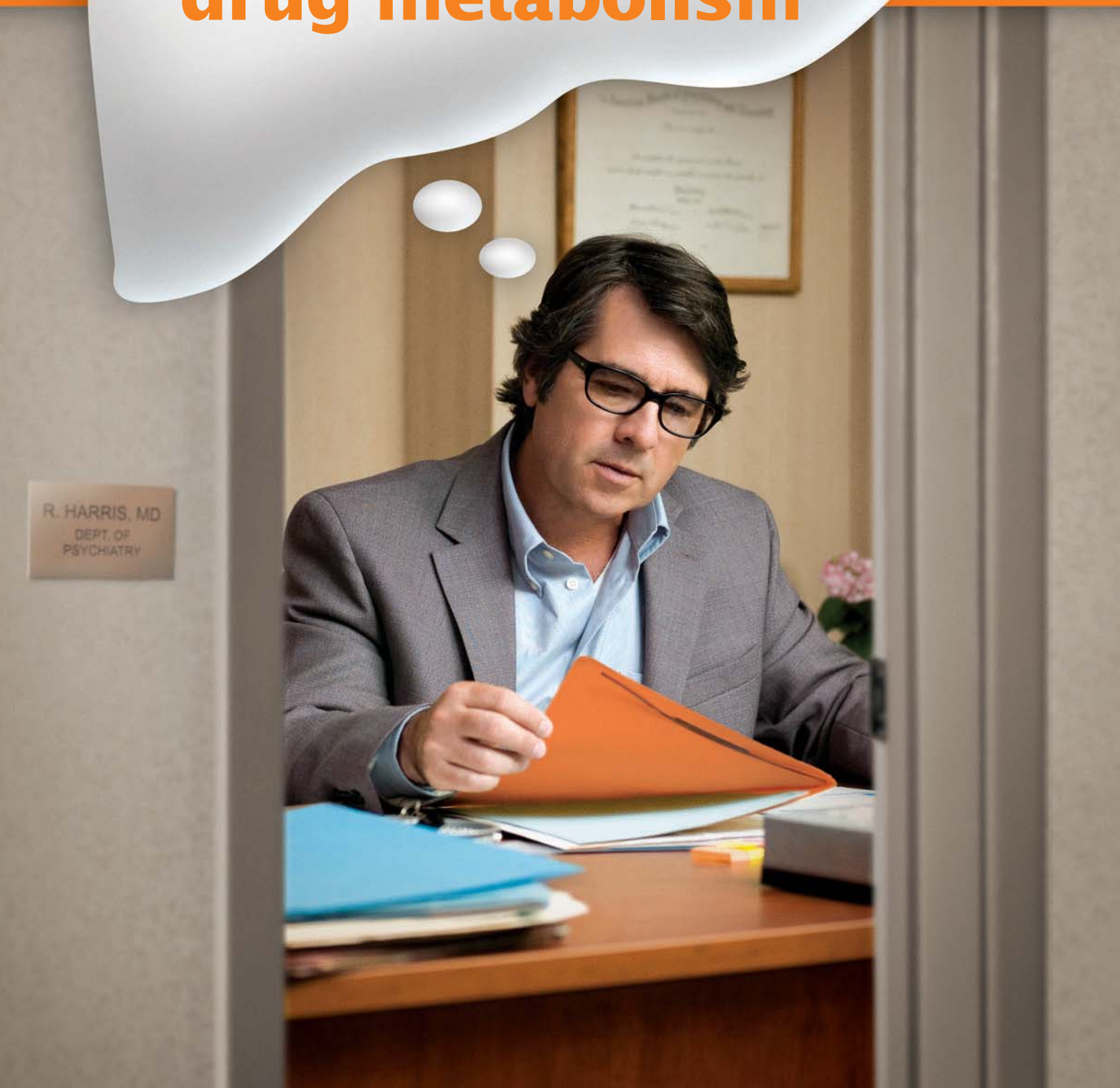
When treating patients with schizophrenia

# Think about drug metabolism



## CYP450 pathways play a limited role in the metabolism of INVEGA®

Less than 10% of the dose is metabolized by each of the 4 identified metabolic pathways (dealkylation, hydroxylation, dehydrogenation, and benzisoxazole scission)

## Primarily excreted unchanged via the kidneys

Total clearance of paliperidone was reduced in subjects with impaired renal function

# INVEGA®
PALIPERIDONE
*Extended-Release Tablets*

### IMPORTANT SAFETY INFORMATION FOR INVEGA®

**WARNING: Increased Mortality in Elderly Patients with Dementia-Related Psychosis**

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

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

**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.

**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.

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

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

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

**Potential for Gastrointestinal Obstruction:** 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.

**Orthostatic Hypotension and Syncope:** 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. Patients should be cautioned about operating hazardous machinery, including motor vehicles, until they are reasonably certain that INVEGA® does not affect them adversely.

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

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

**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.

**Drug Interactions:** Co-administration of INVEGA® 6 mg once daily with carbamazepine 200 mg twice daily caused a decrease of approximately 37% in the mean steady-state $C_{max}$ and AUC of paliperidone. On initiation or discontinuation of carbamazepine, the dose of INVEGA® should be re-evaluated and adjusted if necessary. Given the primary CNS effects of INVEGA®, INVEGA® should be used with caution in combination with other centrally acting drugs and the use of alcohol should be avoided.

**Extrapyramidal Symptoms (EPS):** Total EPS-related adverse events in the higher 9-mg and 12-mg treatment groups were 25% and 26%, respectively, versus 11% for the placebo group.

**Weight Gain:** The proportion of subjects having a weight gain of ≥7% body weight were comparable to placebo (5%) for 3 mg (7%) and 6 mg (6%). A higher incidence was seen for 9 mg (9%) and 12 mg (9%).

**Renal Impairment:** Dosing must be individualized according to the patient's renal function status. The maximum recommended dose of INVEGA® is 6 mg for patients with mild renal impairment and 3 mg for patients with moderate to severe renal impairment (see Dosing for Special Populations).

**Elderly:** No dosage adjustment is recommended based on age alone. However, dose adjustment may be required because of age-related decreases in creatinine clearance (see Dosing for Special Populations).

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

**Use with Risperidone:** Concomitant use of paliperidone with risperidone has not been studied. Since paliperidone is the major active metabolite of risperidone, consideration should be given to the additive paliperidone exposure if risperidone is co-administered.

**Please see brief summary of full Prescribing Information for INVEGA® on adjacent page.**

Janssen™
Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc.

www.invega.com

 June 2009 01JN09057A

# INVEGA®
(paliperidone) Extended-Release Tablets

**Brief Summary**
**BEFORE PRESCRIBING INVEGA®, PLEASE SEE FULL PRESCRIBING INFORMATION, INCLUDING BOXED WARNING.**

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

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

INVEGA® (paliperidone) Extended-Release Tablets are indicated for the acute and maintenance treatment of schizophrenia *[see Clinical Studies (14) in full PI]*.

**CONTRAINDICATIONS**
Hypersensitivity reactions, including anaphylactic reactions and angioedema, have been observed in patients treated with risperidone and paliperidone. INVEGA® (paliperidone) is a metabolite of risperidone and is therefore contraindicated in patients with a known hypersensitivity to either paliperidone or risperidone, or to any of the excipients in INVEGA®.

**WARNINGS AND PRECAUTIONS**
**Increased Mortality in Elderly Patients with Dementia-Related Psychosis: Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. INVEGA® (paliperidone) is not approved for the treatment of dementia-related psychosis *[see Boxed Warning]*.**

**Cerebrovascular Adverse Reactions, 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 reactions (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 and Warnings and Precautions]*.

**Neuroleptic Malignant Syndrome:** A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs, including paliperidone. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure.

The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to identify cases in which the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever, and primary central nervous system pathology.

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. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS.

If a patient appears to require antipsychotic drug treatment after recovery from NMS, reintroduction of drug therapy should be closely monitored, since recurrences of NMS have been reported.

**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=50) 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 ng/mL 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.

**Tardive Dyskinesia:** A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to predict which patients will develop the syndrome. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown.

