included a 14-week run-in and stabilization phase, during which patients received INVEGA (3 mg to 15 mg) once daily until they were deemed stable, followed by a double-blind phase in which patients were maintained on a stable dose of INVEGA or given placebo for up to 11 months. The average dose of INVEGA was 10.8 mg (average 24 weeks). The trial was ended at a predetermined interim analysis due to occurrence of a total number of relapses between the 2 groups (mean duration of therapy with INVEGA and placebo was 74 days and 56 days, respectively).[1,2]

BENEFITS OF INVEGA

WEIGHT CHANGE FROM BASELINE WITH INVEGA[1,2]

Short term (6 weeks)[c,d]

3-mg and 6-mg doses	1.3 lb
9-mg dose	2.2 lb
12-mg dose	2.4 lb
Placebo	−0.9 lb

Longer term (24 weeks)[d,e]

Data on file[1] and adapted from Kramer et al.[2]
[c]Pooled results from three 6-week pivotal trials.
[d]The proportion of patients gaining ≥7% of body weight with INVEGA was 7% (3 mg), 6% (6 mg), 9% (9 mg), and 9% (12 mg) versus 5% (placebo) in 6-week trials, and 20% (average 10.8 mg) versus 12% (placebo) in a longer-term, flexible-dose trial.
[e]Results from a longer-term trial of up to 11 months (average 24 weeks that includes a 14-week run-in and stabilization phase). The average dose of INVEGA was 10.8 mg.

Please see Important Safety Information, including Boxed Warning, on adjacent page.
Please see accompanying brief summary of full Prescribing Information for INVEGA.

INVEGA™
PALIPERIDONE
Extended-Release Tablets
STRENGTH FOR THE WHOLE PERSON

INVEGA™

(paliperidone)
Extended-Release Tablets

BEFORE PRESCRIBING, PLEASE CONSULT COMPLETE PRESCRIBING INFORMATION OF WHICH THE FOLLOWING IS A BRIEF SUMMARY

Rx only

Increased Mortality in Elderly Patients with Dementia-Related Psychosis
Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of 17 placebo-controlled trials (modal duration of 10 weeks) in these subjects revealed a risk of death in the drug-treated subjects of between 1.6 to 1.7 times that seen in placebo-treated subjects. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated subjects 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. INVEGA™ (paliperidone) Extended-Release Tablets is not approved for the treatment of patients with dementia-related psychosis.

INDICATIONS AND USAGE: INVEGA™ (paliperidone) Extended-Release Tablets is indicated for the acute and maintenance treatment of schizophrenia.

CONTRAINDICATIONS: INVEGA™ (paliperidone) is contraindicated in patients with a known hypersensitivity to paliperidone, risperidone, or to any components in the INVEGA™ formulation.

WARNINGS: Increased Mortality in Elderly Patients with Dementia-Related Psychosis – Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. INVEGA™ (paliperidone) Extended-Release Tablets is not approved for the treatment of dementia-related psychosis (see Boxed Warning). QT Prolongation: Paliperidone causes a modest increase in the corrected QT (QTc) interval. The use of paliperidone should be avoided in combination with other drugs that are known to prolong QTc including Class 1A (e.g., quinidine, procainamide) or Class III (e.g., amiodarone, sotalol) antiarrhythmic medications, antipsychotic medications (e.g., chlorpromazine, thioridazine), antibiotics (e.g., gatifloxacin, moxifloxacin), or any other class of medications known to prolong the QTc interval. Paliperidone should also be avoided in patients with congenital long QT syndrome and in patients with a history of cardiac arrhythmias. 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 QTc interval, including (1) bradycardia; (2) hypokalemia or hypomagnesemia; (3) concomitant use of other drugs that prolong the QTc interval; and (4) presence of congenital prolongation of the QT interval. The effects of paliperidone on the QT interval were evaluated in a double-blind, active-controlled (moxifloxacin 400 mg single dose), multicenter QT study in adults with schizophrenia and schizoaffective disorder, and in three placebo- and active-controlled 6-week, fixed-dose efficacy trials in adults with schizophrenia. In the QT study (n = 141), the 8 mg dose of immediate-release oral paliperidone (n=44) showed a mean placebo-subtracted increase from baseline in QTcLD of 12.3 msec (90% CI: 8.9; 15.6) on day 8 at 1.5 hours post-dose. The mean steady-state peak plasma concentration for this 8 mg dose of paliperidone immediate-release was more than twice the exposure observed with the maximum recommended 12 mg dose of INVEGA™ ($C_{max\ ss}$ = 113 and 45 ng/mL, respectively, when administered with a standard breakfast). In this same study, a 4 mg dose of the immediate-release oral formulation of paliperidone, for which $C_{max\ ss}$ = 35 ng/mL, showed an increased placebo-subtracted QTcLD of 6.8 msec (90% CI: 3.6; 10.1) on day 2 at 1.5 hours post-dose. None of the subjects had a change exceeding 60 msec or a QTcLD exceeding 500 msec at any time during this study. For the three fixed-dose efficacy studies, electrocardiogram (ECG) measurements taken at various time points showed only one subject in the INVEGA™ 12 mg group had a change exceeding 60 msec at one time-point on Day 6 (increase of 62 msec). No subject receiving INVEGA™ had a QTcLD exceeding 500 msec at any time in any of these three studies. **Neuroleptic Malignant Syndrome:** A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported with antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability. Other signs may include elevated creatinine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. Management should include: discontinuation of the antipsychotic and other drugs not essential to therapy; intensive symptomatic treatment and medical monitoring; and treatment of other serious medical problems. If a patient requires antipsychotic drugs after recovery from NMS, the reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences have been reported. **Tardive Dyskinesia:** A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. The risk of developing and likelihood that it will become irreversible are believed to increase with the duration of treatment and the total cumulative dose. However, tardive dyskinesia can develop, after brief treatment periods at low doses. There is no known treatment for established cases of tardive dyskinesia, although it may remit, partially or completely, if the antipsychotic is withdrawn. Prescribing should be in a manner to minimize the occurrence. In patients who require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically. If signs and symptoms should appear drug discontinuation should be considered. **Hyperglycemia and Diabetes Mellitus:** Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with all atypical antipsychotics. Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. **Gastrointestinal:** Because the INVEGA™ tablet is non-deformable and does not appreciably change in shape in the gastrointestinal tract, INVEGA™ should ordinarily not be administered to patients with pre-existing severe gastrointestinal narrowing (pathologic or iatrogenic, for example: esophageal motility disorders, small bowel inflammatory disease, "short gut" syndrome due to adhesions or decreased transit time, past history of peritonitis, cystic fibrosis, chronic intestinal pseudoobstruction, or Meckel's diverticulum). There have been rare reports of obstructive symptoms in patients with known strictures in association with the ingestion of drugs in non-deformable controlled-release formulations. Because of the controlled-release design of the tablet, INVEGA™ should only be used in patients who are able to swallow the tablet whole (see PRECAUTIONS: Information for Patients). A decrease in transit time, e.g., as seen with diarrhea, would be expected to decrease bioavailability and an increase in transit time, e.g., as seen with gastrointestinal neuropathy, diabetic gastroparesis, or other causes, would be expected to increase bioavailability. These changes in bioavailability are more likely when the changes in transit time occur in the upper GI tract. **Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients With Dementia-Related Psychosis:** In placebo-controlled trials with risperidone, aripiprazole, and olanzapine in elderly subjects with dementia, there was a higher incidence of cerebrovascular adverse events (cerebrovascular accidents and transient ischemic attacks) including fatalities compared to placebo-treated subjects. INVEGA™ was not marketed at the time these studies were performed. INVEGA™ is not approved for the treatment of patients with dementia-related psychosis (see also Boxed WARNING, WARNINGS: Increased Mortality in Elderly Patients with Dementia-Related Psychosis).

PRECAUTIONS

General: Orthostatic Hypotension and Syncope: Paliperidone can induce orthostatic hypotension and syncope in some patients because of its alpha-blocking activity. In pooled results of the three placebo-controlled, 6-week, fixed-dose trials, syncope was reported in 0.8% (7/850) of subjects treated with INVEGA™ (3, 6, 9, 12 mg) compared to 0.3% (1/355) of subjects treated with placebo. INVEGA™ should be used with caution in patients with known cardiovascular disease (e.g., heart failure, history of myocardial infarction or ischemia, conduction abnormalities), cerebrovascular disease, or conditions that predispose the patient to hypotension (dehydration, hypovolemia, and treatment with antihypertensive medications). Monitoring of orthostatic vital signs should be considered in patients who are vulnerable to hypotension. **Seizures:** Like other antipsychotic drugs, INVEGA™ should be used cautiously in patients with a history of seizures or other conditions that potentially lower the seizure threshold. **Hyperprolactinemia:** Like other drugs that antagonize dopamine D_2 receptors, paliperidone elevates prolactin levels and the elevation persists during chronic administration. Paliperidone has a prolactin-elevating effect similar to that seen with risperidone, a drug that is associated with higher levels of prolactin than other antipsychotic drugs. Galactorrhea, amenorrhea, gynecomastia, and impotence have been reported in patients receiving prolactin-elevating compounds. An increase in the incidence of pituitary gland, mammary gland, and pancreatic islet cell neoplasia (mammary adenocarcinomas, pituitary and pancreatic adenomas) was observed in the risperidone carcinogenicity studies conducted in mice and rats (see PRECAUTIONS: Carcinogenesis, Mutagenesis, Impairment of Fertility). 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, but the available evidence is too limited to be conclusive. **Dysphagia:** Esophageal dysmotility and aspiration have been associated with antipsychotic drug use. Aspiration pneumonia is a common cause of morbidity and mortality in patients with advanced Alzheimer's dementia. INVEGA™ and other antipsychotic drugs should be used cautiously in patients at risk for aspiration pneumonia. **Suicide:** The possibility of suicide attempt is inherent in psychotic illnesses, and close supervision of high-risk patients should accompany drug therapy. **Potential for Cognitive and Motor Impairment:** Somnolence and sedation were reported in subjects treated with INVEGA™ (see ADVERSE REACTIONS). Antipsychotics, including INVEGA™, have the potential to impair judgment, thinking, or motor skills. Patients should be cautioned about performing activities requiring mental alertness, such as operating hazardous machinery or operating a motor vehicle, until they are reasonably certain that paliperidone therapy does not adversely affect them. **Priapism:** No cases of priapism have been reported in clinical trials with INVEGA™. **Thrombotic Thrombocytopenia Purpura (TTP):** No cases of TTP were observed during clinical studies with paliperidone. Although cases of TTP have been reported in association with risperidone administration, the relationship to risperidone therapy is unknown. **Body Temperature Regulation:** Disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic agents. Appropriate care is advised when prescribing INVEGA™ to patients who will be experiencing conditions which may contribute to an elevation in core body temperature. **Antiemetic Effect:** An antiemetic effect was observed in preclinical studies with paliperidone. This effect, if it occurs in humans, may mask the signs and symptoms of overdosage with certain drugs or of conditions such as intestinal obstruction, Reye's syndrome, and brain tumor. **Use in Patients with Concomitant Illness:** Clinical experience with INVEGA™ in patients with certain concomitant illnesses is limited (see CLINICAL PHARMACOLOGY: Pharmacokinetics: Special Populations: Hepatic Impairment and Renal Impairment in full PI). Patients with Parkinson's Disease or Dementia with Lewy Bodies are reported to have an increased sensitivity to antipsychotic medication. Manifestations of this increased sensitivity include confusion, obtundation, postural instability with frequent falls, extrapyramidal symptoms, and clinical features consistent with the neuroleptic malignant syndrome. INVEGA™ 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 trials. Because of the risk of orthostatic hypotension with INVEGA™, caution should be observed in patients with known cardiovascular disease (see PRECAUTIONS: General: Orthostatic Hypotension and Syncope). **Information for Patients:** Physicians are advised to discuss the following issues with patients for whom they prescribe INVEGA™. **Orthostatic Hypotension:** Patients should be advised that there is risk of orthostatic hypotension, particularly at the time of initiating treatment, re-initiating treatment, or increasing the dose. **Interference With Cognitive and Motor Performance:** As INVEGA™ has the potential to impair judgment, thinking, or motor skills, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that INVEGA™ therapy does not affect them adversely. **Pregnancy:** Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during treatment with INVEGA™. **Nursing:** Patients should be advised not to breast-feed an infant if they are taking INVEGA™. **Concomitant Medication:** Patients should be advised to inform their physicians if they are taking, or plan to take, any prescription or over-the-counter drugs, as there is a potential for interactions. **Alcohol:** Patients should be advised to avoid alcohol while taking INVEGA™. **Heat Exposure and Dehydration:** Patients should be advised regarding appropriate care in avoiding overheating and dehydration. **Administration:** Patients should be informed that INVEGA™ should be swallowed whole with the aid of liquids. Tablets should not be chewed, divided, or crushed. The medication is contained within a nonabsorbable shell designed to release the drug at a controlled rate. The tablet shell, along with insoluble core components, is eliminated from the body; patients should not be concerned if they occasionally notice something that looks like a tablet in their stool. **Drug Interactions: Potential for INVEGA™ to Affect Other Drugs** – Paliperidone is not expected to cause clinically important pharmacokinetic interactions with drugs that are metabolized by cytochrome P450 isozymes. *In vitro* studies in human liver microsomes showed that paliperidone does not substantially inhibit the metabolism of drugs metabolized by cytochrome P450 isozymes, including CYP1A2, CYP2A6, CYP2C8/9/10, CYP2D6, CYP2E1, CYP3A4, and CYP3A5. Therefore, paliperidone is not expected to inhibit clearance of drugs that are metabolized by these metabolic pathways in a clinically relevant manner. Paliperidone is also not expected to have enzyme inducing properties. At therapeutic concentrations, paliperidone did not inhibit P-glycoprotein. Paliperidone is therefore not expected to inhibit P-glycoprotein-mediated transport of other drugs in a clinically relevant manner. Given the primary CNS effects of paliperidone (see ADVERSE REACTIONS), INVEGA™ should be used with caution in combination with other centrally acting drugs and alcohol. Paliperidone may antagonize the effect of levodopa and other dopamine agonists. Because of its potential for inducing orthostatic hypotension, an additive effect may be observed when INVEGA™ is administered with other therapeutic agents that have this potential (see PRECAUTIONS: General: Orthostatic Hypotension and Syncope). **Potential for Other Drugs to Affect INVEGA™** – Paliperidone is not a substrate of CYP1A2, CYP2A6, CYP2C9, and CYP2C19, so that an interaction with inhibitors or inducers of these isozymes is unlikely. While *in vitro* studies indicate that CYP2D6 and CYP3A4 may be minimally involved in paliperidone metabolism, *in vivo* studies do not show decreased elimination by these isozymes and they contribute to only a small fraction of total body clearance. **Carcinogenesis, Mutagenesis, Impairment of Fertility: Carcinogenesis:** Carcinogenicity studies of paliperidone have not been performed. Carcinogenicity studies of risperidone, which is extensively converted to paliperidone in rats, mice, and humans, were conducted in Swiss albino mice and Wistar rats. Risperidone was administered in the diet at daily doses of 0.63, 2.5, and 10 mg/kg for 18 months to mice and for 25 months to rats. A maximum tolerated dose was not achieved in male mice. There were statistically significant increases in pituitary gland adenomas, endocrine pancreas adenomas, and mammary gland adenocarcinomas. The no-effect dose for these tumors was less than or equal to the maximum

INVEGA™ (paliperidone) extended-release tablets is indicated for the acute and maintenance treatment of schizophrenia.

IMPORTANT SAFETY INFORMATION FOR INVEGA

Increased Mortality in Elderly Patients with Dementia-Related Psychosis

Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of 17 placebo-controlled trials (modal duration of 10 weeks) in these patients revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times that seen 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. INVEGA™ (paliperidone) is not approved for the treatment of patients with Dementia-Related Psychosis.

Commonly observed adverse events: The most commonly observed adverse events, occurring at an incidence of ≥5% and at least 2 times placebo, were akathisia and extrapyramidal disorder.

QT Prolongation: INVEGA causes a modest increase in the corrected QT (QTc) interval. INVEGA should be avoided in combination with other drugs that are known to prolong the QTc interval, in patients with congenital long QT syndrome or a history of cardiac arrhythmias. Certain circumstances may increase the risk of torsades de pointes and/or sudden death in association with the use of drugs that prolong the QTc interval.

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

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

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

Gastrointestinal: INVEGA should ordinarily not be administered to patients with pre-existing severe gastrointestinal narrowing. Rare instances of obstructive symptoms have been reported in patients with known strictures taking nondeformable formulations. INVEGA should only be used in patients who are able to swallow the tablet whole.

Cerebrovascular Adverse Events (CAEs): CAEs, including fatalities, have been reported in elderly patients with dementia-related psychosis taking atypical antipsychotics in clinical trials. INVEGA is not approved for treating these patients.

Seizures: INVEGA should be used cautiously in patients with a history of seizures.

Hyperprolactinemia: As with other drugs that antagonize dopamine D_2 receptors, INVEGA elevates prolactin levels and the elevation persists during chronic administration.

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

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

Potential for Cognitive and Motor Impairment: INVEGA has the potential to impair judgment, thinking, or motor skills. Caregivers and patients should use caution until they are reasonably certain that INVEGA does not affect them adversely.

Maintenance Treatment: Physicians who elect to use INVEGA for extended periods should periodically re-evaluate the long-term risks and benefits of the drug for the individual patient.

References: 1. Data on file. Janssen, L.P., Titusville, NJ. **2.** Kramer M, Simpson G, Maciulis V, et al. Paliperidone extended-release tablets for prevention of symptom recurrence in patients with schizophrenia: a randomized, double-blind, placebo-controlled study. *J Clin Psychopharmacol.* 2007;27(1):6-14. **3.** Kane J, Canas F, Kramer M, et al. Treatment of schizophrenia with paliperidone extended-release tablets: a 6-week placebo-controlled trial. *Schizophr Res.* 2007;90:147-161.

Please see accompanying brief summary of full Prescribing Information for INVEGA.

recommended human dose of risperidone on a mg/m^2 basis (see risperidone package insert). An increase in mammary, pituitary, and endocrine pancreas neoplasms has been found in rodents after chronic administration of other antipsychotic drugs and is considered to be mediated by prolonged dopamine D_2 antagonism and hyperprolactinemia. The relevance of these tumor findings in rodents in terms of human risk is unknown (see PRECAUTIONS: General: Hyperprolactinemia). **Mutagenesis:** No evidence of genotoxic potential for paliperidone was found in the Ames reverse mutation test, the mouse lymphoma assay, or the *in vivo* rat micronucleus test. **Impairment of Fertility:** In a study of fertility, the percentage of treated female rats that became pregnant was not affected at oral doses of paliperidone of up to 2.5 mg/kg/day. However, pre- and post-implantation loss was increased, and the number of live embryos was slightly decreased, at 2.5 mg/kg, a dose that also caused slight maternal toxicity. These parameters were not affected at a dose of 0.63 mg/kg, which is half of the maximum recommended human dose on a mg/m^2 basis. The fertility of male rats was not affected at oral doses of paliperidone of up to 2.5 mg/kg/day, although sperm count and sperm viability studies were not conducted with paliperidone. In a subchronic study in Beagle dogs with risperidone, which is extensively converted to paliperidone in dogs and humans, all doses tested (0.31-5.0 mg/kg) resulted in decreases in serum testosterone and in sperm motility and concentration. Serum testosterone and sperm parameters partially recovered, but remained decreased after the last observation (two months after treatment was discontinued). **Pregnancy: Pregnancy Category C:** In studies in rats and rabbits in which paliperidone was given orally during the period of organogenesis, there were no increases in fetal abnormalities up to the highest doses tested (10 mg/kg/day in rats and 5 mg/kg/day in rabbits, which are 8 times the maximum recommended human dose on a mg/m^2 basis). In rat reproduction studies with risperidone, which is extensively converted to paliperidone in rats and humans, increases in pup deaths were seen at oral doses which are less than the maximum recommended human dose of risperidone on a mg/m^2 basis (see risperidone package insert). Use of first generation antipsychotic drugs during the last trimester of pregnancy has been associated with extrapyramidal symptoms in the neonate. These symptoms are usually self-limited. It is not known whether paliperidone, when taken near the end of pregnancy, will lead to similar neonatal signs and symptoms. There are no adequate and well controlled studies of INVEGA™ in pregnant women. INVEGA™ should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Labor and Delivery:** The effect of INVEGA™ on labor and delivery in humans is unknown. **Nursing Mothers:** In animal studies with paliperidone and in human studies with risperidone, paliperidone was excreted in the milk. Therefore, women receiving INVEGA™ should not breast-feed infants. **Pediatric Use:** Safety and effectiveness of INVEGA™ in patients < 18 years of age have not been established. **Geriatric Use:** The safety, tolerability, and efficacy of INVEGA™ were evaluated in a 6-week placebo-controlled study of 114 elderly subjects with schizophrenia (65 years of age and older, of whom 21 were 75 years of age and older). In this study, subjects received flexible doses of INVEGA™ (3 to 12 mg once daily). In addition, a small number of subjects 65 years of age and older were included in the 6-week placebo-controlled studies in which adult schizophrenic subjects received fixed doses of INVEGA™ (3 to 15 mg once daily, see CLINICAL PHARMACOLOGY: Clinical Trials in full PI). Overall, of the total number of subjects in clinical studies of INVEGA™ (n = 1796), including those who received INVEGA™ or placebo, 125 (7.0%) were 65 years of age and older and 22 (1.2%) were 75 years of age and older. 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 response between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. This drug is known to be substantially excreted by the kidney and clearance is decreased in patients with moderate to severe renal impairment (see CLINICAL PHARMACOLOGY: Pharmacokinetics: Special Populations: Renal Impairment in full PI), who should be given reduced doses. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function (see DOSAGE AND ADMINISTRATION: Dosing in Special Populations in full PI).

ADVERSE REACTIONS

The information below is derived from a clinical trial database for INVEGA™ consisting of 2720 patients and/or normal subjects exposed to one or more doses of INVEGA™ for the treatment of schizophrenia. Of these 2720 patients, 2054 were patients who received INVEGA™ while participating in multiple dose, effectiveness trials. The conditions and duration of treatment with INVEGA™ varied greatly and included (in overlapping categories) open-label and double-blind phases of studies, inpatients and outpatients, fixed-dose and flexible-dose studies, and short-term and longer-term exposure. Adverse events were assessed by collecting adverse events and performing physical examinations, vital signs, weights, laboratory analyses and ECGs. Adverse events during exposure were obtained by general inquiry and recorded by clinical investigators using their own terminology. Consequently, to provide a meaningful estimate of the proportion of individuals experiencing adverse events, events were grouped in standardized categories using MedDRA terminology. The stated frequencies of adverse events represent the proportions of individuals who experienced 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. The information presented in these sections was derived from pooled data from the three placebo-controlled, 6-week, fixed-dose studies based on subjects with schizophrenia who received INVEGA™ at daily doses within the recommended range of 3 to 12 mg (n = 850). Additional safety information from the placebo-controlled phase of the long-term maintenance study, in which subjects received INVEGA™ at daily doses within the range of 3 to 15 mg (n = 104), is also included. **Adverse Events Observed in Short-Term, Placebo-Controlled Trials of Subjects with Schizophrenia** The information presented in these sections were derived from pooled data from the three placebo-controlled, 6-week, fixed-dose studies based on subjects with schizophrenia who received INVEGA™ at daily doses within the recommended range of 3 to 12 mg (n = 850). Adverse Events Occurring at an Incidence of 2% or More Among INVEGA™-Treated Patients with Schizophrenia and More Frequent on Drug than Placebo Table 1 enumerates the pooled incidences of treatment-emergent adverse events that were spontaneously reported in the three placebo-controlled, 6-week, fixed-dose studies, listing those events that occurred in 2% or more of subjects treated with INVEGA™ in any of the dose groups, and for which the incidence in INVEGA™-treated subjects in any of the dose groups was greater than the incidence in subjects treated with placebo. **Treatment-Emergent Adverse Events in Short-Term, Fixed-Dose, Placebo-Controlled Trials in Adult Subjects with Schizophrenia.* Body System or Organ Class** (Dictionary-derived Term) Percentage of Patients Reporting Event INVEGA™ Placebo (N=355) first, INVEGA™ dosage once daily 3 mg (N=127) second, 6 mg N=235) third, 9 mg (N=246) fourth, 12 mg (N=242) fifth, **Percentage of subjects with adverse events** 66, 72, 66, 70, 76; **Cardiac disorders:** Atrioventricular block first degree 1, 2, 0, 2, 1; Bundle branch block 2, 3, 1, 3, <1; Sinus arrhythmia 0, 2, 1, 1, <1; Tachycardia 7, 14, 12, 12, 14; **Eye disorders:** Vision blurred 1, 1, <1, 0, 2; **Gastrointestinal disorders:** Abdominal pain upper 1, 1, 3, 2, 2; Dry mouth 1, 2, 3, 1, 3; Dyspepsia 4, 2, 3, 2, 5; Nausea 5, 6, 4, 4, 4; Salivary hypersecretion <1, 0, <1, 1, 4; **General disorders**: Asthenia 1, 2, <1, 2, 2; Fatigue 1, 2, 1, 2, 2; Pyrexia 1, 1, <1, 2, 2; **Investigations:** Blood insulin increased 1, 2, 1, 1, <1; Blood pressure increased 1, 2, <1, <1, 1; Electrocardiogram QT corrected interval prolonged 3, 3, 4, 3, 5; Electrocardiogram T wave abnormal 1, 2, 1, 2, 1; **Musculoskeletal and connective tissue disorders**: Back pain 1, 1, 1, 1, 2; Pain in extremity 1, 0, 1, 0, 2; **Nervous system disorders**: Akathisia 4, 4, 3, 8, 10; Dizziness 4, 6, 5, 4, 5; Dystonia 1, 1, 1, 5, 4; Extrapyramidal disorder 2, 5, 2, 7, 7; Headache 12, 11, 12, 14, 14; Hypertonia 1, 2, 1, 4, 3; Parkinsonism 0, 0, <1, 2, 1; Somnolence 7, 6, 9, 10, 11; Tremor 3, 3, 3, 4, 3; **Psychiatric disorders**: Anxiety 8, 9, 7, 6, 5; **Respiratory, thoracic and mediastinal disorders**: Cough 1, 3, 2, 3, 2; **Vascular disorders**: Orthostatic hypotension 1, 2, 1, 2, 4; *Table includes adverse events that were reported in 2% or more of subjects in any of the INVEGA™ dose groups and which occurred at greater incidence than in the placebo group. Data are pooled from three studies; one included once-daily INVEGA™ doses of 3 and 9 mg, the second study included 6, 9, and 12 mg, and the third study included 6 and 12 mg (see CLINICAL PHARMACOLOGY: Clinical Trials in full PI). Events for which the INVEGA™ incidence was equal to or less than placebo are not listed in the table, but included the following: constipation, diarrhea, vomiting, nasopharyngitis, agitation, and insomnia. **Dose-Related Adverse Events in Clinical Trials:** Based on the pooled data from the three placebo-controlled, 6-week, fixed-dose studies, adverse events that occurred with a greater than 2% incidence in the subjects treated with INVEGA™, the incidences of the following adverse events increased with dose: somnolence, orthostatic hypotension, salivary hypersecretion, akathisia, dystonia, extrapyramidal disorder, hypertonia and Parkinsonism. For most of these, the increased incidence was seen primarily at the 12 mg, and in some cases the 9 mg dose. **Common and Drug-Related Adverse Events in Clinical Trials** In the pooled data from three placebo-controlled, 6-week, fixed-dose studies, adverse events reported in 5% or more of subjects treated with INVEGA™ and at least twice the placebo rate for at least one dose included: akathisia and extrapyramidal disorder. **Extrapyramidal Symptoms (EPS) in Clinical Trials:** Pooled data from the three placebo-controlled, 6-week, fixed-dose studies provided information regarding treatment-emergent EPS. Several methods were used to measure EPS: (1) the Simpson-Angus global score (mean change from baseline) which broadly evaluates Parkinsonism, (2) the Barnes Akathisia Rating Scale global clinical rating score (mean change from baseline) which evaluates akathisia, (3) use of anticholinergic medications to treat emergent EPS, and (4) incidence of spontaneous reports of EPS. For the Simpson-Angus Scale, spontaneous EPS reports and use of anticholinergic medications, there was a dose-related increase observed for the 9 mg and 12 mg doses. There was no difference observed between placebo and INVEGA™ 3 mg and 6 mg doses for any of these EPS measures. **Percentage of Patients INVEGA™** Placebo (N=355) first, INVEGA™ dosage once daily 3 mg (N=127) second, 6 mg N=235) third, 9 mg (N=246) fourth, 12 mg (N=242) fifth, **EPS Group:** Parkinsonism [a] 9, 11, 3, 15, 14; Akathisia [b] 6, 6, 4, 7, 9; Use of anticholinergic medications [c] 10, 10, 9, 22, 22; [a]: For Parkinsonism, percent of patients with Simpson-Angus global score > 0.3 (Global score defined as total sum of items score divided by the number of items). [b]: For Akathisia, percent of patients with Barnes Akathisia Rating Scale global score ≥ 2. [c]: Percent of patients who received anticholinergic medications to treat emergent EPS. **Percentage of Patients INVEGA™** Placebo (N=355) first, INVEGA™ dosage once daily 3 mg (N=127) second, 6 mg N=235) third, 9 mg (N=246) fourth, 12 mg (N=242) fifth, **EPS Group**: Overall percentage of patients with EPS-related AE 11.0, 12.6, 10.2, 25.2, 26.0; Dyskinesia 3.4, 4.7, 2.6, 7.7, 8.7; Dystonia 1.1, 0.8, 1.3, 5.3, 4.5; Hyperkinesia 3.9, 3.9, 3.0, 8.1, 9.9; Parkinsonism 2.3, 3.1, 2.6, 7.3, 6.2; Tremor 3.4, 3.1, 2.6, 4.5, 3.3: Dyskinesia group includes: Dyskinesia, Extrapyramidal disorder, Muscle twitching, Tardive dyskinesia Dystonia group includes: Dystonia, Muscle spasms, Oculogyration, Trismus. Hyperkinesia group includes: Akathisia, Hyperkinesia. Parkinsonism group includes: Bradykinesia, Cogwheel rigidity, Drooling, Hypertonia, Hypokinesia, Muscle rigidity, Musculoskeletal stiffness, Parkinsonism. Tremor group includes: Tremor. **Adverse Events Associated with Discontinuation of Treatment in Controlled Clinical Studies:** Based on the pooled data from the three placebo-controlled, 6-week, fixed dose studies, there was no difference in the incidence of discontinuation due to adverse events between INVEGA™-treated (5%) and placebo-treated (5%) subjects. The types of adverse events that led to discontinuation were similar for the INVEGA™-and placebo-treated subjects, except for Nervous System Disorders events which were more common among INVEGA™-treated subjects than placebo-treated subjects (2% and 0%, respectively), and Psychiatric Disorders events which were more common among placebo-treated subjects than INVEGA™-treated subjects (3% and 1%, respectively). **Demographic Differences in Adverse Reactions in Clinical Trials:** An examination of population subgroups in the three placebo-controlled, 6-week, fixed-dose studies did not reveal any evidence of differences in safety on the basis of age, gender or race (see PRECAUTIONS: Geriatric Use). **Laboratory Test Abnormalities in Clinical Trials:** In the pooled data from the three placebo-controlled, 6-week, fixed-dose studies, between-group comparisons revealed no medically important differences between INVEGA™ and placebo in the proportions of subjects experiencing potentially clinically significant changes in routine hematology, urinalysis, or serum chemistry, including mean changes from baseline in fasting glucose, insulin, c-peptide, triglyceride, HDL, LDL, and total cholesterol measurements. Similarly, there were no differences between INVEGA™ and placebo in the incidence of discontinuations due to changes in hematology, urinalysis, or serum chemistry. However, INVEGA™ was associated with increases in serum prolactin (see PRECAUTIONS: General: Hyperprolactinemia). **Weight Gain in Clinical Trials:** In the pooled data from the three placebo-controlled, 6-week, fixed-dose studies, the proportions of subjects having a weight gain of ≥ 7% of body weight were similar for INVEGA™ 3 mg and 6 mg (7% and 6%, respectively) and placebo (5%), but there was a higher incidence of weight gain for INVEGA™ 9 mg and 12 mg (9% and 9%, respectively). **Other Events Observed During the Premarketing Evaluation of INVEGA™:** The following list contains all serious and non-serious treatment-emergent adverse events reported at any time by individuals taking INVEGA™ during any phase of a trial within the premarketing database (n = 2720), except (1) those listed in Table 1 above or elsewhere in labeling, (2) those for which a causal relationship to INVEGA™ use was considered remote, and (3) those occurring in only one subject treated with INVEGA™ and that were not acutely life-threatening. Events are classified within body system categories using the following definitions: *very frequent* adverse events are defined as those occurring on one or more occasions in at least 1/10 subjects, *frequent* adverse events are defined as those occurring on one or more occasions in at least 1/100 subjects, *infrequent* adverse events are those occurring on one or more occasions in 1/100 to 1/1000 subjects, and *rare* events are those occurring on one or more occasions in less than 1/1000 subjects. **Blood and Lymphatic System Disorders:** *rare*: thrombocytopenia; **Cardiac Disorders:** *frequent*: palpitations; *infrequent*: bradycardia; **Gastrointestinal Disorders:** *frequent:* abdominal pain; *infrequent*: swollen tongue; **General Disorders:** *infrequent*: edema; **Immune Disorder:** *rare*: anaphylactic reaction; **Nervous System Disorders:** *rare*: coordination abnormal; **Psychiatric Disorders:** *infrequent*: confusional state; **Respiratory, Thoracic and Mediastinal Disorders:** *frequent*: dyspnea; *rare*: pulmonary embolus; **Vascular Disorders:** *rare*: ischemia, venous thrombosis; The safety of INVEGA™ was also evaluated in a long-term trial designed to assess the maintenance of effect with INVEGA™ in adults with schizophrenia (see CLINICAL PHARMACOLOGY: Clinical Trials in full PI). In general, adverse event types, frequencies, and severities during the initial 14-week open-label phase of this study were comparable to those observed in the 6-week, placebo-controlled, fixed-dose studies. Adverse events reported during the long-term double-blind phase of this study were similar in type and severity to those observed in the initial 14-week open-label phase. **Adverse Events Reported With Risperidone**; Paliperidone is the major active metabolite of risperidone. Adverse events reported with risperidone can be found in the ADVERSE REACTIONS section of the risperidone package insert.

DRUG ABUSE AND DEPENDENCE

Controlled Substance: INVEGA™ (paliperidone) is not a controlled substance.

For more information on symptoms and treatment of overdosage, see full Prescribing Information.

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Janssen

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Better Mental Health May Be Upside of Getting Old

Could it be that mental health, like a good wine, improves with age? Evidence is building that this might be the case, even for people who have a mental illness.

BY JOAN AREHART-TREICHEL

Physical health tends to be better when people are young, but could the opposite be true for mental health?

Barring the onset of dementia or a terminal illness, the answer is often yes, a building body of provocative evidence suggests.

Take, for example, a study reported in the March 2006 *Canadian Journal of Psychiatry* by David Streiner, Ph.D., a professor of psychiatry at the University of Toronto, and colleagues. They assessed the prevalence of mood and anxiety disorders in a nationally representative population of Canadians aged 55 and older to see if the prevalence of these disorders changed with age. They found that there was in fact a linear decrease for these disorders after age 55. This was true for men and women and for people born in Canada and those who immigrated to Canada after age 18.