The risk of developing tardive dyskinesia and the likelihood that it will become irreversible appear to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increase, but the syndrome can develop after relatively brief treatment periods at low doses, although this is uncommon.

There is no known treatment for established tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic treatment itself may suppress (or partially suppress) the signs and symptoms of the syndrome and may thus mask the underlying process. The effect of symptomatic suppression on the long-term course of the syndrome is unknown.

Given these considerations, INVEGA® should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic treatment should generally be reserved for patients who suffer from a chronic illness that is known to respond to antipsychotic drugs. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically.

If signs and symptoms of tardive dyskinesia appear in a patient treated with INVEGA®, drug discontinuation should be considered. However, some patients may require treatment with INVEGA® despite the presence of the syndrome.

**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. These cases were, for the most part, seen in post-marketing clinical use and epidemiologic studies, not in clinical trials, and there have been few reports of hyperglycemia or diabetes in trial subjects treated with INVEGA®. 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. Given these confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse events in patients treated with the atypical antipsychotics. Because INVEGA® was not marketed at the time these studies were performed, it is not known if INVEGA® is associated with this increased risk.

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. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.

**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.

Hyperprolactinemia, regardless of etiology, may suppress hypothalamic GnRH, resulting in reduced pituitary gonadotrophin secretion. This, in turn, may inhibit reproductive function by impairing gonadal steroidogenesis in both female and male patients. Galactorrhea, amenorrhea, gynecomastia, and impotence have been reported in patients receiving prolactin-elevating compounds. Long-standing hyperprolactinemia when associated with hypogonadism may lead to decreased bone density in both female and male subjects.

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 considered in a patient with previously detected breast cancer. 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 Nonclinical Toxicology (13.1) in full PI]*. 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.

**Potential for Gastrointestinal Obstruction:** 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 Dosage and Administration (2.2) and Patient Counseling Information (17.8) in full PI]*.

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.

**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 mg, 6 mg, 9 mg, 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 (e.g., dehydration, hypovolemia, and treatment with antihypertensive medications). Monitoring of orthostatic vital signs should be considered in patients who are vulnerable to hypotension.

**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.

**Seizures:** During premarketing clinical trials (the three placebo-controlled, 6-week, fixed-dose studies and a study conducted in elderly schizophrenic subjects), seizures occurred in 0.22% of subjects treated with INVEGA® (3 mg, 6 mg, 9 mg, 12 mg) and 0.25% of subjects treated with placebo. 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. Conditions that lower the seizure threshold may be more prevalent in patients 65 years or older.

**INVEGA®** (paliperidone) Extended-Release Tablets

**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. Prescriptions for INVEGA® should be written for the smallest quantity of tablets consistent with good patient management in order to reduce the risk of overdose.

**Priapism:** Drugs with alpha-adrenergic blocking effects have been reported to induce priapism. Priapism has been reported with INVEGA® during postmarketing surveillance. Severe priapism may require surgical intervention.

**Thrombotic Thrombocytopenic 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, e.g., exercising strenuously, exposure to extreme heat, receiving concomitant medication with anticholinergic activity, or being subject to dehydration.

**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 (12.3) 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 Warnings and Precautions]*.

**Monitoring: Laboratory Tests:** No specific laboratory tests are recommended.

**ADVERSE REACTIONS**

The following are discussed in more detail in other sections of the labeling:

- Increased mortality in elderly patients with dementia-related psychosis *[see Boxed Warning and Warnings and Precautions]*
- Cerebrovascular adverse events, including stroke, in elderly patients with dementia-related psychosis *[see Warnings and Precautions]*
- Neuroleptic malignant syndrome *[see Warnings and Precautions]*
- QT prolongation *[see Warnings and Precautions]*
- Tardive dyskinesia *[see Warnings and Precautions]*
- Hyperglycemia and diabetes mellitus *[see Warnings and Precautions]*
- Hyperprolactinemia *[see Warnings and Precautions]*
- Potential for Gastrointestinal Obstruction *[see Warnings and Precautions]*
- Orthostatic hypotension and syncope *[see Warnings and Precautions]*
- Potential for cognitive and motor impairment *[see Warnings and Precautions]*
- Seizures *[see Warnings and Precautions]*
- Dysphagia *[see Warnings and Precautions]*
- Suicide *[see Warnings and Precautions]*
- Priapism *[see Warnings and Precautions]*
- Thrombotic thrombocytopenic purpura (TTP) *[see Warnings and Precautions]*
- Disruption of body temperature regulation *[see Warnings and Precautions]*
- Antiemetic effect *[see Warnings and Precautions]*
- Increased sensitivity in patients with Parkinson's disease or those with dementia with Lewy bodies *[see Warnings and Precautions]*
- Diseases or conditions that could affect metabolism or hemodynamic responses *[see Warnings and Precautions]*

The most common adverse reactions in clinical trials (reported in 5% or more of subjects treated with INVEGA® and at least twice the placebo rate in any of the dose groups) were akathisia and extrapyramidal disorder.

The most common adverse reactions that were associated with discontinuation from clinical trials (causing discontinuation in 2% of INVEGA®-treated subjects) were nervous system disorders *[see Adverse Reactions]*.

The safety of INVEGA® was evaluated in 1205 adult subjects with schizophrenia who participated in three placebo-controlled, 6-week, double-blind trials, of whom 850 subjects received INVEGA® at fixed doses ranging from 3 mg to 12 mg once daily. The information presented in this section was derived from pooled data from these three trials. 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 mg to 15 mg (n=104), is also included.

Adverse events during exposure to study treatment were obtained by general inquiry and recorded by clinical investigators using their own terminology. Consequently, to provide a meaningful estimate of the proportion of individuals experiencing adverse events, events were grouped in standardized categories using MedDRA terminology.

Throughout this section, adverse reactions are reported. Adverse reactions are adverse events that were considered to be reasonably associated with the use of INVEGA® (adverse drug reactions) based on the comprehensive assessment of the available adverse event information. A causal association for INVEGA® often cannot be reliably established in individual cases. Further, because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

**Commonly-Observed Adverse Reactions in Double-Blind, Placebo-Controlled Clinical Trials:** *Table 1* enumerates the pooled incidences of adverse reactions reported in the three placebo-controlled, 6-week, fixed-dose studies, listing those 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.

**Table 1. Adverse Reactions in Short-Term, Fixed-Dose, Placebo-Controlled Trials in Adult Subjects with Schizophrenia*: Body System or Organ Class** Dictionary-derived Term followed by **Percent of Patients Reporting Event Placebo (N=355)** first, **INVEGA® 3 mg once daily (N=127)** second, **6 mg once daily (N=235)** third, **9 mg once daily (N=246)** fourth, **12 mg once daily (N=242)** fifth: **Total percentage of subjects with adverse reactions** 37, 48, 47, 54, 60; **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; **Gastrointestinal disorders:** Abdominal pain upper 1, 1, 3, 2, 2; Dry mouth 1, 2, 3, 1, 3; Salivary hypersecretion <1, 0, <1, 1, 4; **General disorders:** Asthenia 1, 2, <1, 2, 2; Fatigue 1, 2, 1, 2, 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; **Vascular disorders:** Orthostatic hypotension 1, 2, 1, 2, 4. *Table includes adverse reactions 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 study included once-daily INVEGA® doses of 3 mg and 9 mg, the second study included 6 mg, 9 mg, and 12 mg, and the third study included 6 mg and 12 mg *[see Clinical Studies (14) in full PI]).* Adverse reactions for which the INVEGA® incidence was equal to or less than placebo are not listed in the table, but included the following: vomiting.

**Less Commonly-Observed Adverse Reactions:** The following list contains all serious and non-serious adverse reactions 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.

**Cardiac disorders:** bradycardia, palpitations

**Gastrointestinal disorders:** abdominal pain, swollen tongue

**General disorders:** edema

**Immune system disorders:** anaphylactic reaction

**Vascular disorders:** ischemia

**Discontinuations Due to Adverse Reactions:** The percentages of subjects who discontinued due to adverse reactions in the three placebo-controlled, 6-week, fixed-dose studies were 3% and 1% in INVEGA®- and placebo-treated subjects, respectively. The most common reasons for discontinuation were nervous system disorders (2% and 0% in INVEGA®- and placebo-treated subjects, respectively).