Or take a study headed by George Vaillant, M.D., a professor of psychiatry at Harvard University and co-director of the Study of Adult Development there. He and his colleagues followed a cohort of 151 inner-city men from adolescence until an average age of 75. The men came from socially disadvantaged families, had dropped out of school, and had a low IQ. Nonetheless, a surprisingly large number enjoyed retirement in their later years. And as Vaillant and his group concluded in a report in the April 2006 *American Journal of Psychiatry*: "The very risk factors associated with bleak young adulthood, and the very risk factors associated with bleak midlife adjustment, appeared to exert relatively little effect on whether the men, followed since 1940, currently enjoyed retirement. . . . It appeared as if retirement created—for these men at least—a new age and a third chance at a contented life."

Research conducted by Dilip Jeste, M.D., a professor of psychiatry at the University of California, San Diego, and colleagues on 205 older people living in San Diego County also bolsters the case that mental health tends to improve with age. The researchers asked the seniors, who ranged in age from 60 to 102 and who had common physical illnesses that often afflict seniors, to rate themselves on a scale of 1 to 10 indicating how well they believed they had aged. A rating of 1 was the worst a subject could give himself or herself, and 10 was the best. The researchers expected most of the subjects to rate themselves with a 3 or 4, but it turned out that the average score was 8.4, the researchers reported in the January 2006 *American Journal of Geriatric Psychiatry*.

Age Benefits Those With Mental Illness

One of the major findings from the National Comorbidity Survey Replication, published in the June 2005 *Archives of General Psychiatry*, was that most mental disorders usually have their onset in childhood or adolescence. Such early onset, the researchers wrote, is "opposite of the patterns found for almost all chronic physical disorders" (*Psychiatric News*, July 15, 2005). Thus one might expect mental illnesses to become well entrenched and more difficult to recover from by the time people reach their 50s and beyond. However, this does not seem to be the case, growing evidence suggests.

For example, Jeste and his colleagues longitudinally followed several hundred adults with schizophrenia. As the subjects grew older, and even as their physical functioning deteriorated, their hallucinations and delusions appeared to decrease considerably, and their negative symptoms decreased somewhat as well.

"There is less depression in late life than any of the epidemiologists expected, especially if you control for Alzheimer's, alcoholism, and major depressive disorder," Vaillant said in an interview with *Psychiatric News*. "And even if you follow people with major depressive disorder—people who are really quite crippled during their adult lives—they are often doing much better in their 70s, at least if they survive the cigarette smoking that goes with depression."

A Swiss psychiatrist—Wulf Roessler, M.D., a professor of clinical and social psychiatry at the University of Zurich—found that a surprisingly large number of people in the general Swiss population showed signs of subthreshold psychosis, but that fewer people showed such signs as they aged (*Psychiatric News*, June 1).

In addition, individuals who abuse substances and those with eating disorders are more likely to get better with age, Joel Paris, M.D., a professor of psychiatry at McGill University in Montreal, told *Psychiatric News*. The same is even the case for people with borderline personality disorder or antisocial personality disorder, Paris has found (*Psychiatric News*, July 7, 2006; June 1). Data from short-term follow-ups of individuals with obsessive-compulsive personality disorder suggest that they too tend to improve as they age, said Paris.

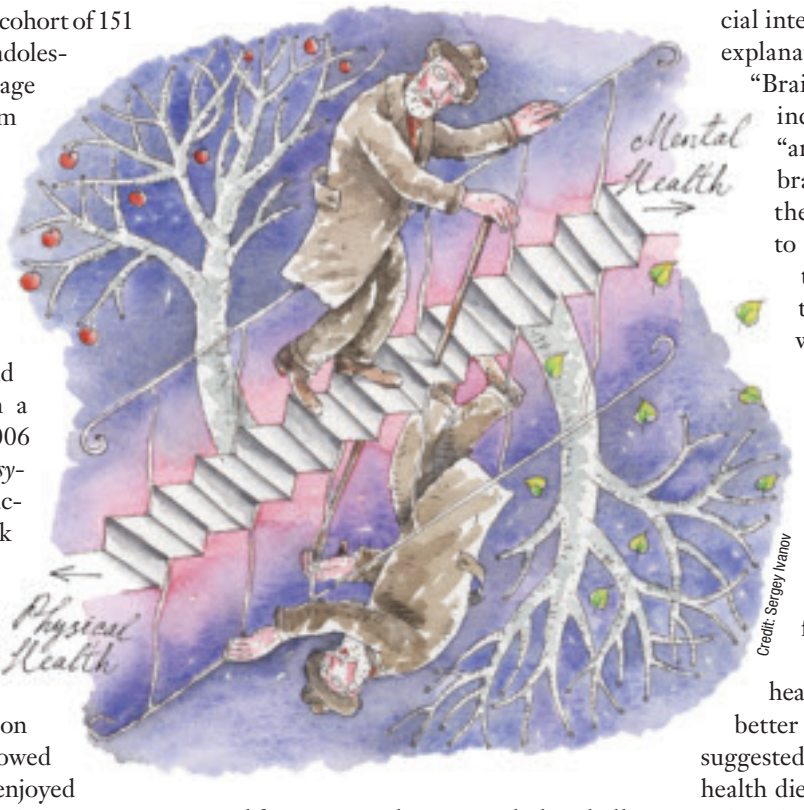
"The big exception is bipolar disorder, which sometimes gets worse with age," Paris pointed out. Jeste, however, is not so sure: "Actually we have some very preliminary data on bipolar disorder in older people. Some of the older bipolar patients seem to be doing better than some of the younger ones."

Hypotheses Offered

Relatively little research has been conducted to find out why mental health and mental illness may improve with age.

However, some psychiatrists with a special interest in the subject offer possible explanations.

"Brain myelinization is known to increase with age," said Vaillant, "and the better insulated your brain is, the better it works. Also, the part of the brain that continues to be integrated last is that part of the brain that connects the emotional life—the limbic system—with the frontal lobes. So instead of being uptight or having 'hissy fits' like you did when you were younger, you are able to gracefully modulate your emotional intelligence as you grow older. In other words, emotional intelligence increases with age as memory for names gets worse."



Credit: Sergey Ivanov

One reason why the mental health of older people may seem to be better than that of younger ones, Jeste suggested, is that those with poorer mental health die earlier. However, his longitudinal study showing that schizophrenia subjects' mental health sometimes improves with age belies this explanation, he noted.

"My own view is that older people may actually be more vulnerable biologically in some ways. . .to developing mental illnesses in late life," Dan Blazer II, M.D., Ph.D., a professor of psychiatry at Duke University, said. "However, I think that from a psychological perspective, and perhaps a little bit from a social perspective too, there are modifiers that maybe protect older persons from developing mental illnesses later in life. And that is one of the reasons we tend to see a somewhat lower frequency of most of the major mental illnesses in late life, except for the dementing disorders."

For example, Blazer said, "older people tend to accumulate wisdom, and one part of wisdom is that they have been through a number of events and know how to deal with them. That in turn may protect them when they experience crises in later life, such as physical illness, loss of a spouse, or loss of friends."

There is also reason to believe that older persons may respond better emotionally to challenges than younger people do because of where they see themselves in life, Blazer suggested. That is, they may be more focused on the present than on the future because they don't have all that many more years to live, and focusing on the present may help them cope better with crises, which in turn helps safeguard their mental health.

A possible reason why individuals with borderline personality disorder, antisocial personality disorder, and substance abuse often improve as they age, Paris proposed, is because people tend to become less impulsive as they grow older, and impulsivity is a key factor in all three of these disorders.

How Do Findings Affect Practice?

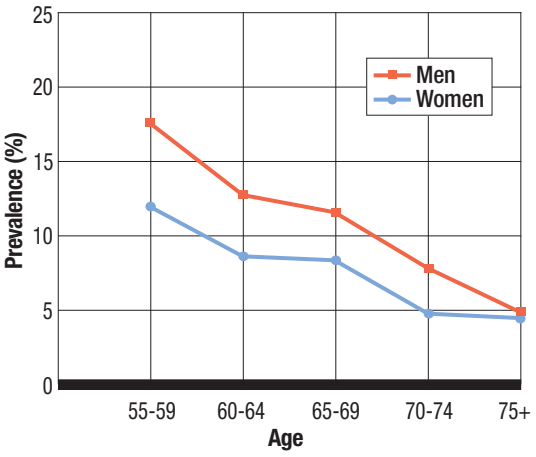
So if people's mental health tends to improve with age—a hypothesis that not all psychiatrists endorse, and one with many exceptions—what are the implications for psychiatric practice?

"We have a cultural belief that it is better to be young than old," said Paris, "but from the point of view of psychological symptoms, it seems to be untrue. So that's worth noting. Another implication is that people may get better with time with or without intervention, even within a shorter time frame, like five years. So that's useful to know. I think the problem is that we [psychiatrists] end up seeing cases that don't get better. This leads to a bias [in our outlook]. The people who get better disappear, so there is a tendency to see illnesses as more chronic than they really are."

Vaillant agreed. "Psychiatrists tend to meet the people who are doing badly. . . . They simply don't have an adequate perspective on adult development. . . . When you study people for 40 years as I have, you see a different world." ■

Risk of Mood Disorders Decreases With Age

Researchers assessed the prevalence of mood and anxiety disorders in a nationally representative population of Canadians aged 55 and older between May and December 2002 to see whether the prevalence of these disorders changed with age. They found that prevalence dropped progressively after age 55 for both men and women. Thus, older Canadians may be less susceptible to mood disorders than younger Canadians are.



Source: David Streiner, Ph.D., et al., *Canadian Journal of Psychiatry*, March 2006

Depression Treatment Program A Good Business Investment

Employers who make it easier for workers with depression to be screened and treated are likely to see a "return on their investment."

BY EVE BENDER

Employees at a number of major U.S. corporations who were randomized to an enhanced depression treatment program that included a telephone outreach intervention experienced less-severe depression symptoms and increased work productivity and job retention compared with employees receiving usual care, according to a study in the September 26 *Journal of the American Medical Association*.

Employers are often reluctant to invest in depression screening and treatment programs due to fears that doing so would be expensive, according to the report. However, the results of a randomized, controlled trial led by principal investigator Philip Wang, M.D., showed that the increased work retention and number of hours worked by employees participating in the enhanced program translated into cost savings for employers.

Wang is director of the Division of Services and Intervention Research at the National Institute of Mental Health (NIMH).

"It will be helpful to start alerting employers to the fact that mental health benefits may actually be an investment opportunity," Wang told *Psychiatric News*. "If they improve employees' mental health, they will get something back and improve their bottom line."

Wang and his colleagues randomly recruited 604 employees from 16 major corporations covered by United Behavioral Health (UBH), a large managed behavioral health company, from January 2004 to February 2005 using a two-phase procedure.

Among the companies were an airline, insurance company, major bank, and public utility, and the participating workers represented a wide variety of occupations.

The employees at those companies first completed a health-risk appraisal, which included questions about various health problems, occupation, and sociodemographics.

Employees were also screened for depression with the Kessler-6 Psychological Depression Scale (K-6), and those who scored positive for depression were invited to participate in a telephone interview that assessed depression using the Quick Inventory of Depression Symptoms Self Report (QIDS-SR).

Employees who had a score indicating moderate depression were randomized to either an intervention group or a "usual care" group. Employees in the usual care group were informed that their responses indicated possible depression and advised to consult with a clinician as part of usual care.

Those in the intervention group had professionals described as "care managers" who via telephone contacts assessed them for treatment and facilitated treatment with medications and/or psychotherapy by encouraging patients and monitoring treatment adherence.

Those in the usual-care group did not receive the telephone case management contacts.

Those randomized to the intervention first completed the Patient Health Questionnaire–9, and care managers recommended to those with a significant level of depressive symptoms face-to-face, community-based psychotherapy and medication evaluation. The care managers provided treatment authorization and referral information.

Care managers recommended and facilitated treatment in the community for the intervention group and monitored the treatment closely. The care managers also maintained regular telephone contact with those in the intervention group who declined to seek treatment.

For those who had symptoms of depression after two months and still refused to seek treatment, care managers provided a structured course of cognitive-behavioral therapy by telephone. This included motivational enhancement exercises, help in focusing on rewarding activities, and identifying and challenging negative thoughts.

The care managers working with the intervention group were licensed, master's-level social workers and psychologists employed by UBH. A psychiatrist employed by UBH was available for consultation to clinicians, and some of the study authors, including Wang, provided about an hour of supervision a week to the care managers.

Wang measured several outcomes for participants in both groups, including work productivity (using the World Health Organization and Productivity Questionnaire) and depressive symptoms (using the QIDS-SR).

He found that after a year, the proportion of employees whose symptoms improved substantially (defined as a 50 percent improvement on the QIDS) was substantially higher in the intervention group (30.9 percent) than in the treatment-as-usual group (21.6 percent).

please see ***Investment*** *on page 28*

Hyperactivity in Children Linked to Food Coloring

In a double-blind, placebo-controlled study, artificial food colors and a benzoate preservative appear to increase hyperactivity in children, including those without attention-deficit/hyperactivity disorder.

BY JUN YAN

British researchers have found evidence that suggests artificial food colors and additives may exacerbate hyperactivity in children, according to a study published online in *The Lancet* on September 6.

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Donna McCann, Ph.D., and others from the University of Southampton in England, tested the effects of commonly used food coloring agents and the preservative sodium benzoate on hyperactivity levels in two groups of children: one group consisted of 153 3-year-olds and the other of 144 8- and 9-year-olds. During the six-week study with a within-subject crossover design, the children consumed a set amount of drink mix every day. The drink mixes used in the study were three mixed fruit juices (two active mixes and one placebo) that looked and tasted the same; the only difference was that the two active drinks contained a mixture of artificial food colors and sodium benzoate (see box for ingredients in the active mixes).

Each week, one of the three drink mixes (active mix A, active mix B, or placebo) was delivered to the children's homes for their consumption during that week. On weeks 2, 4, and 6, mix A, mix B, and placebo were delivered in a random sequence. The actual drink delivered to each home at any given week was blinded to the child, the parents, the teachers, and the researchers. Weeks 1, 3, and 5 were washout periods when the children received the placebo drink.

The children's behavior was measured throughout the study period using a global hyperactivity aggregate (GHA) score. The scores were compiled based on observation and ratings by parents and teachers. The children, parents, teachers, and researchers were unaware of the actual drink (active or placebo) given to the children at any given time. The study was commissioned by the U.K. Food Standards Agency (FSA), which regulates food safety.

The children had statistically significant increases in GHA scores associated with the active drink mixes in most but not all analyses. Among the 73 3-year-olds who did drink more than 85 percent of the assigned mixes in all six weeks and had all the GHA scores, and after controlling for several potentially confounding factors, mix A had a significant effect on GHA scores compared with placebo. Mix B, however, did not have a significant effect compared with placebo. Among the 91 8- and 9-year-olds who drank more than 85 percent of the assigned drinks, both mix A and mix B had a significant effect on their GHA scores compared with placebo.

"This is a very important study, rigorously designed by outstanding investigators, and represents an important cautionary note on the need for more studies of the impact of various food additives on children's behavior," psychiatrist Peter Jensen, M.D., the director of the REACH (Resource for Advancing Children's Health) Institute, commented to *Psychiatric News*. "While it could not be determined from this study alone that such additives have a causative role in ADHD, the findings do suggest that additional, similarly carefully designed studies are needed in children generally and in children at risk for ADHD specifically."

Previous studies had implicated artificial food colors and additives in increased hyperactivity in children with ADHD. In contrast, this study recruited a representative sample of children in the community with and without ADHD and showed increased hyperactivity within the overall study population.

Because of the composition of the active drink mixes, the authors acknowledged that it was not possible to parse out an individual additive's effect on hyperactivity. They pointed out that sodium benzoate has an important preservative function, and the implication of these findings could be substantial for the food industry.

> **"This is a very important study . . .and represents an important cautionary note on the need for more studies of the impact of various food additives on children's behavior."**

If these findings are replicated by other investigators and in other populations, said Jensen, regulatory agencies should scrutinize the risks of the widespread use on such additives in foods. Based on this study, the FSA recently updated its advice to consumers, BBC News reported.

"If [children show] signs of ADHD, then eliminating the colors used in the Southamptom study from their diet might have some beneficial effects," said Andrew Wadge, director of food safety policy and chief scientist at the FSA.

Both Wadge and Jim Stevenson, Ph.D., senior author of the study and a professor at Southampton University, both acknowledged that many other factors contribute to ADHD and simply eliminating artificial food colors and sodium benzoate will not necessarily prevent hyperactivitiy disorders.

An abstract of "Food Additives and Hyperactive Behaviour in 3-Year-Old and 8/9-Year-Old Children in the Community: A Randomised, Double-Blinded, Placebo-Controlled Trial" is posted at <www.thelancet.com/journals/lancet/article/PIIS0140673607613063/abstract>. ■

©Tetra Images/Corbis

Researchers tested the effects of commonly used food-coloring agents and the preservative sodium benzoate on hyperactivity levels in two groups of children. The drink mixes used in the study were three mixed fruit juices—two active mixes, designated A and B, and one placebo. Mix A was linked to significantly increased hyperactivity compared with placebo in both 3-year-old children and 8/9-year-olds. Mix B was linked to significantly increased hyperactivity in 8/9-year-olds, but not in 3-year-olds.

Mix A	Mix B
Sunset yellow	Sunset yellow
Carmoisine	Carmoisine
Tartrazine	Quinoline yellow
Ponceau	Allura red AC
Sodium benzoate	Sodium benzoate

Retiring Because of Depression Can Worsen Illness

Depression may push workers into premature retirement, a prospect that helps neither them nor their employers.

BY AARON LEVIN

At least half the burden of depression among adults in the United States comes from work impairment, disability, or absence. For some workers, being depressed means giving up on work altogether, well before people their own age leave the workforce, according to University of Pennsylvania researchers.

Their study found that premature retirement is 40 percent more likely among workers with depression.

Early retirement can be a double hardship for workers in their late 50s or early 60s who retire without Social Security benefits. Those benefits don't start until at least age 62, and Medicare kicks in at age 65, said Jalpa Doshi, Ph.D., a research assistant professor of medicine; Daniel Polsky, Ph.D., an associate professor of medicine; and biostatistician Liyi Cen, M.S., all of the Department of General Internal Medicine at the University of Pennsylvania.

"In addition to financial hardship, earlier retirement as a result of depression may potentially have far-reaching detrimental effects on the health of late-middle-aged workers," they wrote for the September online *Health Services Research*. Incomes decline for early retirees, and many may be without health insurance.

In the past, employers might have been happy to see workers impaired by depression or other causes of poor health leave. But like many aspects of retirement, a realistic view today is more ambiguous, said Debra Lerner, M.S. Ph.D., and David Adler, M.D., of the Health Institute at Tufts–New England Medical Center in Boston. Lerner and Adler have collaborated on several studies examining how depression affects job status and performance. They have found that treating depression improves work performance

please see ***Retiring*** *on page 21*

COMPILED BY JUN YAN

Regulatory Briefs

• The safety sections in the labeling of ***risperidone*** (Risperdal)**,** ***carbamazepine,*** and ***modafinil*** (Provigil) have been revised to include new data on adverse effects. The risperidone package insert now includes adverse reactions reported in clinical trials in children as well as adults. The Food and Drug Administration (FDA) recently expanded the drug's indications to include short-term treatment of schizophrenia and bipolar disorders in pediatric patients (*Psychiatric News*, September 21).

The changes to carbamazapine's package insert include the drug's cardiac adverse effects, possible adverse fetal effects, contraindication in patients with hepatic porphyria, and its interaction with nefazodone.

For modafinil, the modified package insert highlights warnings about serious rashes, including Stevens-Johnson syndrome in adults and children and hypersensitivity or anaphylaxis-like reactions. The FDA's concerns over serious rashes had previously prevented the approval of Cephalon's application for modafinil as a treatment for attention-deficit/hyperactivity disorder (*Psychiatric News*, April 21, 2006).

The changes to package inserts for these drugs can be accessed at <www.fda.gov/medwatch/safety/2007/aug07.htm>.

• The FDA's Division of Drug Marketing, Advertising, and Communications issued a "Notice of Violation" letter in October to Eli Lilly regarding misleading promotional material in a pamphlet mailed to physicians for ***duloxetine hydrochloride*** (Cymbalta). The pamphlet promoted the drug's indication for treating neuropathic pain associated with diabetic peripheral neuropathy. The letter refers to the promotional information in the pamphlet as "false or misleading in that it overstates the efficacy of Cymbalta and omits some of the most serious and important risk information associated with its use." The FDA also charged that the two other approved indications for duloxetine, the treatment of major depressive disorder and generalized anxiety disorder, were not mentioned in the promotional pamphlet.

The FDA requested that Lilly immediately stop using the material and any other promotional materials with similar content.

The FDA's warning letter is posted at <www.fda.gov/cder/warn/2007/Cymbalta_wl.pdf>.

Industry Briefs

• Shire announced voluntary withdrawal of some ***methylphenidate transdermal system patches*** (Daytrana patches) from the market in September because of reported difficulty in removing the release liner. The packages withdrawn include those with an expiration date of March 31, 2009, and earlier and those with lot numbers 2563511, 2563611, and 2570411. In the announcement, Shire stated that the patches affected by the withdrawals can still be used unless the liner cannot be removed or the patches are damaged while being opened.

The press release about the patch withdrawal is posted at <www.shire.com/shire/NewsAndMedia/PressReleases/showShirePress.jsp?ref=821&tn=3&m1=8&m2=>.

Research Briefs

• A study in the September 27 *New England Journal of Medicine* adds to the mountain of evidence indicating that childhood vaccines do not cause autism. William Thompson, Ph.D., from the Centers for Disease Control and Prevention (CDC) and colleagues studied more than 1,000 children from ages 7 to 10 and found no association between their current neuropsychological performance and past exposure to mercury in ***thimerosal***, a preservative used in vaccines and immune globulin products.

Each child was assessed on 42 neuropsychological outcomes. Their past mercury exposure, from the mothers' pregnancy through 7 months after birth, was calculated based on the vaccines and immune globulins the child had received in his or her medical and immunization records and through interviews with the mothers. Only a few statistically significant associations between neurological performance and the level of early mercury exposure were detected, which were "small and almost equally divided between positive and negative effects." The authors concluded that there was no causal association between early exposure to mercury from thimerosal and neurological functioning in 7- to 10-year-olds.

"Early Thimerosal Exposure and Neuropsychological Outcomes at 7 to 10 Years" is posted at <http://content.nejm.org/cgi/content/full/357/13/1281>

• A drug used to treat breast cancer, ***tamoxifen***, was shown to have a rapid effect on symptoms of mania in a small pilot study conducted by Carlos Zarate, M.D., and other researchers at the National Institute of Mental Health. Sixteen adult patients were randomly assigned to receive either tamoxifen or placebo for three weeks in a 1:1 ratio. All patients had a current manic or mixed episode with or without psychotic features. The dose of tamoxifen tested ranged from 20 mg a day to 140 mg a day. At the end of three weeks, five of the eight patients taking tamoxifen achieved a 50 percent or greater response on Young Mania Rating Scale scores, while only 13 percent on placebo did. The superiority of tamoxifen treatment became significant at as early as day 5. The authors suggested that tamoxifen's rapid antimanic effect is due to the drug's blockade of protein kinase C (PKC), a family of enzymes important to the regulation of neurotransmission in the brain. The PKC signaling pathways have been implicated in the pathology of bipolar disorders and may be a promising target for a new class of drugs that can control bipolar symptoms faster than conventional treatments. The study was published online in the September *Bipolar Disorders*.

"Efficacy of a Protein Kinase C Inhibitor (Tamoxifen) in the Treatment of Acute Mania: A Pilot Study" is posted at <www.blackwell-synergy.com/doi/full/10.1111/j.1399-5618.2007.00530.x>.

• British researchers found ***donepezil*** (Aricept) to be no more effective than placebo in reducing agitation in patients with Alzheimer's disease; the study was published in the October 4 *New England Journal of Medicine*. Patients with clinically significant agitation who had not responded to psychosocial treatment were randomly assigned to 10 mg a day donepezil treatment (128 patients) or placebo (131 patients). At the end of 12 weeks, patients' level of agitation symptoms, measured by change from baseline in the Cohen-Mansfield Agitation Inventory score, was not significantly different between the donepezil group and the placebo group. Patients, caregivers, clinicians, and outcome-assessing personnel were all blinded to treatment assignment during the study.

Donepezil, a cholinesterase inhibitor, carries a general indication approved by the FDA for the treatment of Alzheimer's disease.

This study was funded by the Medical Research Council at Neurogeneration Research Centre under the Institute of Psychiatry, King's College London, and the Alzheimer's Society, a U.K. organization.

An abstract of "Donepezil for the Treatment of Agitation in Alzheimer's Disease" is posted at <content.nejm.org/cgi/content/abstract/357/14/1382>. ■

Lead in Children's Blood May Contribute To ADHD's Hyperactivity Component

Researchers have found that very low levels of lead in the blood may contribute to the development of attention-deficit/hyperactivity disorder in children.

BY JOAN AREHART-TREICHEL

Thanks to government regulation, lead poisoning in children is no longer common in the United States. However, American youngsters are still widely exposed to low levels of lead in water, soil, and other venues.

But even these lower levels of lead in turn may contribute to attention-deficit/hyperactivity disorder (ADHD) in some American children, a new study suggests.

The study was headed by Joel Nigg, Ph.D., a professor of clinical psychology at Michigan State University. Results are in press with *Biological Psychiatry*.

Studies done in the 1980s have already linked the amount of lead in children's blood with ADHD. But the levels—10-20 ug/dl—were higher than the levels usually found in American children today, which average 1-2 ug/dl. So Nigg and his colleagues wanted to see whether these lower blood levels could also be associated with ADHD.

The researchers recruited subjects for the study from schools, clinics, and advertisements. To obtain the broadest and most representative sample possible, the investigators advertised for both healthy children and children suspected of having or diagnosed with ADHD. A total of 845 families expressed interest in participating in the study.

The children in these families were then screened extensively with various instruments—say, the Child Behavior Checklist and the Kiddie Schedule for Affective Disorders and Schizophrenia—to determine whether they had ADHD or other psychiatric disorders.

One hundred-and-fifty children aged 8 to 17 were finally selected to participate in the study. A third had ADHD, combined type; a third had ADHD, predominantly inattentive type; and the remainder did not have ADHD and could thus serve as controls. Moreover, the levels of lead in the blood of all the subjects closely matched the American average of 1-2 ug/dl, with a maximum level of 3.4 ug/dl.

Blood lead levels were significantly higher in the children with ADHD, combined type, than in the control children, but this was not the case in children who had ADHD, predominantly inattentive type. So Nigg and his group believe that low lead levels in the blood might play a role in the hyperactivity component of ADHD, but not in the inattention component of it.

How lead might contribute to hyperactivity is not clear. It does not seem to be mediated by lead's negative impact on intelligence, because while the researchers found that blood lead levels in their subjects were correlated with IQ, they also found that IQ could not explain the link between lead and hyperactivity. Low-level lead exposure is known to disrupt midbrain dopamine circuitry, and this circuitry, however, is involved in ADHD.

Although the researchers suspect that low blood levels of lead may play a role in a number of cases of ADHD-related hyperactivity, they do not believe that this is so in all cases, because some of their subjects with mildly elevated blood levels did not have ADHD-related hyperactivity, while some of their subjects with ADHD-related hyperactivity did not have elevated blood levels of lead.

The study's results have public health policy implications, Nigg told *Psychiatric News*, emphasizing that "prevention of lead exposure may be important at even lower levels than we thought."

The study was financed by Michigan State University and the Centers for Disease Control and Prevention.

An abstract of "Low Blood Lead Levels Associated With Clinically Diagnosed Attention-Deficit/Hyperactivity Disorder and Mediated by Weak Cognitive Control" is posted at <www.journals.elsevierhealth.com//periodical/bps> under "Articles in Press." ■

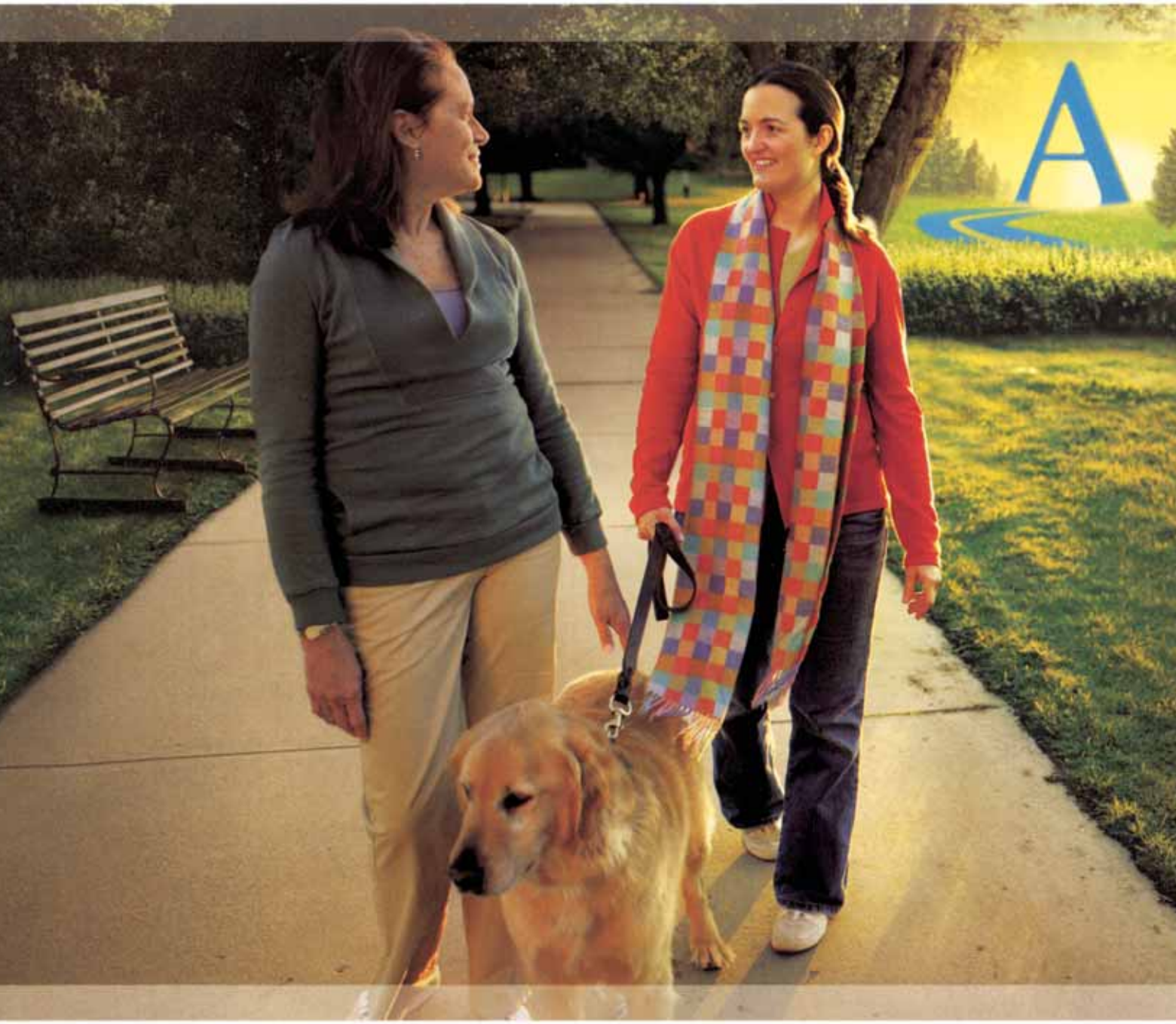
The things that may describe a patient with schizophrenia…

Delusions
Emotional withdrawal
Disorganized behavior

Family history of high cholesterol

…can obscure the person

ABILIFY Helps Reveal



ABILIFY is indicated for the treatment of schizophrenia.

Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk (1.6 to 1.7 times) of death compared to placebo (4.5% vs 2.6%, respectively). ABILIFY is not approved for the treatment of patients with dementia-related psychosis.

HELP ILLUMINATE

The Person Within.

Meet Kristen, age 31. She is a patient with schizophrenia, but she's also an animal lover, daughter, and friend. She's so much more than her illness.

Do you have someone like Kristen in your practice?

ABILIFY significantly reduced positive and negative symptoms, as measured by PANSS™ Total Score, at primary endpoint (Week 4) in a 4-week, double-blind, placebo-controlled trial in patients with schizophrenia.[1]

In a long-term (26-week), placebo-controlled trial there were no medically important differences between the ABILIFY and placebo patients in the mean change from baseline in triglyceride, HDL, LDL, and total cholesterol measurements.

PANSS™ (Positive and Negative Syndrome Scale) is a trademark of Multi-Health Systems, Inc.

Please see IMPORTANT SAFETY INFORMATION, including **Boxed WARNING**, on following page.

THE PERSON WITHIN

ABILIFY®
(aripiprazole)
TABLETS and ORAL SOLUTION 1 mg/mL

IMPORTANT SAFETY INFORMATION for ABILIFY

Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk (1.6 to 1.7 times) of death compared to placebo (4.5% vs 2.6%, respectively). ABILIFY is not approved for the treatment of patients with dementia-related psychosis (see Boxed WARNING).

- **Neuroleptic malignant syndrome (NMS)**–As with all antipsychotic medications, a rare and potentially fatal condition known as NMS has been reported with ABILIFY. 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 is recommended
- **Tardive dyskinesia (TD)**–The risk of developing TD and the potential for it to become irreversible may increase as the duration of treatment and the total cumulative dose increase. Prescribing should be consistent with the need to minimize TD. If signs and symptoms appear, discontinuation should be considered since TD may remit, partially or completely
- **Cerebrovascular adverse events** (eg, stroke, transient ischemic attack), including fatalities, have been reported at an increased incidence in clinical trials of elderly patients with dementia-related psychosis treated with ABILIFY
- **Hyperglycemia and diabetes mellitus**–Hyperglycemia, in some cases associated with ketoacidosis, coma, or death, has been reported in patients treated with atypical antipsychotics including ABILIFY. Patients with diabetes should be monitored for worsening of glucose control; those with risk factors for diabetes should undergo baseline and periodic fasting blood glucose testing. Patients who develop symptoms of hyperglycemia should also undergo fasting blood glucose testing. There have been few reports of hyperglycemia with ABILIFY

Treatment-emergent adverse events reported with:

ABILIFY Oral

In short-term trials of patients with schizophrenia (up to 6 weeks) or bipolar disorder (up to 3 weeks), the following were reported at an incidence ≥10% and greater than placebo, respectively: headache (30% vs 25%), anxiety (20% vs 17%), insomnia (19% vs 14%), nausea (16% vs 12%), vomiting (12% vs 6%), dizziness (11% vs 8%), constipation (11% vs 7%), dyspepsia (10% vs 8%), and akathisia (10% vs 4%).

ABILIFY Injection

In short-term (24 hour) trials, the following were reported at an incidence ≥5% and greater than placebo, respectively: headache (12% vs 7%), nausea (9% vs 3%), dizziness (8% vs 5%), and somnolence (7% vs 4%).