**Dose-Related Adverse Reactions:** Based on the pooled data from the three placebo-controlled, 6-week, fixed-dose studies, among the adverse reactions that occurred with a greater than 2% incidence in the subjects treated with INVEGA®, the incidences of the following adverse reactions increased with dose: somnolence, orthostatic hypotension, akathisia, dystonia, extrapyramidal disorder, hypertonia, Parkinsonism, and salivary hypersecretion. For most of these, the increased incidence was seen primarily at the 12 mg dose, and, in some cases, the 9 mg dose.

**INVEGA®** (paliperidone) Extended-Release Tablets

**Demographic Differences:** 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 gender or race alone; there was also no difference on the basis of age *[see Use in Specific Populations]*.

**Extrapyramidal Symptoms (EPS):** 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 (*Table 2*), and (4) incidence of spontaneous reports of EPS (*Table 3*). 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.

**Table 2. Treatment-Emergent Extrapyramidal Symptoms (EPS) Assessed by Incidence of Ratings Scales and Use of Anticholinergic Medication: EPS Group** followed by **Percentage of Patients Placebo (N=355)** first, **INVEGA® 3 mg once daily (N=127)** second, **6 mg once daily (N=235)** third, **9 mg once daily (N=246)** fourth, **12 mg once daily (N=242)** fifth, 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

**Table 3. Treatment-Emergent Extrapyramidal Symptoms (EPS)-Related Adverse Events by MedDRA Preferred Term: EPS Group** followed by **Percentage of Patients Placebo (N=355)** first, **INVEGA® 3 mg once daily (N=127)** second, **6 mg once daily (N=235)** third, **9 mg once daily (N=246)** fourth, **12 mg once daily (N=242)** fifth, Overall percentage of patients with EPS-related AE 11, 13, 10, 25, 26; Dyskinesia 3, 5, 3, 8, 9; Dystonia 1, 1, 1, 5, 5; Hyperkinesia 4, 4, 3, 8, 10; Parkinsonism 2, 3, 3, 7, 6; Tremor 3, 3, 3, 4, 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

**Laboratory Test Abnormalities:** In the pooled data from the three placebo-controlled, 6-week, fixed-dose studies, a between-group comparison revealed no medically important differences between INVEGA® and placebo in the proportions of subjects experiencing potentially clinically significant changes in routine serum chemistry, hematology, or urinalysis parameters. Similarly, there were no differences between INVEGA® and placebo in the incidence of discontinuations due to changes in hematology, urinalysis, or serum chemistry, including mean changes from baseline in fasting glucose, insulin, c-peptide, triglyceride, HDL, LDL, and total cholesterol measurements. However, INVEGA® was associated with increases in serum prolactin *[see Warnings and Precautions]*.

**Weight Gain:** In the pooled data from the three placebo-controlled, 6-week, fixed-dose studies, the proportions of subjects meeting a weight gain criterion of ≥ 7% of body weight were compared, revealing a similar incidence of weight gain for INVEGA® 3 mg and 6 mg (7% and 6%, respectively) compared with placebo (5%), and a higher incidence of weight gain for INVEGA® 9 mg and 12 mg (9% and 9%, respectively).

**Other Findings Observed During Clinical Trials:** 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 Studies (14) in full PI]*. In general, adverse reaction 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 reactions 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.

**Postmarketing Experience:** The following adverse reaction has been identified during postapproval use of INVEGA®; because this reaction was reported voluntarily from a population of uncertain size, it is not possible to reliably estimate its frequency: priapism.

**Adverse Reactions Reported With Risperidone:** Paliperidone is the major active metabolite of risperidone. Adverse reactions reported with risperidone can be found in the ADVERSE REACTIONS section of the risperidone package insert.

**DRUG INTERACTIONS**

**Potential for INVEGA® to Affect Other Drugs:** 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 Warnings and Precautions]*.

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.

Paliperidone is a weak inhibitor of P-glycoprotein (P-gp) at high concentrations. No *in vivo* data are available and the clinical relevance is unknown.

**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. *In vitro* studies have shown that paliperidone is a P-gp substrate.

Co-administration of INVEGA® 6 mg once daily with carbamazepine 200 mg twice daily caused a decrease of approximately 37% in the mean steady-state Cmax and AUC of paliperidone. This decrease is caused, to a substantial degree, by a 35% increase in renal clearance of paliperidone. A minor decrease in the amount of drug excreted unchanged in the urine suggests that there was little effect on the CYP metabolism or bioavailability of paliperidone during carbamazepine co-administration. On initiation of carbamazepine, the dose of INVEGA® should be re-evaluated and increased if necessary. Conversely, on discontinuation of carbamazepine, the dose of INVEGA® should be re-evaluated and decreased if necessary.

Paliperidone is metabolized to a limited extent by CYP2D6 *[see Clinical Pharmacology (12.3) in full PI]*. In an interaction study in healthy subjects in which a single 3 mg dose of INVEGA® was administered concomitantly with 20 mg per day of paroxetine (a potent CYP2D6 inhibitor), paliperidone exposures were on average 16% (90% CI: 4, 30) higher in CYP2D6 extensive metabolizers. Higher doses of paroxetine have not been studied. The clinical relevance is unknown.

**USE IN SPECIFIC POPULATIONS**

**Pregnancy:** Pregnancy Category C: 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.

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.

In animal reproduction studies, there were no increases in fetal abnormalities when pregnant rats and rabbits were treated during the period of organogenesis with up to 8 times the maximum recommended human dose of paliperidone (on a mg/m$^2$ basis).

In rat reproduction studies with risperidone, which is extensively converted to paliperidone in rats and humans, there were increases in pup deaths 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).

**Labor and Delivery:** The effect of INVEGA® on labor and delivery in humans is unknown.

**Nursing Mothers:** Paliperidone is 9-hydroxyrisperidone, the active metabolite of risperidone. In animal studies, risperidone and 9-hydroxyrisperidone were excreted in milk. Risperidone and 9-hydroxyrisperidone are also excreted in human breast milk. Caution should be exercised when INVEGA® is administered to a nursing woman. The known benefits of breastfeeding should be weighed against the unknown risks of infant exposure to paliperidone.

**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 mg 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 mg to 15 mg once daily) *[see Clinical Studies (14) 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 (12.3) 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 (2.4) in full PI]*.

**Renal Impairment:** Dosing must be individualized according to the patient's renal function status *[see Dosage and Administration (2.4) in full PI]*.

**Hepatic Impairment:** No dosage adjustment is required in patients with mild to moderate hepatic impairment. INVEGA® has not been studied in patients with severe hepatic impairment.

**PATIENT COUNSELING INFORMATION**

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 *[see Warnings and Precautions]*.

**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 *[see Warnings and Precautions]*.

**Pregnancy:** Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during treatment with INVEGA® *[see Use in Specific Populations]*.

**Nursing:** Caution should be exercised when INVEGA® is administered to a nursing woman. The known benefits of breastfeeding should be weighed against the unknown risks of infant exposure to paliperidone. *[See Use in Specific Populations]*.

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

**Alcohol:** Patients should be advised to avoid alcohol while taking INVEGA® *[see Drug Interactions]*.

**Heat Exposure and Dehydration:** Patients should be advised regarding appropriate care in avoiding overheating and dehydration *[see Warnings and Precautions]*.

**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 *[see Dosage and Administration (2.2) in full PI]*.

Manufactured by:
ALZA Corporation
Mountain View, CA 94043
OR
Janssen Cilag Manufacturing, LLC
Gurabo, Puerto Rico 00778


Manufactured for:
Janssen, Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc.
Titusville, NJ 08560



10105904B
Revised: December 2008

01JN08030BS

# SEE ME FOR WHO I CAN BE

Lisa, 32*
Part-time Caterer
Diagnosis: Bipolar Disorder
Recent Episode: Mixed

*Not an actual patient.

## Do you see your patients' full potential?

GEODON is indicated for the treatment of acute manic or mixed episodes associated with bipolar disorder, with or without psychotic symptoms.