ABILIFY for Schizophrenia:

- Rapid control of agitation*
- Early† and sustained positive and negative symptom control
- Low incidence of somnolence/sedation‡
- Low mean weight change in clinical trials
  - — In a 52-week schizophrenia trial, weight change averaged 1 kg for ABILIFY-treated patients (BMI <23, 2.6 kg; BMI 23 to 27, 1.4 kg; BMI >27, -1.2 kg). The percentage of ABILIFY-treated patients with ≥7% increase in baseline body weight was 30% for those with BMI <23, 19% for those with BMI 23 to 27, and 8% for those with BMI >27.
- Lipid profile comparable to placebo

*With ABILIFY Injection at primary endpoint (2 hours). ABILIFY Injection is indicated for the treatment of agitation associated with schizophrenia.
†As early as Week 1 through study endpoint (Week 4).
‡ABILIFY 10%, placebo 8%.

Physicians who elect to use ABILIFY for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

Like other antipsychotics, ABILIFY may have the potential to **impair judgment, thinking, or motor skills.** Patients should not drive or operate hazardous machinery until they are certain ABILIFY does not affect them adversely.

ABILIFY®
(aripiprazole)
TABLETS and ORAL SOLUTION 1 mg/mL

HELP ILLUMINATE THE PERSON WITHIN

Please see BRIEF SUMMARY OF FULL PRESCRIBING INFORMATION, including **Boxed WARNING,** on adjacent pages.

Reference: 1. Potkin SG, Saha AR, Kujawa MJ, et al. Aripiprazole, an antipsychotic with a novel mechanism of action, and risperidone vs placebo in patients with schizoaffective disorder. *Arch Gen Psychiatry.* 2003;60:681-690.

570US07AB09902 June 2007 AB07A-0027 Printed in USA Printed on recycled paper

ABILIFY® (aripiprazole) TABLETS
ABILIFY® (aripiprazole) ORAL SOLUTION
ABILIFY® DISCMELT™ (aripiprazole) Orally Disintegrating Tablets
ABILIFY® (aripiprazole) INJECTION FOR INTRAMUSCULAR USE ONLY

Rx only

BRIEF SUMMARY: PLEASE CONSULT PACKAGE INSERT FOR COMPLETE PRESCRIBING INFORMATION.

INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks) in these patients revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times that seen 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 (eg, heart failure, sudden death) or infectious (eg, pneumonia) in nature. ABILIFY is not approved for the treatment of patients with dementia-related psychosis.

CONTRAINDICATIONS: Known hypersensitivity to aripiprazole

WARNINGS: Increased Mortality In Elderly Patients With Dementia-Related Psychosis - Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. ABILIFY (aripiprazole) is not approved for the treatment of patients with dementia-related psychosis (see Boxed WARNING).

Neuroleptic Malignant Syndrome (NMS): Potentially fatal NMS has been reported in association with administration of antipsychotic drugs, including ABILIFY. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. If signs and symptoms appear, immediate discontinuation is recommended (see **Full Prescribing Information for additional information on management of NMS).** Patients requiring antipsychotic drug treatment after recovery from NMS should be carefully monitored since recurrences of NMS have been reported.

Tardive Dyskinesia (TD): Potentially irreversible TD may develop in patients treated with antipsychotic drugs. Although the prevalence of TD appears to be highest among the elderly, especially elderly women, it is impossible to predict which patients are more likely to develop the syndrome. The risk of developing TD and the potential for it to become irreversible may increase as the duration of treatment and the total cumulative dose increase. Prescribing should be consistent with the need to minimize TD. If signs and symptoms appear, discontinuation should be considered since TD may remit, partially or completely. Antipsychotic treatment, itself, may suppress (or partially suppress) the signs and symptoms of the syndrome and, thereby, may possible mask the underlying process. Chronic antipsychotic treatment should generally be reserved for patients who suffer from a chronic illness that (1) is known to respond to antipsychotic drugs, and (2) for whom alternative, equally effective, but potentially less harmful treatments are not available or appropriate. The need for continued treatment should be reassessed periodically.

Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients with Dementia-Related Psychosis: In placebo-controlled clinical studies (two flexible-dose and one fixed-dose study) of dementia-related psychosis, there was an increased incidence of cerebrovascular adverse events (eg, stroke, transient ischemic attack), including fatalities, in aripiprazole-treated patients. In the fixed-dose study, there was a statistically significant dose response relationship for cerebrovascular adverse events in patients treated with aripiprazole. ABILIFY is not approved for the treatment of patients with dementia-related psychosis. (See also **Boxed WARNING**, **WARNINGS** and **PRECAUTIONS** in **Full Prescribing Information**)

Hyperglycemia and Diabetes Mellitus: Hyperglycemia, in some cases associated with ketoacidosis, hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics including ABILIFY. Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Patients diagnosed with diabetes who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control; patients with risk factors for diabetes should undergo baseline and periodic fasting blood glucose (FBG) testing. Any patient being treated with an atypical antipsychotic should be monitored for symptoms of hyperglycemia and those who develop symptoms of hyperglycemia should also undergo FBG testing.

PRECAUTIONS: General:

Orthostatic Hypotension: ABILIFY may be associated with orthostatic hypotension, perhaps due to its α_1-adrenergic receptor antagonism. The incidence of orthostatic hypotension-associated events from five short-term, placebo-controlled trials in schizophrenia (n=926) on oral ABILIFY included: orthostatic hypotension (1.9%), postural dizziness (0.8%), and syncope (0.6%). The incidence of orthostatic hypotension-associated events from short-term, placebo-controlled trials in bipolar mania (n=597) on oral ABILIFY included: orthostatic hypotension (0.7%), postural dizziness (0.5%), and syncope (0.3%). The incidence of orthostatic hypotension-associated events from short-term, placebo-controlled trials in agitation associated with schizophrenia or bipolar mania (n=501) on ABILIFY Injection included: orthostatic hypotension (0.6%), postural dizziness (0.2%), and syncope (0.4%). The incidence of a significant orthostatic change in blood pressure (defined as a decrease of at least 30 mmHg in systolic blood pressure when changing from a supine to standing position) for aripiprazole was not statistically different from placebo in trials in patients with schizophrenia, bipolar mania, or agitation associated with schizophrenia or bipolar mania. ABILIFY should be used with caution in patients with known cardiovascular disease (history of myocardial infarction or ischemic heart disease, heart failure or conduction abnormalities), cerebrovascular disease, or conditions which would predispose patients to hypotension (dehydration, hypovolemia, and treatment with antihypertensive medications). If parenteral benzodiazepine therapy is deemed necessary in addition to ABILIFY Injection treatment, patients should be monitored for excessive sedation and for orthostatic hypotension.

Seizures: In short-term trials, seizures/convulsions occurred in 0.1% (1/926) of oral aripiprazole-treated patients with schizophrenia, in 0.3% (2/597) of oral aripiprazole-treated patients with bipolar mania, and in 0.2% (1/501) of aripiprazole injection-treated patients with agitation associated with schizophrenia or bipolar mania. Use cautiously in patients with a history of seizures or with conditions that lower the seizure threshold. Conditions that lower the seizure threshold may be more prevalent in a population of 65 years or older.

Potential for Cognitive and Motor Impairment: Despite the relatively modest increased incidence of somnolence compared to placebo, ABILIFY, like other antipsychotics, may have the potential to impair judgment, thinking, or motor skills. In short-term trials, somnolence (including sedation) was reported in 10% of patients with schizophrenia on oral ABILIFY compared to 8% of patients on placebo; 14% of patients with bipolar mania on oral ABILIFY compared to 7% of patients on placebo; and in 9% of patients with agitation associated with schizophrenia or bipolar mania on ABILIFY Injection compared to 6% of patients on placebo. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that therapy with ABILIFY does not affect them adversely.

Body Temperature Regulation: Disruption of body temperature regulation has been attributed to antipsychotic agents. Use appropriate care when prescribing aripiprazole for patients who will be experiencing conditions that may contribute to an elevation in core body temperature.

Dysphagia: Esophageal dysmotility and aspiration have been associated with antipsychotic drug use, including ABILIFY. Aspiration pneumonia is a common cause of morbidity and mortality in patients with advanced Alzheimer's disease. ABILIFY and other antipsychotic drugs should be used cautiously in patients at risk for aspiration pneumonia.

Suicide: The possibility of a suicide attempt is inherent in psychotic illnesses and bipolar disorder, and close supervision of high-risk patients should accompany drug therapy. Prescriptions for ABILIFY should be written for the smallest quantity consistent with good patient management.

Use in Patients with Concomitant Illness: Clinical experience with ABILIFY in patients with certain concomitant systemic illnesses is limited. ABILIFY has not been evaluated or used to any appreciable extent in patients with a recent history of myocardial infarction or unstable heart disease.

In three, 10-week, placebo-controlled studies of aripiprazole in elderly patients with psychosis associated with Alzheimer's disease (n=938), the treatment-emergent adverse events that were reported at an incidence of ≥3% and aripiprazole incidence at least twice that for placebo were lethargy, somnolence (including sedation), incontinence (primarily, urinary incontinence), excessive salivation, and lightheadedness. ABILIFY is not approved for treatment of patients with dementia-related psychosis. If the prescriber elects to treat such patients with ABILIFY, vigilance should be exercised, particularly for the emergence of difficulty swallowing or excessive somnolence, which could predispose to accidental injury or aspiration (See **Boxed WARNING**, **WARNINGS** and **CLINICAL PHARMACOLOGY: Special Populations** in **Full Prescribing Information**).

Information for Patients: Physicians are advised to discuss the following issues with patients for whom they prescribe ABILIFY (aripiprazole) see full Prescribing Information for the complete information to discuss with patients taking aripiprazole:

Interference with Cognitive and Motor Performance: Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that ABILIFY does not affect them adversely.

Pregnancy: Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy with ABILIFY.

Nursing: Patients should be advised not to breast-feed an infant if they are taking ABILIFY.

Concomitant Medication: Patients should be advised to inform their physicians if they are taking, or plan to take, any prescription or over-the-counter drugs, since there is a potential for interactions.

Heat Exposure and Dehydration: Patients should be advised regarding appropriate care in avoiding overheating and dehydration.

Phenylketonurics: Phenylalanine is a component of aspartame. Each ABILIFY DISCMELT orally disintegrating tablet contains the following amounts: 10 mg - 1.12 mg phenylalanine and 15 mg - 1.68 mg phenylalanine.

Sugar Content: Patients should be advised that each mL of ABILIFY oral solution contains 400 mg of sucrose and 200 mg of fructose.

Drug Interactions: Use caution when ABILIFY is taken in combination with other centrally acting drugs and alcohol. ABILIFY may enhance the effect of certain antihypertensive agents. ABILIFY is unlikely to cause clinically important drug interactions mediated by the enzymes CYP1A1, CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, or CYP2E1 enzymes. *In vivo* studies using 10- to 30-mg/day doses of aripiprazole had no significant effect on metabolism by CYP2D6 (dextromethorphan), CYP2C9 (warfarin), CYP2C19 (omeprazole, warfarin), and CYP3A4 (dextromethorphan) substrates. No clinically significant effect of famotidine, valproate, or lithium was seen on the pharmacokinetics of aripiprazole.

Inducers of CYP3A4 (eg, carbamazepine) could cause an increase in aripiprazole clearance and lower blood levels. When a **CYP3A4** inducer is added to ABILIFY, the dose of ABILIFY should be doubled. Additional dose increases should be based on clinical evaluation. When the CYP3A4 inducer is withdrawn from combination therapy, the ABILIFY dose should be reduced.

Carbamazepine: Coadministration of carbamazepine (200 mg BID) with ABILIFY (30 mg QD) resulted in an approximate 70% decrease in C_{max} and AUC values of aripiprazole and its active metabolite, dehydro-aripiprazole.

Inhibitors of CYP3A4 (eg, ketoconazole) or **CYP2D6** (eg, quinidine, fluoxetine, or paroxetine) can inhibit the elimination of aripiprazole and cause increased blood levels. When a strong **CYP3A4** or **CYP2D6** inhibitor is added to ABILIFY, the dose of ABILIFY should be reduced to one-half of the usual dose. When the CYP3A4 or CYP2D6 inhibitor is withdrawn from the combination therapy, the ABILIFY dose should then be increased.

Ketoconazole: Coadministration of ketoconazole (200 mg/day for 14 days) with a 15-mg single dose of ABILIFY increased the AUC of aripiprazole and its active metabolite by 63% and 77%, respectively.

Quinidine: Coadministration of a 10-mg single dose of ABILIFY with quinidine (166 mg/day for 13 days) increased the AUC of aripiprazole by 112% but decreased the AUC of its active metabolite, dehydro-aripiprazole, by 35%.

Alcohol: There was no significant difference between aripiprazole coadministered with ethanol and placebo coadministered with ethanol on performance of gross motor skills or stimulus response in healthy subjects. As with most psychoactive medications, patients should be advised to avoid alcohol while taking ABILIFY.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Carcinogenesis: Carcinogenicity studies were conducted in ICR mice and in Sprague-Dawley (SD) and F344 rats. Aripiprazole was administered for 2 years in the diet at doses of 1, 3, 10, and 30 mg/kg/day to ICR mice and at 10, 20, 40, 60 mg/kg/day (3 to 19 times the maximum recommended human dose [MRHD] based on mg/m^2) to SD rats and 1, 3, and 10 mg/kg/day to F344 rats (0.2 to 5 and 0.3 to 3 times the MRHD based on mg/m^2, respectively). In addition, SD rats were dosed orally for 2 years. Aripiprazole did not induce tumors in male mice or rats. In female mice, the incidences of pituitary gland adenomas and mammary gland adenocarcinomas and adenoacanthomas were increased at dietary doses of 3 to 30 mg/kg/day (0.1 to 0.9 times human exposure at MRHD based on AUC and 0.5 to 5 times the MRHD based on mg/m^2). In female rats, the incidence of mammary gland fibroadenomas was increased at a dietary dose of 10 mg/kg/day (0.1 times human exposure at MRHD based on AUC and 3 times the MRHD based on mg/m^2); and the incidences of adrenocortical carcinomas and combined adrenocortical adenomas/carcinomas were increased at an oral dose of 60 mg/kg/day (14 times human exposure at MRHD based on AUC and 19 times the MRHD based on mg/m^2). These findings are considered to be prolactin-mediated. Increases in serum prolactin were observed in a 13-week dietary study in female mice at doses used in the carcinogenicity study. Serum prolactin was not increased in a 4- and 13-week dietary study in female rats. The relevance for human risk of prolactin-mediated endocrine tumors in rodents is unknown. **Mutagenesis:** Aripiprazole and a metabolite (2,3-DCPP) were clastogenic in the *in vitro* chromosomal aberration assay in Chinese hamster lung (CHL) cells, with and without metabolic activation. The metabolite, 2,3-DCPP, produced increases in numerical aberrations in the *in vitro* assay in CHL cells in the absence of metabolic activation. A positive response was obtained in the *in vivo* micronucleus assay in mice; however, the response was shown to be due to a mechanism not considered relevant to humans. **Impairment of Fertility:** Female rats were treated with oral doses of 2, 6, and 20 mg/kg/day (0.6, 2, and 6 times the MRHD on an mg/m^2 basis) of aripiprazole from 2 weeks prior to mating through day 7 of gestation. Estrus cycle irregularities and increased corpora lutea were seen at all doses, but no impairment of fertility was seen. Increased pre-implantation loss was seen at 6 and 20 mg/kg, and decreased fetal weight was seen at 20 mg/kg. Male rats were treated with oral doses of 20, 40, and 60 mg/kg/day (6, 13, and 19 times the MRHD on an mg/m^2 basis) of aripiprazole from 9 weeks prior to mating through mating. Disturbances in spermatogenesis were seen at 60 mg/kg, and prostate atrophy was seen at 40 and 60 mg/kg, but no impairment of fertility was seen.

Pregnancy Category C: There are no adequate and well-controlled studies in pregnant women. Aripiprazole should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus. In animal studies, aripiprazole demonstrated developmental toxicity, including possible teratogenic effects in rats and rabbits.

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

Nursing Mothers: Aripiprazole was excreted in milk of rats during lactation. It is not known whether aripiprazole or its metabolites are excreted in human milk. It is recommended that women receiving aripiprazole should not breast-feed.

Pediatric Use: Safety and effectiveness in pediatric and adolescent patients have not been established.

Geriatric Use: Placebo-controlled studies of oral aripiprazole in schizophrenia or bipolar mania did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. There was no effect of age on the pharmacokinetics of a single 15-mg dose of aripiprazole. Aripiprazole clearance was decreased by 20% in elderly subjects (≥65 years) compared to younger adult subjects (18 to 64 years), but there was no detectable effect of age in the population pharmacokinetic analysis in schizophrenia patients. Studies of elderly patients with psychosis associated with Alzheimer's disease have suggested that there may be a different tolerability profile in this population compared to younger patients with schizophrenia. (See also **Boxed WARNING, WARNINGS** and **PRECAUTIONS** in **Full Prescribing Information**)

ADVERSE REACTIONS

Aripiprazole has been evaluated for safety in 8456 patients who participated in multiple-dose, clinical trials in schizophrenia, bipolar mania, and dementia of the Alzheimer's type, and who had approximately 5635 patient-years of exposure to oral aripiprazole and 749 patients with exposure to aripiprazole injection. A total of 2442 patients were treated with oral aripiprazole for at least 180 days and 1667 patients treated with oral aripiprazole had at least 1 year of exposure.

Adverse Events Associated with Discontinuation of Treatment: Overall, there was little difference in the incidence of discontinuation due to adverse events in placebo-controlled oral aripiprazole trials (aripiprazole vs placebo: schizophrenia, 7% vs 9%; bipolar mania, 11% vs vs 9%; or in placebo-controlled intramuscular aripiprazole injection trials (aripiprazole injection, 0.8%; placebo 0.5%). The types of adverse events that led to discontinuation were similar between the oral aripiprazole and placebo-treated patients.

Commonly Observed Adverse Events: (≥5% incidence and at a rate at least twice the rate of placebo for ABILIFY vs placebo, respectively): In 4- to 6-week, placebo-controlled, schizophrenia trials (2 to 30 mg/day), the one commonly observed adverse event associated with the use of oral aripiprazole was: akathisia (8%, 4%). In 3-week, placebo-controlled, bipolar mania trials (15 or 30 mg/day), the most common adverse events associated with oral aripiprazole were: akathisia (15%, 3%), constipation (13%, 6%), sedation (8%, 3%), tremor (7%, 3%), restlessness (6%, 3%), extrapyramidal disorder (5%, 2%). In 24-hour placebo-controlled trials of intramuscular aripiprazole injection for agitation associated with schizophrenia or bipolar mania, nausea was the one adverse event observed (9%, 3%).

Adverse Events with an Incidence ≥2% in Oral Aripiprazole Trials: The following treatment-emergent

events were reported at an incidence of ≥2% with oral aripiprazole (doses ≥2 mg/d), and at a greater incidence with aripiprazole than with placebo in short-term placebo-controlled trials (aripiprazole N=1523, placebo N=849), respectively, were: headache (30%, 25%), anxiety (20%, 17%), insomnia (19%, 14%), nausea (16%, 12%), vomiting (12%, 6%), dizziness (11%, 8%), constipation (11%, 7%), dyspepsia (10%, 8%), akathisia (10%, 4%), sedation (7%, 4%), fatigue (6%, 5%), extrapyramidal disorder (6%, 4%), somnolence (5%, 4%), dry mouth (5%, 4%), arthralgia (5%, 4%), tremor (5%, 3%), restlessness (5%, 3%), pharyngolaryngeal pain (4%, 3%), pain in extremity (4%, 2%), cough (3%, 2%), nasal congestion (3%, 2%), abdominal discomfort (3%, 2%), stomach discomfort (3%, 2%), pain (3%, 2%), vision blurred (3%, 1%), salivary hypersecretion (2%, 1%), peripheral edema (2%, 1%), hypertension (including blood pressure increased) (2%, 1%). The following events were reported by patients treated with oral aripiprazole with an incidence equal to or less than placebo: diarrhea, toothache, upper abdominal pain, abdominal pain, musculoskeletal stiffness, back pain, myalgia, agitation, psychotic disorder, dysmenorrhea (percentage based on gender total), and rash.

Adverse Events with an Incidence ≥1% in Intramuscular Aripiprazole Injection Trials: The following treatment-emergent events were reported at an incidence ≥1% with intramuscular aripiprazole injection (doses ≥5.25 mg/day) and at incidence greater than placebo in 24-hour, placebo-controlled trials (aripiprazole injection N=501, placebo N=220) in agitated patients with schizophrenia or bipolar mania, respectively, include: headache (12%, 7%), nausea (9%, 3%), dizziness (8%, 5%), somnolence (7%, 4%), sedation (3%, 2%), vomiting (3%, 1%), fatigue (2%, 1%), tachycardia (2%, <1%), akathisia (2%, 0%), dyspepsia (1%, <1%), dry mouth (1%, <1%), blood pressure increased (1%, <1%), musculoskeletal stiffness (1%, <1%). The following events were reported by patients treated with aripiprazole injection with an incidence equal to or less than placebo: injection site pain, injection site burning, insomnia, agitation.

Dose-Related Adverse Events: Dose response relationships for the incidence of treatment-emergent adverse events were evaluated from four trials in patients with schizophrenia comparing various fixed doses (2, 5, 10, 15, 20, and 30 mg/day) of oral aripiprazole to placebo. The one adverse event to have a possible dose response relationship was somnolence (including sedation) which was most prominent at the 30 mg/day dose (placebo, 7.1%; 10 mg, 8.5%; 15 mg, 8.7%; 20 mg, 7.5%; 30 mg, 12.6%).

Extrapyramidal Symptoms: In the short-term, placebo-controlled trials of schizophrenia, the incidence of reported EPS-related events, excluding events related to akathisia was (oral aripiprazole 13%, placebo 12%) and the incidence of akathisia-related events was (oral aripiprazole 8%, placebo 4%). In the short-term, placebo-controlled trials in bipolar mania, the incidence of reported EPS-related events, excluding events related to akathisia was (oral aripiprazole 15%, placebo 8%) and the incidence of akathisia-related events was (oral aripiprazole 15%, placebo 4%). In the placebo-controlled trials in patients with agitation associated with schizophrenia or bipolar mania, the incidence of reported EPS-related events excluding events related to akathisia was (aripiprazole injection 2%, placebo 2%) and the incidence of akathisia-related events was (aripiprazole injection 2%, placebo 0%).

Laboratory Test Abnormalities: A between group comparison for 3- to 6-week, placebo-controlled trials revealed no medically important differences between the aripiprazole and placebo groups in the proportions of patients experiencing potentially clinically significant changes in routine serum chemistry, hematology, or urinalysis parameters. Similarly, there were no aripiprazole/placebo differences in the incidence of discontinuations for changes in serum chemistry, hematology, or urinalysis. In a long-term (26-week), placebo-controlled trial there were no medically important differences between the aripiprazole and placebo patients in the mean change from baseline in prolactin, fasting glucose, triglyceride, HDL, LDL, and total cholesterol measurements.

Weight Gain: In 4- to 6-week trials in schizophrenia, there was a slight difference in mean weight gain between aripiprazole and placebo patients (+0.7 kg vs. -0.05 kg, respectively), and also a difference in the proportion of patients meeting a weight gain criterion of ≥7% of body weight [aripiprazole (8%) compared to placebo (3%)]. In 3-week trials in mania, the mean weight gain for aripiprazole and placebo patients was 0.0 kg vs. -0.2 kg, respectively. The proportion of patients meeting a weight gain criterion of ≥7% of body weight was aripiprazole (3%) compared to placebo (2%). In a 26-week schizophrenia trial, weight change, respectively, for ABILIFY (aripiprazole)- and placebo-treated patients was -0.5 kg and -0.5 kg for those with BMI <23, -1.3 kg and -0.6 kg for those with BMI 23 to 27, and -2.1 kg and -1.5 kg for those with BMI >27. The percentage of ABILIFY- and placebo-treated patients, respectively, with ≥7% increase in baseline body weight was 6.8% and 3.7% for those with BMI <23, 5.1% and 4.2% for those with BMI 23 to 27, and 5.7% and 4.1% for those with BMI >27. In a 52-week schizophrenia trial, weight change for ABILIFY-treated patients was 2.6 kg for those with BMI <23, 1.4 kg for those with BMI 23 to 27, and -1.2 kg for those with BMI >27. The percentage of ABILIFY-treated patients with ≥7% increase in baseline body weight was 30% for those with BMI <23, 19% for those with BMI 23 to 27, and 8% for those with BMI >27.

ECG Changes: Pooled analysis of placebo-controlled trials in patients with schizophrenia or bipolar mania treated with oral aripiprazole or in patients with agitation associated with schizophrenia or bipolar mania treated with intramuscular aripiprazole injection, revealed no significant differences between aripiprazole and placebo of potentially important changes in ECG parameters. Oral aripiprazole was associated with a median increase in heart rate of 5 beats per minute compared to a 1 beat per minute increase among placebo patients.

Adverse Events in Long-Term, Double-Blind, Placebo-Controlled Trials

The adverse events reported in a 26-week, double-blind trial comparing oral ABILIFY and placebo in patients with schizophrenia or bipolar mania were generally consistent with those reported in the short-term, placebo-controlled trials, except for a higher incidence of tremor (ABILIFY 8% vs placebo 2%).

Other Adverse Events Observed During the Premarketing Evaluation of Oral Aripiprazole

The following adverse events were reported with oral aripiprazole at multiple doses ≥2 mg/day in clinical trials (8456 patients, 5365 patient-years of exposure). This list may not include events previously listed elsewhere in the labeling, those events for which a drug cause was remote, those terms which were so general as to be uninformative, and those events reported with an incidence of ≤0.05% and which did not have a substantial probability of being acutely life-threatening. *Frequent events* are those occurring in at least 1/100 patients; *infrequent events* are those occurring in 1/100 to 1/1000 patients; *rare events* are those occurring in fewer than 1/1000 patients. ***Blood and Lymphatic System Disorders:*** *Infrequent* - anaemia, lymphadenopathy, leukopenia (including agranulocytosis, neutropenia); *Rare* - leukocytosis, thrombocytopenia, idiopathic thrombocytopenic purpura, thrombocythaemia. ***Cardiac Disorders:*** *Frequent* - tachycardia (including ventricular, supraventricular, sinus); *Infrequent* - bradycardia, palpitations, cardiac failure (including congestive and acute), myocardial infarction, cardiac arrest, atrial fibrillation, atrioventricular block (including first degree and complete), extrasystoles (including ventricular and supraventricular), angina pectoris, cyanosis, bundle branch block (including left, right), myocardial ischaemia; *Rare* - atrial flutter, cardiomegaly, cardiomyopathy, cardiopulmonary failure. ***Ear and Labyrinth Disorders:*** *Infrequent* - ear pain, vertigo, tinnitus; *Rare* - deafness. ***Endocrine Disorders:*** *Infrequent* - hypothyroidism; *Rare* - goitre, hyperparathyroidism, hyperthyroidism. ***Eye Disorders:*** *Frequent* - conjunctivitis; *Infrequent* - eye redness, eye irritation, dry eye, blepharospasm, visual disturbance, eye pain, eye discharge, blepharitis, cataract, lacrimation increased; *Rare* - eyelid function disorder, oculogyration, eyelid oedema, photophobia, diplopia, eyelid ptosis, eye haemorrhage. ***Gastrointestinal Disorders:*** *Frequent* - loose stools; *Infrequent* - flatulence, dysphagia, gastroesophageal reflux disease, gastritis, haemorrhoids, abdominal distension, faecal incontinence, haematochezia, gingival pain, rectal haemorrhage, abdominal pain lower, oral pain, retching, faecaloma, gastrointestinal haemorrhage, ulcer (including gastric, duodenal, peptic), tooth fracture, gingivitis, lip dry; *Rare* - abdominal tenderness, chapped lips, periodontitis, aptyalism, gastrointestinal pain, hypoaesthesia oral, inguinal hernia, swollen tongue, colitis, haematemesis, hyperchlorhydria, irritable bowel syndrome, oesophagitis, faeces hard, gingival bleeding, glossodynia, mouth ulceration, reflux oesophagitis, cheilitis, intestinal obstruction, pancreatitis, eructation, gastric ulcer haemorrhage, melaena, glossitis, stomatitis. ***General Disorders and Administration Site Conditions:*** *Frequent* - asthenia, pyrexia, chest pain, gait disturbance; *Infrequent* - malaise, oedema, influenza-like illness, chills, general physical health deterioration, feeling jittery, mobility decreased, thirst, feeling cold, difficulty in walking, facial pain, sluggishness, condition aggravated; *Rare* - inflammation localized, swelling, energy increased, inflammation, abasia, xerosis, feeling hot, hyperthermia, hypothermia. ***Hepatobiliary Disorders:*** *Infrequent* - cholecystitis (including acute and chronic); *Rare* - cholelithiasis, hepatitis. ***Immune System Disorders:*** *Infrequent* - hypersensitivity. ***Infections and Infestations:*** *Frequent* - respiratory tract infection (including upper and lower), pneumonia; *Infrequent* - cellulitis, dental caries, vaginitis, vaginal infection, cystitis, vaginal mycosis, eye infection, gastroenteritis, onychomycosis, vaginal candidiasis, otitis media, folliculitis, candidiasis, otitis externa, pyelonephritis, rash pustular; *Rare* - appendicitis, septic shock. ***Injury, Poisoning, and Procedural Complications:*** *Frequent* - fall, skin laceration, contusion, fracture; *Infrequent* - blister, scratch, joint sprain, burn, muscle strain, periorbital haematoma, arthropod bite/sting, head injury, sunburn; *Rare* - joint dislocation, alcohol poisoning, road traffic accident, self mutilation, eye penetration, injury asphyxiation, poisoning, heat exhaustion, heat stroke. ***Investigations:*** *Frequent* - weight decreased, blood creatine phosphokinase increased; *Infrequent* - blood glucose increased, heart rate increased, body temperature increased, alanine aminotransferase increased, blood cholesterol increased, white blood cell count increased, haemoglobin decreased, aspartame aminotransferase increased, blood urea increased, electrocardiogram ST segment abnormal (including depression, elevation), haematocrit decreased, hepatic enzyme increased, blood bilirubin increased, blood glucose decreased, blood creatinine increased, blood alkaline phosphatase increased, blood pressure decreased, blood potassium decreased, blood urine present, electrocardiogram QT corrected interval prolonged; *Rare* - transaminases increased, blood triglycerides increased, blood uric acid increased, cardiac murmur, eosinophil count increased, neutrophil count increased, platelet count increased, red blood cell count decreased, white blood cell count decreased, white blood cells urine positive, bacteria urine identified, blood lactate dehydrogenase increased, blood potassium increased, neutrophil count decreased, urine output decreased, blood creatine phosphokinase MB increased, ECG signs of myocardial ischemia, electrocardiogram T-wave inversion, heart rate decreased, tuberculin test positive, glucose urine present, glycosylated haemoglobin increased, glucose tolerance decreased, glycosylated haemoglobin decreased, muscle enzyme increased. ***Metabolism and Nutrition Disorders:*** *Frequent* - decreased appetite (including diet refusal, markedly reduced dietary intake), dehydration; *Infrequent* - anorexia, increased appetite, hypercholesterolaemia, hypokalaemia, hyperglycaemia, diabetes mellitus, hypoglycaemia, hyponatremia, diabetes mellitus non-insulin-dependent, hyperlipidaemia, obesity (including overweight), polydipsia; *Rare* - hypertriglyceridaemia, gout, hypernatraemia, weight fluctuation, diabetes mellitus inadequate control. ***Musculoskeletal and Connective Tissue Disorders:*** *Frequent* - musculoskeletal pain (including neck, jaw, chest wall, bone, buttock, groin, flank, musculoskeletal chest, pubic, and sacral), muscle rigidity, muscle cramp; *Infrequent* - muscle twitching, joint swelling, muscle spasms, muscle tightness, arthritis, osteoarthritis, muscular weakness, joint range of motion decreased, sensation of heaviness; *Rare* - tendonitis, osteoporosis, trismus, arthropathy, bursitis, exostosis, night cramps, coccydynia, joint contracture, localised osteoarthritis, osteopenia, rhabdomyolysis, costochondritis, rheumatoid arthritis, torticollis. ***Nervous System Disorders:*** *Frequent* - lethargy, dyskinesia; *Infrequent* - disturbance in attention, parkinsonism, dystonia, drooling, cogwheel rigidity, dysarthria, paraesthesia, hypoaesthesia, loss of consciousness (including depressed level of consciousness), hypersomnia, psychomotor hyperactivity, balance disorder, cerebrovascular accident, hypokinesia, tardive dyskinesia, memory impairment, amnesia, ataxia, dementia, hypotonia, burning sensation, dysgeusia, restless leg syndrome, hypertonia, Parkinson's disease, akinesia, dysphasia, transient ischaemic attack, facial palsy, hemiparesis, myoclonus, sciatica; *Rare* - bradykinesia, coordination abnormal, cognitive disorder, syncope vasovagal, carpal tunnel syndrome, hyporeflexia, intention tremor, muscle contractions involuntary, sleep apnea syndrome, dementia Alzheimer's type, epilepsy, hyperreflexia, mastication disorder, mental impairment, nerve compression, parkinsonian gait, tongue paralysis, aphasia, choreoathetosis, formication, masked facies, neuralgia, paresthesia oral, parkinsonian rest tremor, cerebral haemorrhage, dizziness exertional, hyperaesthesia, haemorrhage intracranial, ischaemic stroke, judgment impaired, subarachnoid haemorrhage. ***Psychiatric Disorders:*** *Frequent* - schizophrenia (including schizoaffective disorder), depression (including depressive symptom), hallucination (including auditory, visual, tactile, mixed, olfactory, and somatic), mood altered (including depressed, euphoric, elevated, and mood swings), paranoia, irritability, suicidal ideation, confusional state, aggression, mania, delusion (including persecutory, perception, somatic, and grandeur); *Infrequent* - tension, nervousness, nightmare, excitability, panic attack (including panic disorder, panic disorder with agoraphobia, and panic reaction), abnormal dreams, apathy, libido decreased, hostility, suicide attempt, bipolar disorder (including bipolar I), libido increased, anger, delirium, acute psychosis, disorientation, bruxism, hypomania, obsessive-compulsive disorder (including obsessive thoughts), mental status changes, crying, dysphoria, completed suicide, flat affect, impulsive behaviour; *Rare* - blunted affect, cognitive deterioration, logorrhea, psychomotor agitation, social avoidant behaviour, psychomotor retardation, suspiciousness, affect lability, anorgasmia, fear, homicidal ideation, tic, premature ejaculation, dysphemia, bradyphrenia, derealisation, depersonalisation. ***Renal and Urinary Disorders:*** *Infrequent* - pollakiuria, dysuria, haematuria, urinary retention, renal failure (including acute and chronic), urinary hesitation, enuresis, nephrolithiasis, micturition urgency, polyuria; *Rare* - nocturia, proteinuria, glycosuria, calculus urinary, azotaemia. ***Reproductive System and Breast Disorders:*** *Infrequent* - erectile dysfunction, vaginal discharge, amenorrhoea, vaginal haemorrhage, menstruation irregular, menorrhagia, premenstrual syndrome, testicular pain, genital pruritus female, ovarian cyst, benign prostatic hyperplasia, prostatitis; *Rare* - gynaecomastia, priapism (including spontaneous penile erection), breast pain, pelvic pain, epididymitis, galactorrhoea, uterine haemorrhage. ***Respiratory, Thoracic, and Mediastinal Disorders:*** *Frequent* - dyspnoea (including exertional); *Infrequent* - sinus congestion, rhinorrhoea, wheezing, epistaxis, asthma, hiccups, productive cough, chronic obstructive airways disease (including exacerbated), rhinitis allergic, pneumonia aspiration, pulmonary congestion, sinus pain, respiratory distress, dry throat, hoarseness; *Rare* - bronchopneumopathy, haemoptysis, respiratory arrest, sneezing, hypoxia, pulmonary embolism, pulmonary oedema (including acute), respiratory failure, brochospasm, nasal dryness, paranasal sinus hypersecretion, pharyngeal erythema, rhonchi, tonsillar hypertrophy, asphyxia, Mendelson's syndrome. ***Skin and Subcutaneous Tissue Disorders:*** *Infrequent* - hyperhydrosis, erythema, pruritis (including generalised), dry skin, decubitus ulcer, dermatitis (including allergic, seborrhoeic, acneiform, exfoliative, bullous, neurodermatitis), ecchymosis, skin ulcer, acne, eczema, hyperkeratosis, swelling face, skin discoloration, photosensitivity reaction, skin irritation, alopecia, rash maculopapular, cold sweat, scab, face oedema, dermal cyst, psoriasis, night sweats, rash erythematous; *Rare* - rash scaly, urticaria, rash maculopapular, rosacea, seborrhoea, periorbital oedema, rash vesicular. ***Vascular Disorders:*** *Frequent* - hypotension; *Infrequent* - hot flush (including flushing), haematoma, deep vein thrombosis, phlebitis; *Rare* - pallor, petechiae, varicose vein, circulatory collapse, haemorrhage, thrombophlebitis, shock.

Other Adverse Events Observed During the Premarketing Evaluation of Aripiprazole Injection

The following adverse events were reported with aripiprazole injection at doses ≥1 mg/day in clinical trials (749 patients). This list may not include events previously listed elsewhere in the labeling, those events for which a drug cause was remote, those terms which were so general as to be uninformative, and those events reported with an incidence of ≤0.05% and which did not have a substantial probability of being acutely life-threatening. *Frequent events* are those occurring in at least 1/100 patients; *Infrequent events* are those occurring in 1/100 to 1/1000 patients; *rare events* are those occurring in fewer than 1/1000 patients. ***Ear and Labyrinth Disorders:*** *Infrequent* - hyperacusis. ***General Disorders and Administration Site Conditions:*** *Infrequent* - injection site stinging, abnormal feeling, injection site pruritus, injection site swelling, venipuncture site bruise. ***Infections and Infestations:*** *Infrequent* - bacteruria, urinary tract infection, urosepsis. ***Investigations:*** *Infrequent* - blood pressure abnormal, heart rate irregular, electrocardiogram T-wave abnormal. ***Psychiatric Disorders:*** *Infrequent* - intentional self-injury. ***Respiratory, Thoracic, and Mediastinal Disorders:*** *Infrequent* - pharyngolaryngeal pain, nasal congestion. ***Vascular Disorders:*** *Infrequent* - blood pressure fluctuation.

Postintroduction Reports: Reported since market introduction and temporally (not necessarily causally) related to aripiprazole therapy: allergic reaction (eg, anaphylactic reaction, angioedema, laryngospasm, oropharyngeal spasm, pruritis, or urticaria), grand mal seizure, and jaundice.

DRUG ABUSE AND DEPENDENCE: Aripiprazole is not a controlled substance.

Abuse and Dependence: Aripiprazole has not been systematically studied in humans for its potential for abuse, tolerance, or physical dependence. While the clinical trials did not reveal any tendency for any drug-seeking behavior, 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. Patients should be evaluated carefully for a history of drug abuse and closely observed for signs of ABILIFY (aripiprazole) misuse or abuse.

OVERDOSAGE: 76 cases of deliberate or accidental overdosage with oral ABILIFY alone or in combination with other substances were reported worldwide [44 cases with known outcome, 33 recovered without sequelae and one recovered with sequelae (mydriasis and feeling abnormal)]. Additionally, 10 of these cases were in children (age 12 and younger) involving oral aripiprazole ingestions up to 195 mg with no fatalities. The largest known acute ingestion was 1080 mg of oral aripiprazole (36 times maximum recommended daily dose) in a patient who fully recovered. Common adverse events (reported in at least 5% of all overdose cases) were vomiting, somnolence, and tremor. **For more information on symptoms of overdose, see Full Prescribing Information.**

Management of Overdosage: No specific information is available on the treatment of overdose with aripiprazole. An electrocardiogram should be obtained in case of overdosage and, if QTc interval prolongation is present, cardiac monitoring should be instituted. Otherwise, management of overdose should concentrate on supportive therapy, maintaining an adequate airway, oxygenation and ventilation, and management of symptoms. Close medical supervision and monitoring should continue until the patient recovers. ***Charcoal:*** In the event of an overdose of ABILIFY, an early charcoal administration may be useful in partially preventing the absorption of aripiprazole. Administration of 50 g of activated charcoal, one hour after a single 15-mg oral dose of aripiprazole, decreased the mean AUC and C_{max} of aripiprazole by 50%. ***Hemodialysis:*** Although there is no information on the effect of hemodialysis in treating an overdose with aripiprazole, hemodialysis is unlikely to be useful in overdose management since aripiprazole is highly bound to plasma proteins.

Tablets manufactured by Otsuka Pharmaceutical Co., Ltd., Tokyo, 101-8535 Japan or Bristol-Myers Squibb Company, Princeton, NJ 08543 USA
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APA Values Residents' Ideas, Encourages Their Contributions

BY ABIGAIL DONOVAN, M.D.

I am frequently asked what I do as APA's member-in-training trustee (MITT). Sometimes I think that even people in my own program aren't quite sure what I do, except that I seem to spend a lot of time in Arlington, Va., where APA has its headquarters and holds meetings.

As the MITT, I attend all five meetings the Board of Trustees has each year. At Board meetings, we discuss a wide array of crucial issues such as increasing access to quality psychiatric care, developing the next *DSM* edition, and promoting humane care of patients. We also hear updates from APA leaders and staff on legislative and regulatory issues affecting psychiatric practice and on the state of APA's finances. At each meeting, I advocate for the best interests of members-in-training on these and other issues.

I also serve on the Committee of Residents and Fellows (CORF), which is dedicated to increasing resident participation and the value of resident membership in APA. Each year CORF organizes workshops at both the annual meeting and Institute on Psychiatric Services that focus on the interests of residents. CORF also publishes a newsletter and, with the Assembly Committee of Members-in-Training (ACOM), has been instrumental in passing initiatives that increase mentorship opportunities for MITs in APA.

But all of this simply tells you what I do, not what my experiences have been or what I think about it all. It is very difficult for me to sum up my experiences in APA in a few words. It has been overwhelming and exhilarating, gratifying and challenging, exhausting and stimulating. It is actually quite a bit like residency.

I remember my first Board meeting in May 2006, at the annual meeting in Toronto. I waited outside the room where the outgoing Board members were holding their last meeting. I was terrified, unsure what would be expected of me, wondering how I could contribute anything to this large, powerful organization. I knew many of the other Board members, not personally, but by their names and numerous contributions to psychiatry—Drs. Steven Sharfstein, Pedro Ruiz, Michelle Riba, Carolyn Robinowitz, just to name a few. The door to the conference room opened, and I knew it was time for the new Board members to go in. I paused at the threshold, almost paralyzed by the site of the long tables with individual microphones, reminiscent of Senate hearings, and the clearly confident and established psychiatrists engaged in what appeared to be important conversations, and by the photographer and observers. I don't know how long I paused there, but it was long enough for Dr. Robinowitz to notice me. She came right over to me and said, "Come in, come right in."

I had not met Dr. Robinowitz before, although, of course, I knew who she was—APA's then president-elect. And apparently, she recognized how overwhelmed I was, because she guided me over the threshold and introduced me to several Board members. She then went back to the door—I assume to guide other newcomers into the inner sanctum of APA.

That moment exemplifies many of my experiences on the Board. From that first moment, I have always felt included as a full Board member, not just a token resident. My thoughts and opinions as a resident have been not only respected, but also sought out and highly valued.

I have received thoughtful mentorship from many Board members, including Dr. Donna Norris, who first called me to ask how I was handling the election process; Dr. Jeffrey Geller, who patiently explained parliamentary procedure to me; and Dr. Nada Stotland, who generously shared her extensive knowledge of APA governance.

I have been continually impressed by how much APA's policymakers value us as residents and future leaders in psychiatry. During my brief tenure, I have seen the creation of a formal mentorship program for residents in APA governance, the start of the resident "Jeopardy" competition called "MindGames," a renewed statement of support for the two resident organizations, CORF and ACOM, the establishment of a funded mentor position for those two organizations, and the creation of a resident-focused version of the *American Journal of Psychiatry*. I can assure you that APA is truly dedicated to the needs and development of its resident members.

And what does APA ask in return? Only that we share our ideas and opinions with our committees and that we share our passion and energy with the organization.

If I can offer one piece of advice to residents, it is to present your ideas freely, shed all inhibition about speaking up, and, as Dr. Robinowitz says, ask the tough questions. Speak your mind—your contributions will be valued. Be as dedicated to APA as it clearly is to us. ■

Abigail Donovan, M.D., is APA's member-in-training trustee.

Retiring

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but does not eliminate all deficits in areas such as mental-interpersonal tasks, time management, or output tasks.

They told *Psychiatric News* that Doshi's study, which is based on a large population sample, "is a good companion to clinical studies of what happens to depressed people at work."

"There's been a change in thinking," said Lerner in an interview with *Psychiatric News*. "Early retirement is seen as not good for the economy, employers, or the employee. Now, keeping people in their jobs longer is important from both an economic and a health point of view."

> **"If it is unplanned and involuntary, retirement has detrimental effects on health, and those effects are worse on people with depression."**

Doshi and her colleagues looked at 2,853 workers aged 53 to 58 years in 1994 who took part in the Health and Retirement Study, a nationally representative survey that has provided data for numerous other studies. Workers were followed every two years through 2002.

Among all labor force participants in the study, depression increased the odds ratio for retirement among men to 1.37 and for women to 1.40, wrote Doshi and colleagues. The effect was graduated: participants with active depression were more likely to retire than those with subthreshold depression, and the latter more than those with no depression.

Among men, the results held true for full- or part-time workers, wrote Doshi and colleagues. "However, for women, the effect of depression on retirement transitions was concentrated on those working part time rather than full time."

The researchers' prospective approach meant that they could see if depression preceded changes in job status, rather than the other way around. They defined "retirement" as transitions form working full or part time to either retired or disabled status, since 89 percent of these workers never returned to the job.

"If it is unplanned and involuntary, retirement has detrimental effects on health, and those effects are worse on people with depression," said Lerner.

Retirement in general can have a positive or negative effect on workers, said her colleague Adler. They may feel released from the day-to-day stresses of their job or they may miss the sense of purpose—and the income—derived from regular work. Nonetheless, he said, "living with depression is not a good outcome."

An abstract of "Depression and Retirement in Late Middle-Aged U.S. Workers Health Services Research" is posted at <www.blackwell-synergy.com/doi/abs/10.1111/j.1475-6773.2007.00782.x>. ■

NIA Offers Web Site For Hispanic Seniors

The National Institute on Aging has created a Web site at <www.nia.nih.gov/Espanol> that offers accurate, up-to-date information on health issues affecting Hispanic seniors. The user-friendly site covers a wide range of health topics, including diseases such as Alzheimer's, and provides tips on maintaining a healthy lifestyle. The site also offers free publications in Spanish and links to other health-related, Spanish-language Web sites such as Medicare and MedlinePlus.

According to the U.S. Census Bureau, the number of older Hispanic adults in the United States is expected to increase from 6 percent in 2003 to 11 percent by 2030. ■

Erratum

An article in the October 5 issue of *Psychiatric News* erroneously stated that 0.1 percent of college students commit suicide. That figure represents the percentage of students *with suicidal ideation* who commit suicide. Overall, approximately 0.0075 percent of college students (or about 7.5 in 100,000) commit suicide, according to several studies. ■

We've Come a Long Way

I enjoyed Dr. Carolyn Robinowitz's article on women in psychiatry in her president's column in the September 21 issue. My experience parallels hers—my medical school class—University of Washington, class of 1964—had about five women and 70 men. We had one or two women in our intern group in medicine and pediatrics at Syracuse, general psychiatric residency in Rochester, N.Y., and child fellowship at Yale.

I have been teaching at the University of California Davis Medical School since I arrived in the area in the early 1970s. Women have been well represented in this medical school and achieved majority status at least 10 years ago. Recently, I have been teaching a doctoring class to second-year medical students. My current class has six women and two men, and of course my goal is to make them all child psychiatrists.

JAMES ALAN MARGOLIS, M.D.
Sacramento, Calif.

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

Collaboration

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PLoS Medicine, a peer-reviewed, open-access journal published by the nonprofit organization Public Library of Science.

As scientific research becomes increasingly global and more clinical trials are outsourced to underdeveloped countries, ethical concerns for the protection of human rights have grown. Even well-meaning philanthropic aid programs conducted by wealthy nations can result in suspicion, resentment, and negative outcomes if the administrators are ignorant of local cultures and geopolitical issues, the ESC program advisors pointed out.

The lack of research oversight by local governments, varying standards of ethical conduct, and economic disadvantages may place people at risk for exploitation and harm, the report noted. The ethical problems and controversies in AIDS research in Africa, for example, have drawn criticism that researchers and sponsors treated subjects in poor African countries using ethical and medical standards lower than those that would be expected in the United States or other affluent countries.

The issues that are cited by ESC advisors range from the need to engage the local community to women's social status in specific places, and obligations/benefit sharing once a clinical trial is completed (see box). The ESC experts maintain that researchers should maximally communicate and collaborate with the local community, as well as with public, government, and nongovernmental organizations. Ignorance about local cultures and preferences could lead to failure, such as the rejection of white anti-malaria bed nets in places where white is a culturally sensitive color.

The concerns were compiled on the basis of interviews and group discussions with research investigators and program officers within GCGH and surveys of experts from academia, governments, nongovernmental organizations, and the private sector in developing countries. This is the first analysis of ethical, social, and cultural issues related to large-scale research and public health initiatives that specifically addresses the developing world, according to the authors.

"It is important to distinguish between issues unique to international research and issues that are relevant to research in all settings, including studies done in developed countries," Paul Appelbaum, M.D., chair of APA's Council on Psychiatry and Law, told *Psychiatric News*. Appelbaum is the Elizabeth K. Dollard Professor of Psychiatry and director of Medicine and Law in the Division of Psychiatry, Law, and Ethics in the Department of Psychiatry at Columbia University; he has written extensively on bioethics.

Collaboration with a local community, for example, is essential to any research setting. One issue raised by the ESC program "particularly salient to the underdeveloped world is whether research participants and the hosting community will benefit from the research outcomes and results. The products of many research studies are so expensive that there is little hope the [host] countries will have wide access to them. It is a major issue in international research and not easy to resolve," Appelbaum said.

An important concern not covered by the list, he noted, is the complex issue of informed consent in rural and poor regions. "One difficulty is how different cultures understand the concept of consent. The idea of choice may be incomprehensible in some cultures where authority carries great weight with the population. Researchers and physicians may represent an authority figure, and people may find it difficult or feel powerless to refuse participation in a study."

He explained that some potential research subjects may not be in a position to make entirely voluntary choices, especially women in places where they need the approval of male figures such as fathers and husbands to participate in a study. There may also be situations in which a male figure can compel a woman to participate in a study against her will. Language barriers and a profound lack of understanding about science in underdeveloped regions can also hinder people's ability to make truly informed decisions.

The GCGH is supported by the Bill and Melinda Gates Foundation, Canadian Institutes of Health Research, Foundation for the National Institutes of Health, and Wellcome Trust. The goal of the initiative is to "achieve scientific breakthroughs against diseases that kill millions of people each year in the world's poorest countries." The projects focus on developing new and better vaccines, preventing insect-transmitted diseases, discovering solutions to drug resistance, and more accurately diagnosing and tracking diseases in poor countries.

"Grand Challenges in Global Health: Ethical, Social, and Cultural Issues Based on Key Informant Perspectives" is posted at <medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371%2Fjournal.pmed.0040268>. ■

Research Issues That Are Critical In Developing Countries

The following are ethical, social, and cultural issues that need to be addressed regarding scientific research and health programs in developing countries:

Community engagement
✓ Work collaboratively with host communities that share a common goal and interest.

Public engagement
✓ Provide people with trustworthy information, and elicit and adopt public input.

Cultural acceptability
✓ Identify and be sensitive to cultural barriers and context.

Gender
✓ Empower and educate women, who are often subject to abuse, discrimination, and exploitation.

Post-trial obligations/benefit sharing
✓ Share the benefits of research with the host communities and individual research participants and offer sustained care after completion.

Collaboration
✓ Collaborate with local public and private sectors and help create sustainable scientific infrastructure.

Role of civil society organizations
✓ Engage civil society and nongovernmental organizations working with local communities.

Affordability
✓ Make new technology affordable and ensure equitable delivery.

Accessibility
✓ Provide adequate equipment, facilities, and staff to ensure accessibility to poor, rural areas.

Regulations
✓ Balance regulatory oversight and intellectual property protection with meeting peoples' needs in dire health emergencies.

Collection, management, and storage of tissue samples
✓ Develop guidance on the use of human tissues in research.

Corruption and poor governance
✓ Beware of corruption and lack of social and political infrastructure as obstacles to accessing new technology.

Unintended consequences
✓ Consider and address consequences such as unintended promotion of sexual practice due to perceived benefits of vaccination and consequences of genetically modified organisms.

Source: Peter Singer et al., *PLoS Medicine,* September 2007.

Military

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This proposal will require not a one-time infusion of additional funding, Blazer said, but "sustained increased funding to shore up mental health care for our soldiers."

One way the military has attempted to increase access with limited personnel is to increase the use of telemedicine, including in Europe. However, technological limitations have restricted its use in Afghanistan and Iraq, according to Col. Elspeth Ritchie, M.C., psychiatric consultant to the Army surgeon general.

Access obstacles also limit the mental health services that the Department of Veterans Affairs (VA) is able to provide, according to several speakers. However, veterans' access problems were attributed more to geography than to staff shortages.

Ira Katz, M.D., deputy chief of patient care services officer for mental health in the VA, said, however, that the 200,000 VA employees—including 2,000 psychiatrists—have been able to meet most of the mental health care needs of U.S. veterans, fewer than 12 percent of whom require treatment for PTSD or other mental health problems. The hiring of 3,600 more "mental health professionals" in the last three years has allowed the VA system to offer increased treatment sought by recent veterans of the wars in Iraq and Afghanistan, who are much more likely than older veterans to seek mental health care. Thirty-six percent of the 250,000 Iraq and Afghanistan veterans who have sought care in the VA system were treated for mental health problems.

Katz stressed, however, that "no matter how much the VA expands access, there will continue to be challenges in providing care, especially in rural areas."

VA Needs to Forge Partnerships

One way to address rural access is for the VA to partner with state and local health care systems in rural areas that lack VA mental health professionals, said Frederick Frese, Ph.D., a member of the NAMI board of directors and a consumer advocate.

Legislation (S 38 and HR 2689) to authorize the VA to contract with community health centers and "other qualified entities" to provide mental health services in areas not adequately served by VA facilities has been introduced in Congress, but has not yet advanced.

Another barrier to mental health care for members of the military is their fear that treatment for psychiatric problems will hurt future chances to advance in rank or get jobs once they leave the military. "Stigma has not gone away," Ritchie emphasized.

The branches of the military have tried to lessen stigma by making psychiatrists and mental health professionals readily accessible to frontline troops, including the assignment of more than 200 Army clinicians to Iraq and Afghanistan, at any given time.

Another way to address stigma, according to Gail Wilensky, Ph.D., a member of the President's Commission on Care for America's Returning Wounded Warriors, is to challenge the belief that treatment blocks career advancement. She encouraged the armed services to have young officers who have received treatment and subsequent promotions share their experiences with other members of the military.

Leaders in each service branch have begun programs to educate their members about mental illness and encourage them to urge their buddies who display the warning signs of mental health problems to seek treatment. Several military installations, such as Fort Bragg in North Carolina, have begun to embed "mental health workers" in their general medical units, which allows soldiers to seek care in a less-obtrusive way.

Challenges Remain

Another challenge facing military and veterans health care providers is the elevated suicide risk their patient populations face. The VA response to increased suicides by veterans has included the assignment of a full-time suicide prevention coordinator to each VA medical center and launching a national suicide prevention hotline (*Psychiatric News*, September 7).

Other challenges with which the military and VA mental health systems are wrestling include better understanding of posttraumatic stress disorder and traumatic brain injury and the best treatments for those conditions.

In addition to the many usual war-related mental health problems, mental health professionals are struggling to understand the best way to treat the effects of repeated concussive injuries and how those interact with PTSD, Wilensky said.

The text of the Veterans Mental Health Outreach and Access Act can be accessed at <http://thomas.loc.gov> by searching on bill number, S 38. The report of the DoD Task Force on Mental Health is posted at <www.ha.osd.mil/dhb/mhtf/MHTF-Report-Final.pdf>. ■

Outcomes

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who had touted the line on better prognosis in developing countries, he believes the new study offers a fresh perspective.

He said the long-held assumption of better prognosis had generated some intriguing, if untested, hypotheses. Among the most prominent of these is the theory put forward by Arthur Kleinman, M.D., of Harvard that schizophrenia patients fare better in "socio-centric" rather than "ego-centric" cultures: that the high level of independence and skill required to thrive in a technological, highly individualistic society causes patients with the cognitive deficits of schizophrenia to languish and fail.

In contrast (so the theory went), patients in less-demanding cultures would more easily find a niche, nurtured by the strong family and social ties commonly said to exist in rural cultures.

But Carpenter concedes that the earlier WHO findings and the subsequent hypothesis obscured the coarseness of some of the measures used to designate a good outcome.

For instance, patients in India might be found to be employed, however marginally, while in Denmark they were invariably found to be unemployed; yet by itself the finding fails to take into account Denmark's strong social welfare network, which ensures that disabled patients have lifelong disability income, while in India patients might be living at subsistence level.

Moreover, the category of "employment" is itself a black box that might conceal a very low level of functioning.

Carpenter relates an anecdote reported by John Strauss, M.D., Carpenter's co-investigator in the pilot study. "In Nigeria we found a patient who was employed tending the family livestock herd," he said. "But when we asked around, we learned that the job was something normally done by a 10-year-old boy."

In the more searching analysis by Cohen and colleagues, they found a similar situation. In one Indian study, for instance, two-thirds of women were rated as having good homemaking functioning.

"However, it is difficult to determine the extent to which functional abilities were required to perform assigned household tasks (cooking, washing clothes and utensils, household maintenance, caring for children and others in the household) because other women in the household generally helped with these tasks," the authors wrote in their report.

"Not all employment is positive," Cohen told *Psychiatric News*. "Too often, it is exploitative or just plain awful. To demonstrate the value of work, it would be necessary to examine the nature of employment available to persons with schizophrenia."

Regarding the assumption of more tightly knit family and social structures in developing countries, Cohen said he believes it may be a "romanticization" of poorer, rural cultures.

"There is nothing wrong with the hypothesis," he said. "The problem comes when it is accepted as true without testing it. The hypothesis is rather static, too. It posits family support as a constant, and this is probably not the case.

"While in Nepal a number of years ago, I was told that Nepali families would do virtually anything to help a member at the time of his or her first psychotic episode, but that extraordinary support would weaken and, at times, break down in the face of chronic psychosis," Cohen said. "I am not saying that families are not supportive—only that the support is a dynamic process that is influenced by many factors and cannot be assumed."

"Questioning an Axiom: Better Prognosis for Schizophrenia in the Developing World?" is posted at <http://schizophreniabulletin.oxfordjournals.org/cgi/content/full/sbm105v1>. ■

VA

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military or in civilian jobs, especially those related to law enforcement.

Veterans advocates have maintained that better coordination of health and criminal-justice services is needed to ensure that veterans with mental illness who have been released from local jails are referred to the VA system for help before they descend into homelessness or suicide.

Frederick Frese, Ph.D., a member of the NAMI board of directors, said at a September congressional briefing on veterans' mental health that coordination with local government agencies could keep many veterans with mental illness from going for years without treatment (see page 1).

Yet another part of the bill requires the VA to make outpatient mental health care for veterans considered at risk for suicide available on a 24-hour basis. Many veterans and their survivors have testified before congress about extended treatment waiting times they endured after reporting suicidal thoughts and requesting mental health care.

The bill also requires a toll-free hotline for veterans, staffed by "appropriately trained mental health personnel" and available at all times, in addition to the 24-hour care requirement.

The measures are needed, said Sen. Tom Harkin (D-Iowa), sponsor of the Senate version, to reduce the more than 5,000 veteran suicides each year. The need is clear from statistics showing that the suicide rate for Iraq veterans is 35 percent higher than that for the general population, he said.

"This is a genuine crisis, and it requires an urgent, stepped-up response from the VA, which is exactly the purpose of my bill," Harkin said.

The bill was endorsed by the American Legion, Veterans of Foreign Wars, Disabled Veterans of America, and other veterans groups.

"The American Legion receives contact from veterans themselves who openly admit they need immediate help because of thoughts of harming themselves," said Shannon Middleton, deputy director for Health at the American Legion, in congressional testimony about the bill. "When the family and the veteran know what services are available, it is easier to seek assistance."

The bill, after being amended in the Senate, was returned to the House in September for final passage.

The Joshua Omvig Veterans Suicide Prevention Act can be accessed at <http://thomas.loc.gov> by searching on the bill number, HR 327. ■

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Neuroleptic malignant syndrome (NMS)—As with all antipsychotic medications, a rare and potentially fatal condition known as NMS has been reported with olanzapine. If signs and symptoms appear, immediate discontinuation is recommended. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis and cardiac dysrhythmia). Additional signs may include elevated creatinine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure.

Tardive dyskinesia (TD)—As with all antipsychotic medications, prescribing should be consistent with the need to minimize the risk of TD. The risk of developing TD and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic increase. The syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn.

Medication dispensing and prescribing errors have occurred between ZYPREXA® (olanzapine) and Zyrtec® (cetirizine HCl). These errors could result in unnecessary adverse events or potential relapse in patients suffering from schizophrenia or bipolar disorder. To reduce the potential for dispensing errors, please write ZYPREXA clearly.

The most common treatment-emergent adverse event associated with ZYPREXA (vs placebo) in 6-week acute-phase schizophrenia trials was somnolence (26% vs 15%). Other common events were dizziness (11% vs 4%), weight gain (6% vs 1%), personality disorder (COSTART term for nonaggressive objectionable behavior; 8% vs 4%), constipation (9% vs 3%), akathisia (5% vs 1%), and postural hypotension (5% vs 2%).

The most common treatment-emergent adverse event associated with ZYPREXA (vs placebo) in 3- and 4-week bipolar mania trials was somnolence (35% vs 13%). Other common events were dry mouth (22% vs 7%), dizziness (18% vs 6%), asthenia (15% vs 6%), constipation (11% vs 5%), dyspepsia (11% vs 5%), increased appetite (6% vs 3%), and tremor (6% vs 3%).

For complete safety profile, see the full Prescribing Information.

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Lilly

ZYPREXA® (Olanzapine Tablets)
ZYPREXA® ZYDIS® (Olanzapine Orally Disintegrating Tablets)
ZYPREXA® IntraMuscular (Olanzapine for Injection)
Brief Summary: Please consult package insert for complete prescribing information.

WARNING

Increased Mortality in Elderly Patients with Dementia-Related Psychosis—Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks) in these patients revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times that seen 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 (eg, heart failure, sudden death) or infectious (eg, pneumonia) in nature. ZYPREXA is not approved for the treatment of patients with dementia-related psychosis.

INDICATIONS AND USAGE: ZYPREXA and ZYPREXA Zydis are indicated for short- and long-term treatment of schizophrenia, for acute manic and mixed episodes of bipolar I disorder, and for maintenance treatment in bipolar disorder. The use of ZYPREXA for extended periods should be periodically re-evaluated as to the long-term usefulness of the drug for the individual patient. ZYPREXA IntraMuscular is indicated for treatment of agitation associated with schizophrenia and bipolar I mania.

CONTRAINDICATIONS: Known hypersensitivity to olanzapine.

WARNINGS: Increased Mortality in Elderly Patients with Dementia-Related Psychosis—Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. ZYPREXA is not approved for the treatment of patients with dementia-related psychosis (*see* BOX WARNING).

In placebo-controlled clinical trials of elderly patients with dementia-related psychosis, the incidence of death in olanzapine-treated patients (3.5%) was significantly greater than placebo-treated patients (1.5%).

Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients with Dementia—Cerebrovascular adverse events (eg, stroke, transient ischemic attack), including fatalities, were reported in patients in trials of olanzapine in elderly patients with dementia-related psychosis. In placebo-controlled trials, there was a significantly higher incidence of cerebrovascular adverse events in patients treated with olanzapine compared to patients treated with placebo. Olanzapine is not approved for the treatment of patients with dementia-related psychosis.

Hyperglycemia and Diabetes Mellitus—Hyperglycemia, in some cases associated with ketoacidosis, coma, or death, has been reported in patients treated with atypical antipsychotics including olanzapine. Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Patients diagnosed with diabetes who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes who are starting treatment with atypicals should have fasting blood glucose (FBG) testing at baseline and periodically during treatment. Any patient treated with atypicals should be monitored for symptoms of hyperglycemia. Patients who develop symptoms of hyperglycemia during treatment with atypicals should undergo FBG testing.

Neuroleptic Malignant Syndrome (NMS)—Potentially fatal NMS has been reported in association with administration of antipsychotic drugs, including olanzapine. See complete prescribing information for information on management of NMS. Patients requiring antipsychotic drug treatment after recovery from NMS should be carefully monitored since recurrences have been reported.

Tardive Dyskinesia (TD)—Potentially irreversible TD may develop in patients treated with antipsychotic drugs. Although the prevalence of TD appears to be highest among the elderly, especially elderly women, it is impossible to predict which patients are more likely to develop the syndrome. If signs and symptoms of TD appear, consider drug discontinuation.

PRECAUTIONS: Hemodynamic Effects—Olanzapine may induce orthostatic hypotension associated with dizziness; tachycardia; and in some patients, syncope. Hypotension, bradycardia with/without hypotension, tachycardia, and syncope were also reported during the clinical trials with intramuscular olanzapine for injection. Incidence of syncope was 0.6%, 15/2500 with oral olanzapine in phase 2-3 trials and 0.3%, 2/722 with intramuscular olanzapine for injection in clinical trials. Three normal volunteers in phase 1 studies with intramuscular olanzapine experienced hypotension, bradycardia, and sinus pauses of up to 6 seconds that spontaneously resolved (in 2 cases the events occurred on intramuscular olanzapine, and in 1 case, on oral olanzapine). The risk for this sequence of events may be greater in nonpsychiatric patients compared to psychiatric patients who are possibly more adapted to certain effects of psychotropic drugs. Patients should remain recumbent if drowsy or dizzy after injection with intramuscular olanzapine for injection until examination has indicated they are not experiencing postural hypotension, bradycardia, and/or hypoventilation. Olanzapine should be used with particular caution in patients with known cardiovascular disease (history of myocardial infarction or ischemia, heart failure, or conduction abnormalities), cerebrovascular disease, and conditions which would predispose patients to hypotension (dehydration, hypovolemia, and treatment with antihypertensive medications) where the occurrence of syncope, or hypotension and/or bradycardia might put them at increased medical risk. Caution is necessary in patients receiving treatment with other drugs having effects that can induce hypotension, bradycardia, respiratory or CNS depression (*see* Drug Interactions). Concomitant administration of intramuscular olanzapine and parenteral benzodiazepine has not been studied and is not recommended. If such combination treatment is considered, careful evaluation of clinical status for excessive sedation and cardiorespiratory depression is recommended.

Seizures—During premarketing testing, seizures occurred in 0.9% (22/2500) of olanzapine-treated patients, regardless of causality. Use cautiously in patients with a history of seizures or with conditions that potentially lower the seizure threshold.

Hyperprolactinemia—Like other drugs that antagonize dopamine D2 receptors, olanzapine elevates prolactin levels; a modest elevation persists during chronic administration. Tissue culture experiments indicate that approximately one third of human breast cancers are prolactin dependent in vitro. However, neither clinical nor epidemiologic studies have shown an association between chronic administration of this class of drugs and tumorigenesis in humans; the available evidence is inconclusive.

Transaminase Elevations—In placebo-controlled studies, clinically significant ALT (SGPT) elevations (≥3 times the upper limit of normal) were observed in 2% (6/243) of patients exposed to olanzapine compared to no (0/115) placebo patients. None of these patients experienced jaundice. Among about 2400 patients with baseline SGPT ≤90 IU/L, 2% (50/2381) had asymptomatic SGPT elevations to >200 IU/L. Most were transient changes that tended to normalize while olanzapine treatment was continued. Among 2500 patients in oral olanzapine trials, about 1% (23/2500) discontinued treatment due to transaminase increases. Rare postmarketing reports of hepatitis have been received. Very rare cases of cholestatic or mixed liver injury have also been reported in the postmarketing period. Exercise caution in patients who have signs and symptoms of hepatic impairment; preexisting conditions associated with limited hepatic functional reserve; or concomitant treatment with potentially hepatotoxic drugs (*see* Laboratory Tests, below).

Potential for Cognitive and Motor Impairment—Somnolence was a commonly reported, dose-related adverse event in premarketing trials (olanzapine 26% vs placebo 15%). Somnolence led to discontinuation in 0.4% (9/2500) of patients in the oral premarketing database.

Body Temperature Regulation—Use appropriate care when prescribing olanzapine for patients who will be experiencing conditions that may contribute to an elevation in core body temperature.

Dysphagia—Esophageal dysmotility and aspiration have been associated with antipsychotic drug use. Aspiration pneumonia is a common cause of morbidity and mortality in patients with advanced Alzheimer's disease. Olanzapine and other antipsychotic drugs should be used cautiously in patients at risk for aspiration pneumonia.

Suicide—The possibility of a suicide attempt is inherent in schizophrenia and in bipolar disorder, and close supervision of high-risk patients should accompany drug therapy. Prescriptions for olanzapine should be written for the smallest quantity of tablets consistent with good patient management.

Use in Patients with Concomitant Illnesses—Olanzapine should be used with caution in patients with clinically significant prostatic hypertrophy, narrow angle glaucoma, or a history of paralytic ileus.

In 5 placebo-controlled studies in elderly patients with dementia-related psychosis (n=1184), these treatment-emergent adverse events were reported with olanzapine at an incidence of ≥2% and significantly greater than with placebo: falls, somnolence, peripheral edema, abnormal gait, urinary incontinence, lethargy, increased weight, asthenia, pyrexia, pneumonia, dry mouth, visual hallucinations. Discontinuation due to adverse events was significantly greater with olanzapine than placebo (13% vs 7%). Elderly patients with dementia-related psychosis treated with olanzapine are at an increased risk of death compared to placebo. Olanzapine is not approved for treatment of patients with dementia-related psychosis. If the prescriber elects to treat this patient population, vigilance should be exercised (*see* BOX WARNING *and* WARNINGS).

Because of the risk of orthostatic hypotension with olanzapine, use caution in cardiac patients (*see* Hemodynamic Effects).

Information for Patients—See full prescribing information for information to discuss with patients taking olanzapine.

Laboratory Tests—Periodic assessment of transaminases is recommended in patients with significant hepatic disease.