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

GEODON is contraindicated in patients with a known history of QT prolongation, recent acute myocardial infarction, or uncompensated heart failure, and should not be used with certain other QT-prolonging drugs. **GEODON has been associated with prolongation of the $QT_c$ interval. In some drugs, QT prolongation has been associated with torsade de pointes, a potentially fatal arrhythmia. Patients who are at risk for significant electrolyte disturbances should have baseline measurements performed before initiating GEODON. Patients on diuretics should be monitored.**

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.

*Please see brief summary of prescribing information on adjacent page.*

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

**GEODON®**
(ziprasidone HCl) **Capsules**

**BRIEF SUMMARY.** See package insert for full prescribing information.

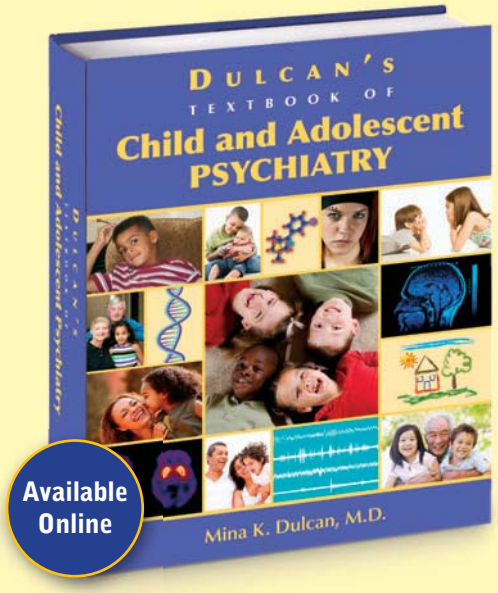
**Increased Mortality in Elderly Patients with Dementia-Related Psychosis—**Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical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

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

**CONTRAINDICATIONS** — ***QT Prolongation:*** Because of GEODON's dose-related prolongation of the QT interval and the known association of fatal arrhythmias with QT prolongation by some other drugs, GEODON is contraindicated in patients with a known history of QT prolongation (including congenital long QT syndrome), with recent acute myocardial infarction or with uncompensated heart failure (see **WARNINGS**). Pharmacokinetic, pharmacodynamic studies between GEODON and other drugs that prolong the QT interval have not been performed. An additive effect of GEODON and other drugs that prolong the QT interval cannot be excluded. Therefore, GEODON should not be given with chlorpromazine, mesoridazine, thioridazine, chlorpromazine, droperidol, pimozide, sparfloxacin, gatifloxacin, moxifloxacin, halofantrine, mefloquine, pentamidine, arsenic trioxide, levomethadyl acetate, dofetilide, or ibutilide mesylate, probucol or tacrolimus. GEODON is also contraindicated for use with drugs that have demonstrated QT prolongation as one of their pharmacodynamic effects and have this effect described in the prescribing information as a contraindication or a boxed or bolded warning (see **WARNINGS**). GEODON is contraindicated in individuals with a known hypersensitivity to the product. **WARNINGS** — ***Increased Mortality in Elderly Patients with Dementia-Related Psychosis:*** **Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. GEODON (ziprasidone) is not approved for the treatment of patients with dementia-related psychosis (see BOXED WARNING).** ***QT Prolongation and Risk of Sudden Death:*** **GEODON use should be avoided in combination with other drugs that are known to prolong the QT$_c$ interval. Additionally, clinicians should be alert to the identification of other drugs that have been consistently observed to prolong the QT$_c$ interval. Such drugs should not be prescribed with GEODON. A study directly comparing the QT/QT$_c$-prolonging effect of GEODON with several other drugs effective in the treatment of schizophrenia was conducted in patient volunteers. The mean increase in QT$_c$ from baseline for GEODON ranged from approximately 9 to 14 msec greater than for four of the comparator drugs (risperidone, olanzapine, quetiapine, and haloperidol), but was approximately 14 msec less than the prolongation observed for thioridazine. In this study, the effect of GEODON on QT$_c$ length was not augmented by the presence of a metabolic inhibitor (ketoconazole 200 mg bid). In placebo-controlled trials, GEODON increased the QT$_c$ interval compared to placebo by approximately 10 msec at the highest recommended daily dose of 160 mg. In clinical trials the electrocardiograms of 2/2988 (0.06%) GEODON patients and 1/440 (0.23%) placebo patients revealed QT$_c$ intervals exceeding the potentially clinically relevant threshold of 500 msec. In the GEODON patients, neither case suggested a role of GEODON. Some drugs that prolong the QT/QT$_c$ interval have been associated with the occurrence of torsade de pointes and with sudden unexplained death. The relationship of QT prolongation to torsade de pointes is clearest for larger increases (20 msec and greater) but it is possible that smaller QT/QT$_c$ prolongations may also increase risk, or increase it in susceptible individuals, such as those with hypokalemia, hypomagnesemia, or genetic predisposition. Although torsade de pointes has not been observed in association with the use of GEODON at recommended doses in premarketing studies, experience is too limited to rule out an increased risk. A study evaluating the QT/QT$_c$ prolonging effect of intramuscular GEODON, with intramuscular haloperidol as a control, was conducted in patient volunteers. In the trial, ECGs were obtained at the time of maximum plasma concentration following two injections of GEODON (20 mg then 30 mg) or haloperidol (4.5 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 4.8 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, e.g., 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 concurrent 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 cases of skin rash had signs and symptoms of associated systemic illness, e.g., elevated WBCs. Most patients in all rash groups improved promptly upon treatment with anti-histamines 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 alpha adrenergic antagonism properties. Syncope was reported in 0.8% 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. No clinical studies or 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 of 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 their 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:*** If GEODON should 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 or dopamine agonists. Effect of Other Drugs on GEODON: *Carbamazepine* 200 mg bid for 21 days results in a decrease of approximately 35% in the AUC of GEODON. *Ketoconazole*, a potent inhibitor of CYP3A4, 400 mg qd for 5 days, increases the AUC and C$_{max}$ of GEODON by about 35%–40%. *Cimetidine*, 800 mg qd for 2 days, did not affect GEODON pharmacokinetics. Dosing with an oral dose 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 the 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. There is no evidence for human risk of the findings of prolactin-related 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 3 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 to 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, the excess no indication of any different tolerability for GEODON 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 slower 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% (102/2/9) 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 the discontinuation of 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 (13%), abnormal vision (6%), asthenia (6%), and vomiting (5%). The following listing 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, akathisia, 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 do not generally show a difference between GEODON and placebo. ***Dystonia:*** Prolonged abnormal contractions of muscle groups may occur in susceptible individuals during first few days of treatment. Dystonia may occur at any dose level but with greater frequency and severity with high potency and at higher doses of first-generation antipsychotic drugs. Elevated risk is observed in males and younger age groups. ***Vital Sign Changes:*** GEODON is associated with orthostatic hypotension (see **PRECAUTIONS**). ***Weight Gain:*** In short-term schizophrenia trials, the proportions of patients meeting a weight gain criterion of ≥7% of body weight were compared, revealing a statistically significantly greater incidence of weight gain for GEODON patients (10%) vs placebo patients (4%). A median weight gain of 0.5 kg was observed in GEODON patients vs 0.0 kg in placebo patients. Weight gain was reported as an adverse event in 0.4% of both GEODON and placebo patients. During long-term therapy with GEODON, a categorization of patients at baseline on the basis of body mass index (BMI) showed the greatest mean weight gain and the highest incidence of clinically significant weight gain (≥7% of body weight) in patients with a low BMI (<23) compared to normal (23–27) or overweight (>27) patients. There was a mean weight gain of 1.4 kg for patients with a "low" baseline BMI (<20 kg/m$^2$) 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:* tachycardia, 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, tenesmus. — *Rare:* hypothyroidism, hyperthyroidism, thyroiditis. Hemic and Lymphatic System — *Infrequent:* anemia, ecchymosis, leukocytosis. *Rare:* 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, hypercholesterolemia, dehydration, lactic dehydrogenase increased, albuminuria, hypokalemia. *Rare:* BUN increased, creatinine increased, hyperlipemia, hypercholesterolemia, hypercalcemia, hypocholesterolemia, hypoglycemia, hypocalcemia, hyperglycemic 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, hypesthesia, abnormal gait, oculogyric crisis, hypesthesia, ataxia, amnesia, coma, hyperkinesia, hypotonia, akinesia, dysarthria, withdrawal syndrome, buccoglossa syndrome, choreoathetosis, diplopia, incoordination, neuropathy. *Infrequent:* paralysis. *Rare:* myoclonus, nystagmus, torticollis, oculogyric crisis, 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, seborrhea, cellulitis, nail disorder. Special Senses — *Frequent:* fungal dermatitis. *Infrequent:* conjunctivitis, dry eyes, tinnitus, blepharitis, cataract, chorioretinal abnormalities. *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:* pyelonephritis, vaginal hemorrhage, nocturia, anuria, 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 group(s) 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 listing 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, mouth and tongue ulcerations. Nervous — dizziness, anxiety, insomnia, somnolence, akathisia, agitation, extrapyramidal syndrome, hypertonia, cogwheel rigidity, paresthesia, personality disorder, dyskinesia, speech disorder. Respiratory — rhinitis. Skin and Appendages — 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 (1920 mg), the only symptoms reported were minimal sedation, slurring of speech, and transitory hypertension (BP 200/95).