Drug Interactions—Use caution when olanzapine is taken in combination with other centrally acting drugs and alcohol. Olanzapine may enhance the effects of certain antihypertensive agents. Olanzapine may antagonize the effects of levodopa and dopamine agonists. Agents that induce CYP1A2 or glucuronyl transferase enzymes (eg, omeprazole, rifampin) may cause an increase in olanzapine clearance. Inhibitors of CYP1A2 could potentially inhibit olanzapine clearance. Although olanzapine is metabolized by multiple enzyme systems, induction or inhibition of a single enzyme may appreciably alter olanzapine clearance. A dosage adjustment may need to be considered with specific drugs.

Activated charcoal (1 g) reduced the Cmax and AUC of oral olanzapine by about 60%. Single doses of cimetidine (800 mg) or aluminum- and magnesium-containing antacids did not affect the oral bioavailability of olanzapine. Carbamazepine (200 mg bid) causes an approximately 50% increase in the clearance of olanzapine. Higher daily doses of carbamazepine may cause an even greater increase in olanzapine clearance. Neither ethanol (45 mg/70 kg single dose) nor warfarin (20 mg single dose) had an effect on olanzapine pharmacokinetics. Fluoxetine at 60 mg (single or multiple doses) causes a small increase in the Cmax of olanzapine and a small decrease in olanzapine clearance; however, the impact of this factor is small in comparison to the overall variability between individuals, and dose modification is not routinely recommended. Fluvoxamine decreases the clearance of olanzapine; lower doses of olanzapine should be considered in patients receiving fluvoxamine concomitantly. In vitro data suggest that a clinically significant pharmacokinetic interaction between olanzapine and valproate is unlikely.

Olanzapine is unlikely to cause clinically important drug interactions mediated by the enzymes CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A. Single doses of olanzapine did not affect the pharmacokinetics of imipramine/desipramine or warfarin. Multiple doses of olanzapine did not influence the kinetics of diazepam/N-desmethyldiazepam, lithium, ethanol, or biperiden. However, coadministration of either diazepam or ethanol potentiated the orthostatic hypotension observed with olanzapine. Multiple doses of olanzapine did not affect the pharmacokinetics of theophylline or its metabolites. Co-administration of intramuscular lorazepam and intramuscular olanzapine for injection added to the somnolence observed with either drug alone (*see* Hemodynamic Effects).

Carcinogenesis, Mutagenesis, Impairment of Fertility—The incidence of liver hemangiomas and hemangiosarcomas in female mice was significantly increased in one carcinogenicity study at 2 times the maximum human daily oral dose (MHDOD) but not in another study at 2-5 times the MHDOD (mg/m^2 basis). In this study there was a high incidence of early mortalities in males in the 30/20 mg/kg/d group. The incidence of mammary gland adenomas and adenocarcinomas was significantly increased in female mice and rats given olanzapine at 0.5 and 2 times the MHDOD respectively (mg/m^2 basis). In other studies, serum prolactin measurements of olanzapine showed elevations up to 4-fold in rats at the same doses used in the carcinogenicity studies. The relevance for human risk of the finding of prolactin mediated endocrine tumors in rodents is unknown. No evidence of mutagenic potential for olanzapine has been found.

In rats, fertility (females) and mating performance (males and females) were affected at doses 1.5-11 times the MHDOD (mg/m^2 basis). Diestrous was prolonged and estrous delayed at 0.6 times the MHDOD (mg/m^2 basis); therefore, olanzapine may produce a delay in ovulation.

Pregnancy Category C—There are no adequate and well-controlled studies in pregnant women. Olanzapine should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus.

Labor and Delivery, Nursing Mothers—Parturition in rats was not affected by olanzapine; its effect on labor and delivery in humans is unknown. In a study in lactating, healthy women, olanzapine was excreted in breast milk. Mean infant dose at steady state was estimated to be 1.8% of the maternal dose. It is recommended that women receiving olanzapine should not breast-feed.

Use in Pediatric and Geriatric Patients—Safety and effectiveness in pediatric patients have not been established. In premarketing clinical trials in patients with schizophrenia, there was no indication of any different tolerability of olanzapine in the elderly compared to younger patients. Studies in elderly patients with dementia-related psychosis have suggested there may be a different tolerability profile in these patients. Elderly patients with dementia-related psychosis treated with olanzapine are at an increased risk of death compared to placebo. Olanzapine is not approved for treatment of patients with dementia-related psychosis. If the prescriber elects to treat these patients, vigilance should be exercised. Consider a lower starting dose for any geriatric patient in the presence of factors that might decrease pharmacokinetic clearance or increase the pharmacodynamic response to olanzapine (*see* BOX WARNING, WARNINGS, *and* PRECAUTIONS).

ADVERSE REACTIONS: The following findings are based on a clinical trial database consisting of 8661 patients with approximately 4165 patient-years of exposure to oral olanzapine and 722 patients with exposure to intramuscular olanzapine for injection, including patients with schizophrenia, bipolar mania, or Alzheimer's disease (oral olanzapine trials) and patients with agitation associated with schizophrenia, bipolar I disorder (manic or mixed episodes), or dementia (intramuscular olanzapine for injection trials). See the full prescribing information for details on these trials. Certain portions of the discussion below relating to dose-dependent adverse events, vital sign changes, weight gain, laboratory changes, and ECG changes are derived from studies in patients with schizophrenia and have not been duplicated for bipolar mania or agitation; however, this information is also generally applicable to bipolar mania and agitation.

Associated with Discontinuation—Overall there was no difference in discontinuations due to adverse events in placebo-controlled oral olanzapine trials (olanzapine vs placebo: schizophrenia, 5% vs 6%; bipolar mania monotherapy, 2% vs 2%; bipolar mania cotherapy, 11% [olanzapine plus lithium or valproate] vs 2% [lithium or valproate alone]); or in placebo-controlled intramuscular olanzapine for injection trials (olanzapine for injection, 0.4%; placebo 0%). Discontinuations in oral schizophrenia trials due to increases in SGPT were considered to be drug related (olanzapine 2% vs placebo 0%; *see* PRECAUTIONS).

Commonly Observed Adverse Events—In 6-week, placebo-controlled, premarketing schizophrenia trials, the most common treatment-emergent adverse events associated with oral olanzapine (incidence ≥5% and olanzapine incidence at least twice that for placebo) were: postural hypotension, constipation, weight gain, dizziness, personality disorder (COSTART term for nonaggressive objectionable behavior), and akathisia. In 3- and 4-week placebo-controlled bipolar mania monotherapy trials, the most common treatment-emergent adverse events associated with oral olanzapine were: asthenia, dry mouth, constipation, dyspepsia, increased appetite, somnolence, dizziness, and tremor. In short-term bipolar mania combination therapy trials, the most common treatment-emergent adverse events observed with olanzapine plus lithium or valproate were dry mouth, weight gain, increased appetite, dizziness, back pain, constipation, speech disorder, increased salivation, amnesia, and paresthesia. In 24-hour placebo-controlled trials of intramuscular olanzapine for injection for agitation associated with schizophrenia or bipolar mania, somnolence was the one adverse event observed at an incidence of ≥5% and at least twice that for placebo (olanzapine for injection 6%, placebo 3%).

Adverse Events with an Incidence ≥2% in Oral Monotherapy Trials—The following treatment-emergent events were reported at an incidence of ≥2% with oral olanzapine (doses ≥2.5 mg/d), and at a greater incidence with olanzapine than with placebo in short-term placebo-controlled trials (olanzapine N=532, placebo N=294): ***Body as a Whole***—accidental injury, asthenia, fever, back pain, chest pain; ***Cardiovascular***—postural hypotension, tachycardia, hypertension; ***Digestive***—dry mouth, constipation, dyspepsia, vomiting, increased appetite; ***Hemic and Lymphatic***—ecchymosis; ***Metabolic and Nutritional***—weight gain, peripheral edema; ***Musculoskeletal***—extremity pain (other than joint), joint pain; ***Nervous System***—somnolence, insomnia, dizziness, abnormal gait, tremor, akathisia, hypertonia, articulation impairment; ***Respiratory***—rhinitis, cough increased, pharyngitis; ***Special Senses***—amblyopia; ***Urogenital***—urinary incontinence, urinary tract infection.

Adverse Events with an Incidence ≥2% in Oral Combination Therapy Trials—The following treatment-emergent events were reported at an incidence of ≥2% with oral olanzapine (doses ≥5 mg/d) plus lithium or valproate (N=229), and at a greater incidence than with placebo plus lithium or valproate (N=115) in short-term placebo-controlled trials: ***Body as a Whole***—asthenia, back pain, accidental injury, chest pain; ***Cardiovascular***—hypertension; **Digestive**—dry mouth, increased appetite, thirst, constipation, increased salivation; ***Metabolic and Nutritional***—weight gain, peripheral edema, edema; ***Nervous System***—somnolence, tremor, depression, dizziness, speech disorder, amnesia, paresthesia, apathy, confusion, euphoria, incoordination; ***Respiratory***—pharyngitis, dyspnea; ***Skin and Appendages***—sweating, acne, dry skin; ***Special Senses***—amblyopia, abnormal vision; ***Urogenital***—dysmenorrhea, vaginitis.

Adverse Events with an Incidence ≥1% in Intramuscular Trials—The following treatment-emergent adverse events were reported at an incidence of ≥1% with intramuscular olanzapine for injection (2.5–10 mg/injection) and at incidence greater than placebo in short-term, placebo-controlled trials in agitated patients with schizophrenia or bipolar mania: ***Body as a Whole***—asthenia; ***Cardiovascular***—hypotension, postural hypotension; ***Nervous System***—somnolence, dizziness, tremor.

Dose Dependency of Adverse Events in Short-Term, Placebo-Controlled Trials—Extrapyramidal Symptoms: In an acute-phase controlled clinical trial in schizophrenia, there was no significant difference in ratings scales incidence between any dose of oral olanzapine (5±2.5, 10±2.5, or 15±2.5 mg/d) and placebo for parkinsonism (Simpson-Angus Scale total score >3) or akathisia (Barnes Akathisia global score ≥2). In the same trial, only akathisia events (spontaneously reported COSTART terms akathisia and hyperkinesia) showed a statistically significantly greater adverse events incidence with the 2 higher doses of olanzapine than with placebo. The incidence of patients reporting any extrapyramidal event was significantly greater than placebo only with the highest dose of oral olanzapine (15±2.5 mg/d). In controlled clinical trials of intramuscular olanzapine for injection, there were no statistically significant differences from placebo in occurrence of any treatment-emergent extrapyramidal symptoms, assessed by either rating scales incidence or spontaneously reported adverse events.

Other Adverse Events: Dose-relatedness of adverse events was assessed using data from this same clinical trial involving 3 fixed oral dosage ranges (5±2.5, 10±2.5, or 15±2.5 mg/d) compared with placebo. The following treatment-emergent events showed a statistically significant trend: asthenia, dry mouth, nausea, somnolence, tremor.

In an 8-week, randomized, double-blind study in patients with schizophrenia, schizophreniform disorder, or schizoaffective disorder comparing fixed doses of 10, 20, and 40 mg/d, statistically significant differences were seen between doses for the following: baseline to endpoint weight gain, 10 vs 40 mg/d; incidence of treatment-emergent prolactin elevations >24.2 ng/mL (female) or >18.77 ng/mL (male), 10 vs 40 mg/d and 20 vs 40 mg/d; fatigue, 10 vs 40 mg/d and 20 vs 40 mg/d; and dizziness, 20 vs 40 mg/d.

Vital Sign Changes—Oral olanzapine was associated with orthostatic hypotension and tachycardia in clinical trials. Intramuscular olanzapine for injection was associated with bradycardia, hypotension, and tachycardia in clinical trials (*see* PRECAUTIONS).

Weight Gain—In placebo-controlled 6-week schizophrenia studies, weight gain was reported in 5.6% of oral olanzapine patients (average 2.8-kg gain) compared to 0.8% of placebo patients (average 0.4-kg loss); 29% of olanzapine patients gained >7% of their baseline weight, compared to 3% of placebo patients. During continuation therapy (238 median days of exposure), 56% of patients met the criterion for having gained >7% of their baseline weight. Average gain during long-term therapy was 5.4 kg.

Laboratory Changes—Olanzapine is associated with asymptomatic increases in SGPT, SGOT, and GGT and with increases in serum prolactin and CPK (*see* PRECAUTIONS). Asymptomatic elevation of eosinophils was reported in 0.3% of olanzapine patients in premarketing trials. There was no indication of a risk of clinically significant neutropenia associated with olanzapine in the premarketing database.

In clinical trials among olanzapine-treated patients with baseline random triglyceride levels of <150 mg/dL (N=659), 0.5% experienced triglyceride levels of ≥500 mg/dL anytime during the trials. In these same trials, olanzapine-treated patients (N=1185) had a mean triglyceride increase of 20 mg/dL from a mean baseline of 175 mg/dL. In placebo-controlled trials, olanzapine-treated patients with baseline random cholesterol levels of <200 mg/dL (N=1034) experienced cholesterol levels of ≥240 mg/dL anytime during the trials more often than placebo-treated patients (N=602; 3.6% vs 2.2% respectively). In these same trials, olanzapine-treated patients (N=2528) had a mean increase of 0.4 mg/dL in cholesterol from a mean baseline of 203 mg/dL, which was significantly different compared to placebo-treated patients (N=1415) with a mean decrease of 4.6 mg/dL from a mean baseline of 203 mg/dL.

ECG Changes—Analyses of pooled placebo-controlled trials revealed no statistically significant olanzapine/placebo differences in incidence of potentially important changes in ECG parameters, including QT, QTc, and PR intervals. Olanzapine was associated with a mean increase in heart rate of 2.4 BPM compared to no change among placebo patients.

Other Adverse Events Observed During Clinical Trials—The following treatment-emergent events were reported with oral olanzapine at multiple doses ≥1 mg/d in clinical trials (8661 patients, 4165 patient-years of exposure). This list may not include events previously listed elsewhere in labeling, those events for which a drug cause was remote, those terms which were so general as to be uninformative, and those events reported only once or twice which did not have a substantial probability of being acutely life-threatening. *Frequent* events occurred in ≥1/100 patients; *infrequent* events occurred in 1/100 to 1/1000 patients; *rare* events occurred in <1/1000 patients. ***Body as a Whole***—*Frequent:* dental pain, flu syndrome; *Infrequent:* abdomen enlarged, chills, face edema, intentional injury, malaise, moniliasis, neck pain, neck rigidity, pelvic pain, photosensitivity reaction, suicide attempt; *Rare:* chills and fever, hangover effect, sudden death. ***Cardiovascular***—*Frequent:* hypotension; *Infrequent:* atrial fibrillation, bradycardia, cerebrovascular accident, congestive heart failure, heart arrest, hemorrhage, migraine, pallor, palpitation, vasodilatation, ventricular extrasystoles; *Rare:* arteritis, heart failure, pulmonary embolus. ***Digestive***—*Frequent:* flatulence, increased salivation, thirst; *Infrequent:* dysphagia, esophagitis, fecal impaction, fecal incontinence, gastritis, gastroenteritis, gingivitis, hepatitis, melena, mouth ulceration, nausea and vomiting, oral moniliasis, periodontal abscess, rectal hemorrhage, stomatitis, tongue edema, tooth caries; *Rare:* aphthous stomatitis, enteritis, eructation, esophageal ulcer, glossitis, ileus, intestinal obstruction, liver fatty deposit, tongue discoloration. ***Endocrine***—*Infrequent:* diabetes mellitus; *Rare:* diabetic acidosis, goiter. ***Hemic and Lymphatic***—*Infrequent:* anemia, cyanosis, leukocytosis, leukopenia, lymphadenopathy, thrombocytopenia; *Rare:* normocytic anemia, thrombocythemia. ***Metabolic and Nutritional***—*Infrequent:* acidosis, alkaline phosphatase increased, bilirubinemia, dehydration, hypercholesteremia, hyperglycemia, hyperlipemia, hyperuricemia, hypoglycemia, hypokalemia, hyponatremia, lower extremity edema, upper extremity edema; *Rare:* gout, hyperkalemia, hypernatremia, hypoproteinemia, ketosis, water intoxication. ***Musculoskeletal***—*Frequent:* joint stiffness, twitching; *Infrequent:* arthritis, arthrosis, leg cramps, myasthenia; *Rare:* bone pain, bursitis, myopathy, osteoporosis, rheumatoid arthritis. ***Nervous System***—*Frequent:* abnormal dreams, amnesia, delusions, emotional lability, euphoria, manic reaction, paresthesia, schizophrenic reaction; *Infrequent:* akinesia, alcohol misuse, antisocial reaction, ataxia, CNS stimulation, cogwheel rigidity, delirium, dementia, depersonalization, dysarthria, facial paralysis, hypesthesia, hypokinesia, hypotonia, incoordination, libido decreased, libido increased, obsessive compulsive symptoms, phobias, somatization, stimulant misuse, stupor, stuttering, tardive dyskinesia, vertigo, withdrawal syndrome; *Rare:* circumoral paresthesia, coma, encephalopathy, neuralgia, neuropathy, nystagmus, paralysis, subarachnoid hemorrhage, tobacco misuse. ***Respiratory***—*Frequent:* dyspnea; *Infrequent:* apnea, asthma, epistaxis, hemoptysis, hyperventilation, hypoxia, laryngitis, voice alteration; *Rare:* atelectasis, hiccup, hypoventilation, lung edema, stridor. ***Skin and Appendages***—*Frequent:* sweating; *Infrequent:* alopecia, contact dermatitis, dry skin, eczema, maculopapular rash, pruritus, seborrhea, skin discoloration, skin ulcer, urticaria, vesiculobullous rash; *Rare:* hirsutism, pustular rash. ***Special Senses***—*Frequent:* conjunctivitis; *Infrequent:* abnormality of accommodation, blepharitis, cataract, deafness, diplopia, dry eyes, ear pain, eye hemorrhage, eye inflammation, eye pain, ocular muscle abnormality, taste perversion, tinnitus; *Rare:* corneal lesion, glaucoma, keratoconjunctivitis, macular hypopigmentation, miosis, mydriasis, pigment deposits lens. ***Urogenital***—*Frequent:* vaginitis*; *Infrequent:* abnormal ejaculation,* amenorrhea,* breast pain, cystitis, decreased menstruation,* dysuria, female lactation,* glycosuria, gynecomastia, hematuria, impotence,* increased menstruation,* menorrhagia,* metrorrhagia,* polyuria, premenstrual syndrome,* pyuria, urinary frequency, urinary retention, urinary urgency, urination impaired, uterine fibroids enlarged,* vaginal hemorrhage*; *Rare:* albuminuria, breast enlargement, mastitis, oliguria. (*Adjusted for gender.)

The following treatment-emergent events were reported with intramuscular olanzapine for injection at one or more doses ≥2.5 mg/injection in clinical trials (722 patients). This list may not include events previously listed elsewhere in labeling, those events for which a drug cause was remote, those terms which were so general as to be uninformative, and those events reported only once or twice which did not have a substantial probability of being acutely life-threatening. ***Body as a Whole***—*Frequent:* injection site pain; *Infrequent:* abdominal pain, fever. ***Cardiovascular***—*Infrequent:* AV block, heart block, syncope. ***Digestive***—*Infrequent:* diarrhea, nausea. ***Hemic and Lymphatic***—*Infrequent:* anemia. ***Metabolic and Nutritional***—*Infrequent:* creatine phosphokinase increased, dehydration, hyperkalemia. ***Musculoskeletal***—*Infrequent:* twitching. ***Nervous System***—*Infrequent:* abnormal gait, akathisia, articulation impairment, confusion, emotional lability. ***Skin and Appendages***—*Infrequent:* sweating.

Postintroduction Reports—Reported since market introduction and temporally (not necessarily causally) related to olanzapine therapy: allergic reaction (eg, anaphylactoid reaction, angioedema, pruritus or urticaria), diabetic coma, jaundice, neutropenia, pancreatitis, priapism, rhabdomyolysis, and venous thromboembolic events (including pulmonary embolism and deep venous thrombosis). Random cholesterol levels of ≥240 mg/dL and random triglyceride levels of ≥1000 mg/dL have been reported.

DRUG ABUSE AND DEPENDENCE: Olanzapine is not a controlled substance.

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Selection

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in a number of schizophrenia-associated genes was found specific to the human lineage, he explained.

In primate evolution the authors also found accelerated DNA sequence changes in the protein coding regions in one of the genes (DISC1) that is implicated in schizophrenia.

"These tests suggest that during the recent evolution, certain variations in the genome were positively selected, and some of these overlap with the genes implicated in schizophrenia," Lin said.

Thaker said the observations are not surprising since schizophrenia is such a uniquely human disease, and evolutionary forces that have endowed individuals with specialized cognitive and social skills may also make them vulnerable to insults that can result in maladaptive behaviors.

"The intriguing part of their findings is that the same genetic variations that lead to devastating illness such as schizophrenia, an illness with serious impairments in cognition and in social and motivational drive, may also provide some advantage," Thaker told *Psychiatric News*.

"To understand this apparent contradiction, one needs to understand that schizophrenia is multifactorial, with several genes in various combinations interacting with the environment, resulting in the overt illness," he said. "Certain patterns of allelic variations across a number of genes may be devastating, but variation in an individual gene by itself may provide advantage."

Thaker noted that Andreas Meyer-Lindenberg, M.D., Ph.D., of the National Institute of Mental Health recently found that the same allelic variation in the DARPP-32 gene—which is associated with schizophrenia—is important for better cognitive performance.

"A larger proportion of relatives of schizophrenia patients are likely to have partial genetic loading than the general population, and schizotypal personality styles are common in this group that are associated with unique cognitive styles, some disadvantageous, but others leading to creativity," Thaker added.

An abstract of "Adaptive Evolution of Genes Underlying Schizophrenia" is posted at <www.journals.royalsoc.ac.uk/content/6215831652282576/?p=7474162914024da08f81333b29c72587&pi=0?p=7474162914024da08f81333b29c72587&pi=0>. ■

Youth

continued from page 14

and that adding CBT to fluoxetine therapy minimized suicidal ideation and treatment-emergent suicidal events.

The TADS team will complete a full year of naturalistic follow-up, with some patients continuing treatment and some not. Grants from NIMH and the National Institute on Drug Abuse will also allow them to track their subjects for five years to record functional outcomes as they transition to college, young adulthood, and the workplace, said March.

TADS is a major contribution to guiding current practice, although only future research can tell if a different SSRI or another form of psychotherapy would give similar results, Kutcher said.

"We now have a safe and effective treatment for a very severe disorder," he said. "Now providers have to ask what is our moral and social responsibility to children, given that probably less than 30 percent of children who need help are getting it."

An abstract of "The Treatment for Adolescents With Depression Study (TADS)" is posted at <http://archpsyc.ama-assn.org/cgi/content/short/64/10/1132>. ■

Investment

continued from page 18

The proportion of employees experiencing recovery from depressive symptoms as indicated by a QIDS score of 5 or less was also significantly higher for the intervention group (26.2 percent) than the usual-care group (17.7 percent).

In addition, employees participating in the study's intervention arm worked an average of two more hours a week than those in the usual-care group.

Wang noted that the monetary value of working two more hours a week translated to about $1,800 per employee annually, and that the cost of similar interventions would range from about $100 to $400 per employee a year, "so there is definitely a cost benefit," he said, adding that employers who implemented such interventions would "experience a positive return on investment from outreach and enhanced treatment of depressed workers."

He said further research will investigate the durability of the gains made by employees in terms of reduced depression and increased workplace productivity.

The study was funded by NIMH and the Robert Wood Johnson Foundation.

An abstract of "Telephone Screening, Outreach, and Care Management for Depressed Workers and Impact on Clinical and Work Productivity Outcomes" is posted at <jama.ama-assn.org/cgi/content/abstract/298/12/1401>. ■

Papers Invited

The Association for the Advancement of Philosophy and Psychiatry will hold its 20th annual meeting May 3 and 4, 2008, in Washington, D.C., on the theme "Political Extremism and Psychopathology." Papers are invited on such questions as these: What role, if any, does psychopathology play in the lives of extremists? Are there coherent ways of distinguishing between healthy and pathological political ideologies? What specific insights can cognitive neurobiology, psychodynamic theory, or evolutionary psychology offer to political scientists? Should psychiatry have a public role in discussing public figures' possible psychopathology?

Abstracts should be 600 words or fewer and sent by November 15 to Donald Mender at donald.mender@yale.edu. Acceptances will be e-mailed by January 1, 2008. ■

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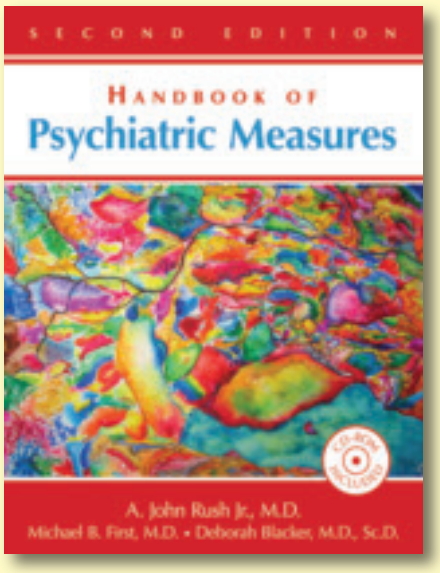

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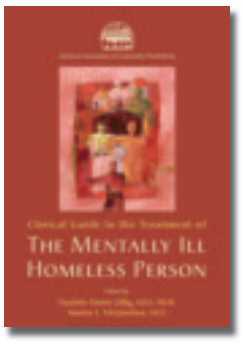

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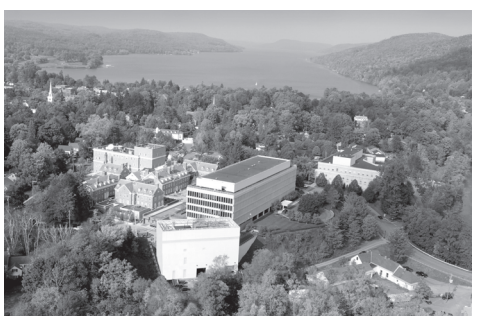

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MHM Services, Inc. is the nation's leading provider of correctional healthcare staffing. As one of the largest employers of mental health professionals in the nation, MHM Services is always looking for dedicated individuals who want a career that is both professionally rewarding and provides greater balance with less stress in their day to day life.

MHM Services is now offering Per Diem and traveling positions throughout the U.S. We offer competitive hourly rates, paid malpractice, paid travel expenses, direct deposit, and now company sponsored benefits for our Per Diem and traveling Psychiatrists.

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ALABAMA

UNIVERSITY OF ALABAMA AT BIRMINGHAM
DEPARTMENT OF PSYCHIATRY
AIMHS Center for Program Evaluation Research

The Department of Psychiatry, Community Psychiatry Program at UAB invites applications for two full-time faculty positions for psychiatrists or psychologists with interest in community mental health program research in the Division of Public Psychiatry. Rank, tenure status and salary commensurate with experience and qualifications. The selected candidates will be at the core of the recently established Alabama Institute for Mental Health Services, a mental health services center of excellence. AIMHS faculty and staff will assist with implementation and evaluation of current and future state-wide initiatives in evidence-based programs for a range of community mental health services. Program evaluation and basic mental health intervention research expertise is an essential qualification for applicants. At least one candidate may be recruited at a junior faculty level while the second position will be filled by a senior researcher. Both individuals will play a key role in the expansion of the institute and in furthering mental health system change, at the state and national level. The senior level candidate would be expected to have a strong record of federal and other grant funding, as well as current projects and funding that would fit with the objectives of the AIMHS. Licensure or license eligibility and clinical experience with the serious mentally ill population are desired. Secondary clinical duties are available for interested candidates. Opportunities exist for teaching and supervision with clinical psychology interns, medical students and psychiatry residents.

The UAB Department of Psychiatry and Behavioral Neurobiology is in a phase of rapid growth under the direction of a new chairman. Basic neuroscience research has been greatly enhanced and the AIMHS project is poised to expand mental health services research at UAB, in Alabama and the southeast region. Candidates should possess a Ph.D. in clinical psychology, or be a BC/BE psychiatrist and demonstrate clear potential for distinguished scientist careers, and demonstrate the ability to attract external funding. Applications should include a letter outlining qualifications, research interests, and potential fit with the AIMHS center. Additionally, applications should include a current vita, and may include selected reprints, and letters of recommendation. Applications should be sent to Robert Savage, Ph.D., Associate Professor, UAB Department of Psychiatry, CCB Room 466, 1530 3rd Avenue South, Birmingham, AL 35294. UAB is a large urban university and major regional medical center with excellent resources and benefits. UAB is an affirmative action/equal opportunity employer.

PSYCHIATRY EMERGENCY DEPARTMENT DIRECTOR

Birmingham - University of Alabama at Birmingham, Department of Psychiatry and Behavioral Neurobiology. Full-time faculty position for BC/BE psychiatrist in the Public Sector Division. Rank, tenure status and salary commensurate with experience and qualifications. Major regional medical center with excellent resources and benefits. Candidate will lead the initiative to develop the state's first psychiatric emergency services continuum. At the hub of this PES will be a psychiatric emergency services (PES) clinic and 23-hour observation unit with expansion to a crisis stabilization unit, mobile crisis teams, crisis residential services and crisis counseling. Participation in the teaching and supervision of medical students and psychiatry residents expected. Involvement in research encouraged. Competitive salary/benefits package. Applications to Jacqueline M. Feldman, M.D., Linton Professor, Division Director, Community Care Building, 4th Floor, 1530 3rd Avenue South, Birmingham, AL 35294-2050. UAB is an affirmative action/equal opportunity employer.

Mountain Lakes Behavioral Healthcare, located in beautiful northeast Alabama, has an excellent opportunity to practice general psychiatry in a community mental health center setting. We have an immediate full time opening in our Scottsboro Office in Jackson County (45 minutes from Huntsville). Looking for someone interested in a diversified caseload and varied work settings. Very good working conditions; eager, cooperative treatment team; competitive salary and benefits. Board certified or Board eligible. J-1; H1-B welcome. Contact: Greg Glasscock, email gglasscock@mlbhc.com; (256) 582-4240 ext. 107.

Sweet Home! Alabama college town seeks ADULT psychiatrist to join hospital group. Top ranked hospital by Money Magazine! Extremely Lucrative Salary, Full Benefits, and Academic Affiliation! For more information on this psychiatry position along with others nationwide, Contact: Lindsay McCartney at: (800) 735-8261 ext 213; FAX your CV to: (703)-995-0647 or Email: lmccartney@medsourceconsultants.com

ALASKA

Fairbanks Memorial Hospital in Fairbanks, AK, is looking for a full-time, adult, inpatient Psychiatrist to join our exceptional team. We have a 20-bed inpatient unit, staffed with a Nurse Director, RNs, an LPN, CNAs, Psych Techs, Counselors, an OT, Social Workers and a Medical Director.

FMH is committed to continually upgrading the level of care in our close-knit community and invite you to join us. Come experience the Alaskan way of life, full of adventure and beauty, and work at a top-notch facility.

For more information, call 888.303.5402 or e-mail Suzan.Bast@bannerhealth.com. Check out our Web site at www.fmhdc.com.

ANCHORAGE: Child or General Psychiatrist. Inpatient & residential treatment center. Join a great staff & physician team. Outstanding compensation potential - salary, benefits & bonus. Contact Joy Lankswert @ 866-227-5415 or email joy.lankswert@uhsinc.com

ARIZONA

Assistant or Associate Professor, Clinical Psychiatry or Professor, Clinical Psychiatry University of Arizona (UPH Hospital-Kino)

The University of Arizona's Department of Psychiatry is recruiting adult psychiatrists to join a progressive and growing academic department located in the beautiful southwest with academic appointments as Assistant or Associate Professor, Clinical Psychiatry, or Professor, Clinical Psychiatry, depending on applicant's qualifications. Individual must be board-certified or -eligible in Psychiatry and have current credentials to practice medicine in the United States. Incumbent will provide clinical care in an inpatient facility with adult and geriatric populations. Other duties may include supervising and teaching adult psychiatry residents and medical students. Competitive salary and excellent benefits package offered. For more complete information about the positions, and to apply, go to **http://www.uacareertrack.com** and reference job **#36355**. If you have questions, please contact **Alesia Gillis, Human Resources, Dept. of Psychiatry, 1501 N. Campbell Avenue, P.O. Box 245002, Tucson, AZ 85724-5002; (520) 626-3819 or agillis@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.

CALIFORNIA

Faculty Positions - UCSD

The Dept. of Psychiatry at the University of California, San Diego, is currently recruiting for contracted positions at the assistant or associate clinical professor level. We are seeking board-certified or board-eligible psychiatrists with a California medical license to practice in our community outpatient clinics. Preference will be given to candidates with a strong track record in clinical care, teaching experience and an interest or experience in clinical research. The positions offer flexible scheduling, along with potential teaching and research opportunities. The appointment level will be determined by the candidate's qualifications, and the salary is based on UC staff psychiatrist pay scales. Applicants should send their curriculum vitae and other supporting documents to: Attn: Dr. Lohr and Dr. Soliman, Search Committee K, UCSD Dept. of Psychiatry, 9500 Gilman Drive, La Jolla, CA 92093-0603. UCSD is an equal-opportunity employer.

The Perfect Position in Northern California!

I have an outstanding Adult Psychiatrist position that is available in one of California's fastest growing communities. It is located 45 minutes south of Sacramento with a population of over 260,000. The position is a highly sought after **Adult Psychiatrist employed outpatient opportunity with no call!** You can have a flexible schedule while you care for the full range of psychiatric cases. Work in an environment of collegiality with other highly trained Adult and C & A psychiatrists along with their superb team of therapists, social workers, nurses, and case managers. This is a perfect position to balance your personal and professional life! **Send your CV to Tina Wilkins at wilkinstina@earthlink.net; fax to 916-536-9281; call 1-888-229-9495.**

UCSF DEPARTMENT OF PSYCHIATRY SAN FRANCISCO GENERAL HOSPITAL

Due to expanding programs, the Department of Psychiatry of the School of Medicine, University of California, San Francisco (UCSF) seeks psychiatrists to serve as clinician-teachers at San Francisco General Hospital, a major teaching hospital of UCSF. The clinician-teacher role offers the opportunity to teach UCSF residents, medical students, and other trainees; to provide clinical leadership for multidisciplinary staff at the unit or team level; and to develop a defined area of scholarship and/or clinical research. The inpatient service features the award-winning Ethnic/Minority Psychiatric Inpatient Programs. Other services include the Psychiatric Emergency Service, community case management programs, and the Divisions of Psychosocial Medicine; Substance Abuse and Addiction Medicine; and Infants, Children, and Adolescent Services. Ideal candidates would be ABPN Board-certified or Board-eligible psychiatrists with inpatient and/or outpatient experience, a commitment to an academic career as a clinician-teacher, and demonstrated interest in working with underserved and culturally diverse populations in a public setting. Bilingual and/or bicultural abilities are desirable.

- Compensation: $154,000-$200,000 + dependent on qualifications and experience
- Relocation package
- Outstanding benefits package

Interested applicants should send or fax ([415] 206-8942) their resume and names and addresses/telephone numbers of three references to: Susan Brekhus, UCSF Department of Psychiatry, San Francisco General Hospital, 1001 Potrero Avenue, Suite 7M, San Francisco, CA 94110. For additional information, you are welcome to call or email Susan Brekhus at (415) 206-3805 or email susan.brekhus@sfdph.org, Francis Lu, MD, Professor of Clinical Psychiatry at (415) 206-8984 or francis.lu@sfdph.org. UCSF seeks candidates whose experience, teaching, research, or community service has prepared them to contribute to our commitment to diversity and excellence. UCSF is an affirmative Action/equal opportunity employer. All qualified applicants are encouraged to apply, including minorities and women.