Revised August 2008




**Coming October 2009!**

# Dulcan's Textbook of Child and Adolescent Psychiatry

## Edited by Mina K. Dulcan, M.D.

*Special Prepublication Price of 215.00*
*until October 31, 2009 (thereafter $239.00)*

*Dulcan's Textbook of Child and Adolescent Psychiatry* supplants the previous textbook edited by Jerry Wiener and Mina Dulcan—not with a new edition, but rather a new book that offers a fresh look at the field of child mental health. It preserves Wiener's vision of a clinically focused textbook useful to trainees and practitioners in a variety of specialties, providing the most up-to-date and comprehensive text in child and adolescent psychiatry as presented by more than 110 contributors who distill their knowledge and expertise into a single authoritative volume.

Each chapter highlights what we know about evidence-based practices in assessment and treatment, while sections on future research point toward current pressing questions. At the end of each chapter are educational summary points. Of the 65 chapters, 56 feature new lead authors, chosen to represent the expertise of disciplines ranging from pediatrics and neurology to sleep medicine and family therapy.

### Among its key features:

- Chapters on evaluation are developmentally focused, with a separate chapter for each age range.
- The section on diagnosis and assessment has been reconfigured and includes a new chapter on neurological examination and the use of EEG and imaging.
- Eighteen chapters on specific disorders encompass clinical description, diagnosis, epidemiology, comorbidity, etiology, prevention, prognosis, evaluation, treatment approaches, and research directions.
- Special topics include new chapters on bereavement and traumatic grief; ethnic, cultural, and religious issues; aggression and violence; and fundamentals of genetics relevant to child and adolescent psychiatry.
- Additional chapters address special clinical considerations such as children of ill parents AND legal/ethical issues
- Wide-ranging emphasis on treatment—expanded from seven to eighteen chapters—includes psychopharmacology, brain-based innovative treatments, and a spectrum of psychosocial approaches that focus on individual, family, therapeutic milieu, and systemic models of care.
- A new section on consultation provides guidance on interactions with schools, primary care practitioners, and the juvenile justice system.

Scholarly and practical, *Dulcan's Textbook of Child and Adolescent Psychiatry* is a core resource for child and adolescent psychiatry training and will also serve as a reference for practitioners in psychiatry, pediatrics, neurology, psychology, nursing, and social work.

American Psychiatric Publishing, Inc.
The *First* and *Last* Word in Psychiatry

2010 • 1,104 pages • ISBN 978-1-58562-323-5 • Hardcover • Item #62323
Special Prepublication Price of $215.00 until October 31, 2009 (thereafter $239.00)

**Order Online: www.appi.org • Toll Free: 1-800-368-5777**
**Fax: 703-907-1091 • Email: appi@psych.org** • Find us on Facebook and Twitter. AH938

# NEW YORK CITY

## OCTOBER 8–11, 2009

**Save the date now to attend the American Psychiatric Association's 61st Institute on Psychiatric Services, APA's leading educational conference on clinical issues and community mental health to meet the service needs of people with severe mental illness. Check out our website at www.psych.org/IPS.**

## *Pride and Practice: Bringing Innovation Into Our Treatments*

This four-day event will feature popular networking events, more than 100 exhibits that complement the educational program, and over 200 expertly-led educational sessions on topics including: Violence, Trauma, and Victimization; Social and Community Psychiatry; Psychopharmacology; Resident and Medical Student Concerns; Disorders; Cross-Cultural and Minority Issues; Child and Adolescent Issues; Treatment Techniques and Outcome Studies; Cognitive Disorders; Health Service Research; Mood Disorders; Schizophrenia, Addiction, and much more…

### Who Should Attend?

- All APA Members
- Psychiatrists and mental health professionals in community practice or the public sector, including state and Veterans Affairs hospitals, community clinics, jails and prisons
- Psychiatric Administrators
- Mental health professionals interested in social issues that have an impact on patients and their families
- Minority psychiatrists and International Medical Graduates
- Psychiatric Residents (only $60 for advance registration)
- Nonmember Residents and Advocacy Group Members (only $85 for advance registration)
- Medical Students (free registration)

### Why Should You Attend?

- This activity has been approved for CME credit and CEs have been applied for
- Receive a 40% discount on APA member registration fees
- Network with colleagues at receptions and other events
- Valuable exhibit hall prizes drawn each day
- Immersion Courses are NEW and FREE this year. They offer intensive all day sessions which will provide a new and clinically applicable skill set to attendees. A certificate of participation/certification will be available for all courses.

The IPS is going "GREEN" this year; therefore, the ***Preliminary Program***, which includes registration, housing, travel, and detailed program information is available online only at www.psych.org/IPS.

61st Institute on Psychiatric Services
APA's Leading Educational Conference on Public and Community Psychiatry

*For more information, please contact:*
American Psychiatric Association
1000 Wilson Blvd., Suite 1825
Arlington, VA 22209-3901
Phone: 1-888-35-PSYCH
or (703) 907-7300
Fax: (703) 907-1090
E-mail: apa@psych.org
Web: www.psych.org/IPS

Drexel UNIVERSITY

Co-sponsored by
Drexel University College of Medicine/
Behavioral Healthcare Education

*Maimonides is Brooklyn's premier specialty care teaching hospital. We pioneer medical breakthroughs, boast state-of-the-art clinical and information technology, train more medical residents than other hospitals in Brooklyn and regularly win awards from independent evaluators for the quality of our care. We are compassionate, patient-centered and focused on employee participation and development. Our Physicians are not only highly trained specialists and medical educators, they are caring men and women who recognize the emotional, psychosocial and spiritual dimensions to illness.*

## Vice Chair, Director of Psychiatry Residency Training Program

We currently have a Full Time position available in our expanding Psychiatry department to direct our accredited four-year program of 27 residents and coordinate the Department's medical educational activities. You will be responsible for oversight of training activities and maintaining compliance with residency training standards. Board certification in psychiatry and experience in training of psychiatry residents required. Candidates should have clinical and administrative experience in psychiatric education.

We offer a competitive compensation and a comprehensive benefits package. Please send your CV to: **C/O Andrew Kolodny, MD, Chair of Psychiatry email: resumes@maimonidesmed.org or fax: 718-283-6540.** EOE.

Maimonides
Medical Center
www.maimonidesmed.org

**Passionate About Medicine. Compassionate About People.**

## PSYCHIATRISTS

*The VA Needs You*

| | | |
|---|---|---|
| Shreveport, LA<br>Alexandria, LA<br>Biloxi, MS<br>Jackson, MS | Pensacola, FL<br>Mt. Vernon, MO<br>Muskogee, OK | Fayetteville, AR<br>Fort Smith, AR<br>Mobile, AL |

Psychiatrist positions require: BE/BC Psychiatrists, current, full, unrestricted licensure (any state), U.S. citizen Great Benefits, Excellent Pay, Rewarding Work. See announcements on www.vacareers.va.gov. Recruitment/Relocation incentives may be authorized, ask contact individual for details.

**BILOXI/PENSACOLA** Outpatient and Inpatient Psychiatry positions. Expertise in substance abuse, geropsychiatry and PTSD preferred. BE/BC psychiatrist, state license (any state), U.S. citizen or permanent resident. Send applications to Jean Williams, HRMS (05A), 400 Veterans Avenue, Biloxi, MS or contact at jean.williams@med.va.gov or (228) 523-5633.

**ALEXANDRIA** Strong Clinical Skills. Prefer experience in General Outpatient, Inpatient Psychiatry, and Substance Abuse. CV/Application to heather.ball@va.gov or mail to Heather Ball/Psychiatry Service (116), P.O. Box 69004, Alexandria, LA 71306-9004. For additional questions, please call (318) 466-2958.

**SHREVEPORT** Prefer experience in general psychiatry, including inpatient, outpatient, consultative, or telemedicine psychiatry. Interested candidates should submit a CV to Sherri Collier, Human Resources (05), Overton Brooks VA Medical Center, 510 E. Stoner Ave, Shreveport, LA 71101 or via email: sherri.collier@va.gov phone: (318) 990-5147.

**FAYETTEVILLE, FORT SMITH, ARKANSAS; BRANSON, MISSOURI** Contact Betty Gray (479)443-4301 ext 5188 or email: betty.gray@va.gov.

**MUSKOGEE, OK** Contact Jason Cleveland, HRMS at 918-577-3800.

**JACKSON, MISSISSIPPI** Duties may involve several aspects of general psychiatry, including inpatient, outpatient, consultative, or telemedicine psychiatry. Interested candidates should submit a CV to Felicia Owens, Human Resources (05P), VA Medical Center, 1500 E. Woodrow Wilson Dr., Jackson, MS 39216 or Felicia.owens@va.gov phone: 601-364-1575. Equal Opportunity Employer.

# Chair, Department of Psychiatry

UMDNJ-Robert Wood Johnson Medical School seeks candidates for the position of Chair, Department of Psychiatry. Closely affiliated with University Behavioral Health Care, one of the largest behavioral health care organizations in the country, the Department has an energetic and productive faculty. Prominent departmental research and clinical programs include consult-liaison/psychosomatics, child/adolescent psychiatry and addictions. Located in Central New Jersey, midway between Philadelphia and New York, the Department has close geographic and collaborative ties with Rutgers and Princeton Universities as well as the area's great concentration of pharmaceutical companies.

The successful candidate will have a MD or MD/PhD, be Board certified, and eligible for licensure in New Jersey. The individual will have international stature in Psychiatry, a history of productive research and scholarship, and serve as a role model and catalyst for intellectual attainment. We seek an outstanding clinician and proven administrator with demonstrated success in developing and implementing programs. A strong commitment to teaching is vital. The individual should be known for personal and professional integrity, excellent interpersonal skills as well as political astuteness, and should be able to articulate a vision for the Department while conveying a sense of energy, openness, and optimism with a collaborative, consensus-building, yet decisive management style.

As one of the nation's leading comprehensive medical schools, Robert Wood Johnson Medical School of the University of Medicine and Dentistry of New Jersey is dedicated to the pursuit of excellence in education, research, health care delivery, and the promotion of community health. In cooperation with Robert Wood Johnson University Hospital, the medical school's principal affiliate, they comprise New Jersey's premier academic health center.

With 2,800 full-time and volunteer faculty, Robert Wood Johnson Medical School encompasses 22 basic science and clinical departments and 6 major institutes. The medical school maintains educational programs at the undergraduate, graduate and postgraduate levels for more than 1,500 students and provides continuing education courses for health care professionals and community education programs.

Review of applications will begin immediately and will continue until the ideal candidate is chosen. Please send letters of nomination and/or application and curriculum vitae to: **Frederick Lepore, MD, Chair of Search Committee, c/o Bonnie Baloga-Altieri, PhD, RN, Director of Administration, Office of the Dean, UMDNJ-Robert Wood Johnson Medical School, 125 Paterson Street, Suite 1400, New Brunswick, NJ 08901, Email: balogabl@umdnj.edu.** UMDNJ is an Affirmative Action/Equal Opportunity Employer. For more information, visit www.umdnj.edu/hrweb.

UMDNJ
ROBERT WOOD JOHNSON MEDICAL SCHOOL
University of Medicine & Dentistry of New Jersey

# Seeking the best: PSYCHIATRISTS

Align your talents and experience with Saudi Aramco and discover the unique advantages this world-leader in petroleum exploration and production offers you and your family in Saudi Arabia.

Work in Saudi Aramco's 350-bed, JCI-accredited hospital and experience rewards both personally and professionally - competitive compensation, six weeks' vacation with paid travel, an outstanding package of benefits, and a quality, family-oriented lifestyle.

You'll need to have three (3) years of experience in a psychiatric residency program approved by the American Board of Psychiatry & Neurology and at least two (2) years as a full-time Psychiatrist, after training.

**For complete details and to apply, visit: www.aramco.jobs/ajp**

ارامكو السعودية
Saudi Aramco

## Mental Health Care Professionals

**Psychiatrists/Psychologists/Social Workers**
**Clinical Nurse Specialists/Addiction Therapists**

Join VA Northern California Health Care System's (NCHCS) mental health care team and support America's heroes. NCHCS is now hiring mental health care professionals to be part of our interdisciplinary care team; you'll treat patients struggling with the full range of emotional and mental disorders, including PTSD, traumatic brain injuries, mood disorders, substance abuse disorders, and sexual trauma. You'll work in an environment where innovation is encouraged and scientific evidence directs our practice.

We are now hiring for full and part time positions in Sacramento, Fairfield, Redding and Chico. Call today and be a part of VA's Mental Health Enhancement Initiative.

- Interdisciplinary care team model of practice
- Practice model is based on care needs, not insurance company regulations
- Your out of state license allows you to practice at any of our facilities
- Diverse professional opportunities – clinical, leadership, research, education, and national policy development
- Salary is competitive and based on credentials and experience
- Exceptional paid time off package
- Excellent health and retirement benefits
- Student loan reimbursement of up to $38,000 for psychiatrists, psychologists and psychiatric nurses

Please email Mary Silva, Human Resources Specialist at **mary.silva@va.gov**

**Department of Veterans Affairs an Equal Opportunity Employer**

## Director, VA Connecticut Healthcare System (VACHS), Mental Health Service Line

The VA Connecticut Healthcare System (VACHS) and the Department of Psychiatry at Yale University School of Medicine are seeking outstanding candidates for the position of Director of the VACHS Mental Health Service Line. As the VACHS is a Dean's Committee VA Medical Center, this individual will lead a large dynamic and complex service with strong commitments to clinical, educational and research missions. The VACHS Mental Health Service Line is a major component of the Yale Department of Psychiatry and its leader is a key member of the Yale Psychiatry Senior Executive Leadership.

The Mental Health Service Line is a full service psychiatric and psychological clinical division with 28 inpatient beds, 32 step-down beds, a psychiatric emergency room and a wide range of outpatient and rehabilitative services. The annual clinical budget of the VACHS Mental Health Service is over $30-million per year, supporting over 270 FTEs, including 50 psychiatrists, 48 psychologists and 48 researchers. In addition, VACHS supports 38 psychiatric residents and fellows on site, including ACGME approved specialty fellowships jointly sponsored by the VA and Yale affiliated entities in addiction, geriatric and psychosomatic medicine. Additional VA Special Advanced Fellowship Programs (PGY-4, PGY-5, and PGY-6) at VACHS include Alcoholism, Addictions, Schizophrenia, PTSD, Mental Illness Research, Psychiatric Neuroscience Research, Psychosocial Rehabilitation, Informatics and Robert Wood Johnson Clinical Scholars. There are also two accredited psychology internship and postdoctoral training programs based at VACHS.

The VACHS Mental Health Service Line is one of the major research sites of the Yale University, Department of Psychiatry. It is home to the VISN I Mental Illness Research, Evaluation and Clinical Center (MIRECC), the Clinical Neuroscience Division and Health Services Division of the VA National Center for PTSD, VA Alcohol Research Center, and two VA Research Enhancement Award Programs (REAP) for Depression and PRIME (Pain, Research, Informatics, Medical Comorbidities and Education). With a research budget of approximately $24 million VA supported direct costs per year, and over 25 funded investigators, the VACHS Mental Health Service Line ranks among the VA's leading academic service lines.