Consultation / Liaison Attending Psychiatrist Langley Porter Psychiatric Institute UC San Francisco

The UCSF Department of Psychiatry at Langley Porter Psychiatric Institute is seeking a psychiatrist to join our Consultation-Liaison Service. This is a full time clinician-educator faculty position, with primary responsibilities for consultation to the inpatient clinical services of UCSF Medical Center, and teaching and supervision of residents and medical students. UCSF Medical Center is a tertiary care hospital which cares for a wide variety of patients from diverse ethnic, cultural, and socio-economic backgrounds. Consultation is also provided to the emergency department and cancer center. This faculty position also offers the opportunity to pursue additional teaching and leadership activities in the School of Medicine, and to develop a defined area of expertise, scholarship, and/or clinical research.

Applicants should be BC/BE in psychiatry, experienced in Consultation-Liaison settings, and interested in an academic career as a clinician-educator. Appointment level will be commensurate with the candidate's qualifications and experience. UCSF is an affirmative action / equal opportunity employer.

Submit letter of interest and cv to:

Stephen E. Hall, M.D.
Director, Intensive Services
Department of Psychiatry
Langley Porter Psychiatric Institute
401 Parnassus Avenue, Box F-0984
San Francisco, CA 94143

Stephenh@lppi.ucsf.edu

GREATER BAY AREA - Modesto, California

General & Child Psychiatrists needed, for unique, stable County Mental Health system in a welcoming community. Serve both public & private sector patients, in both inpatient/outpatient settings that have been benchmarked for their quality. Possibilities for Resident teaching & consultation with a full range of providers. When patients require hospitalization, inpatient & outpatient staff work **TOGETHER** to optimize care. Stanislaus County is located only 1 1/2 hours from both San Francisco and Yosemite, enjoying the best of both worlds.

Excellent salary scale, with steps from $159K to $194K; **PLUS** full benefits; **PLUS** 5% additional for each of following: Inpatient, General Boards, Child Boards; **PLUS** extra for limited On-Call; **PLUS** Union-negotiated increases already set for next few years. Negotiable hourly contract also an option. Fax CV to Marshall Lewis, MD, 209-558-8641 or call 209-558-4639.

Central California Psychiatric group looking for Board eligible/ Board certified psychiatrist to join a mature practice, with an enjoyable lifestyle, in a great setting, with in a short drive to mountains (Yosemite and Sequoia), coast and San Francisco. Practice consists of inpatient, outpatient and/or mixed schedule. Group primary orientation is psychopharmacology. Appointment with UCSF local program available. Competitive salary and benefits with ample opportunity to increase income.

Please send curriculum vitae and inquiries to:
Mateo F. De Soto, M.D.
E-mail: bbmc@bbmc-inc.com
Fax: (559) 437-1118
Mailing address:
1060 W. Sierra Ave., Ste 105
Fresno, CA 93711

UC DAVIS SCHOOL OF MEDICINE DEPARTMENT OF PSYCHIATRY AND BEHAVIORAL SCIENCES

Health Sciences Assistant Clinical Professor. The University of California, Davis, Department of Psychiatry and Behavioral Sciences invites applicants for a full-time academic psychologist to serve at the Assistant Clinical Professor level and to be a member of the department's growing program in schizophrenia research led by Professor Cameron Carter.

Applicant should have a Ph.D. in Clinical Psychology and be licensed in California. Position involves providing clinical care and conducting research to individuals in the early phases of serious mental disorders, including schizophrenia and mood disorders. The applicant should have significant research training and experience working with this population. Expertise using SIPS, the SCID, the Kid SCID, and in the administration and scoring of cognitive and neuropsychological measures are essential. A working knowledge of the use of algorithmic treatment approaches as well as the PIER Model of Multi Family Psychoeducation and support therapies will be an asset. Expertise and interest in conducting innovative research into risk prediction, predicting functional outcome, the measurement of functional and early identification of individuals at risk for serious mental disorders is essential. Experience in using neurobiological measures, including Neuroimaging, to predict outcome in high risk and early psychosis individuals is also desirable. Appointment will be at a level commensurate with experience and qualifications.

For full consideration, applications must be received by December 31,2007. Position is open until filled, but no later than February 29, 2008. Interested candidates should email a curriculum vitae and letter of interest in response to Position #_PY 06R 08_ to Cecilia Mafnas at Cecilia.mafnas@ucdmc.ucdavis.edu. In conformance with applicable law and University policy, the University of California, Davis, is an equal opportunity/affirmative action employer.

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

PSYCHIATRISTS

San Francisco Bay Area - Alameda County Behavioral Health Care Services - offers a full range of accessible mental health, alcohol and drug services to clients throughout all parts of the County. We are actively recruiting for full-time, part-time and services-as-needed Psychiatrists to provide psychiatric evaluation and treatment to adults in the Outpatient Services and Criminal Justice Mental Health Program.

Our network of services currently consists of over 400 individual practitioners, more than 90 community-based agencies, 20 hospitals and other institutions. Clients and their family members can now find geographically accessible services throughout all parts of the County. Services are available in all languages and are provided by a multicultural and multidisciplinary panel of service providers, many of whom have developed specialties that meet the often unique needs of our clientele. For more information, please visit: www.acbhcs.org

Physician III (Psych Option) $69.19-$84.01/hr.
Physician III SAN (Psych Option) $90.71/hr.

Additional Compensation to Base Salary:
5% Board Eligibility/Certification; 5% Lead Psychiatrist; 25% Criminal Justice

Min Req: Possession of a valid license to practice medicine in CA & completion of residency in psychiatry.

We offer highly competitive salaries and an extensive benefit package. Please contact Karl D. Adler, MD via his assistant Bernie Mullen at BMullen@acbhcs.org or (510) 567-8106, and apply on-line at www.acgov.org

Mental health consumers and bilingual applicants are strongly encouraged to apply
EOE

BAY AREA DOCTORS INC. BE/BC psychiatrists for CA facilities. **UP TO $260 AN HOUR**. Earn up to $43,600 a month, working 4 ten hr days a week with no call. Flexible schedules, weekends possible. Extra for on call. Fax CV to 415-814-5764. Tel 707-694-6890. Email bayareadoctors@sbcglobal.net

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COLORADO

Medical Director
J-1 Visa Waiver Available

Horizon Health, the nation's leader in Psychiatric Contract Management seeks a **Medical Director** for a new **10-bed Gero-psych** unit at **Colorado Plains Medical Center**, a 50-bed acute-care hospital located in Fort Morgan, CO, serving a two-county area of 35,000. The hospital is fully accredited by JCAHO, and has a Level III Trauma Center, a 24-hour Emergency Room and many other services including diagnostic imaging services such as MRI, Nuclear Medicine, CT, Radiography, ACR-certified Mammography and Ultrasound. Rehab services include Physical, Occupational and Speech Therapies. Other services include Cardiopulmonary, Surgery, complete Lab Services, Obstetrics, Social Services, Dietary and Home Health.

Fort Morgan is big enough to have it all, and small enough to be a delightful home town. Fort Morgan has been thriving on the eastern plains of Colorado since it was established in 1884. The city now serves as the commercial and retail hub for all of Northeastern Colorado, and continues to grow into the 21st Century. Fort Morgan is located only 80 miles northeast of Denver on U.S. Interstate 76 and U.S. Highway 34, less than an hour's drive to 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

Two Full Time Faculty Positions At Yale School of Medicine.

Two full-time Attendings needed for Psychiatry Service at the Yale-New Haven Psychiatric Hospital: 1) General Adult Inpatient and 2) Dual Diagnosis Unit. Candidates must be board certified or eligible, and license eligible in the State of Connecticut. Inpatient experience and demonstrated excellence in clinical teaching required for Inpatient position. Addiction training required and potential of added credentials in addiction psychiatry preferable for Dual Diagnosis position - balance of academic work in teaching and service negotiable. Both positions will involve teaching of medical students and Yale psychiatric residents. Academic appointment at the Assistant or Associate Professor level. Review of applications will begin immediately.

Interested candidates please send resumes and letters of recommendation by December 15, 2007 to: William H. Sledge, MD, Medical Director, Yale-New Haven Psychiatric Hospital, 300 George Street, Suite 901, New Haven, CT 06511. Yale University is an equal opportunity, affirmative action employer. Applications from women and minority group members are encouraged.

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.

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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

Inpatient and Ambulatory Services at Yale/CMHC

The Yale University School of Medicine seeks psychiatrists for one full-time faculty position in an Inpatient Service and up to two positions in the Ambulatory Services of the Connecticut Mental Health Center [CMHC] for July 2008 that will carry academic appointments at the Assistant or Associate Professor level in the Department of Psychiatry. Outstanding clinical and teaching skills are required for roles in patient care as well as supervision of psychiatry residents and other trainees at CMHC, a core site for training and research within Yale's Department of Psychiatry. The positions include protected time for participation in a variety of Departmental research and educational activities. Applicants must be board certified or eligible in psychiatry, licensed to practice in CT and be legally employable. Please send a CV and 3 references by February 1st to Jeanne Steiner, D.O., Medical Director CMHC, 34 Park St., New Haven, CT, 06519. Direct inquiries to jeanne.steiner@yale.edu. Yale University is an affirmative action/equal opportunity employer; applications from women and minority group members are specifically invited.

Latino Services at Yale/CMHC

The Yale University School of Medicine seeks a bilingual and bicultural psychiatrist for a full-time faculty position in the Latino Services of the Connecticut Mental Health Center [CMHC] for July 2008 that will carry an academic appointment at the Assistant or Associate Professor level. CMHC is expanding its services through a Regional Latino Behavioral Health initiative, which will provide direct service, consultation, teaching, and research within an array of community sites. Outstanding clinical and teaching skills are required for roles in patient care as well as supervision of psychiatry residents and other trainees at CMHC, a core site for training and research within Yale's Department of Psychiatry. The position includes protected time for participation in a variety of Departmental research and teaching activities. Applicants must be board certified or eligible in psychiatry, licensed to practice in CT and be legally employable. Please send a CV and 3 references by February 1st to Jeanne Steiner, D.O., Medical Director CMHC, 34 Park St., New Haven, CT, 06519. Direct inquiries to jeanne.steiner@yale.edu. Yale University is an affirmative action/equal opportunity employer; applications from women and minority group members are specifically invited.

CHILD PSYCHIATRISTS- Connecticut

Opportunities for Inpatient and Outpatient Child Psychiatrists to join Behavioral Health Services affiliated with Saint Francis Hospital and Medical Center, a major teaching hospital distinguished as a leader in clinical excellence.

Outpatient opportunity includes working with a multidisciplinary team of master's level therapist, nurse practitioners, and psychologist in behavioral health centers located throughout the greater Hartford area.

Inpatient opportunity includes working with a multidisciplinary team on a 12-bed inpatient child psychiatry unit for children ages 5-12 located on the Mount Sinai Campus in Hartford, Connecticut. On-site fully accredited school, which supports the educational needs of the young patients.

Our central Connecticut location offers a wide range of upscale suburban living choices and all the amenities of the New England region, including first-rate schools, and the pleasures of country and coastal environments. Close proximity to professional sporting events, concerts, ballet, theatres, skiing and boating, and less than 2 hours to Boston and New York.

For more information about this opportunity, please contact Christine Bourbeau in the Recruitment Office at 800.892.3846 or fax/email your CV to 860.714.8894.

Email address CBourbea@stfranciscare.org
Visit our website at www.saintfranciscare.com

EEO/AA-M/F/D/V, Pre-employment drug testing

University of Connecticut Health Center

CORRECTIONAL MANAGED HEALTH CARE

Seeking board certified and board eligible psychiatrists to provide care to patients in the Connecticut Department of Correction. Opportunities include patient care, research, teaching, and leadership in both an academic and public health care setting. Opportunities exist throughout the state. Exciting employment, excellent state benefits, regular working hours, and competitive salaries. Please contact Noreen Logan, Human Resources, for information and an application at (860) 679-7691 or e-mail at logan@uchc.edu.

AA/EEO M/F/PWD/V

DELAWARE

Mental Health-Psychiatrist Child/Adol (BC/BE) to provide evaluations, Medication therapy and consult with staff in a highly regarded, private, not-for-profit child guidance clinic in Dover, DE.
Full-time. No weekends. Competitive package. Send cover letter and resume to: Delaware Guidance Services, HR, 1213 Delaware Ave., Wilmington, DE 19806. Fax: 302-652-8297
EOE.

DOVER: General Psychiatrist - Inpatient & Partial programs. Staff position. Offering base salary, benefits and more... Contact Joy Lankswert @ 866-227-5415 or email joy.lankswert@uhsinc.com

FLORIDA

MIAMI AREA (Aventura, FL): PSYCHIATRIST, FT; FL LICENSE REQ'D; also hiring ARNP and/or P.A.; private practice (adoles/adult/geriatric pts); Office/SNF/IP; Excellent Salary & Benefits; **FAX CV** to Dusty: **305-935-1717** or **EMAIL:** aventuraoffices@bellsouth.net

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DAYTONA - MELBOURNE - ORLANDO - MIAMI - FORT LAUDERDALE - PALM BEACH - OCALA - GAINESVILLE - FORT MYERS - SARASOTA - PENSECOLA - JACKSONVILLE - Psychiatrists needed for rapidly expanding Nursing Home Service. Great support. No call. Average Salary 210K + benefits. Part-time available. Some travel required. Must have FL Medicare & FL Medicaid individual provider #s. No Restrictions (H1B Candidates Considered). Call our administrator, Christy, at 866-936-5250.

PSYCHIATRIST

The country's first residential eating disorder treatment facility, **The Renfrew Center** has a **part-time** opening at its Florida site. FL License required, competitive salary & benefits.

APPLY TO:
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Atlantic Coast organization needs a fifth psychiatrist for ALL OUTPATIENT practice. Combine a strong salary, full benefits, gorgeous beaches, and great lifestyle options. Contact Jim Ault at St. John Associates, 1-800-737-2001 or jault@stjohnjobs.com. Visit www.stjohnjobs.com.

Psychiatrist Opportunities

Mental Health Resource Center, Inc. (MHRC) currently has two Psychiatrist positions available in Jacksonville: one Psychiatrist is needed for its Adult Florida Assertive Community Treatment (FACT) Program; and one Psychiatrist is needed to provide outpatient and inpatient psychiatric services (the inpatient services will be provided at Shands Jacksonville Medical Center). Both are full-time salaried positions with a comprehensive benefits package. Florida licensure and Board Eligibility/Certification required. MHRC is a JCAHO accredited comprehensive community mental health center. To apply, contact Dr. Robert Sommers, President/CEO, MHRC/RBHS, P.O. Box 19249, Jacksonville, FL 32245. e-mail: rbhspres@bellsouth.net. Fax: (904) 743-5109. Phone: (904) 743-1883, ext. 219.

GEORGIA

Quiet Country Setting close to large metro area in Beautiful NW GA. Community Mental Health Opportunity for BC/BE Psychiatrist. FT/PT Adult and C&A opportunities available. We offer excellent benefits and competitive salary. Opportunities for employment are available in our crisis unit and clinics. Agency serves Whitfield, Polk, Floyd, Bartow, Gilmer and Fannin Counties. Extra call available if desired. Send CV to our HR Dept. at jobs@highlandrivers.org or fax 706-270-5129.

IDAHO

Eastern Idaho Regional Medical Center Behavioral Health Center

The Behavioral Health Center of Eastern Idaho Regional Medical Center has two different exceptional opportunities with a very competitive compensation for qualified psychiatrists. Idaho Falls is a very livable and affordable city and is located in a marvelous area, less than two hour drive from Jackson Hole, Yellowstone National Park, and the Grand Tetons. Idaho Falls is a community of 60,000+ people and the Behavioral Health Center serves a market area of over 300,000 people. The Behavioral Health Center is a 76 bed free standing psychiatric hospital with 30 residential treatment beds and 46 acute care beds. BHC is located two blocks from the medical center and has direct access to all of the relevant medical services.

The practice opportunities which are available for a board certified or board eligible child psychiatrist include the following primary options:

1. An affiliation with the hospital with an income guarantee, sign-on bonus and an executive relocation package to help a physician establish their private practice. There are opportunities to enter a practice association with one of the other psychiatric practices or counseling groups in the community.
2. A full time employment arrangement which would include inpatient and outpatient work.

Currently the Behavioral Health Center has 4 full time affiliated psychiatrists and 1 psychiatrist who cover one weekend of call every month. Until the recruitment is complete, locum tenens coverage will be continued. With the addition of the new psychiatrists we anticipate an average weekday call of 1 in 6 and a weekend call that would average 1 in 10.

If you would like to learn more about this tremendous opportunity, please contact me at your earliest convenience.

Regards,

Eric Mack, Market Manager
HCA Physician Services
Office: (949) 366-4154
Cell: (714) 404-9683
Fax: (866) 824-9444
www.hcahealthcare.com

ILLINOIS

Medical Director and Staff Psychiatrist

Chicago Read Mental Health Center is seeking a qualified individual to serve as Medical Director for a 130 bed adult psychiatric hospital located on the northwest side of Chicago. We are looking for a board certified psychiatrist with a Recovery focus, who can provide leadership to a dynamic clinical team in the delivery of quality care to persons with serious mental illness. We are also seeking a board eligible psychiatrist to work on one of our patient care units. The hospital serves both acute and specialty psychiatric populations. Chicago Read is both Joint Commission and CMS accredited.
Please send resume to

Nancy Heneghan,
Human Resource Specialist
4200 N. Oak Park Ave.
Chicago, IL 60634
Nancy.Heneghan@Illinois.gov

CHAIR
DEPARTMENT OF PSYCHIATRY AND BEHAVIORAL MEDICINE

THE UNIVERSITY OF ILLINOIS COLLEGE OF MEDICINE AT PEORIA (UICOMP) seeks candidates with demonstrated leadership, teaching skills, and GME experience to lead a growing department with broad community faculty participation in a thriving city with many cultural amenities and moderate cost of living, few big city hassles. Candidates must be board certified and eligible for Illinois medical license. Rank and tenure dependent on qualifications. Candidates must be committed to educational excellence and collegiality and will be expected to develop a Psychiatry Residency in collaboration with Methodist Medical Center, a regional tertiary care facility. Excellent salary and benefits package.

Job description available upon request by mail or e-mail (ksciorti@uic.edu). For fullest consideration, submit letter of interest and curriculum vitae by February 1, 2008 to:

Rodney Lorenz, MD
Chair, Psychiatry Search Committee
University of Illinois College of Medicine
Attention: Kathy Sciortino
One Illini Drive
Peoria, IL 61605

Electronic submissions welcome at ksciorti@uic.edu. Applications considered until position is filled. AA/EOE; women and minorities are encouraged to apply.

PSYCHIATRIST EDUCATOR: Assist. Prof., Univ. of IL Coll. of Medicine at Peoria, Dept. of Psychiatry & Behav. Medicine is seeking a brd-cert./elig. PSYCHIATRIST to join a collegial community-based psychiatry department. Primary responsibilities include classroom/clinical teaching and outpt. clinical care. Applications accepted until position is filled. Reply to: Peter Alahi, M.D., Chair, Psychiatry Search Committee, Dept. of Psychiatry & Behav. Medicine, UIC College of Medicine at Peoria, 221 NE Glen Oak Ave., 7 West, Peoria, IL 61636; Phone (309) 671-2165; FAX (309) 671-8384 e-mail: palahi@uic.edu The University of Illinois is an AA/EO Employer.

Join an outpatient practice located in the Bloomington-Normal area midway between Chicago and St. Louis. Practice offers great flexibility and includes two psychiatrists and a therapist. Friendly college and residential community provide excellent location to raise a family and potential for further growth. Contact Dr. Raju Paturi 309/862-0064 and Fax CV with photo 309/862-1542.

INDIANA

Psychiatrists wanted

Midtown Community Mental Health Center, Indianapolis, IN is seeking several BC/BE Psychiatrists. Seeking one (1) outpatient psychiatrist to work with ACT Team as well as provide care for patients with SMI. Seeking one (1) psychiatrist to work in our Adult Outpatient services.

Need to be licensed to practice medicine in the state of Indiana. J-1 Visa applicants are welcome. Comparable salary and benefits package plus paid malpractice insurance.

Send CV to Steve Fekete, M.D., Medical Director, Midtown CMHC, 850 N. Meridian St., Indianapolis, IN 46204 or FAX: 317-554-2721. Telephone: 317-554-2703.

KENTUCKY

ASHLAND, KY / HUNTINGTON, WV - Seeking a Staff Psychiatrist to join a top-notch team of behavioral health professionals on a 27-bed adult unit at a general hospital in northeastern KY. Call 1 in 4. Offering salary with benefits plus bonus plan and relocation package. Enjoy a much more laid back quality of life in a lovely area. Please **call Terry B. Good at 1-866-865-7380**, Fax #: 804-684-5663; Email: terry.good@horizonhealth.com. Or mail CV to: 1663 Denton Lane, Hayes, VA 23072. EOE

LOUISVILLE area: Medical Director for private inpatient/outpatient treatment facility. Limited call - great salary & benefits. Contact Joy Lankswert @ 866-227-5415 or email joy.lankswert@uhsinc.com

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45 minutes from Nashville!!! Facility in one of the fastest growing and prettiest towns in Kentucky is looking for Adult and C&A psychiatrists. Position is 100% Outpatient with NO CALL!! 40 hour work week and NO CALL! Enjoy the security of a salaried position with a comprehensive benefits package. Possible sign on bonus and federal loan repayment as well! OPPORTUNITIES FOR J1 visa holders available nearby!!! Please contact Ariana Sanjabi @ 800.735.8261 ext.214, fax your CV to 703.378.0016 or e-mail: asanjabi@medsourceconsultants.com.

LOUISIANA

The Louisiana Office of Mental Health is seeking psychiatrists to work across the state in a variety of positions. We have a unique mental health care delivery system that is transforming itself in a number of ways to better meet the needs of our citizens. With the challenges we are facing from the 2005 hurricane season, our system has had to be creative and responsive. Come be a part of the recovery of our beautiful state! Positions are available in urban and rural areas, inpatient and outpatient facilities, and forensic and civil settings; adult and child psychiatrists are needed. For more information, please contact Kathleen Crapanzano, M.D., Office of Mental Health Medical Director, 628 PO Box 4049, Baton Rouge, LA 70821-4049 or phone at 225-342-2550 or e-mail at kcrapanz@dhh.la.gov.

Ochsner Health System

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, 600+ member physician group, and 28 health centers
- Very competitive salary and benefits
- Family-oriented community with year-round outdoor activities
- Favorable malpractice environment in Louisiana
- J-1 visa candidates are welcome to apply
- Ochsner Health System is an equal opportunity employer.

Please email CVs to: profrecruiting@ochsner.org or call (800) 488-2240.
Ref# APSYN4.

Medical Director
Baton Rouge, LA

A Medical Director is needed for a 19-bed geriatric psychiatric program in Baton Rouge, Louisiana. In this position, the Medical Director will be responsible for a complete practice experience working on inpatient program, which would include admission, diagnosis, treatment, management, and discharge of patients. Excellent Stipend offered with lucrative private practice potential. For more information please contact Diane Odom, 972-420-4083, fax 972-420-8233, e-mail diane.odom@horizonhealth.com

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DEPARTMENT OF PSYCHIATRY AND NEUROLOGY, TULANE UNIVERSITY SCHOOL OF MEDICINE in New Orleans, LA, is recruiting for several general and forensic psychiatrists (clinical track) for our growing department, at the Assistant/Associate Professor level. Candidates must have completed an approved general psychiatry residency and be board certified/eligible in general psychiatry and forensic psychiatry, respectively. Responsibilities will include direct patient care, teaching of medical students and house officers (including those in our accredited forensic psychiatry fellowship program), and research (clinical and basic science) at various state hospitals, state correctional institutions, and at Tulane University Health Sciences Center. Time allocations will be based upon individual situations. Applicants must be eligible to obtain a Louisiana medical license. Applications will be accepted until suitable qualified candidates are found. Send CV and list of references to John W. Thompson, Jr., M.D., Vice Chair, Adult Psychiatry and Director, Division of Forensic Neuropsychiatry, Tulane University School of Medicine, Department of Psychiatry and Neurology, 1440 Canal Street TB53, New Orleans, LA 70112. For further information onsite, please contact Dan Winstead, MD, Chair of Psychiatry and Neurology, at 504-473-5246 or winstead@tulane.edu. Tulane is strongly committed to policies of nondiscrimination and affirmative action in student admission and in employment.

MAINE

Dartmouth Faculty Psychiatrists

Dartmouth Medical School, Department of Psychiatry, in collaboration with the State of Maine Department of Health and Human Services, seeks faculty psychiatrists for the Riverview Psychiatric Center in Augusta, Maine. The Center is the flagship inpatient hospital serving central and southern Maine's system of public mental health care. A 92-bed, state of the art, replacement hospital opened in the Spring of 2004. Preference will be given to candidates with forensic training and/or experience. Maine licensure required. These are full-time Dartmouth faculty appointments with salary and rank commensurate with experience and academic accomplishments. Protected time for scholarly activities. Central and southern Maine offers exceptional opportunities to enhance your quality of life. We have safe communities, with very low crime, good schools and unparalleled four season recreational activities. Augusta is less than one hour from the Maine coast and closer to numerous crystal clear lakes and mountains. It is no wonder Maine is called "vacationland." Please send CV and three letters of reference to: **Alan I. Green, MD, Professor and Chair of Psychiatry, Dartmouth Hitchcock Medical Center, One Medical Center Drive, Lebanon, NH 03756**. Dartmouth Medical School is an EOE/AA Employer and encourages applications from women and members of minority groups.

MARYLAND

The University of Maryland School of Medicine is seeking a full-time adult psychiatrist to work in the area of emergency psychiatry. The position includes work as Medical Director of the Psychiatric Emergency Service with the opportunity to work in other mental health care settings. The position is unique in that the Psychiatric Emergency Service of the University of Maryland is one of the few freestanding psychiatric emergency service providers in the country. This is an opportunity to work with elite specially-trained nursing staff in emergency psychiatry, and with its unique position, it provides opportunities for new research in emergency psychiatry. The position is an academic appointment with opportunities in teaching and research. Candidates must be ABPN certified or eligible. Academic rank and salary are commensurate with experience. Successful candidates will be members of the faculty of the School of Medicine. Send C.V. to: **Angela Onwuanibe, M.D., Box 351, University of Maryland Medical Center, 22 South Greene Street, Baltimore, MD 21201. FAX 410-328-2672 or email AOnwuani@Psych.UMaryland.edu**
The University of Maryland School of Medicine is an AA, EEO, ADA employer. Minorities and women are encouraged to apply.

PT Psychiatrist-Well established, Pvt, Multi-Discipline Grp Practice in Montgomery County MD, has an immediate opening for BC adult/adolescent psychiatrist. 15-20 Hrs wkly. Flexible schedule. Team approach. Email CV apcadmin2@verizon.net or fax to 301-258-7482.

Faculty Position
Assistant Professor (Tenure Track)
Department of Psychiatry

The Department of Psychiatry at the Uniformed Services University of the Health Sciences, Bethesda, MD is seeking to fill an Assistant Professor, tenure-track, teaching and research position. The Department is comprised of twenty full-time faculty and has active research interests in the neurobiology and behavior of stress, PTSD, anxiety, depression, and substance abuse. The successful candidate will participate in and develop medical student and resident education, a research program and provide clinical care. Individuals who hold an M.D., have completed an approved psychiatric residency and are board eligible/certified are invited to apply. Send curriculum vitae, description of current and anticipated research interests and the names and addresses of four references to: Robert J. Ursano, M.D., Chairman, Department of Psychiatry, Uniformed Services University, 4301 Jones Bridge Road, Bethesda, MD 20814 (psychiatry@usuhs.mil). Review of applications is ongoing. The University is an affirmative action/equal opportunity employer.

Clifton T. Perkins Hospital Center, a JCAHO-accredited institution and Maryland's only maximum security forensic hospital, is seeking candidates for the position of staff psychiatrist. Candidates with forensic interest or experience would be especially well-suited. Responsibilities include the provision of high quality psychiatric care on an inpatient unit in a state-of-the-art forensic facility. Additional opportunities include evaluations of dangerousness, competency to stand trial, and criminal responsibility.

Join a vibrant medical staff with expertise in care of the seriously mentally ill within a forensic setting. Faculty appointments are available at University of Maryland and Johns Hopkins Hospitals, if eligible. The hospital is centrally located 20 minutes from Baltimore, 35 minutes from DC, and 20 minutes from Annapolis. Competitive salary with excellent benefits, flexible working hours, and the opportunity for paid overnight call.

Interested candidates should contact Robert Wisner-Carlson, MD at 410-724-3078 or P.O. Box 1000, 8450 Dorsey run Road, Jessup, MD 20794 (wisnerr@dhmh.state.md.us.)

Faculty Opportunity
Division of Child and Adolescent Psychiatry
University of Maryland, Baltimore

The University of Maryland School of Medicine, Division of Child and Adolescent Psychiatry is seeking a full-time child and adolescent psychiatrist at the Assistant or Associate Professor level.

The position carries faculty appointments at the University and offers exciting opportunities for clinical care, teaching and research. All clinical work is done in combination with the residents in our large and successful child and adolescent psychiatry training program. Our program and professionals are very interested in family driven treatment as exemplified by the recently received SAMHSA National Child Trauma Stress Center in family-informed trauma treatment. Academic rank and salary are commensurate with experience. We are looking for a good colleague to work in a team approach. Send a letter of introduction and CV to:

David B. Pruitt, M.D
Professor of Psychiatry and Pediatrics
Director
Division of Child and Adolescent Psychiatry
701 W. Pratt St., #429
Baltimore, Maryland 21201

The University of Maryland is an AA, EOE, and ADA Employer. Minorities and women are encouraged to apply.

Psychiatrist

Springfield Hospital Center - a 405 bed psychiatric in patient facility, operated by The Maryland State Mental Hygiene Administration seeks Maryland licensed Psychiatrists. Our rural 400 acre campus is located 22 miles west of Baltimore and convenient to Washington, DC. via routes 70 & 29. We offer full time and part time positions with comprehensive benefits, which include 27 days of paid leave, medical coverage and access to Maryland State Employees Pension at retirement. Additionally, Contractual day/night positions available. Both Board & Non-Board Certified physicians will be considered. Salary for these positions is negotiable. Please send CV to: Jonathan Book, M.D., Clinical Dir, SHC, 6655 Sykesville Rd. Sykesville, Maryland 21784. For questions call 410-970-7006 or email Jbook@dhmh.state.md.us. EOE

MASSACHUSETTS

CHILD/ADOLESCENT PSYCHIATRIST

Child/Adolescent Psychiatrist needed to provide consultation, evaluation, & follow-up services to adolescents at DYS programs located in Framingham & Worcester. Flex hrs; 10-15 hrs/wk.

Please send CV to Deborah Garfield, LICSW, Director of Clinical Services, Eliot Community Human Services, Inc., 111 Old Road to Nine Acre Corner, Concord, MA 01742, FAX (978) 369-0908, dgarfie@eliotchs.org.

SUPERVISORY PSYCHIATRIST

Opportunity for a Board-Certified/Board-Eligible Psychiatrist to join the expanding Mental Health Service at the Northampton VAMC. Experience or specialized training in geriatrics is highly desired, teaching, PTSD, supervisory experience and/or primary care psychiatry are a plus. This is a leadership position that includes supervision of psychiatrists and exciting program development opportunities to meet the needs of the new veteran population. Northampton is an active, diversified Medical Center, with 3 satellite outpatient clinics, a 16-bed substance abuse/compensated work therapy Psycho-social Residential Rehabilitation Treatment Program, 85 psychiatric inpatient beds, and 66 nursing home care unit beds. Specialized programs include PTSD, substance abuse, chronically mentally ill, and acute psychiatry. Opportunities are currently available for teaching residents as well as psychology and social work interns. Congenial work atmosphere, stimulating colleagues, and minimal night and weekend duties make this a very pleasant place to work. Northampton is located in the heart of the "five college" area of Western Massachusetts and abounds in cultural attractions. Two hours from Boston, three hours from Times Square, yet in its own cultural base, the area is ideal for raising a family. This Medical Center is affiliated to the Dartmouth Medical School. Competitive salary and federal benefits. EOE employer.
Send CV to: Michelle Zehelski, Human Resource Staffing Clerk (05-HR), Northampton VA Medical Center, Leeds, MA 01053, (413) 584-4040, ext. 2124; FAX (413) 582-3146.

Child and/or Adult Psychiatrists BC/BE Child and/or Adult Psychiatrists needed at MSPCC

FT & PT opportunities available in New Bedford, Springfield and Holyoke, MA

MSPCC (Massachusetts Society for the Prevention of Cruelty to Children) is a private, nonprofit society with a legacy of strengthening families and preventing child abuse through essential child welfare and mental health treatment and effective public advocacy. In this role, you will evaluate the psychological, neurological, and psycho-pharmacological status of clients; provide ongoing medication follow-up of clients; and provide direct psychotherapy when indicated.

Please send CV to: **Email: recruitment@mspcc.org; OR Fax: 617.587.1586; OR Mail: Kim Wong and Dr. Sam Kelley, MSPCC, HR, 99 Summer St. 6th Floor, Boston, MA 02110.**

EOE

www.mspcc.org

Boston North Shore: Northeast Hospital Corporation, a locally-based nonprofit medical and psychiatric system recently named one of the nation's top 100 integrated healthcare systems by Solucient, has opportunities for board certified or eligible psychiatrists at two of its facilities:

Beverly Hospital; inpatient or inpatient/C and L combination. Help take this general hospital psychiatry program to the next level! Two positions available, including Medical Director position for experienced psychiatrist with leadership skill; C/L fellowship training a plus. Salary is competitive with an excellent benefit package including generous time off and reimbursement for malpractice insurance and CME. Limited call, and lucrative coverage opportunities are available.

BayRidge Hospital: This well-established 62-bed psychiatric hospital located in Lynn, a teaching site for Boston University Medical School, has a full-time position for an inpatient psychiatrist. Work with an excellent and supportive staff in a friendly atmosphere. There is no required night call, but lucrative coverage opportunities are available. Salary is competitive with an excellent benefit package including generous time off, and reimbursement for malpractice insurance and CME.

Contact: Barry Ginsberg, M.D., Chief, Department of Psychiatry. Phone (781) 477-6965, Fax (781) 477-6967; email address: bginsber@nhs-healthlink.org

CAMBRIDGE Health Alliance: Women's Health

Position available at Cambridge Health Alliance Department of Psychiatry, Harvard Medical School. Part time opportunity in Women's Health/outpatient C/L Psychiatry. 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 and a fellowship training program in Psychosomatic Medicine (C/L) 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, experience in women's mental health, strong clinical skills, excellent collaborator, problem solver. Bilingual and/or bicultural abilities and training in C/L Psychiatry are desirable. Competitive compensation, excellent benefit package. Cambridge Health Alliance is an Equal Employment Opportunity employer, and women and minority candidates are strongly encouraged to apply. **CV & letter to Derri Shtasel, MD, Dept. of Psychiatry, 1493 Cambridge Street, Cambridge, MA 02139. Fax 617-665-2521. Email: DShtasel@challiance.org** (email preferred).

CAMBRIDGE HEALTH ALLIANCE—Part-time psychiatrist, approximately 10 hours/week, for multidisciplinary Psychiatric Emergency Service at Cambridge Hospital. Candidates should have experience with emergency psychiatry, comfort with screening of general medical issues, and strong skills with substance abuse populations. Interest in teaching is desired. Child and adolescent expertise, added qualifications in addictions, knowledge of forensic issues, and/or fluency in Spanish or Portuguese a plus. Responsibilities include direct clinical care as well as supervision of trainees and other mental health providers. Schedule flexible-salaried position. Harvard Medical School appointment for qualified candidates as determined by the criteria of Harvard Medical School. Cambridge Health Alliance is an Equal Employment Opportunity employer, and women and minority candidates are strongly encouraged to apply. Email CV to Dr. Derri Shtasel, Chief of Adult Psychiatry at dshtasel@challiance.org or Fax to 617-665-2521.

BOSTON & SUBURBS! Part-time & fulltime - NO CALL. Salary, benefits & bonus offered. **Jamaica Plain, Brookline, Attleboro, Pembroke locations**. Child, General & Geriatric Psychiatrists for inpatient/partial programs. Moonlighting DOC shifts also available. Contact Joy Lankswert @ 866-227-5415 or email joy.lankswert@uhsinc.com

Harvard Vanguard Medical Associates
Atrius Health

Adult, Child, Subspecialty Psychiatry - Boston, MA

Harvard Vanguard Medical Associates (http://www.harvardvanguard.org), an eminent and growing multispecialty, ambulatory group practice, is expanding its Behavioral Health Departments at several of our Boston and surrounding area offices. We are one of the most active and successful outpatient psychiatric practices in New England, with a long tradition of innovation and collaboration with our medical colleagues. Our psychiatrists work closely with their medical colleagues (internists, pediatricians and gynecologists) in addition to their multidisciplinary teams of behavioral health clinicians (psychologists, social workers and clinical nurse specialists) in a collaborative approach to mental health care.

Responsibilities include outpatient psychiatric evaluation, treatment planning and treatment, medication management services, participation in a multidisciplinary team, and supervision of clinical nurse specialists and trainees in our behavioral health fellowship program. Opportunities range from half-time to full-time. Our practice features a state-of-the-art electronic medical record, e-prescribing, and excellent practice supports (billing and authorization matters are all taken care of for you). We are an affiliate of Harvard Medical School where teaching opportunities and an academic appointment are available for the right candidates through the Department of Psychiatry. We offer a very competitive compensation and benefits package.

Please forward your CV to: Brenda Reed, Physician Recruitment, Harvard Vanguard Medical Associates, 275 Grove Street, Suite 3-300, Newton, MA, 02466-2275. Fax: 617-559-8255; e-mail: brenda_reed@vmed.org, or call: 800-222-4606; or 617-559-8275 within Massachusetts. EOE/AA. Sorry, not a J-1 visa opportunity.

STAFF PSYCHIATRIST

Opportunity for a Board-Certified/Board-Eligible Psychiatrist to join the expanding Mental Health Service at the Northampton VAMC. Experience or specialized training in geriatrics is highly desired, teaching, PTSD, and/or primary care psychiatry are a plus. Northampton is an active, diversified Medical Center, with 3 satellite outpatient clinics, a 16-bed substance abuse/compensated work therapy Psycho-social Residential Rehabilitation Treatment Program, 85 psychiatric inpatient beds, and 66 nursing home care unit beds. Specialized programs include PTSD, substance abuse, chronically mentally ill, and acute psychiatry. Opportunities are currently available for teaching residents as well as psychology and social work interns. Congenial work atmosphere, stimulating colleagues, and minimal night and weekend duties make this a very pleasant place to work. Northampton is located in the heart of the "five college" area of Western Massachusetts and abounds in cultural attractions. Two hours from Boston, three hours from Times Square, yet in its own cultural base, the area is ideal for raising a family. This Medical Center is affiliated with Dartmouth Medical School for education and research. Competitive salary and federal benefits. EOE employer.
Send CV to: Michelle Zehelski, Human Resource Staffing Clerk (05-HR), Northampton VA Medical Center, Leeds, MA 01053, (413) 584-4040, ext. 2124; FAX (413) 582-3146.

Chief of Psychiatry

A multifaceted position at Harrington Memorial Hospital overseeing both inpatient and outpatient psychiatric services. Individual will have the opportunity to play a major role in strategic planning and growth for the future, as well as participate in all relevant hospital wide initiatives. Harrington Memorial Hospital is a community hospital located in central MA, approximately 1 hour west of Boston. Competitive salary and benefits.

Please respond to:
Don Brechner
G.B. Wells Human Services Center
Ph: 508-765-9167 ex. 4233
Email: dbrechne@harringtonhospital.org.

CAMBRIDGE: Inpatient Unit Director/ Attending Psychiatrist

Position available at Cambridge Health Alliance Department of Psychiatry, Harvard Medical School. Full time inpatient unit Medical Director with clinical responsibility for a 9 patient team on an 18-bed teaching service. Clinical care is provided through a multidisciplinary team approach with psychiatrist leadership. The inpatient medical director will also oversee provision of care on the unit, lead quality initiatives on the unit, oversee teaching of residents, medical students and psychology interns, and demonstrate commitment to clinical excellence.

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: Board-certified, 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. Competitive compensation, excellent benefit package. Cambridge Health Alliance is an Equal Employment Opportunity employer, and women and minority candidates are strongly encouraged to apply. **CV & letter to Derri Shtasel, MD, Dept. of Psychiatry, 1493 Cambridge Street, Cambridge, MA 02139. Fax 617-665-2521. Email: DShtasel@challiance.org** (email preferred).

Outpatient and Inpatient Psychiatrists - VA Boston Healthcare System

The VA Boston Healthcare System is recruiting board certified (BC) or board eligible (BE) psychiatrists for outpatient and inpatient positions in Brockton and Boston. Outpatient/inpatient psychiatrists at our Brockton site and outpatient psychiatrists at our Boston sites will have important teaching roles in the Harvard South Shore and Boston University Psychiatry Residency Training programs. Experience and accomplishments will be commensurate with appointment as a faculty member at Boston University School of Medicine and/or Harvard Medical School. These positions offer a highly competitive VA salary and exist in an outstanding academic environment with prominent teaching and research programs. Recruitment bonus is available to qualified candidates. To apply, candidates should send a letter of interest, CV, and the names of three persons to contact for references to Joseph Felton (05D), Human Resources Specialist at VA Boston Healthcare System, Brockton Division; E-mail vhabhsjobs@med.va.gov and a copy to : Gary.Kaplan@med.va.gov For further information regarding the position, please contact Dr. Gary Kaplan, Director, Mental Health Service, VA Boston Healthcare System, 940 Belmont Street Brockton, MA 02301. Phone: 774-826-2486.

We are an Affirmative Action/Equal Opportunity Employer with a strong institutional commitment to diversity in all areas.

Massachusetts: MHM Services, Inc. is proud to announce our affiliation with the Massachusetts Department of Correction. Positions currently exist at MCI Shirley (PT 28hrs/wk) and NCCI/Gardner (PT 28hrs/wk). Hours may be combined to form a full-time position or may be divided to form a variety of part-time options. We are seeking Psychiatrists who are ready to make a difference to an underserved population while being part of an elite organization that offers outstanding benefits and generous compensation. Gain personal and professional satisfaction, while utilizing your skills in a safe and supportive work environment. Guide the delivery of mental health services to this diverse population of incarcerated individuals. Contact Holley Schwieterman at (866) 204-3920 or email: hschwieterman@mhm-services.com to learn more. www.mhm-services.com

EEO/AA

CENTRAL MASSACHUSETTS - Child and Adolescent Psychiatrist/Medical Director Faculty Positions
The University of Massachusetts Medical School (UMMS), Department of Psychiatry, is seeking child psychiatrists to serve as Medical Directors at the UMass Intensive Residential Treatment Programs located at Westborough State Hospital and Worcester State Hospital, each serving adolescents ages 13-19 years. Length of stay of several months or more supports a milieu treatment program/team approach. Positions may be full or part-time (28 hours/week). Candidates must be BC/BE in Child and Adolescent Psychiatry. Experience in teaching and training residents and medical students is desirable. Faculty appointment, teaching, and research opportunities available. Competitive salary and excellent benefits. Join a vital and growing academic division of Child Psychiatry. Send letter of interest and C.V. to: W. Peter Metz, M.D., Director, Child & Adolescent Psychiatry, UMass Medical School, 55 Lake Avenue North, Worcester, MA 01655 or e-mail peter.metz@umassmed.edu AA/EOE

MICHIGAN

GRAND RAPIDS: General & Child Psychiatrists. Inpatient & outpatient for general & specialty programs. Great practice & patient care, collegial staff and community to live in. Top salary, benefits and more. Contact Joy Lankswert @ 866-227-5415; email joy.lankswert@uhsinc.com

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Medical Director
Sault Ste. Marie, MI

Horizon Health, in partnership with **War Memorial Hospital** in **Sault Ste. Marie, MI**, seeks a **Medical Director** for a new 20-bed Adult Inpatient Psychiatric Program. The Upper Peninsula of Michigan is known as one of the most beautiful locations in all of the U.S., abounding in outdoor/recreational activities and possessing some of the most breathtaking scenery in North America. Excellent practice and income opportunity with attractive salary/full benefits/malpractice ins./CME/relocation, and more offered through the hospital. Additional generous Medical Director stipend offered through Horizon Health for Administrative duties. Contact: Mark Blakeney, Horizon Health, 972-420-7473, fax CV: 972-420-8233, or email mark.blakeney@horizonhealth.com. EOE.

MISSOURI

PSYCHIATRIST

Southwest Missouri Psychiatric Rehabilitation Center, a state run In-patient facility serving both acute and long-term clients, located in the scenic Ozarks of Southwest Missouri is seeking a half-time Psychiatrist. The position will have an active role as lead member of an interdisciplinary treatment setting dedicated to quality service. Minimum qualifications include: M.D. or D.O. with residency completion in psychiatry, board eligible or board certified, and licensed to practice in Missouri. The facility is located in a relaxed rural setting within a short driving distance of major metropolitan and lake resort areas. Salary and schedule negotiable.

Please forward Curriculum Vita to:
Human Resources, Southwest Missouri Rehabilitation Center,
1301 Industrial Parkway
East, El Dorado Springs, Missouri 64744,
Fax to 417-876-1004 or e-mail
james.stacy@dmh.mo.gov

The Missouri Department of Mental Health does not deny employment or services because of race, sex, creed, marital status, national origin, disability or age of applicants or employees.

Staff Psychiatrist
Jefferson City- MO State Capital!

A Staff Psychiatrist is needed for a 15-bed adult/geriatric psychiatric program in Jefferson City, Missouri. In this position, the Psychiatrist will be responsible for a complete practice experience working on inpatient program, which would include admission, diagnosis, treatment, management, and discharge of patients. For this position, an attractive salary, benefits, and relocation will be provided.

Jefferson City is the state capital of Missouri and the county seat of Cole County. Located in the Ozarks on the Missouri River near the geographic center of the state. Only 30 miles from Columbia, MO and 2 hrs from St. Louis, MO. Contact Diane Odom, 972-420-4083, fax 972-420-8233, e-mail diane.odom@horizonhealth.com

MONTANA

PSYCHIATRIST-Seeking full-time board certified psychiatrist to fill staff position 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. Fort Harrison Hospital is located in Helena, the State Capital. Competitive salary, benefits and liability included. Additional information can be found at www.vacareers.va.gov. Fax curriculum vitae to 406-447-7978 or call at 406-447-7566 for additional information. EOE.

NEBRASKA

Medical Director
Omaha, Nebraska!

DUE TO GROWTH, Horizon Health seeks a Medical Director for a NEW freestanding psychiatric hospital located in Omaha, Nebraska. Innovative 64-bed adult psychiatric hospital scheduled to open April 2008.

Psychiatrist will be hired as Medical Director to oversee hospital program, which will provide sub-acute, acute, and crises intervention services. Medical Director will be responsible for administrative duties, clinical direction, and patient-care. Ideal candidate will have active Nebraska license, Board Certification and experience working in Community Mental Health, State Hospital, and Private Practice settings. Attractive compensation provided.

Please contact Diane Odom, 972-420-4083, Fax 972-420-8233, e-mail: **diane.odom@horizonhealth.com**

NEVADA

SOUTHERN NEVADA ADULT MENTAL HEALTH SERVICES

ADULT PSYCHIATRISTS: Southern Nevada Adult Mental Health Services, a JCAHO accredited State Agency, is recruiting BC/BE adult psychiatrists to join an integrated community mental health system of 50 psychiatrists and allied mental health providers in Las Vegas, NV. Area qualified for J1/H1 visa psychiatrists. Our practice is focused on the seriously mentally-ill and our philosophy is based on the community recovery model. In-patient and out-patient positions are available. Rawson-Neal is a 235 bed state-of-the-art facility which includes a 30-bed psychiatric observation unit. Community clinics offer walk-in, counseling, medication and pharmacy services. Treatment support programs include residential, case coordination and PACT/ACT teams. Specialized community services are available for co-occurring disorders, seniors, court diversion and more. Competitive salary, excellent benefits, limited on-call and malpractice make this an attractive opportunity. Teaching affiliation with the University of Nevada School of Medicine and relocation package are also available. Nevada has NO STATE INCOME TAX.

For additional information see our web site http://mhds.state.nv.us/sn/index.shtml.
Submit letter of interest and CV to Jackie Arellano at jarellano@snamhs.nv.gov

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THE 1ST CHOICE IN PSYCHIATRIC RECRUITMENT
Las Vegas
Hospital in need of Medical Director
For more information contact:
WES ROBERTSON
(800) 783-9152 FAX (270) 782-1055
www.fcspsy.com
admin@fcspsy.com

NEW HAMPSHIRE

ADULT PSYCHIATRIST

Monadnock Family Services is a community mental health center offering assessment, counseling, support, education and referral services to children and adults of all ages. Position available with an innovative behavioral health agency with a 100-year history. Monadnock Family Services is a leader in area health and social services, alliances, and partnerships. Creative, innovative and supportive climate in the beautiful Monadnock region of N.H. - 90 miles from Boston; near many excellent recreational and cultural activities. MFS is seeking a 5-day per week general psychiatrist to work primarily with adult clients (including the geriatric population) with persistent mental illness for our community mental health center. The psychiatrist in this position works as a clinical leader in an interdisciplinary team consisting of various mental health professionals who provide services based in the recovery and evidence-based practice models of treatment. Candidate must be Board Certified or eligible in psychiatry, have current credentials to practice medicine in the US, and have a desire to work with individuals with severe and persistent mental illness. Competitive salary and fringe benefits with generous vacation leave, 11 paid holidays and sabbatical program. Infrequent on-call coverage required. *Our staff enjoys a generous benefit package, including health, dental, flexible-spending plan and company-provided LTD, AD&D and Life insurance and 3 weeks of vacation during the first year of employment.*
Please send resumes in confidence to: MONADNOCK FAMILY SERVICES ATTN: Human Resources, 17 93rd Street, Dept. PN, Keene, NH 03431 Or to Humanresources@mfs.org

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Staff Psychiatrist
Community Council of Nashua, NH

Our dynamic comprehensive community mental health center located in scenic New England, is seeking a full time BE/BC psychiatrist to join our medical staff. Responsibilities include providing psychiatric evaluations and on going psychiatric service in an adult, outpatient clinic setting. The psychiatrist heads a treatment team and provides direct supervision and management of clinical staff. Research opportunities available. Paid call is shared with 5 other physicians. Attractive compensation and benefits package, 45 minutes from Boston, in tax free New Hampshire. Nashua, NH is easily accessible to major airports, mountains and lake regions.
Send CV to:

Hisham Hafez, MD
Executive Director/Chief Medical Officer
Community Council of Nashua, NH
7 Prospect St., Nashua, NH 03060.
hr@cofnashua.org

PSYCHIATRIST
Portsmouth, NH

Beautiful Seacoast area with four seasons, 55 minutes from Boston. Expanding private, non-profit community mental health center seeks two psychiatrists, one child and adolescent and one adult, to join a staff of seven psychiatrists, for outpatient care. Vibrant collegial atmosphere with competitive salary and excellent benefits package.

Interested candidates should send cover letter and C.V. to W.M. Hanna. M.D., Medical Director.

Seacoast Mental Health Center, Inc.
1145 Sagamore Avenue
Portsmouth, NH 03801
Fax: 603-433-5093

NEW JERSEY

Child/Adol. or Adult Psychiatrists

Child/Adol. or Adult Psychiatrists - needed for multi-disciplinary group in affluent community in North/Central N.J. NO Managed Care! Call Dr. S. Reiter at 908-598-2400 x1 and/or fax CV to 908-598-2408.

Psychiatrist - Established, for profit outpatient mental health practice with offices in South Jersey and Philadelphia. Immediate opening for experienced Adult Psychiatrist and Child and Adolescent Psychiatrist. Excellent referral base and reputation. Private practice model within comprehensive multi-disciplinary group of highly qualified clinicians. Fax CV to 856-985-8148 or call 856-983-3866 ext. 3018.

SOUTH JERSEY near Cherry Hill. General or Addiction Psychiatrist for adult general psych & dual diagnoses inpatient treatment programs. Salary, benefits, and bonus plan offered. Nominal call. Contact Joy Lankswert @ 866-227-5415 or email joy.lankswert@uhsinc.com

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NJ Beach resort community!
Great opportunity for a Child Psychiatrist! Local CMHC is seeking a full-time Child Psychiatrist to work **100% OUTPATIENT, NO CALL, 35 hours**!! Salary starting at $160K, depending on boards and experience, and full benefits (even at the 35 hours). Benefits are 28% on top of the salary! Please contact Loree Frazitta @ 800-735-8261 Ext. 216, fax your CV to 703-995-0647, or email your CV to lfrazitta@medsourceconsultants.com

NEW MEXICO

PRESBYTERIAN

Albuquerque, NM

PHS is New Mexico's largest private, non-profit integrated healthcare system.

The Behavior Medicine Program is a full-service psychiatry department with 2 adult and 1 child/adolescent inpatient units, a multidisciplinary outpatient department, intensive outpatient treatment, emergency and consultative programs.

We have an opening for an adult or geriatric psychiatrist who is interested in varied professional life. Opportunities include inpatient, outpatient and emergency/consultative care.

This is a full time employed position with the 500+ provider Presbyterian Medical Group.

Competitive salary and benefit package, includes malpractice insurance and relocation allowance.

Additional information about PHS may be found at www.PHS.org
For MD benefits info click on tab for 'Careers' and then from the left drop down menu under 'Careers' chose 'Physicians' and then 'Physician Benefits'.

Contact: Kay Kernaghan, Physician Recruiter, PHS
E-mail: kkernagh@phs.org
Phone: 1-866-757-5263

Mental Health Resources, Inc. of Clovis, New Mexico has an immediate need for a full-time or part-time psychiatrist to add to its medical staff. Vacancy is for a psychiatric generalist who would enjoy a small town environment. Area is approved for J-1 or H-1 placement. Contact Dr. Cecilia Carpio, Medical Director, Mental Health Resources, Inc., 1100 West 21st St., Clovis, NM 88101. mhrnewmex@yucca.net

NEW YORK CITY & AREA

Psychiatrist - Child/Adolescent

The George Jervis Clinic at the Institute for Basic Research in Developmental Disabilities seeks a Board-Certified or Eligible Child/Adult Psychiatrist, Full or Part-Time to serve as a member of a multidisciplinary team. We provide diagnostic and evaluative services to persons with disabilities and their families. Must be licensed or eligible in the State of New York. Experience with MR/DD and Autistic population preferred. Teaching or research background a plus. Research opportunities with basic researchers or collaboration with clinicians are available. Affiliation with State University system is possible. Regular hours with no call responsibilities. Excellent benefits package. Salary based on qualifications and/or experience. We offer a unique opportunity for the dedicated professional who wishes to provide needed services while contributing to the body of research in Developmental Disabilities. Fax application to (718) 494-7917 or mail to Human Resources Office; please include posting **# S-07-20**, Institute for Basic Research in Developmental Disabilities, 1050 Forest Hill Road, Staten Island, NY 10314. IBR/DD is an EO/AA Employer.

PSYCHIATRISTS
Lutheran Medical Center and Lutheran Family Health Centers in Southwest Brooklyn, offering a continuum of community-oriented behavioral health services under the auspices of the Department of Psychiatry, has openings for the following:

F/T MEDICAL DIRECTOR/OUTPATIENT BEHAVIORAL HEALTH-provide overall clinical leadership for ambulatory behavioral health services in an FQHC network in Southwest Brooklyn. Includes leadership and supervision of psychiatrists, nurse practitioners, and non-psychiatric behavioral health clinicians. Evaluate and treat patients, collaborate with Administrative Director on programs and operations, lead incident reviews, participate in audits, design and implement quality improvement activities, participate in ongoing development and implementation of an EMR. Report to Chairman, Dept. of Psychiatry, Lutheran Medical Center. Requires Board Certification in Psychiatry and 5+ years post-residency clinical/administrative experience (Unit Chief, Service Director, etc.) Additional Fellowship training/ certification and language capability preferred but not required. Clinical academic appointment at affiliated SUNY Downstate is available and encouraged. Position is ideal for a candidate with career goal of advancing as physician administrator/physician executive.

F/T INPATIENT PSYCHIATRIST-participate in multidisciplinary teamwork on a 35-bed IP Psychiatric Unit with 2 psychiatric colleagues and a Chief. Provide once-weekly psychiatric consultation on adjacent Detox Unit. Includes medical student teaching. Bilingual Spanish, Mandarin Chinese or Arabic a plus.

F/T OUTPATIENT ADDICTION PSYCHIATRIST-Fellowship -trained, addiction-Boarded or ASAM-certified psychiatrist to join OP adult substance abuse/MICA team for direct patient care, including buprenorphine treatment, in FQHC network site. Qualifying for loan repayment may be possible due to HPSA designation.

MOONLIGHTING PSYCHIATRISTS-opportunities in Inpatient/ ED/CL/Detox Services on select weekly shifts.

Please fax 718-630-8594, email: bgoff@lmcmc.com or send resume/CV to: Bradford M. Goff, M.D., Chairman, Dept. of Psychiatry, Lutheran Medical Center, Suite 2-45, 150 55th Street, Brooklyn, NY 11220. EOE/AA M/F/D/V

LUTHERAN MEDICAL CENTER
www.LutheranMedicalCenter.com

ASSOCIATE CLINICAL DIRECTOR
Manhattan Psychiatric Center, an OMH facility and NYU affiliate, is seeking a Board Certified Psychiatrist for the position of Associate Clinical Director (Psychiatrist 3). The applicant must have a license to practice in NYS, another state or Canada and 1 year post board certification experience. Preferred qualifications are 5 years post residency experience and have worked in a supervisory capacity.
The position involves responsibility for the supervision of staff psychiatrists, teaching of residents and medical students and opportunities for research.
Manhattan Psychiatric Center is a specialized facility for the treatment of the severe and persistent mentally ill with manualized programs for violence, diabetes and neurocognitive remediation.

Please fax resume to:
Samuel J. Langer, M.D., Chief of Psychiatry
646 672 6386
Manhattan Psychiatric Center
Wards Island, NY 10035
MPC is an equal opportunity employer

Premier HealthCare

BC/BE Psychiatrists

Child/Adolescent & Adult
Brooklyn, Bronx & Manhattan
Full Time/Part Time/Fee for Service

YAI/Premier Healthcare is a nationally recognized, well-established NYC diagnostic & treatment center for people with disabilities and their families. We are currently seeking NY Licensed psychiatrists.
Brooklyn Heights or Sheepshead Bay Brooklyn, Throgs Neck Bronx & Midtown Manhattan.
This is an opportunity to work with a professional team of doctors and nurses in a multi-cultural, team environment. Send CV to:
Karen Meyers, Clinical Recruiter, Premier HealthCare, 460 West 34 Street, N.Y., N.Y. 10001 Fax 212-563-4836 Email: kmeyers@yai.org

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Westchester Suburb or Upper Manhattan Child & Adol IP, FT- choose either Westchtr (easy NYC drive) **or** Manhttan. Option for teaching, Little mg'd care, long LOS, no call, no evenings, no weekends! Strong C/A grp. Write in strictest confidence to AdolMD@gmail.com

NEW YORK STATE

Psychiatrist

The Columbia County Mental Health Center has an immediate opening for a **Psychiatrist** in our outpatient clinic. The position will enjoy working in a brand new facility, flexible hours and a competitive salary. We are located in beautiful upstate New York, two hours from NYC, adjacent to the Berkshires.

Columbia County is an Equal Opportunity Employer

Send resume and inquires to

Michael G. O'Leary, DSW
Director of Community Services
Columbia County Department of Human Services
325 Columbia Street
Hudson, New York 12534

518 828-9446
moleary@govt.co.columbia.ny.us

GREATER BINGHAMTON HEALTH CENTER

ADULT PSYCHIATRISTS
and
CHILD/ADOLESCENT PSYCHIATRISTS

GBHC (JCAHO-Accredited New York State Office of Mental Health facility) is seeking full time; board certified/board eligible **ADULT PSYCHIATRISTS** for its adult inpatient facility and **CHILD/ADOLESCENT PSYCHIATRISTS** for its Child/Adolescent Behavioral Health Center. Abundant on-site CME. Salaried, permanent positions with excellent New York State benefits. No evening or weekend call required. Compensated optional call available. Enjoy the reasonable cost of living Central New York offers with easy access to NYC and other major cities.

Submit CV to:
Human Resources
Greater Binghamton Health Center
425 Robinson St., Binghamton, NY 13904
Fax: (607) 773-4117. EOE/AAE

NORTH CAROLINA

Psychiatrist/Faculty Positions: The Department of Psychiatric Medicine at the Brody School of Medicine at ECU is now accepting applications for two full-time faculty positions. The positions offer an excellent blend of clinical care, teaching, and clinical supervision of medical students, residents, physician extender(s), and other health professionals/trainees. Primary clinical assignment will be at the community-based clinical teaching sites. Requirements include MD or equivalent degree, completion of accredited psychiatric residency training in psychiatry, and preferably board certification in Psychiatry. Salary and academic rank commensurate with experience and academic background. Applications will be accepted until positions are filled. Greenville is the hub of Eastern NC and the home of East Carolina University, the 3rd largest public university in the state. Located near many recreational areas, including the Atlantic Ocean coastal resorts, Greenville is a university town, rich in cultural activities with charm and an easy pace of life. To apply, please send a letter of interest and CV to: Kathleen M. Seibel, M.D., M.H.A., Chair of Search Committee, Department of Psychiatric Medicine, Brody School of Medicine, 600 Moye Blvd., Greenville, NC 27834. In addition, applicants should submit an on-line application to **www.jobs.ecu.edu** (position #66013) (position # 66040) with attached cover letter, CV, and list of references. For more information please contact Dr. Seibel at seibelk@ecu.edu or telephone number 252-744-8744. East Carolina University is an AA/EO Employer.

CLOSE TO RALEIGH AND GREENVILLE - VERY LUCRATIVE COMPENSATION PACKAGE - Horizon Health seeks a Psychiatrist for a Medical Director position on an adult unit and CD unit in a very impressive general hospital in Rocky Mount. Offering a salary with benefits plus bonus plan or practice guarantee and stipend. What a great location! Enjoy the wonderful climate and quality of life this lovely area offers-only 45 minutes from Raleigh and Greenville & an easy drive to the mountains or the beach. Please **call Terry B. Good at 1-866-865-7380**, Fax #: 804-684-5663; Email: terry.good@horizonhealth.com. Or mail CV to: 1663 Denton Lane, Hayes, VA 23072.

Eastern NC - Convenient to Outer Banks, NC and Norfolk/VA Beach - Horizon Health has a very attractive salaried position with benefits in a general hospital located in an area that is becoming one of THE places to retire in NC. This is more of a Hospitalist position as it primarily inpatient work. You would work with a great group of people that make work a pleasure every day. What could be better: low stress small town living with a wonderful climate and easy drive to the coast plus a very rewarding professional opportunity. Join two other psychiatrists making call 1 in 3. Please **call Terry B. Good at 1-866-865-7380**, Fax #: 804-684-5663; Email: terry.good@horizonhealth.com. Or mail CV to: 1663 Denton Lane, Hayes, VA 23072.

Wilmington, North Carolina
Psychiatry Opportunity

Wilmington, NC

New Hanover Regional Medical Center seeks to hire Inpatient-based Psychiatrists to provide services within the medical center and the Behavioral Health Hospital, The Oaks. A 62-bed psychiatric hospital on the New Hanover Regional Medical Center campus, The Oaks provides inpatient and outpatient psychiatric programs for adults. The Oaks staff is specially trained to evaluate and treat patients for depressions, adjustment disorders, bipolar disorder, schizophrenia, psychotic and personality disorders. Inpatient units include: Dual-Diagnosis Unit, Behavioral Medicine Unit and Progressive Treatment Unit. Team consists of four physicians and a mid-level provider. Call is 1 in 4.

Ideal candidates must have a strong work ethic, good interpersonal and communication skills, a commitment to excellent patient care and a team-oriented attitude.

Being a Southern coastal town, Wilmington offers a variety of activities from a historic riverfront downtown, Thalian Hall performing arts center, museums, beaches and water activities, fishing, nightlife and great restaurants. Wilmington offers many family oriented communities and activities. Additionally, area schools are identified as some of the top in the state while the local university provides further educational opportunities. For more information about the Wilmington area, you may go to http://www.wilmingtonchamber.org/

Position is a hospital employment model with excellent salary and benefits. Interested candidates should forward their CV to Kathy Gresham, Director, Physician Relations, New Hanover Regional Medical Center, 910-452-8772 or email Kathy.Gresham@nhhn.org

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Private Practice Opportunities in North Carolina.

Carolina Partners in Mental HealthCare, PLLC is seeking BE/BC psychiatrists for our practices in Raleigh, Chapel Hill and Wake Forest, NC. Private outpatient practices, full partnership from day one - no investment required. FT, PT flexible. Carolina Partners has seven offices in Raleigh, Durham, 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 801-729-9867; EMail carolinapartners @bellsouth.net.

OHIO

Full-time opportunity for a child/adolescent psychiatrist or general psychiatrist willing to treat adolescents. MHS is a comprehensive community mental health center offering inpatient, outpatient, partial hospital, and community support programs. Located in a safe, family-friendly, community located less than an hour from Columbus and Dayton and offering an abundance of natural, cultural, educational and entertainment venues. Competitive salary and benefit package including 20 days vacation, plus paid sick and personal time, health, dental and life insurance, FSA, company-funded retirement plan, CME, and professional dues. Must be board-certified or board-eligible. Visit www.mhscc.org for more information and to download a brochure. Please send letter of interest and vita to J. Marenberg, HR Director, Mental Health Services for Clark Co. 1345 N. Fountain Blvd. Springfield, OH 45504, Jo.Marenberg@mhscc.org or fax to 937 342-4254. Equal Opportunity Employer.

All outpatient practice with no night call! Great salary and full benefits less than an hour to Cleveland. Contact Jim Ault at St. John Associates, jault@stjohnjobs.com or 800-737-2001. Visit www.stjohnjobs.com for more opportunities nationwide.

THE 1ST CHOICE IN PSYCHIATRIC RECRUITMENT
Cincinnati
G/A Psych, CMHC, All O/P, No call
For more information contact:
BOB TOTH
(800) 783-9152 FAX (270) 782-1055
www.fcspsy.com
admin@fcspsy.com

OKLAHOMA

Medical Director
Near TULSA!

A Medical Director is needed for a 16-bed geriatric psychiatric program in Okmulgee, Oklahoma **(35 minutes from Tulsa, OK)**. In this position, the Medical Director will be responsible for a complete practice experience working on inpatient program, which would include admission, diagnosis, treatment, management, and discharge of patients. Excellent Stipend offered with lucrative private practice potential. For more information please contact Diane Odom, 972-420-4083, fax 972-420-8233, e-mail diane.odom@horizonhealth.com

OREGON

Private Practice opportunity in Bend, Oregon. This is both an outpatient and inpatient practice. The inpatient units are primarily adult-20 beds total, with consult/liaison services. We are jointly recruiting with St. Charles Medical Center, the largest medical center east of the Cascades. The hospital is offering a practice guarantee, interview and moving expenses. Bend is nestled in the beautiful Cascades three hours driving time from Portland, with great restaurants, golf, skiing, kayaking, mountain biking and many other recreational activities.
Email CV to Magnus Lakovics, MD, Medical Director, Behavioral Health Services, St. Charles Medical Center at mlakovics@msn.com or call 541-390-4418.

PRIVATE PRACTICE: Unique opportunity for solo practitioner to share office space, overhead/operating expenses, and a collegial atmosphere with 11 well-established, well-esteemed, psychodynamically oriented solo private practice psychiatrists in a remodeled historic home in NW Portland. Please contact Richard Alden MD (503-228-5909, ext.110) for further information.

PENNSYLVANIA

Pennsylvania: MHM Correctional Services, Inc. the leading national specialist in providing mental health programs and services to correctional systems invites you to join us in one of these outstanding opportunities with the Pennsylvania Department of Corrections. Full-time positions currently exist at SCI Camp Hill (Harrisburg, PA) and SCI Huntingdon (Central PA) as well as a part-time (12 hrs/wk) positions at SCI Pine Grove (Indiana, PA). We are seeking Psychiatrists who are ready to make a difference to an underserved population while being part of an elite organization that offers outstanding benefits and generous compensation. Gain personal and professional satisfaction, while utilizing your skills in a safe and supportive work environment. Guide the delivery of mental health services to this diverse population of incarcerated individuals. Contact Holley Schwieterman at: (866) 204-3920 or email: hschwieterman@mhm-services.com to learn more. www.mhm-services.com

EEO/AA

STATE COLLEGE: Child or General Psychiatrist to see children & adults - outpatient only.
CLARION-General Psychiatrist for inpatient and partial programs.
SHIPPENSBURG-near Harrisburg. General Psychiatrist. Inpatient & sub acute programs for general psychiatric & addiction services.
Salary, bonus, & benefits. Contact Joy Lankswert @ 866-227-5415 or email joy.lankswert@uhsinc.com

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PSYCHIATRIST PART- TIME

Consulting Psychiatrist or psychiatric resident needed for Mental Health Out-Patient Clinic in Western PA. Clinic is 45 minutes from Pittsburgh, 45 minutes from Youngstown and 20 minutes from Sharon, PA. Flexible schedule- any weekday, evening, or Saturday. Seeking Adult and Child/Adolescent Psychiatrists, MD/DO. Email CV/Resume to: sharon@pinpa.org, Fax - 724-657-3326 or telephone Dr. Sharon Hodge at 724-657-3303 ext. 105.

CRISIS MEDICAL DIRECTOR

Mercy Fitzgerald Hospital in Southeastern Delaware County is recruiting a full time Psychiatrist for weekday work as Medical Director of our crisis center. Full time is with group practice involvement and includes benefits, malpractice and high income potential. Part time positions in crisis also considered. Please contact Jeffrey J. Dekret, M.D., Director of Psychiatry by fax 610-237-4695, email: jdekret@mercyhealth.org or call 610-237-4123.

PITTSBURGH, PA - Calling all Pittsburgh Steelers Fans!
Several job opportunities available in the Pittsburgh, PA area!! Exceptional opportunities for **ADULT and C&A** psychiatrists. ADULT psychiatrist can do a mix of inpatient and outpatient, all inpatient or mostly outpatient. C&A psychiatrist can do a mix of inpatient and outpatient or mostly outpatient. Salary **starts at $175,000** and goes up depending on experience and boards. Potential for upward mobility or partnership down the road. Great place to work!!!! Please contact Carrley Ward @ 800-735-8261 x219, fax your CV to 703-995-0647, or email your CV to: cward@medsourceconsultants.com

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Medical Director
Aetna Behavioral Health
King of Prussia, PA

Aetna Behavioral Health is looking for a board certified psychiatrist with clinical experience to take a leadership role in a new and innovative approach to behavioral health care management.

Full benefit package. Salary commensurate with experience.

To apply, please submit your CV to our company website, **www.aetna.com/working**, and view details under Req. # 16944.

We want you to know℠
Aetna®

Aetna is an equal opportunity/affirmative action employer.

RHODE ISLAND

PSYCHIATRIST

NEEDED IMMEDIATELY @ NAVAL HOSPITAL NEWPORT, RI

FAX RESUMES (210) 930-4520 TO MARLOW BASS
OR WWW.MAGOTECH.COM

TENNESSEE

East Tennessee State University - College of Medicine - Department of Psychiatry and Behavioral Sciences - Two Full-Time Positions - General Psychiatrist and Child Psychiatrist - 770160, 814300 - RE-ADVERTISED. Full-time positions available for General Psychiatrist and Child Psychiatrist. General Psychiatrist 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 37614-1707. Telephone inquires should be made at 423-439-2235 or e-mail at lovedayc@etsu.edu. AA/EOE**

VANDERBILT UNIVERSITY FACULTY POSITION

Vanderbilt University Department of Psychiatry (Nashville, TN) is recruiting BE/BC full-time faculty psychiatrists (Adult or Child) with interest in inpatient psychiatry in an academic setting. Teaching and participation in clinical research will complement the clinical work. Appointment will be at the Assistant Professor level or above. Salary is negotiable dependent upon qualifications and experience.

For further information, please contact: Sherron Buchanan, Assistant to Chair, 1601 23rd Avenue South, Suite 3060, Nashville, TN 37212 - Phone: 615-322-2665; Fax: 615-343-8400

TEXAS

Child & Adult Psychiatrists - Assistant Professors
Adult Psychiatrist - Associate Professor

The **Department of Psychiatry at The University of Texas M.D. Anderson Cancer Center** is recruiting board-certified/eligible child & adult psychiatrists at the Assistant Professor level and an adult psychiatrist at the Associate Professor level to join its full-time faculty. We seek individuals with experience or training in clinical consultation-liaison psychiatry/psycho-oncology and an interest in research. Our faculty provide clinical expertise in patient care and management for patients suffering with psychiatric and behavioral disturbances related to cancer treatment. The successful candidates would also participate in the training of psychiatry fellows, residents and medical students in the specialty of psycho-oncology. In addition, they would be responsible for the development and conduct of research related to behavioral, psychiatric and psychosocial problems in cancer patients and their families.

Interested applicants should submit a curriculum vitae and a letter describing their clinical and academic interests to: **Alan Valentine, M.D., Department of Psychiatry, P.O. Box 301402, Unit 453, Houston, Texas 77230, Phone: 713-792-7546 Fax: 713-792-8242, E-mail: avalenti@mdanderson.org**

M. D. Anderson Cancer Center is an equal opportunity employer and does not discriminate on the basis of race, color, national origin, gender, sexual orientation, age, religion, disability or veteran status except where such distinction is required by law. All positions at The University of Texas M. D. Anderson Cancer Center are security sensitive and subject to examination of criminal history record information. Smoke-free and drug-free environment.

AUSTIN: Busy private practice group seeking adult and/or child psychiatrist. Texas license and BE/BC required. Primarily out-patient. In patient optional. Ample referrals. Office well staffed and equipped. Austin is a great place to live and raise a family. Contact Neuropsychiatric Associates of Austin @ (512) 454-5716 or e-mail np_associates@prodigy.net.

Come to beautiful San Antonio, Texas!!

Psychiatrists

The Center for Health Care Services, a 2006 APA Gold Award winner, is actively seeking full-time/part-time/contract psychiatrists for our Adult & Child Programs. The Center Psychiatrists are at the leading edge of the delivery of mental health service, providing assessment and treatment of clients, and leadership of a team of skilled and dedicated mental health professionals. Must be board eligible or board certified.

The Center offers:
- *Attractive salary*
- *Excellent benefits package, including retirement benefits and an internal CME program.*

San Antonio offers:
- *Great climate year round*
- *Ranked among the best value cost of living*
- *Arts, Theatre, Sports and Entertainment, Amusement parks and more*
- *Easy access to beaches, Mexico, the Texas Hill Country, more*

If you are interested in learning more about service at The Center, please submit your C.V. in confidence to:

The Center for Health Care Services
Attn: HR Director
3031 IH 10 West
San Antonio, Texas 78201
Fax: 210-731-1310
staffing@chcs.hhscn.org

EOE

Presbyterian Hospital of Dallas
Texas Health Resources

Medical Director needed in Dallas, Texas!

We are looking for a medical director to staff our adult psych inpatient unit that has recently expanded to 41 beds. Unit specialty areas include detox, eating disorders, geropsych, and ECT.

Please contact Norma Ondarza, Texas Health Resources (800) 945-0430, NormaOndarza@TexasHealth.org. Please visit us at www.texashealth.org

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Psychiatrist or PCP experienced in Geriatrics
Clinical, Supervisory and Administrative Responsibility with Geriatric Psychiatry Group. FT $200,000.00/yr compensation DOE. Benefits+Bonus+Sign on Bonus
Chart Review, Supervision of NP/PA, Phone Consults. PT 5 - 20hrs/mth $100.00+/hr DOE $1000.00/mth min+Sign on Bonus.
Expertise in psychopharmacology, psychotherapy, community or geriatric psychiatry desired.
Willingness to work with multidisciplinary team. Will train on special needs of Geriatric Population. TX license required. Positions available in Houston and San Antonio.
Visit: www.seniorpsychiatry.com/Fax CV: 800-318-0120/Email: hr@seniorpsychiatry.com

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DALLAS area (Sherman); McALLEN and SAN ANGELO: Diverse TX locations. Private practice opportunities - General, Geriatric or Child Psychiatrists. Service Directorship & caseload stipend offered as well as other financial support depending on location. Contact Joy Lankswert @ 866-227-5415 or email joy.lankswert@uhsinc.com

UTAH

PROVO/OREM: Child Psychiatrist - Adolescent Residential Treatment. Duties include admission evaluations, treatment planning & follow-up, parent contacts, & participation in medical staff meetings. Manageable caseload - patients seen on varied schedules per treatment needs. Compensation package to include salary & benefits. Contact Joy Lankswert @ 866-227-5415 or email joy.lankswert@uhsinc.com

VASLCHCS is affiliated with the University of Utah School of Medicine, seeks a full time BC/BE staff psychiatrist. The primary duty will be to provide psychiatric medication management to patients in satellite clinics utilizing telepsychiatry. Limited overnight travel to outlying clinics may be required. Applicants must qualify for academic appointment at University of Utah School of Medicine. Academic appointment will be commensurate with experience and may be adjunct or in the full time clinical or tenure track. Opportunities exist to teach and supervise medical students and psychiatry residents. On-call requirements are minimal. The VA Salt Lake City Health Care System offers excellent benefit programs. Must be U.S. Citizen. Closes once position is filled. Send CV and names/addresses of three references to VA Salt Lake City Health Care System, Human Resources (Mail Code 05C), Attn: Tonya Mackintosh, Salt Lake City, Utah 84148. Reference Announcement #C06-246. For additional information contact Tonya Mackintosh at 1-801-584-1284, ext. 2267 or Nikki Morris, ext. 4403. Equal Opportunity Employer.

VERMONT

The Counseling Service of Addison County (CSAC) is currently seeking a Psychiatrist to join an innovative interdisciplinary practice of a highly regarded non-profit community mental health center located in a uniquely desirable small, New England college community. Child/adolescent expertise desired, but not required. Qualifications: BC/BE psychiatrist. CSAC Offers a collaborative environment, rewarding work, a culture of caring, top ranked services, committed staff, excellent benefits, and a lovely location in the Champlain Valley. The Middlebury and Burlington areas offer an outstanding quality of life that boasts magnificent restaurants, world-class shopping, cultural amenities, vibrant downtowns and a natural playground for outdoor activities like golf, tennis, sailing, hiking, biking and, of course, great skiing.

We are people helping people.

Please submit cover letter and resume to Cheryl Huntley via email at chuntley@csac-vt.org, fax at (802) 388-8183, or mail to 89 Main Street, Middlebury, VT 05753. For more information you may call her at (802) 388-0302 ext. 493. Visit our website: www.csac-vt.org.

VIRGINIA

Central State Hospital is seeking a psychiatrist with expertise in Public and/or Forensic Psychiatry. Applicants must be licensed or eligible for licensing by the Virginia Board of Medicine (Board certification is preferred.) CSH offers an outstanding benefits package, competitive salaries (up to $173,289 based on training and experience), a high quality of life, and career enhancement opportunities. For more information on CSH and to apply for this position, please visit our website: www.csh.dmhmrsas.virginia.gov EEO/AA

Central State Hospital
26317 W. Washington Street
Petersburg, VA 23803
p: 804-524-4451/7111
e: employment@csh.dmhmrsas.virginia.gov

VIRGINIA COMMONWEALTH UNIVERSITY: Dept. of Psychiatry recruiting BE/BC **faculty psychiatrist at Assistant or Associate Professor level,** for mixed inpatient-outpatient position. Inpatient responsibilities include daily teaching rounds on nine beds acute inpatient unit, and outpatient work includes supervision, faculty practice, and visiting community geriatric locations. Fellowship in geriatrics preferred. Pursuit of scholarly work encouraged and supported. VCU is a large urban university with robust health science campus and 750 beds university hospital. Department of Psychiatry employs over 85 full time faculty and is nationally ranked in federally funded research. Richmond, the State Capital, has moderate climate and a rich mix of historical and contemporary facilities. Excellent suburban housing, public/private schools. Internet provides comparative cost of living. Send CV to Marie Baker-Roach, Human Resources, Department of Psychiatry, VCU/MCV, Box 980710, Richmond, VA 23298. VCU is an EEO/AA employer. Women, minorities, and persons with disabilities encouraged to apply.

Chair, Addictions Psychiatry

The Department of Psychiatry, Medical College of Virginia at Virginia Commonwealth University, in collaboration with VCU Institute for Drug and Alcohol Studies, is recruiting a strong academic leader to chair the Division of Addiction Psychiatry. Doctoral level applicant should have career commitment to addictions research and a track record of research/funding. Responsible for developing teaching and clinical programs needed to support teaching/research. Resources available to support an expanded research program. Funded ACGME accredited Fellowship Program. We have strong programs in psychiatric genetics, epidemiology, pharmacology, toxicology, and women's health. Laboratory and community based research are active areas for collaboration. New Dean is a strong supporter of psychiatric research. Department of Psychiatry has over 85 full-time faculty, 38 residents, multiple fellowships and research centers. VCU is a large urban 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.

Virginia Licensed Psychiatrist to join a large multi-disciplinary group of providers w/ several locations in the Virginia Beach area. Excellent compensation & benefits. Fax Resume to: Christian Psychotherapy Service, 757-497-1327 or call 757-490-0377.

CARILION CLINIC
finding better ways

Psychiatrist - Multiple Opportunities Available
Carilion Clinic - Virginia

Carilion Clinic in Roanoke, VA has an opening for a full-time BE/BC adult Psychiatrist at Carilion Roanoke Memorial Hospital, an 843-bed academic/tertiary referral center in with 32 acute adult psychiatric beds. Responsibilities include outpatient clinical services for the Department of Psychiatry and Behavioral Medicine, along with teaching medical students and supervising residents in psychiatry. In collaboration with Virginia Tech, Carilion Clinic is establishing its own allopathic medical school opening Fall 2010 with a problem-based learning curriculum. Call 1:10.

Carilion New River Valley Medical Center in Christiansburg, VA has an opening for a full-time BE/BC adult Psychiatrist at Saint Albans Behavioral Health, located a new, 36-bed wing of the medical center. The inpatient psychiatry unit includes an ECT suite, intensive treatment area, geriatric observation, and adjacent outpatient offices for continuity of care. Saint Albans is a training site for medical students at Via College of Osteopathic Medicine on the campus of Virginia Tech in nearby Blacksburg. Call 1:7.

Weekend positions also available in Roanoke and Christiansburg locations. See new patients, do consults and round on 75% of patients over course of two 16-hour weekend shifts (Saturday/Sunday). One weekend off per quarter. Work an additional 2 hours per week with Chair of Psychiatry on projects and qualify for full-time benefits.

Positions include a competitive base salary augmented with a substantial bonus for quality, plus additional compensation for meeting productivity targets and comprehensive benefits package, including relocation. For more information or to submit your CV and cover letter for consideration, contact:

Rhonda B. Creger, Senior Consultant,
Professional Staffing
Carilion Clinic
800-856-5206 or rhondac@carilion.com
Visit www.carilion.com

Child Psychiatrist

Virginia Commonwealth University: Medical College of Virginia Hospitals, Division of Child & Adolescent Psychiatry in the Department of Psychiatry, recruiting Virginia license-eligible BE/BC child psychiatrist faculty as Inpatient/Outpatient attending. Position located in professional shortage area; J-1 candidates welcome to apply. Will be responsible for administration and clinical care as well as teaching and supervision of medical students, residents and child fellows. In addition, consultation work with community agencies will be available. Interest in teaching and academic work, as well as ability to work on interdisciplinary team, required. Department has nine fulltime child psychiatrists and child research institute, over 85 fulltime faculty and well-funded research in genetics, addictions, child and women's mental health and psychopharmacology. VCU is a large urban university with robust health science campus and 750-bed university hospital. Richmond, the State Capital, has moderate climate and rich mix of history with modern facilities, excellent suburban housing, public/private schools. See comparative cost of living via Internet at www.coli.org/. Send CV to Bela Sood, MD, c/o Marie Baker-Roach, VCU, Box 980710, Richmond VA 23298. Virginia Commonwealth University is an Equal Opportunity/Affirmative Action employer. Women, minorities, and persons with disabilities are encouraged to apply.

WASHINGTON

Adult Psychiatrist
Seattle, Washington

Pacific Medical Centers is one of the largest, not-for-profit networks of multi-specialty groups in the Greater Seattle area. Our team of over 130 primary and specialty care providers representing 24 specialties has a proud history of providing quality medical care in an evidence-based, collaborative environment.

We are seeking an experienced BC/BE, general adult psychiatrist to join our dynamic multidisciplinary behavioral medicine team. A strong psychopharmacology background and excellent interpersonal skills are essential. This is a .8 - 1.0 FTE outpatient position with time divided between two of our area clinics. An unrestricted DEA and WA medical license will be required.

Seattle is a sophisticated yet charming city with diverse cultures, professional sports, excellent shopping, and outstanding schools. Statewide we enjoy vast outdoor recreation opportunities, a temperate climate with four seasons and no state income tax!

Our competitive compensation and comprehensive benefits package will support and enhance a lifelong career. For additional information about PMC, and to apply directly online, please visit our website: www.pacificmedicalcenters.org.

Contact: Deborah Akins, Physician Recruiter
Toll Free: 888-901-1122
Email: DeborahA@pacmed.org

AA/EOE

pacific medical centers

Western Washington State: Adult/Geriatric/Forensic Psychiatrist (BE/BC with a WA state license) applications considered. Western State Hospital is a fully accredited (JCAHO) and certified (CMS) 997 bed hospital serving adult, geriatric and forensic populations. Annual salary up to $158,304 DOQ. Excellent benefits, including hospitalization/medical insurance, retirement and vacation leave, plus optional deferred income plan. Send CV to Norma Jones, Medical Staff Coordinator; Western State Hospital; 9601 Steilacoom Blvd. SW; Lakewood, WA 98498-7213. E-Mail: JONESNL2@DSHS.WA.GOV.

WEST VIRGINIA

PSYCHIATRIST - William R. Sharpe, Jr. Hospital, a 150-bed, JCAHO-accredited, state psychiatric hospital and winner of APA Award for state/university collaboration, is searching for a BE/BC psychiatrist. This is a full time faculty position with West Virginia University with regionally competitive salaries and excellent benefits and no call duty. Position will remain open until filled. Contact Abe Adel, MD at 304-269-1210 or email a CV and cover letter to bettygumfoster@wvdhhr.org. WVU is an AA/EO employer.

WISCONSIN

Adult Psychiatrist - La Crosse, WI
BC/BE general adult psychiatrist needed to join four psychiatrists. In-patient and out-patient practice (1:5 call) with Franciscan Skemp Healthcare - Mayo Health System, multispecialty group/healthcare network including 200+ physicians/associate providers. Initial salary guarantee with subsequent productivity-based compensation and excellent benefit package. La Crosse, city of 52,000 (metro area 120,000), is located in west-central Wisconsin on the scenic Mississippi River, offering unlimited recreational, cultural and educational opportunities in a family environment. Contact Bonnie Guenther, Physician Services, at 800-269-1986 or email: guenther.bonnie@mayo.edu.

Franciscan Skemp
Mayo Health System

Hospitalist - Addictionologist
Meriter Health Services
Madison, WI

The NewStart Program of Meriter Hospital, located in beautiful Madison, Wisconsin, has an exciting opening for an Addictionologist. This is an excellent opportunity to join the hospital based inpatient and outpatient practice of ASAM President Michael Miller, MD and Ian Powell, MD. This position will provide supervision of adult and adolescent IOP services plus participating in a busy three-physician outpatient and inpatient addiction medicine practice including inpatient detoxification services (alcohol, sedatives, and opioids) as well as small hospital-based rehab and dual-diagnosis inpatient services for adults. The position includes two to three days per week in large community-based teaching hospital with a world-class consultation-liaison service in addiction medicine, as well as an active outpatient practice. Other opportunities include teaching and working with a new addiction psychiatry fellowship program. The health insurance/managed care climate is far more favorable than most practice situations. Practice and live in one of America's most desirable communities with tremendous recreational, cultural, and educational resources. Adolescent medicine and psychiatry applicants preferred, but all addictionists invited to apply to this multi-disciplinary addiction medicine service including internal medicine, family medicine, and psychiatry colleagues. Meriter Health Services provides an outstanding benefit package. For more information, contact Kris Holmes at kholmes@meriter.com or 608-417-6589.

Adult Psychiatrists

Child and Adolescent Psychiatrists

The University of Wisconsin Department of Psychiatry is seeking BC/BE Child and Adolescent Psychiatrists and BC/BE Adult Psychiatrists to join our expanding clinical and research programs. Primary responsibilities include outpatient or inpatient clinical care, supervision of residents, and teaching of medical students and residents. Administrative and research experience is highly valued. Candidates will also have the opportunity to participate in collaborative and independent research within a Department nationally recognized for excellence in developmental and emotions research.

Please send letter of interest and your CV to:

Jeff Charlson
Department Administrator
University of Wisconsin School of Medicine
and Public Health
Department of Psychiatry
6001 Research Park Boulevard
Madison, WI 53719
or via email to jtcharls@wisc.edu

WYOMING

WYOMING: General Psychiatrist. Position duties include covering Inpatient and Outpatient services in a private hospital setting. Salary, benefits and bonus. Join a great staff & stable physician team. Contact Joy Lankswert @ 866-227-5415 or email joy.lankswert@uhsinc.com

International

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Fellowships

FELLOWSHIP IN REPRODUCTIVE PSYCHIATRY: The Department of Psychiatry at the University of North Carolina at Chapel Hill is offering a two-year fellowship in reproductive psychiatry. Applications are being accepted for July 1, 2008 from psychiatrists who have completed their residency. The fellowship is designed to train psychiatrists in women's mental health, reproductive endocrinology, reproductive neuroscience, biostatistics and clinical research design. To apply for the position, send, your letter of interest and CV to David R. Rubinow, M.D., Meymandi Distinguished Professor of Psychiatry and Chair, Department of Psychiatry, Campus Box 7160, University of North Carolina, Chapel Hill, NC 27599-7160. You may also fax the same information to 919 966-7659 or email david_rubinow@med.unc.edu. The University of North Carolina at Chapel Hill is an Equal Opportunity employer.

THE 2008 PAUL JANSSEN FELLOWSHIP IN TRANSLATIONAL NEUROSCIENCE RESEARCH AT COLUMBIA UNIVERSITY

The Paul Janssen Fellowship is awarded, for up to two years, to an outstanding young physician-investigator (must have M.D. degree) to conduct novel translational research in the field of neuroscience as it relates to psychiatric disease and medicine. The Paul Janssen Fellow will be assigned both a basic scientist mentor and a clinical investigator mentor from the faculty at Columbia University to serve as joint mentors. The fellow will take a basic observation made by the basic science mentor and apply it to the study of disease or treatment with the clinical research mentor. Candidates from the international neuroscience community, holding an M.D. or M.D./Ph.D. degrees, and preferably having completed initial fellowship research training, are invited to apply. The award provides a stipend, commensurate with experience, as well as some funding for research costs. The stipend provided may require supplemental funding by the mentors.
Preliminary/open application period: 9/1/07 - 11/30/07. For details on how to apply, contact Renee Azima Heller, M.A., Administrator, tel: 212-543-6774, email: rla2117@columbia.edu or visit our website (http://excalibur.cpmc.columbia.edu/janssen_app_2008.html). Columbia University is an AA/EOE.

YALE FACULTY FELLOWSHIP IN ADDICTIONS MEDICATIONS DEVELOPMENT RESEARCH

Department of Psychiatry, Yale School of Medicine, seeks psychiatrist or clinical psychologist to participate in a multi-disciplinary faculty level research training program in medications development for tobacco and stimulant addiction. Position supported by NIDA K12 training grant with protected research time. Strong background in substance abuse or psychopharmacology research preferred. Position carries academic appointment at the rank of Assistant Professor or Associate Research Scientist. Training program aims to launch independent research careers in drug abuse medications development. Required qualifications include: M.D. or Ph.D. degree, completion of specialty training, commitment to a career in substance abuse research and U.S. Citizenship or permanent resident status. For further information contact: Bruce Rounsaville, M.D., tel 203-937-3486, extension 7401, bruce.rounsaville@yale.edu. Yale University is an Equal Opportunity/Affirmative Action Employer.

Geriatric Psychiatry Fellowship with Emphasis on Integrated Consultation-Liaison Psychiatry

Stony Brook University's Department of Psychiatry and Behavioral Science announces the availability of an innovative ACGME-accredited geriatric psychiatry fellowship position starting July 2008 with the option for special emphasis on consultation-liaison psychiatry. With eight board-certified geriatric psychiatrists on the faculty, the geriatric psychiatry fellow will have dedicated experiences in geriatric inpatient, long-term care, outpatient, ECT, and consultation-liaison psychiatry at both the University Hospital as well as several community settings. Located within the new Stony Brook Division of Medical and Geriatric Psychiatry, fellows in geriatric psychiatry will participate in a clinical milieu emphasizing understanding the psychiatric aspects of medical conditions along with the medical aspects of psychiatric conditions. Fellows have the unusual opportunity through collaborative consultation-liaison work to develop added clinical expertise and professional relationship skills working closely with trainees and faculty in geriatric medicine, neurology, and family medicine. To apply for the position send by U.S. mail, fax (631) 444-7534, or e-mail *steven.cole@stonybrook.edu* your letter of interest, your CV, and three letters of reference to Steven Cole, M.D., Head, Division of Medical and Geriatric Psychiatry Health Sciences Center, 10th Floor, Room 042, Stony Brook NY 11794-8101. Equal opportunity/affirmative action employer. Visit *www.stonybrook.edu/jobs* for employment information.

Psychiatry Research Fellowships

The Mount Sinai School of Medicine's Department of Psychiatry is ranked among the top 10 research departments in the country. This department has opportunities for 2008 Psychiatry Research Fellowships in Mood & Personality Disorders, Mood & Anxiety disorders, Autism, & Schizophrenia, as well as ACGME Fellowships in Addiction, Geriatric Psychiatry & Psychosomatic Medicine. Visit holders must have attended an ACGME approved 4 year residency.

Please send inquiries to Alison.McInnes@mssm.edu. Call 718-584-9000 ext 6821. Visit our website at http://www.mssm.edu/psychiatry/fellowships/clinical_research.html. EOE.

Geriatric Psychiatry Fellowship Training University of Rochester Medical Center Rochester, NY

The University of Rochester Medical Center is a nationally recognized center for excellence in geriatric psychiatry along with allied fields including neurobiology and aging, gerontology, and geriatric medicine. Since 1983, we have offered fellowship training in geriatric psychiatry as part of a rich educational tradition in multidisciplinary, clinical and academic activities.

We offer one-year PGY-5 clinical fellowships in geriatric psychiatry. Upon successful completion of our ACGME-accredited program, our graduates will be eligible for the ABPN subspecialty examination in geriatric psychiatry.

We also offer a 2-year HRSA-funded Interdisciplinary Geriatrics Fellowship, which integrates the core disciplines of psychiatry, medicine, and dentistry, and prepares trainees for careers in academic medicine as clinical and educational leaders.

Both fellowships offer training in the care of older patients in a variety of inpatient, long-term care, outpatient, consultation, and palliative care settings. Supervised clinical experiences are complemented by a didactic program, elective offerings, and opportunities to develop individual scholarly and research interests. In addition to the breadth of our clinical programs and patient populations, we have a large cadre of experienced and nationally recognized clinicians, teachers, and researchers serving on our faculty. We pride ourselves on providing a stimulating, rewarding educational experience in a supportive and nurturing environment.

For more information please contact:
Jeffrey M. Lyness, MD
Director, Geriatric Psychiatry
Fellowship Program
University of Rochester Medical Center
Phone: 585.275.6741
Email: Jeffrey_Lyness@urmc.rochester.edu
Or visit our website at:
www.urmc.rochester.edu/smd/psych/educ_train/fellowship/geriatrics/index.cfm

Research Fellowships in Psychiatry at the University of North Carolina

Applications are currently being accepted for NIMH-funded research fellowship positions in clinical and applied neuroscience at the University of North Carolina at Chapel Hill. This two-year fellowship is intended for psychiatrists who have completed their residency training, are U.S. citizens or permanent residents of the U.S., and are eligible for a North Carolina medical license. Exceptional candidates entering their fourth year of training will be considered. Fellowship positions are also available for Ph.D. trained applicants.

Areas of active clinical investigation include schizophrenia, bipolar illness, women's mood disorders, depression, eating disorders, alcoholism and neurodevelopmental disorders. A wide variety of clinical research methodologies are represented, including structural and functional neuroimaging, psychopharmacology, genetics, and psychophysiology. Opportunities for basic research in neuropathology, neuropharmacology, developmental neurobiology, and animal models of psychiatric disease are available as well.

More information about the Research Fellowship Program, the UNC Department of Psychiatry and its investigators is available at http://www.psychiatry.unc.edu/. Fellows are eligible for the NIH Loan Repayment Program (see http://lrp.info.nih.gov for details).

Applicants should send a letter outlining their interests, a CV, and three letters of reference to: John H. Gilmore, M.D., Vice Chairman for Research, Department of Psychiatry, Campus Box #7160, University of North Carolina School of Medicine, Chapel Hill, N.C. 27599-7160; jgilmore@med.unc.edu. The University of North Carolina at Chapel Hill is an equal opportunity employer.

INFANT PSYCHIATRY FELLOWSHIP. The Section of Child and Adolescent Psychiatry at Tulane University Health Sciences Center is seeking a full-time Fellow in Infant Psychiatry. This one or two year fellowship includes clinical and research experiences with the multidisciplinary Infant Mental Health group at Tulane. Completion of a fellowship in Child and Adolescent Psychiatry preferred. Faculty appointment at the Instructor level is possible. Applications will be accepted until a suitable qualified candidate is found. Applicants should send letter of interest, updated CV and list references to Charles Zeanah, MD, Vice Chair and Director of Child and Adolescent Psychiatry, 1440 Canal Street TB52, New Orleans, LA 70112. Interested eligible applicants may obtain further information regarding this position by contacting Dr. Zeanah at 504-988-5402 or czeanah@tulane.edu. Tulane is strongly committed to policies of non-discrimination and affirmative action in student admission and in employment.

Psychiatry Fellowships

Virginia Commonwealth University, Department of Psychiatry is offering ACGME fellowships in Geriatrics, Psychosomatics and Forensics. Competitive salary and allowances. Fellowships offer broad-based training in inpatient/outpatient settings, focusing on acute and chronic disease, consultation services, private evaluations, seminars, research and teaching experiences. Applicants must demonstrate good communication skills, and have completed approved residency in psychiatry. J-1 applicants eligible. Applications should be sent to Joel Silverman, MD, Chairman, c/o Marie Baker-Roach, Department of Psychiatry, Box 980710, Richmond, VA 23298-0710. Virginia Commonwealth University is Equal Opportunity/Affirmative Action employer and encourages applications from women, minorities, and persons with disabilities.

Psychosomatic Medicine Fellowship, Portland, Oregon. Recruiting for 07/01/08 ACGME-accredited PGY5 level, at Oregon Health & Science Univ and Portland VA Med Center. Flexible program with clinical and research opportunities. Training sites include ambulatory care, specialty services, and consultation to inpatient med/surg. Research and clinical strengths in health services, mental disorders in primary care, pain, end-of-life/palliative care, ethics, mood disorders, Parkinson's disease, and substance abuse. Contact Dr. Steve Dobscha, Portland VA Med. Ctr., PO Box 1034 (R&D 66), Portland, OR 97207; (503) 220-8262, Ext. 156444; or at steven.dobscha@va.gov. EOE.

PSYCHOSOMATIC MEDICINE FELLOWSHIPS 7/08-6/09 NY Medical College/Westchester Medical Center

Established C/L Group in tertiary care hospital. 45 minutes from NYC. Opportunity to work in Burn, High-Risk OB, HIV, Transplant as well as General Med/Surg. Research opportunities. Psychiatry residency & NYS limited permit or license required. Competitive salary and benefits. Contact: Yvette Smolin, MD, Training Director, BHC Room N301, Valhalla, NY 10595 (914) 493-8424 y.smolin@worldnet.att.net

PSYCHOSOMATIC MEDICINE FELLOWSHIP UNIVERSITY OF MICHIGAN

A Psychosomatic Medicine fellowship position is available at the University of Michigan, Department of Psychiatry. The one-year fellowship program (PGY-5) provides a broad-based clinical experience, with a strong multidisciplinary emphasis, and opportunities to achieve skills in research, education and administration, in an extraordinarily rich academic environment, with no night or weekend on-call. Supervision is provided by full-time attendings with board certification in Psychosomatic Medicine. The fellowship begins on July 1, 2008. Excellent salary and benefits. Candidates must have completed an approved residency in Psychiatry and must have passed USMLE Step III prior to entry into program.

Applications will be accepted through January 15, 2008. Please email/mail/fax CV to Michelle Riba, MD, Associate Director, Psychosomatic Medicine Services, Department of Psychiatry, University of Michigan Health System, 1500 E. Medical Center Drive, Room F6236 MCHC, Ann Arbor, MI, 48109-0295. Tel: (734) 764-6879; FAX: (734) 936-1130; web: http://www.med.umich.edu/psych/education, Email: gacioch@umich.edu.

UNIVERSITY OF MICHIGAN GERIATRIC PSYCHIATRY FELLOWSHIP

ACGME-accredited Geriatric Psychiatry Fellowship at Univ. of Michigan and Ann Arbor VA Healthcare System (VAHS) available July 1, 2008. One-year fellowship program (PGY-5) provides broad-based clinical experience in inpatient, outpatient, nursing home settings, with unique multidisciplinary emphasis, in an extraordinarily rich academic environment. Two-year fellowship program (PGY-5 & 6) available to selected candidates and includes all clinical experience of one-year program, plus a research training component (available in basic, clinical and health services research) designed to prepare trainee for academic career. University has NIH-funded Geriatric Research and Training Center and Alzheimer's Disease Research Center, as well as the nation's first comprehensive academic Depression Center. VAHS has Geriatric Research, Educational and Clinical Center (GRECC). Candidates must have completed an approved U.S residency in Psychiatry, and must have passed USMLE Step III prior to entry into program. Applications accepted through November 15, 2007. Please send CV to Alan M. Mellow, M.D., Ph.D., Chief, University of Michigan Section of Geriatric Psychiatry at amell@umich.edu or MHSL/116MH, Ann Arbor VA Medical Ctr., 2215 Fuller Road, Ann Arbor, MI 48105

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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 atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of seventeen placebo controlled trials (modal duration of 10 weeks) in these patients revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times that seen 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. GEODON (ziprasidone) is not approved for the treatment of patients with Dementia-Related Psychosis.

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 atypical antipsychotic drugs are at an increased risk of death compared to placebo. 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/m² basis). Fertility rate was reduced at 160 mg/kg/day (8 times the MRHD on a mg/m² basis). There was no effect on fertility at 40 mg/kg/day (2 times the MRHD on a mg/m² 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. ***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).

References: 1. Daniel DG, Potkin SG, Reeves KR, Swift RH, Harrigan EP. Intramuscular (IM) ziprasidone 20 mg is effective in reducing acute agitation associated with psychosis: a double-blind, randomized trial. *Psychopharmacology*. 2001;155:128-134. **2.** Lesem MD, Zajecka JM, Swift RH, Reeves KR, Harrigan EP. Intramuscular ziprasidone, 2 mg versus 10 mg, in the short-term management of agitated psychotic patients. *J Clin Psychiatry*. 2001;62:12-18. **3.** Brook S, Walden J, Benattia I, Siu CO, Romano SJ. Ziprasidone and haloperidol in the treatment of acute exacerbation of schizophrenia and schizoaffective disorder: comparison of intramuscular and oral formulations in a 6-week, randomized, blinded-assessment study. *Psychopharmacology*. 2005;178:514-523. **4.** Brook S, Lucey JV, Gunn KP, for the Ziprasidone IM Study Group. Intramuscular ziprasidone compared with intramuscular haloperidol in the treatment of acute psychosis. *J Clin Psychiatry*. 2000;61:933-941. **5.** Data on file. Pfizer Inc, New York, NY.

Revised November 2006

Control acute agitation with

GEODON®

for ***Injection*** *(ziprasidone mesylate)*

In schizophrenia. . .

Rapid control* with low EPS[1-4]

- **Low incidence of movement disorders[1-4]**
- **Smooth transition, with continued improvement, from IM to oral therapy[3,4]**
- **May be used concomitantly with benzodiazepines[2,3,5]**

*In 2 pivotal studies vs control, significance was achieved at the 2-hour primary end point (10 mg study) and at the 4-hour primary end point (20 mg study).

GEODON®
Oral Capsules *(ziprasidone HCl)*
and ***Injection*** *(ziprasidone mesylate)*

GEODON for Injection is indicated for the treatment of acute agitation in schizophrenic patients for whom treatment with GEODON is appropriate and who need intramuscular antipsychotic medication for rapid control of the agitation.

Elderly patients with dementia-related psychosis treated with atypical 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 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.

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 fixed-dose, pivotal studies, the most commonly observed adverse events associated with the use of GEODON for Injection (incidence ≥5%) and observed at a rate in the higher GEODON dose groups (10 mg, 20 mg) of at least twice that of the lowest GEODON dose group (2 mg control) were somnolence (20%), headache (13%), and nausea (12%).

Please see brief summary of prescribing information on adjacent page.