Successful candidates must have demonstrated dynamic leadership with outstanding academic and clinical experience, management skills, and the ability to advance and develop superior programs in education, clinical service, and basic and clinical research. Candidates must have experience at the senior level rank in an academic medical environment with qualifications that fulfill the Yale University School of Medicine criteria for Associate Professor or Professor (full appointment, not voluntary faculty). A track record of independent grant support, scientific publications, or other comparable evidence of academic achievement is considered favorably. Also, VA or military experience is desired. The candidate must demonstrate the energy and vision to integrate and lead one of the largest and most dynamic veterans mental health programs in the United States.

Interested individuals should send, fax or e-mail a letter of intent, a CV, and three references to Emily Wayne-Lane of Human Resources-05, VA Connecticut Healthcare System, 950 Campbell Avenue, West Haven, CT 06516; fax to 203 937-4718 or e-mail to Emily.Wayne-Lane@va.gov. Closing date for applications is September 9, 2009 with an expected start date of July 1, 2010.

*VA Connecticut and Yale University are Equal Opportunity/Affirmative Action Employers. Women and members of underrepresented minority groups are encouraged to apply. All applicants tentatively selected for VA employment in a testing designated position are subject to urinalysis to screen for illegal drug use prior to appointment. Applicants who refuse to be tested will be denied employment with VA.*

## Atascadero State Hospital

**BE/BC Psychiatrist**

Atascadero State Hospital now pays board certified psychiatrists starting at $223,464 and advancing stepwise to $255,732. Atascadero is the nation's premier center for the treatment of forensically committed mentally ill patients. Our hospital is a teaching site affiliated with the University of California, accredited by JCAHO, and recipient of the prestigious Codman Award. All of our psychiatrists are board eligible and most are board certified. Many of our psychiatrists have forensic subspecialty boards.

We are located midway between San Francisco and Los Angeles on the scenic central California Coast, south of Big Sur. We offer a spectacularly beautiful environment in San Luis Obispo County with temperate climate, beaches, world class wineries, cultural activities, golfing, sailing, riding, clean air, and excellent schools through the University level.

Our benefit package is valued at an additional 30%, which includes retirement plans (including safety retirement), health plans, professional liability coverage, paid holidays, educational leave, and generous annual leave. On-call duty is compensated hour for hour over and above the base salary. Applicants must hold a current California license, or have pending application with the Medical Board of California.

For a prompt and confidential review, send CV to:

Jeanne Garcia, M.D.
P. O. Box 7001
Atascadero, CA 93423-7001
(805) 468-2005 or fax (805) 468-2138
or e-mail us: jeanne.garcia@ash.dmh.ca.gov

**We are an equal opportunity employer.**

KVC
Behavioral HealthCare

# PSYCHIATRIST

## An innovative practice for a passionate heart.

At KVC Behavioral HealthCare, our passion and expertise make the difference between doing a job and pursuing our life's work. KVC is a leader in child welfare improvements and innovations and offers one of the most extensive networks of child welfare services in the nation. We're seeking a **BE/BC Psychiatrist** to join a multi-disciplinary team and train in our unique and innovative system of care. Working in the KVC Psychiatric Hospital and Psychiatric Residential Treatment Center, you'll provide direct services to children, adolescents and families who are at-risk or in crisis. Position requires a valid Kansas medical license with unrestricted clinical privileges to practice general or child psychiatry. KVC offers a competitive salary and comprehensive benefits. To apply, please email your resume to: **tseaman@kvc.org**; or fax: 913-621-5631. EOE

# Department of Veterans Affairs

## Psychiatrists - VA Boston Healthcare System

The VA Boston Healthcare System (VABHS) is recruiting academically oriented psychiatrists for a number of key positions in our growing Mental Health Service, which has strong and longstanding affiliations with Harvard Medical School (HMS) and Boston University School of Medicine (BUSM) and major campuses located in Boston (Jamaica Plain and West Roxbury) and Brockton. VABHS is a New England regional referral center for veterans' health care.

### Medical Director, Consultation-Liaison Psychiatry

**West Roxbury campus:**

VABHS is recruiting a Medical Director for the Psychiatry Consultation-Liaison service, West Roxbury campus. We seek a board certified academic psychiatrist with at least 5 years' post-residency experience full time (or equivalent) on an academic C-L service, demonstrated excellence in clinical teaching, strong administrative skills, and the motivation and ability to lead this outstanding clinical teaching service. The C-L service receives more than 1200 consultation requests per year, and is an integral part of a vibrant and exceptional academic environment that features nationally recognized training and research programs, and several VA Clinical Centers of Excellence. Academic appointment is through HMS, commensurate with qualifications. The Medical Director oversees the VA-Brigham Women's Hospital Psychosomatic Fellowship and BUSM and HMS resident and medical student C-L rotations. *If you are interested in this position, please send a letter of interest, CV, and contact information for three references to:* **Gary B. Kaplan, M.D., Director, Mental Health Service, VA Boston Healthcare System, 940 Belmont Street, Brockton, MA 02301. Email: Gary.Kaplan@va.gov with a copy to: vhabhsjobs@med.va.gov**

### Inpatient/Outpatient Psychiatrist

**Brockton campus:**

VABHS is recruiting a full-time board-certified (board eligible if less than 2 years post-residency) psychiatrist with a demonstrated commitment to academic psychiatry. This position is divided evenly between inpatient and outpatient programs. Inpatient duties: The psychiatrist will join a well-staffed multidisciplinary inpatient treatment team (7 psychiatrists, 3 psychiatry nurse practitioners, 4 psychologists and 4 social workers) to provide direct clinical services to our acutely ill patient population. The inpatient service has had a major transformation and expansion of its clinical staffing the past year to support the academic and clinical mission of the medical center. Outpatient duties: The psychiatrist will join a vibrant multidisciplinary PTSD treatment team (1 psychiatrist, three psychologists and four social workers) that provides evidence-based clinical care to veterans of all eras including a large cohort of veterans who have recently returned from Iraq and Afghanistan. Duties include support of the academic mission of the medical center, including supervision of psychiatry residents and the opportunity to participate in teaching and research. This position offers a highly competitive VA salary and a faculty appointment at Harvard Medical School commensurate with experience. *If you are interested in this position, please send a letter of interest, CV, and contact information for three references to:* **Gary B. Kaplan, M.D., Director, Mental Health Service, VA Boston Healthcare System, 940 Belmont Street, Brockton, MA 02301. Email: Gary.Kaplan@va.gov with a copy to vhabhsjobs@med.va.gov**

### Emergency Department Moonlighting Positions

**Brockton Campus:**

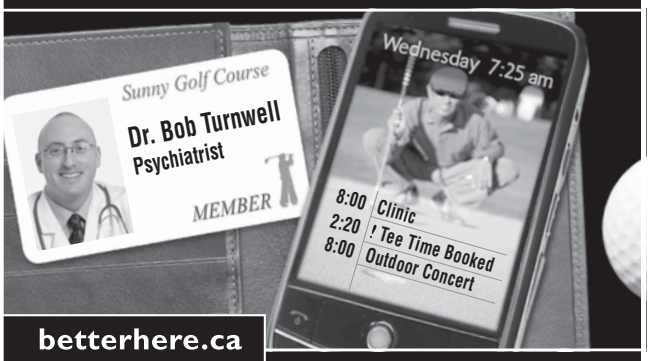
VABHS is recruiting board certified (board eligible if less than 5 years post-residency) psychiatrists to provide direct clinical services and clinical supervision of psychiatry residents on evenings and weekends in the Urgent Care Department on our Brockton campus. In addition to an outstanding academic environment, this position offers competitive compensation and the possibility of an academic appointment for qualified individuals. Hours are 4pm-11pm weekdays and 7am-3pm or 3pm-11pm on Saturdays and Sundays. Please send a letter of interest, CV, and contact information for three references to: **Dr. Ronald Gurrera, Director of Urgent Care Services, Mental Health Service, VA Boston Healthcare System, 940 Belmont Street, Brockton, MA 02301. Phone: 774-826-2473; Email: Ronald.Gurrera@va.gov with a copy to: vhabhsjobs@med.va.gov**

VA Boston is an Affirmative Action/Equal Opportunity Employer with a strong institutional commitment to diversity in all areas. These positions will be filled without discrimination. You must be a U.S. citizen to apply.

# Chief, Psychiatrist

**VA Medical Center St Louis, MO**, is seeking a full time Psychiatrist. Must also qualify for an appointment as Associate Chair in the Department of Neurology and Psychiatry at St. Louis University. The individual will be charged with strategic alignment of efforts between the VAMC and the Department of Neurology & Psychiatry. They will oversee joint educational research and clinical initiatives; perform primary recruitment of psychiatric faculty at both facilities and work closely with the Associate Chief of Staff of Mental Health at the VA and the Chair of the Department of Neurology & Psychiatry at St. Louis University to promote the strategic goals of both organizations. The individual should have an established research program and demonstrate expert clinical, educational and administrative expertise. The St. Louis VAMC offers comprehensive mental health services, including acute and residential inpatient care, consultation and liaison, programs in general mental health, neuropsychiatry, PTSD, Substance Use Disorders, and Psychosocial Rehabilitation and Recovery. Both St. Louis VA Medical Center and St. Louis University are Equal Opportunity Employers. Contact Nekisha Ladd from VA at 314-894-6620 or email CV to nekisha.ladd@va.gov.

## *Life is better for psychiatrists in the sunny Southern Interior of BC, Canada*




**betterhere.ca**

### *Here's Why...*

Whether you are looking to improve your golf game, longing to hit the trails or looking for cultural enrichment at the community level, you can work and enjoy our exceptional four-season playground all in the same day. Enjoy the advantages of a less hurried lifestyle in the Interior communities of Trail or Cranbrook.

Psychiatrist candidates are eligible for funded recruitment visits and relocation support; other rural recruitment and retention incentives are available (specific eligibility criteria applies). American boards required.

Contact us today and find out why it's better here.

Trail Cranbrook Trail Cranbrook Trail Cranbrook

betterhere.ca 1-877-522-9722 physicianrecruitment@interiorhealth.ca

Interior Health

## DIRECTOR of CHILD and ADOLESCENT PSYCHIATRY (Tenure-Track)

State University of New York
Upstate Medical University, Syracuse

The Department of Psychiatry at SUNY Upstate Medical University is seeking an outstanding Director for its flourishing Division of Child and Adolescent Psychiatry. The Division has a regional reputation for excellence in clinical care and education, a fellowship training program, telepsychiatry, expanding clinical programs, and internationally acclaimed researchers, including Drs. Faraone, Barkley, Kates, Gordon, Fremont, Staller and Glatt, who receive over $3 million in NIH funding each year. SUNY Upstate encompasses a major medical school, a graduate school, research facilities, and a new Children's Hospital.

This is a tenure-track position at the rank of Associate or Full Professor. Candidates must have an established national reputation as an academic leader having a record of accomplishment in clinical care and education. Experience with funded research is preferred but not required. Candidates must possess mentoring and leadership skills necessary for faculty development and advancement of the Division.

The rolling hills of Upstate New York boast excellent schools, low cost of living, several major liberal arts colleges and universities, and numerous recreational and entertainment opportunities.

For a prompt and confidential review, please apply on-line to job #024651 via the SUNY Upstate Human Resources website **jobs.upstate.edu**, **or for information only, please contact Jean Pollock at (315) 464-3105 or pollockj@upstate.edu**.

State University of New York
**Upstate Medical University**

***An AA/EEO/ADA employer engaging excellence through diversity.***

**EASTERN VIRGINIA MEDICAL SCHOOL (EVMS)** has initiated a search for a talented faculty member at the rank of Assistant or Associate Professor in the Department of Psychiatry and Behavioral Sciences. EVMS is located in a beautiful, coastal area of Virginia in the second largest metropolitan area in the state. This is a full-time position in a department that has a major commitment to clinical, educational and teaching activities. Clinical responsibilities include inpatient treatment, consultations, and emergency room evaluations at Sentara Norfolk General Hospital, as well as outpatient services at Eastern Virginia Medical School's Department of Psychiatry and Behavioral Sciences. Teaching responsibilities include education and supervision of psychiatric residents and medical students, as well as students from related disciplines, including Psychology and Art Therapy. The position will also emphasize participation in research activities within an academic culture, which places EVMS at the forefront of mental health advances. Currently the EVMS Department of Psychiatry includes 21 full-time faculty members, and the Residency Training Program has 16 residents and is fully accredited by ACGME. The successful candidate should have the ability to significantly contribute to the tripartite mission of education, research and patient-centered quality care. Eastern Virginia Medical School encourages all inquiries and all applications will be held in strictest confidence. Qualified applicants will be reviewed in the order by which their applications are received, and the process will continue until the current position is filled. Please send letters of interest, accompanied by three letters of reference, to Paul Sayegh MD, Vice-Chair, Department of Psychiatry and Behavioral Sciences, Suite 710, Hofheimer Hall, 825 Fairfax Avenue, Norfolk, VA. 23507, or fax to 757-446-5918. Inquiries may also be addressed to sayeghpa@evms.edu. EVMS is an AA/EOE/Drug Free Workplace.

# Index to Advertisers August 2009

The publication of an advertisement in this journal does not imply endorsement of the product or service by the American Psychiatric Association.




**Subscription and Business Information**

The American Journal of Psychiatry, ISSN 0002-953X, is published monthly by the American Psychiatric Association, 1000 Wilson Blvd., Suite 1825, Arlington, VA 22209-3901. Subscriptions (per year): individual $205.00, international $308.00. For additional subscription options, including single issues and student rates, please contact Customer Service at 1-800-368-5777 or email appi@psych.org. Institutional subscriptions are tier priced. For institutional site license or pricing information, contact Customer Service or visit http://highwire.stanford.edu/tfocis/.

Business communications, address changes, and subscription questions from APA members should be directed to the Division of Member Services: (888) 35-PSYCH (toll-free). Nonmember subscribers should call the Circulation Department (800) 368-5777. Author inquiries should be directed to the Journal editorial office: (703) 907-7885 or (703) 907-7884; fax (703) 907-1096; e-mail ajp@psych.org.

Business Management: Nancy Frey, Director, Publishing Services; Laura G. Abedi, Associate Director, Production; Alison Jones, Advertising Prepress Manager; Robert Pursell, Director, Sales and Marketing.

Pharmaceutical Print Advertising: Frank Cox, Kathleen Harrison, Valentin Torres, Pharmaceutical Media, Inc. 30 East 33rd Street, New York, NY 10016. (212) 685-5010; fax (212) 685-6126; e-mail vtorres@pminy.com.

Nonpharmaceutical and Online Sales: Brian Skepton, (703) 907-7332; e-mail bskepton@psych.org.

Pages are produced using Adobe FrameMaker+ SGML 6.0. Printed by RR Donnelley, Mendota, IL., on acid-free paper effective with Volume 164, Number 11, November 2007.

Periodicals postage paid at Arlington, VA, and additional mailing offices. POSTMASTER: Send address changes to The American Journal of Psychiatry, Circulation Department, American Psychiatric Association, 1000 Wilson Blvd., Suite 1825, Arlington, VA 22209-3901.

Indexed in Abstracts for Social Workers, Academic Abstracts, Biological Abstracts, Chemical Abstracts, Chicago Psychoanalytic Literature Index, Cumulative Index to Nursing Literature, Excerpta Medica, Hospital Literature Index, Index Medicus, International Nursing Index, Nutrition Abstracts, Psychological Abstracts, Science Citation Index, Social Science Source, and Social Sciences Index.

# RELAPSE.

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

# RELAPSE.

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

# RETHINK.

Is it time we took another look at treatment for schizophrenia?

While no medication can guarantee a relapse will not occur, using long-acting therapies earlier can help you recognize the opportunity for missed doses and intervene when it matters most.

Janssen® is dedicated to finding innovative ways of helping patients with schizophrenia get the medication they need.

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



Janssen®
Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc.