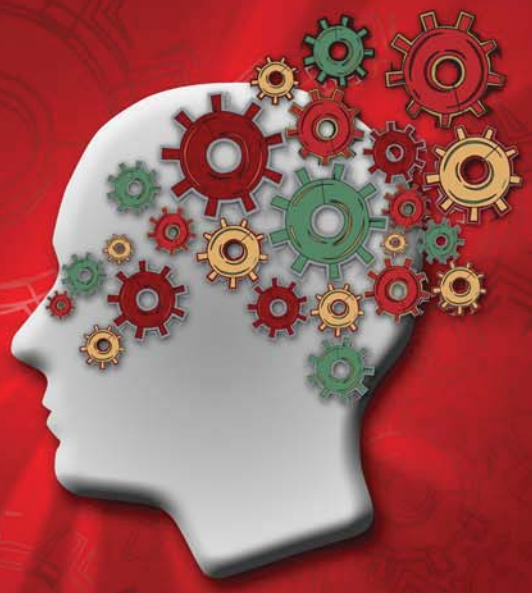


ADHD FAQ's:

Practical Answers for the Office-Based Practitioner

APA 2009 Annual Meeting • San Francisco, California
Monday, May 18, 2009 • Marriott-San Francisco, Salons 7/8

Breakfast
6:30 AM–7:00 AM

Scientific Session
7:00 AM–9:00 AM

Welcome and Preactivity Educational Outcomes Measurement
7:00 AM–7:05 AM — Gabriel Kaplan, MD

How Do I Identify and Treat Adult ADHD?
7:05 AM–7:25 AM — Gabriel Kaplan, MD

Cardiovascular Effects of Stimulants–Is There Cause for Concern?
7:25 AM–7:45 AM — Donald E. Greydanus, MD

How Do I Approach the Bipolar vs ADHD Issue?
7:45 AM–8:05 AM — Jeffrey H. Newcorn, MD

How Do I Manage the ADHD/SUD Comorbidity?
8:05 AM–8:25 AM — Iliyan Ivanov, MD

Postactivity Measurement
8:25 AM–8:30 AM — Gabriel Kaplan, MD

Discussion, Q&A
8:30 AM–9:00 AM — Gabriel Kaplan, MD and Faculty

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

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

Learning Objective
At the conclusion of this session, the participant should be able to enumerate adult ADHD criteria, and understand the cardiovascular risks of stimulants, the process of ADHD/bipolar differential diagnosis, and the outcome findings of ADHD/SUD comorbidity.

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

Registered conference participants and registered guests may attend any industry-supported symposium at the APA meeting.

Program Chair
Gabriel Kaplan, MD
Clinical Associate Professor of Psychiatry
University of Medicine and Dentistry of New Jersey
Newark, New Jersey
Executive Director, Psychiatry
Hoboken University Medical Center
Hoboken, New Jersey

Distinguished Faculty
Donald E. Greydanus, MD
Pediatrics Program Director
MSU/Kalamazoo Center for Medical Studies
Kalamazoo, Michigan

Iliyan Ivanov, MD
Assistant Professor, Psychiatry
Mt Sinai School of Medicine
New York, New York

Jeffrey H. Newcorn, MD
Associate Professor, Psychiatry and Pediatrics
Mount Sinai School of Medicine
New York, New York

Sponsored by

Supported by an educational grant from
Shire

2009 Annual Meeting sponsored by
the American Psychiatric Association

Effective Treatment of Alzheimer's Disease

Translating Guidelines into Practice

An Interactive Panel Discussion

Sunday, May 17, 2009
12:00–12:30 PM Lunch
12:30–2:30 PM Symposium

San Francisco Marriott
Salon 7/8, Lower B-2 Level
55 Fourth Street
San Francisco, California

Faculty/Presenters

George T. Grossberg, MD (Chair)
Samuel W. Fordyce Professor
Director, Geriatric Psychiatry
Department of Neurology and Psychiatry
Saint Louis University School of Medicine
St. Louis, Missouri

Charles A. Cefalu, MD, MS
Professor and Chief, Section of Geriatric Medicine
Department of Medicine
Louisiana State University Health Sciences Center
and School of Medicine at New Orleans
New Orleans, Louisiana

Martin R. Farlow, MD
Professor and Vice Chairman for Research
Department of Neurology
Associate Director, Indiana Alzheimer Disease Center
Indiana University School of Medicine
Indianapolis, Indiana

Wm Maurice Redden, MD
Geriatric Psychiatry Fellow
Department of Neurology and Psychiatry
Saint Louis University School of Medicine
St. Louis, Missouri

Gary W. Small, MD
Parlow-Solomon Professor on Aging
Professor of Psychiatry and Biobehavioral Sciences
David Geffen School of Medicine
University of California, Los Angeles (UCLA)
Director, UCLA Center on Aging
Director, Memory and Aging Research Center
Semel Institute for Neuroscience and Human Behavior
Los Angeles, California

Agenda

12:00–12:30 PM	*Lunch*
12:30–12:45 PM	*Introduction/Welcome* **George T. Grossberg, MD**
12:45–1:00 PM	*The Clinical Pharmacology of Approved AD Therapies* **Wm Maurice Redden, MD**
1:00–1:15 PM	*The Psychiatry Point of View: The AAGP and APA Guidelines for Pharmacologic Management of Patients With AD* **Gary W. Small, MD**
1:15–1:30 PM	*The Neurology Point of View: The AAN Guidelines for Pharmacologic Management of Patients With AD* **Martin R. Farlow, MD**
1:30–1:45 PM	*The General Practitioner Point of View: The ACP/AAFP Guidelines for Pharmacologic Management of Patients With AD* **Charles A. Cefalu, MD, MS**
1:45–2:25 PM	*Moderated Debate and Question & Answer Session*
2:25–2:30 PM	*Closing Remarks* **George T. Grossberg, MD**

Learning Objectives

At the end of this activity, participants should be able to

1. Evaluate and contrast pharmacologic therapies available for treating patients with Alzheimer's disease (AD)
2. Appraise and contrast the published guidelines for pharmacologic management of patients with AD
3. Have increased confidence in the pharmacologic and nonpharmacologic management of patients with AD

Accreditation and Credit Designation Statements

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

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

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

Registered conference participants and registered guests may attend any industry-supported symposium at the APA meeting.

Sponsored by
the American Psychiatric Association.

Forest Laboratories, Inc.

Supported by an educational grant from
Forest Laboratories, Inc.

APA 2009 Annual Meeting in San Francisco, CA

Development of New Agents for the Treatment of Schizophrenia

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

Learning Objectives

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

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

Accreditation Statement

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

Credit Designation

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

Registration

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

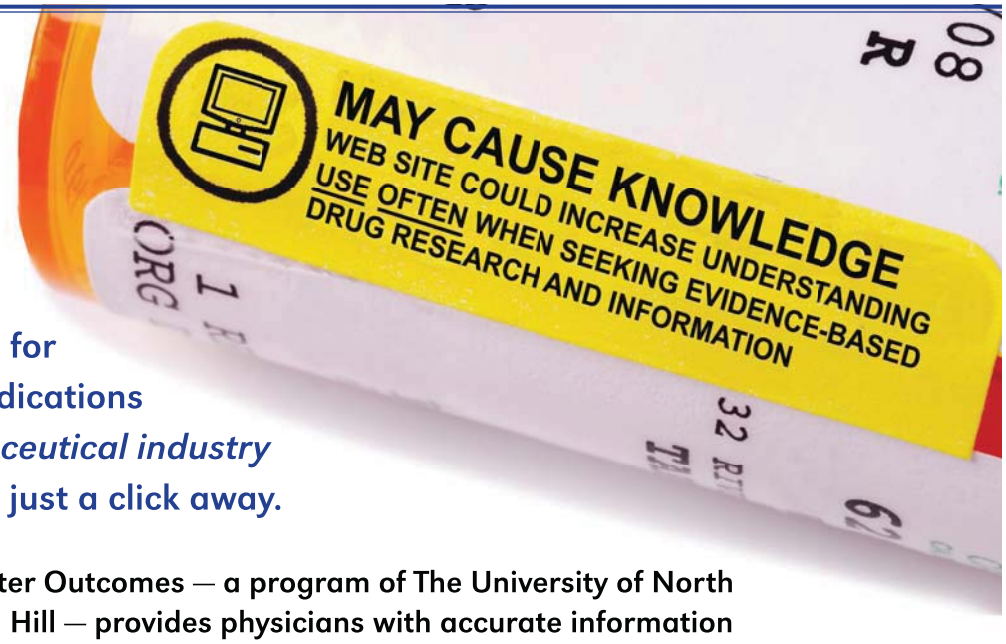
Sponsored by the American Psychiatric Association

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

DAINIPPON SUMITOMO PHARMA

Agenda

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



Credible research

about the most appropriate use for prescription medications *without pharmaceutical industry influence* is now just a click away.

Prescribing for Better Outcomes — a program of The University of North Carolina at Chapel Hill — provides physicians with accurate information about the uses of anti-epileptic drugs in the treatment of bipolar disorder.

www.PrescribingforBetterOutcomes.org

Text "RX" to 54608 to learn more about this program.

Rx PRESCRIBING *for* BETTER OUTCOMES

This program will be conducted on May 17, 2009, during the APA 2009 Annual Meeting

Augmentation STRATEGIES *for* MAJOR DEPRESSIVE DISORDER:

The Evidence for Effective Clinical Decision-Making in Improving Patient Care

SUNDAY, MAY 17, 2009 • Dinner: 6:30–7:00 PM • Symposium: 7:00–9:00 PM
San Francisco, California • Yerba Buena Ballroom, Salons 7 & 8 • SAN FRANCISCO MARRIOTT

AGENDA

6:30–7:00 PM	Breakfast
7:00–7:05 PM	Introduction & Overview MADHUKAR H. TRIVEDI, MD (Chairperson) University of Texas Southwestern Medical Center
7:05–7:30 PM	Inadequate Treatment Response in Major Depressive Disorder: Predictors and Strategies for Selecting Next-Step Treatments ROY H. PERLIS, MD, MSC Harvard Medical School
7:30–7:55 PM	Effective Management of Treatment-Resistant Depression: Evidence-Based Approaches Beyond First-Line Antidepressant Monotherapy MADHUKAR H. TRIVEDI, MD
7:55–8:20 PM	Atypical Antipsychotics as Augmentation Agents for Major Depressive Disorder: Efficacy and Tolerability GEORGE I. PAPAKOSTAS, MD Harvard Medical School
8:20–9:00 PM	Panel Discussion/Question and Answer Session ALL FACULTY

Sponsored by the American Psychiatric Association

GREEN Symposium™

Supported by an educational grant from Bristol-Myers Squibb

EDUCATIONAL ACTIVITY LEARNING OBJECTIVES

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

- Discuss and interpret the clinical implications of factors underlying inadequate response to antidepressant therapy in patients with MDD
- Compare and contrast the rationale for using different second-line strategies in patients who do not respond adequately to antidepressants
- Evaluate the clinical trial evidence for the use of atypical antipsychotics in the management of MDD

CME STATEMENT

This symposium will be conducted on May 17, 2009, during the APA 2009 Annual Meeting. The American Psychiatric Association (APA) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. The APA designates this educational activity for a maximum of 2 *AMA PRA Category 1 Credits*™. Physicians should only claim credit commensurate with the extent of their participation in the activity. Attendees must be registered for the APA Annual Meeting to attend this symposium. Seating is limited and will be based on first-come, first-served. For more information about the meeting, please visit the APA Web site at www.psych.org or contact the APA toll free at 1-888-357-7924 (within the US or Canada) or 703-907-7300.

If any participant of this activity given by The France Foundation is in need of accommodation, please fax written requests to 1-860-434-5390.

APA JOB BANK

The best source for psychiatric job placement

APA Job Bank
psych.org/jobbank

Candidates and Employers Connect through the APA Job Bank at the APA Annual Meeting

- Visit the APA Job Bank to search the most comprehensive online listing of psychiatric positions.
- Connect with prospective employers at the APA Annual Meeting with the APA Job Bank Conference Connection tool.
- Ask APA Job Bank representatives for a demonstration of site features.
- Visit the APA Job Bank today to find the ideal position!

Located in the APA Member Center, next to registration and at the Career Center in the Exhibit Hall

Saturday, May 16
10:00 am - 5:00 pm

Sunday, May 17
10:00 am - 4:30 pm

Monday, May 18
10:00 am - 5:00 pm

Tuesday, May 19
10:00 am - 5:00 pm

Wednesday, May 20
10:00 am - 3:00 pm

SEE ME FOR WHO I CAN BE

GREG, 35*
Diner Worker
Diagnosis: Schizophrenia

*Not an actual patient.

Do you see your patients' full potential?

GEODON is indicated for the treatment of schizophrenia.

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

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

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

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

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

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

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

Please see brief summary of prescribing information on adjacent page.

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

GEODON®
(ziprasidone HCl) **Capsules**

BRIEF SUMMARY. See package insert for full prescribing information.

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

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

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

Revised August 2008

APA 2009 Annual Meeting in San Francisco

Anxious Depression: Diagnostic and Treatment Issues

Hilton–San Francisco
Ballroom 4/5/6

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

Agenda

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

Learning Objectives

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

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

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

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

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

Sponsored by the American Psychiatric Association

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

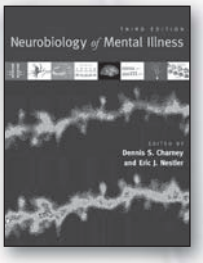
New from

OXFORD

NEUROBIOLOGY OF MENTAL ILLNESS

Third Edition

Dennis S. Charney and **Eric J. Nestler**

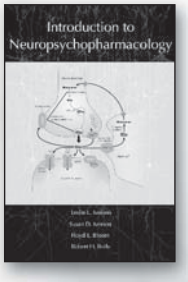


This is a new edition of the first comprehensive text to show how the advances in molecular and cellular biology and in the basic neurosciences have brought the revolution in molecular medicine to the field of psychiatry.

2009 1504 pp.; 240 illus.
9780195325331 cloth $225.00

INTRODUCTION TO NEUROPSYCHOPHARMACOLOGY

Leslie Iversen, **Susan D. Iversen**, **Floyd E. Bloom**, and **Robert H. Roth**



Authored by four founders of modern neuroscience, this concise and comprehensive text covers the current series of medications used to treat diseases of the brain and nervous system—both psychiatric and neurologic—as well as legal and illegal recreational drugs and the neuroscientific information that explains how these medications act on the brain from the molecular to the clinical level.

2009 576 pp.
9780195380538 paper $45.00

OXFORD AMERICAN HANDBOOK OF PSYCHIATRY

David Kupfer, **Michelle S. Horner**, **David Brent**, **David Lewis**, **Charles Reynolds**, **Michael Thase**, **Michael Travis** and **Michelle X. Horner**

This book is a flexi-covered, pocket clinical book, providing practical guidance in quick reference, note form. This new handbook is ideal for students, residents and anyone wanting a succinct, comprehensive, and affordable volume in the proven format of the Oxford Handbook Series.

2008 1260 pp.; 15 illus.
9780195308846 flexi-cover $39.95

CAMPBELL'S PSYCHIATRIC DICTIONARY

Ninth Edition

Robert J. Campbell

The newest edition of a work that has been widely recognized as the definitive dictionary of psychiatry-up-to-date, comprehensive, and authoritative.

2009 1280 pp.
9780195341591 cloth $59.95

PSYCHIATRY IN LONG-TERM CARE

Second Edition

Edited by **William E. Reichman** and **Paul R. Katz**

This book comprehensively reviews the present state of knowledge on how to identify the major psychiatric disorders affecting residents of long-term care facilities and how to intervene.

2009 527 pp.
9780195160949 cloth $69.95

PSYCHIATRIC ETHICS

Fourth Edition

Sidney Bloch and **Stephen Green**

The newest edition of the major, comprehensive text and core reference in the field, covering a range of complex ethical dilemmas that face clinicians and researchers in their everyday practice.

2009 560 pp.; 8 illus.
9780199234318 paper $57.50

NEW OXFORD TEXTBOOK OF PSYCHIATRY

Second Edition

Edited by **Michael Gelder**, **Nancy Andreasen**, **Juan Lopez-Ibor** and **John Geddes**

Destined to be used by those in higher training, for continuing education and reaccreditation, and as a specialist's reference, this book will be the one reference work that everyone in the field will want on their shelves.

2009 1,952 pp.
9780199206698 cloth $390.00

OXFORD TEXTBOOK OF SUICIDOLOGY

Danuta Wasserman and **Camilla Wasserman**

Written by world-leading specialists, this book describes all aspects of suicidal behavior and suicide prevention.

2009 620 pp.
9780198570059 cloth $150.00

PRESCRIPTIONS FOR THE MIND

A Critical Review of Contemporary Psychiatry

Joel Paris

2008 272 pp.
9780195313833 cloth $29.50

PSYCHIATRIC ASPECTS OF NEUROLOGIC DISEASES

Practical Approaches to Patient Care

Edited by **Constantine G. Lyketsos**, **Peter V. Rabins**, **John P. Lipsay**, and **Phillip R. Slavney**

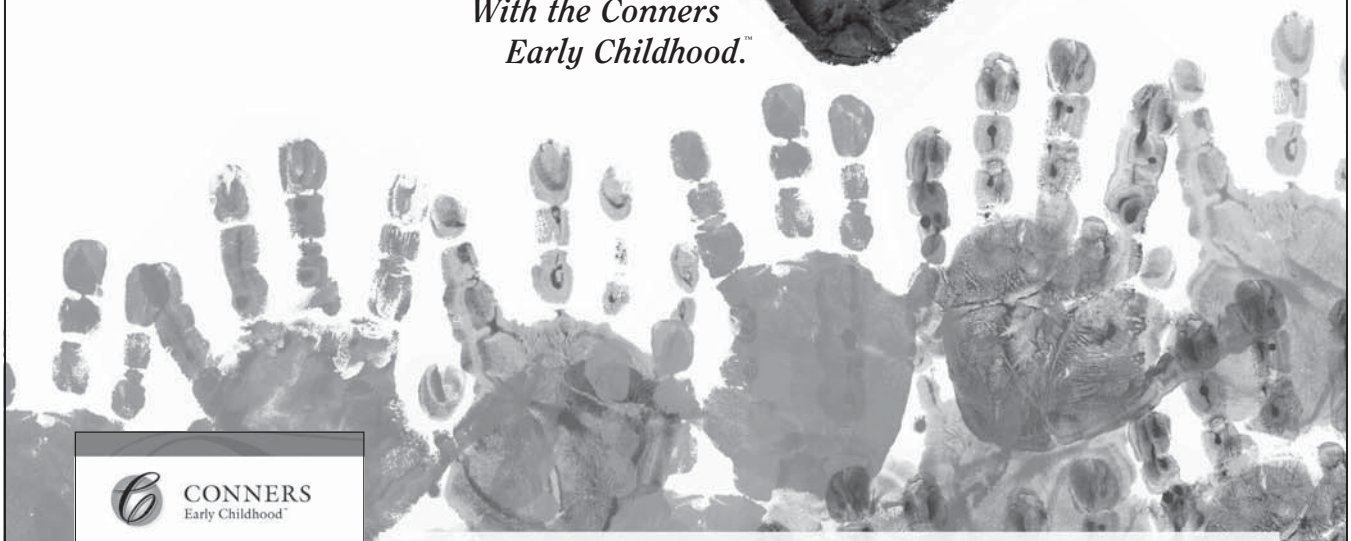
2008 464 pp.
9780195309430 cloth $42.95

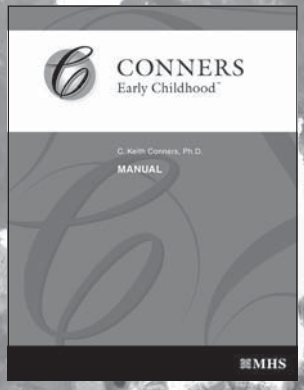
To place your order, contact customer service at **1-800-451-7556** or visit us online at **www.oup.com/us**. Prices are subject to change and apply only in the US.

OXFORD UNIVERSITY PRESS

Leave Your Mark.

Set the New Standard With the Conners Early Childhood.™





SAVE $100.00
when you order the Conners Early Childhood Complete Scoring Software Kit before August 1, 2009.

When ordering, please quote promotional code SE18.

There is more than one layer to a child's psychological and developmental health. Young children between the ages of 2 to 6 are multi-faceted and complex. Let the *Conners Early Childhood* assist you in identifying when early intervention is required.

The *Conners Early Childhood* is designed to assess the concerns of parents and childcare providers in preschool-aged children and aids in the early identification of a multitude of problems; behavioral, social, and emotional.

The *Conners Early Childhood* also measures whether or not a child's developmental milestones (Adaptive Skills, Communication, Motor Skills, Play, and Pre-Academic/Cognitive) are being met.

The *Conners Early Childhood* provides:

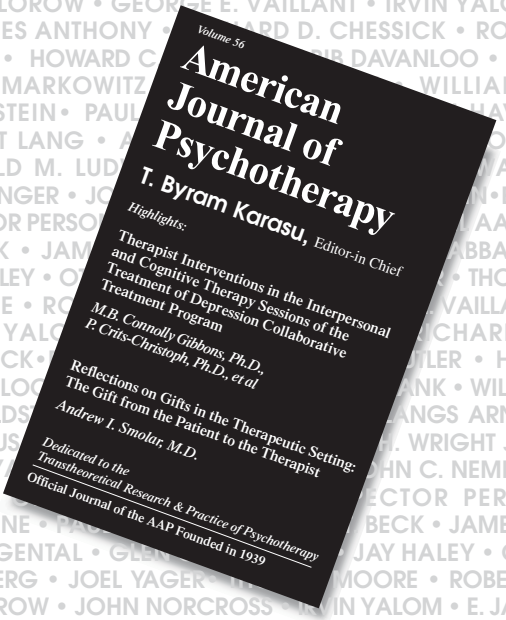
- Multi-informant (parent, teacher/ childcare provider) assessment that allows for easy comparison across raters
- Full-length, Short, Behavior, Developmental Milestones, and Global Index forms
- Validity scales
- Clear and direct links to the *Individuals with Disabilities Education Improvement Act 2004* (IDEA 2004)
- Excellent reliability and validity
- Easy administration, scoring, and results interpretation
- Spanish versions

The *Conners Early Childhood* sets a new standard in assessing and identifying problems in preschool-aged children. Order your copy today.

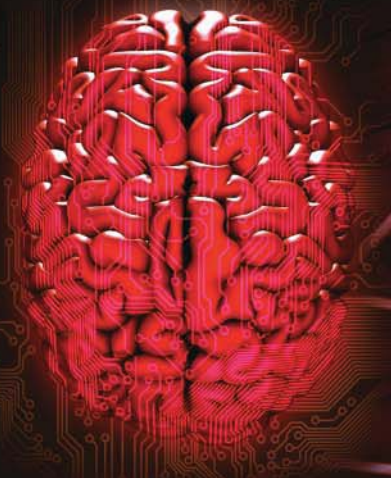
MHS, committed to bringing you the very best in assessments and rating scales.

MHS **USA** Tel: 1.800.456.3003 **WEBSITE** www.mhs.com/conners
CAN Tel: 1.800.268.6011 **EMAIL** customerservice@mhs.com

CONNERS
As always. As never before.™



Incorporating the *Journal of Psychotherapy Practice and Research*
Published four times per annum: *American Journal of Psychotherapy*
Belfer Center, Room 405 • 1300 Morris Park Avenue • Bronx, NY 10461
Telephone: (718) 430-3503, FAX: (718) 430-8907
E-mail: info@ajp.org; Web site: www.ajp.org



The Pathophysiology of ADHD: Implications for Treatment

Program Chair

Timothy E. Wilens, MD
Associate Professor, Psychiatry
Harvard Medical School
Director, Substance Abuse Services
Pediatric Psychopharmacology Research Program
Massachusetts General Hospital
Boston, Massachusetts

Distinguished Faculty

Darin D. Dougherty, MD
Associate Professor, Psychiatry
Harvard Medical School
Boston, Massachusetts
Director of Neurotherapeutics, Psychiatry
Massachusetts General Hospital
Charlestown, Massachusetts

Paul G. Hammerness, MD
Assistant Professor, Psychiatry
Harvard Medical School
Boston, Massachusetts
Scientific Coordinator, Pediatric ADHD Research
Pediatric Psychopharmacology Research and Adult ADHD
Massachusetts General Hospital
Cambridge, Massachusetts

Avis B. Hains, PhD
Postdoctoral Scholar, Neurobiology
Yale University
New Haven, Connecticut

Sponsored by the American Psychiatric Association

Supported by an educational grant from Shire.
Shire

APA 2009 Annual Meeting

San Francisco, California • Sunday, May 17, 2009
Hilton San Francisco • Grand Ballroom, Salon B

Dinner
6:30 PM

Welcome and Preactivity Educational Outcomes Measurement
7:00 PM — Timothy E. Wilens, MD

The Neurobiology of ADHD: Overview of the Mechanisms of Efficacious Agents
7:10 PM — Paul G. Hammerness, MD

Role of Dopamine in ADHD
7:30 PM — Darin D. Dougherty, MD

Alpha Agonists in the Prefrontal Cortex
7:50 PM — Avis B. Hains. PhD

Nicotinic Receptors and Agonists in ADHD
8:10 PM — Timothy E. Wilens, MD

Discussion, Q&A
8:30 PM — Chair and Faculty

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

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

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

Registered conference participants and registered guests may attend any industry-supported symposium at the APA meeting.

Learning Objectives

After attending this educational activity, a participant should be able to:

1. Differentiate the mechanisms of action of medications used to treat ADHD.
2. Explain the roles of dopamine and norepinephrine in ADHD pathophysiology and treatment.
3. Discuss the role of nicotinic receptor agonists as future treatments for ADHD.

“EACH DAY IS CHALLENGING. EACH DAY IS DIFFERENT. EACH DAY IS REWARDING...”

Lieutenant Wendy Pettit, Behavioral Health Social Worker
U.S. Public Health Service Commissioned Corps

BE A LEADER IN MENTAL HEALTH.

Mental health officers in the U.S. Public Health Service Commissioned Corps are part of an elite team bringing mental and behavioral health services to people most in need. Under a new partnership with the U.S. Department of Defense, Commissioned Corps officers may be detailed to military medical treatment facilities. These officers will provide psychiatric services, counseling, and family and group therapy to returning war fighters, their family members, and military retirees. Corps officers are rewarded with an excellent package of salary and benefits, including health coverage, tax-free allowances for housing and food, 30 days of vacation each year, and much more.

AMERICA'S HEALTH RESPONDERS
COMMISSIONED CORPS
U.S. PUBLIC HEALTH SERVICE

READY TO MAKE A DIFFERENCE?

MAKE THE U.S. PUBLIC HEALTH SERVICE COMMISSIONED CORPS THE HIGHLIGHT OF YOUR CAREER.

The U.S. Department of Health and Human Services is an equal opportunity employer.

www.usphs.gov **1-800-279-1605**

DEPARTMENT OF HEALTH AND HUMAN SERVICES • USA
U.S. PUBLIC HEALTH SERVICE • 1798 •

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

BC/BE ADULT PSYCHIATRIST

McLeod Health is seeking a Full-Time BC/BE Adult Psychiatrist for our Behavioral Health Psychiatric Center located in a beautiful rural setting in Darlington, SC, just minutes away from the main flagship hospital, McLeod Regional Medical Center in Florence, SC.

We have an extensive support staff for the hospital and ED consults and a twenty-four hour Access Center. Our state-of-the-art 23-bed crisis intervention in-patient facility was built and designed specifically for the needs of the psychiatric patient. We also provide out-patient therapy for patients in a private-practice setting.

We offer a competitive salary, comprehensive benefits and retirement package, paid professional liability insurance, CME allowance, relocation assistance, and sign-on bonus.

McLeod Regional Medical Center is a 453 bed, tertiary care, and teaching facility serving a primary market of 6 counties, and receiving tertiary referrals from 12 counties for a total population of 1 million people.

McLeod is leading the way for the nation in patient care by improving quality and safety. We are committed to developing patient-centered, evidence-based, physician-led quality health care in a not-for-profit hospital system that values each individual patient.

If you are interested in joining this nationally recognized hospital, please contact Janisyn McLaurin at 843-777-5169 or by email at jmclaurin@mcleodhealth.org.

Apex Medical Center

Great Opportunity Beautiful Las Vegas!

Psychiatrist

Multi-speciality group seeking friendly motivated second Psychiatrist.

Competitive compensation package including: Medical/dental insurance, 401K paid malpractice, paid vacation/CME, relocation assistance, etc.

Main office at Central Las Vegas
JI/H Visa May Apply!

Fax Resume to: 702-947-6702
Or E-mail: drez@apexmedicalcenter.net

APEX MEDICAL CENTER

University of Pennsylvania School of Medicine

Assistant Professor

The Department of Psychiatry at the University of Pennsylvania School of Medicine seeks candidates for an Assistant Professor position in the tenure track.

The successful applicant will have experience in the field of psychiatry with a focus on translational neuroscience. Responsibilities include the development of an independent academic laboratory within the Translational Neuroscience Program.

The successful candidate will participate in clinical service and clinical research. Applicants must have an M.D or M.D./Ph.D. degree. Board certification in Psychiatry with a PA medical license or eligibility is required.

The successful applicant must have substantial post graduate research experience and have the capability to direct an independent laboratory that will be highly integrated into the Translational Neuroscience Program, including participation in joint grant applications and studies.

Experience with treatment development, animal models, circuit modeling or clinical research is required. Experience spanning pre-clinical/clinical studies is preferred. The successful applicant should have a record of independent funding.

Please submit curriculum vitae, a cover letter, and references to:

Dwight L. Evans, M.D.
Ruth Meltzer Professor and Chair; Steven Siegel, Associate Professor and Dir., Translational Neuroscience Program; REF#148
c/o A. Plotnick, Department of Psychiatry
University of Pennsylvania School of Medicine
305 Blockley Hall, 423 Guardian Drive, Philadelphia, PA 19104
E-mail: plotnick@upenn.edu

The University of Pennsylvania is an equal opportunity, affirmative action employer. Women and minority candidates are strongly encouraged to apply.

Complex puzzles. Comprehensive solutions.

At Western Psychiatric Institute and Clinic of UPMC, we take on complex disorders that some other centers won't even attempt to treat.

But whether a patient has a difficult-to-treat disorder or one more easily treated, teams of specialists in psychiatry, psychopharmacology, clinical psychology, and medicine craft complete, individualized treatment plans that draw upon the latest clinical research, much of it conducted by our own investigators. Whether we're interpreting our clinical trial data or a patient's lab results, our work to advance the understanding and treatment of bipolar disorder, eating disorders, autism, and geriatric behavioral health issues is world-class. In fact, we have one of the world's most comprehensive programs for mood disorders, with research-based treatments for patients at every level of need, at every stage of life.

With more than 400 inpatient psychiatric beds and 75 ambulatory programs, we care for people when they're feeling their worst *and* support them when they're at their best, back with their families in their home towns. Each year, Western Psychiatric helps some 30,000 people of all ages — at all stages of recovery, from all over the world — live healthier and more productive lives.

UPMC

upmc.com | 1-800-533-UPMC

Affiliated with the **University of Pittsburgh School of Medicine**,
UPMC is ranked among the nation's best hospitals by *U.S.News & World Report*.

Index to Advertisers
May 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.

therefore, patients with raised intraocular pressure or those at risk of acute narrow-angle glaucoma (angle-closure glaucoma) should be monitored. **Activation of Mania/Hypomania-**During all MDD and VMS (vasomotor symptoms) phase 2 and phase 3 studies, mania was reported for approximately 0.1% of patients treated with Pristiq. Activation of mania/hypomania has also been reported in a small proportion of patients with major affective disorder who were treated with other marketed antidepressants. As with all antidepressants, Pristiq should be used cautiously in patients with a history or family history of mania or hypomania. **Cardiovascular/Cerebrovascular Disease-**Caution is advised in administering Pristiq to patients with cardiovascular, cerebrovascular, or lipid metabolism disorders [*see Adverse Reactions (6.1)*]. Increases in blood pressure and heart rate were observed in clinical studies with Pristiq. Pristiq has not been evaluated systematically in patients with a recent history of myocardial infarction, unstable heart disease, uncontrolled hypertension, or cerebrovascular disease. Patients with these diagnoses, except for cerebrovascular disease, were excluded from clinical studies. **Serum Cholesterol and Triglyceride Elevation-**Dose-related elevations in fasting serum total cholesterol, LDL (low density lipoprotein) cholesterol, and triglycerides were observed in the controlled studies. Measurement of serum lipids should be considered during treatment with Pristiq [*see Adverse Reactions (6.1)*]. **Discontinuation of Treatment with Pristiq-**Discontinuation symptoms have been systematically and prospectively evaluated in patients treated with Pristiq during clinical studies in Major Depressive Disorder. Abrupt discontinuation or dose reduction has been associated with the appearance of new symptoms that include dizziness, nausea, headache, irritability, insomnia, diarrhea, anxiety, fatigue, abnormal dreams, and hyperhidrosis. In general, discontinuation events occurred more frequently with longer duration of therapy. During marketing of SNRIs (Serotonin and Norepinephrine Reuptake Inhibitors) and SSRIs (Selective Serotonin Reuptake Inhibitors), there have been spontaneous reports of adverse events occurring upon discontinuation of these drugs, particularly when abrupt, including the following: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesia, such as electric shock sensations), anxiety, confusion, headache, lethargy, emotional lability, insomnia, hypomania, tinnitus, and seizures. While these events are generally self-limiting, there have been reports of serious discontinuation symptoms. Patients should be monitored for these symptoms when discontinuing treatment with Pristiq. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose, but at a more gradual rate [*see Dosage and Administration (2.4) and Adverse Reactions (6.1) in full prescribing information*]. **Renal Impairment-**In patients with moderate or severe renal impairment or end-stage renal disease (ESRD) the clearance of Pristiq was decreased, thus prolonging the elimination half-life of the drug. As a result, there were potentially clinically significant increases in exposures to Pristiq [*see Clinical Pharmacology (12.6) in full prescribing information*]. Dosage adjustment (50 mg every other day) is necessary in patients with severe renal impairment or ESRD. The doses should not be escalated in patients with moderate or severe renal impairment or ESRD [*see Dosage and Administration (2.2) in full prescribing information*]. **Seizure-** Cases of seizure have been reported in premarketing clinical studies with Pristiq. Pristiq should be prescribed with caution in patients with a seizure disorder. **Hyponatremia-** Hyponatremia can occur as a result of treatment with SSRIs and SNRIs, including Pristiq. In many cases, this hyponatremia appears to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Elderly patients can be at greater risk of developing hyponatremia with SSRIs and SNRIs. Also, patients taking diuretics or who are otherwise volume depleted can be at greater risk [*see Use in Specific Populations (8.5) and Clinical Pharmacology (12.6) in full prescribing information*]. Discontinuation of Pristiq should be considered in patients with symptomatic hyponatremia and appropriate medical intervention should be instituted. **Coadministration of Drugs Containing Desvenlafaxine and Venlafaxine-** Desvenlafaxine is the major active metabolite of venlafaxine. Products containing desvenlafaxine and products containing venlafaxine should not be used concomitantly with Pristiq. **Interstitial Lung Disease and Eosinophilic Pneumonia-** Interstitial lung disease and eosinophilic pneumonia associated with venlafaxine (the parent drug of Pristiq) therapy have been rarely reported. The possibility of these adverse events should be considered in patients treated with Pristiq who present with progressive dyspnea, cough, or chest discomfort. Such patients should undergo a prompt medical evaluation, and discontinuation of Pristiq should be considered.

ADVERSE REACTIONS: Clinical Studies Experience: The most commonly observed adverse reactions in Pristiq-treated MDD patients in short-term fixed-dose studies (incidence ≥5% and at least twice the rate of placebo in the 50- or 100-mg dose groups) were nausea, dizziness, insomnia, hyperhidrosis, constipation, somnolence, decreased appetite, anxiety, and specific male sexual function disorders. Adverse reactions reported as reasons for discontinuation of treatment- The most common adverse reactions leading to discontinuation in at least 2% of the Pristiq-treated patients in the short-term studies, up to 8 weeks, were nausea (4%); dizziness, headache and vomiting (2% each); in the long-term study, up to 9 months, the most common was vomiting (2%). Common adverse reactions in placebo-controlled MDD studies- Table 3 in full PI shows the incidence of common adverse reactions that occurred in ≥2% of Pristiq-treated MDD patients at any dose in the 8-week, placebo-controlled, fixed-dose, premarketing clinical studies. In general, the adverse reactions were most frequent in the first week of treatment. Cardiac disorders: Palpitations, Tachycardia, Blood pressure increased; Gastrointestinal disorders: Nausea, Dry mouth, Diarrhea, Constipation, Vomiting; General disorders and administration site conditions: Fatigue, Chills, Feeling jittery, Asthenia; Metabolism and nutrition disorders: Decreased appetite, weight decreased; Nervous system disorders: Dizziness, Somnolence, Headache, Tremor, Paraesthesia, Disturbance in attention; Psychiatric Disorders: Insomnia, Anxiety, Nervousness, Irritability, Abnormal dreams; Renal and urinary disorders: Urinary hesitation; Respiratory, thoracic, and mediastinal disorders: Yawning; Skin and subcutaneous tissue disorders: Hyperhidrosis, Rash; Special Senses: Vision blurred; Mydriasis, Tinnitus, Dysgeusia; Vascular Disorders: Hot flush. Sexual function adverse reactions-Table 4 shows the incidence of sexual function adverse reactions that occurred in ≥2% of Pristiq-treated MDD patients in any fixed-dose group (8-week, placebo-controlled, fixed and flexible-dose, premarketing clinical studies). Men Only: Anorgasmia, Libido decreased, Orgasm abnormal, Ejaculation delayed, Erectile dysfunction, Ejaculation disorder, Ejaculation failure, Sexual dysfunction; Women Only: Anorgasmia Other adverse reactions observed in premarketing clinical studies: Other infrequent adverse reactions occurring at an incidence of <2% in MDD patients treated with Pristiq were: *Immune system disorders* – Hypersensitivity. *Investigations* – Liver function test abnormal, blood prolactin increased. *Nervous system disorders* – Convulsion, syncope, extrapyramidal disorder. *Psychiatric disorders* – Depersonalization, hypomania. *Respiratory, thoracic and mediastinal disorders* – Epistaxis. *Vascular disorders* – Orthostatic hypotension. In clinical studies, there were uncommon reports of ischemic cardiac adverse events, including myocardial ischemia, myocardial infarction, and coronary occlusion requiring revascularization; these patients had multiple underlying cardiac risk factors. More patients experienced these events during Pristiq treatment as compared to placebo *[see Warnings and Precautions (5.7)*]. Discontinuation events-Adverse events reported in association with abrupt discontinuation, dose reduction or tapering of treatment in MDD clinical studies at a rate of ≥5% include dizziness, nausea, headache, irritability, insomnia, diarrhea, anxiety, abnormal dreams, fatigue, and hyperhidrosis. In general, discontinuation events occurred more frequently with longer duration of therapy [*see Dosage and Administration (2.4) and Warnings and Precautions (5.9) in full prescribing information*]. Laboratory, ECG and vital sign changes observed in MDD clinical studies- The following changes were observed in placebo-controlled, short-term, premarketing MDD studies with Pristiq. *Lipids*-Elevations in fasting serum total cholesterol, LDL (low density lipoproteins) cholesterol, and triglycerides occurred in the controlled studies. Some of these abnormalities were considered potentially clinically significant [*see Warnings and Precautions (5.8)*]. *Proteinuria*-Proteinuria, greater than or equal to trace, was observed in the fixed-dose controlled studies (see Table 6 in full prescribing information). This proteinuria was not associated with increases in BUN or creatinine and was generally transient. *ECG changes*-Electrocardiograms were obtained from 1,492 Pristiq-treated patients with major depressive disorder and 984 placebo-treated patients in clinical studies lasting up to 8 weeks. No clinically relevant differences were observed between Pristiq-treated and placebo-treated patients for QT, QTc, PR, and QRS intervals. In a thorough QTc study with prospectively determined criteria, desvenlafaxine did not cause QT prolongation. No difference was observed between placebo and desvenlafaxine treatments for the QRS interval. *Vital sign changes*-Table 7 summarizes the changes that were observed in placebo-controlled, short-term, premarketing studies with Pristiq in patients with MDD (doses 50 to 400 mg). Relative to placebo, Pristiq was associated with mean increase of up to 2.1 mm Hg in systolic blood pressure, 2.3 mm Hg in diastolic blood pressure, and 4.1 bpm with supine pulse. At the final on-therapy assessment in the 6-month, double-blind, placebo-controlled phase of a long-term study in patients who had responded to Pristiq during the initial 12-week, open-label phase, there was no statistical difference in mean weight gain between Pristiq- and placebo-treated patients. **DRUG INTERACTIONS: Central Nervous System (CNS)-Active Agents-**The risk of using Pristiq in combination with other CNS-active drugs has not been systematically evaluated. Consequently, caution is advised when Pristiq is taken in combination with other CNS-active drugs [*see Warnings and Precautions (5.13)*]. **Monoamine Oxidase Inhibitors (MAOIs)-** Adverse reactions, some of which were serious, have been reported in patients who have recently been discontinued from a monoamine oxidase inhibitor (MAOI) and started on antidepressants with pharmacological properties similar to Pristiq (SNRIs or SSRIs), or who have recently had SNRI or SSRI therapy discontinued prior to initiation of an MAOI [*see Contraindications (4.2)*]. **Serotonergic Drugs-** Based on the mechanism of action of Pristiq and the potential for serotonin syndrome, caution is advised when Pristiq is coadministered with other drugs that may affect the serotonergic neurotransmitter systems [*see Warnings and Precautions (5.2)*]. **Drugs that Interfere with Hemostasis (e.g., NSAIDs, Aspirin, and Warfarin)-** Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies of case-control and cohort design have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. These studies have also shown that concurrent use of an NSAID or aspirin may potentiate this risk of bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when SSRIs and SNRIs are coadministered with warfarin. Patients receiving warfarin therapy should be carefully monitored when Pristiq is initiated or discontinued. **Ethanol-** A clinical study has shown that desvenlafaxine does not increase the impairment of mental and motor skills caused by ethanol. However, as with all CNS-active drugs, patients should be advised to avoid alcohol consumption while taking Pristiq. **Potential for Other Drugs to Affect Desvenlafaxine-**Inhibitors of CYP3A4 (ketoconazole)- CYP3A4 is a minor pathway for the metabolism of Pristiq. Concomitant use of Pristiq with potent inhibitors of CYP3A4 may result in higher concentrations of Pristiq. Inhibitors of other CYP enzymes- Based on *in vitro* data, drugs that inhibit CYP isozymes 1A1, 1A2, 2A6, 2D6, 2C8, 2C9, 2C19, and 2E1 are not expected to have significant impact on the pharmacokinetic profile of Pristiq. **Potential for Desvenlafaxine to Affect Other Drugs-** Drugs metabolized by CYP2D6 (desipramine)- *In vitro* studies showed minimal inhibitory effect of desvenlafaxine on CYP2D6. Clinical studies have shown that desvenlafaxine does not have a clinically relevant effect on CYP2D6 metabolism at the dose of 100 mg daily. Concomitant use of desvenlafaxine with a drug metabolized by CYP2D6 can result in higher concentrations of that drug. Drugs metabolized by CYP3A4 (midazolam)- *In vitro*, desvenlafaxine does not inhibit or induce the CYP3A4 isozyme. Concomitant use of Pristiq with a drug metabolized by CYP3A4 can result in lower exposures to that drug. Drugs metabolized by CYP1A2, 2A6, 2C8, 2C9 and 2C19- *In vitro*, desvenlafaxine does not inhibit CYP1A2, 2A6, 2C8, 2C9, and 2C19 isozymes and would not be expected to affect the pharmacokinetics of drugs that are metabolized by these CYP isozymes. **P-glycoprotein Transporter-** *In vitro*, desvenlafaxine is not a substrate or an inhibitor for the P-glycoprotein transporter. The pharmacokinetics of Pristiq are unlikely to be affected by drugs that inhibit the P-glycoprotein transporter, and desvenlafaxine is not likely to affect the pharmacokinetics of drugs that are substrates of the P-glycoprotein transporter. **Electroconvulsive Therapy-**There are no clinical data establishing the risks and/or benefits of electroconvulsive therapy combined with Pristiq treatment. **USE IN SPECIFIC POPULATIONS: Pregnancy-** Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy. Teratogenic effects – Pregnancy Category C- There are no adequate and well-controlled studies of Pristiq in pregnant women. Therefore, Pristiq should be used during pregnancy only if the potential benefits justify the potential risks. Non-teratogenic effects- Neonates exposed to SNRIs (Serotonin and Norepinephrine Reuptake Inhibitors), or SSRIs (Selective Serotonin Reuptake Inhibitors), late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Such complications can arise immediately upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. These features are consistent with either a direct toxic effect of SSRIs and SNRIs or, possibly, a drug discontinuation syndrome. It should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome [*see Warnings and Precautions (5.2)*]. When treating a pregnant woman with Pristiq during the third trimester, the physician should carefully consider the potential risks and benefits of treatment [*see Dosage and Administration (2.2)*]. **Labor and Delivery-** The effect of Pristiq on labor and delivery in humans is unknown. Pristiq should be used during labor and delivery only if the potential benefits justify the potential risks. **Nursing Mothers-** Desvenlafaxine (O-desmethylvenlafaxine) is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from Pristiq, a decision should be made whether or not to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. Only administer Pristiq to breastfeeding women if the expected benefits outweigh any possible risk. **Pediatric Use-** Safety and effectiveness in the pediatric population have not been established [*see Box Warning and Warnings and Precautions (5.1)*]. Anyone considering the use of Pristiq in a child or adolescent must balance the potential risks with the clinical need. **Geriatric Use-**Of the 3,292 patients in clinical studies with Pristiq, 5% were 65 years of age or older. No overall differences in safety or efficacy were observed between these patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out. For elderly patients, possible reduced renal clearance of desvenlafaxine should be considered when determining dose [*see Dosage and Administration (2.2) and Clinical Pharmacology (12.6) in the full prescribing information*]. **Renal Impairment-** In subjects with renal impairment the clearance of Pristiq was decreased. In subjects with severe renal impairment (24-hr CrCl < 30 mL/min) and end-stage renal disease, elimination half-lives were significantly prolonged, increasing exposures to Pristiq; therefore, dosage adjustment is recommended in these patients [*see Dosage and Administration (2.2) and Clinical Pharmacology (12.6) in the full prescribing information*]. **Hepatic Impairment-**The mean $t_{1/2}$ changed from approximately 10 hours in healthy subjects and subjects with mild hepatic impairment to 13 and 14 hours in moderate and severe hepatic impairment, respectively. No adjustment in starting dosage is necessary for patients with hepatic impairment.

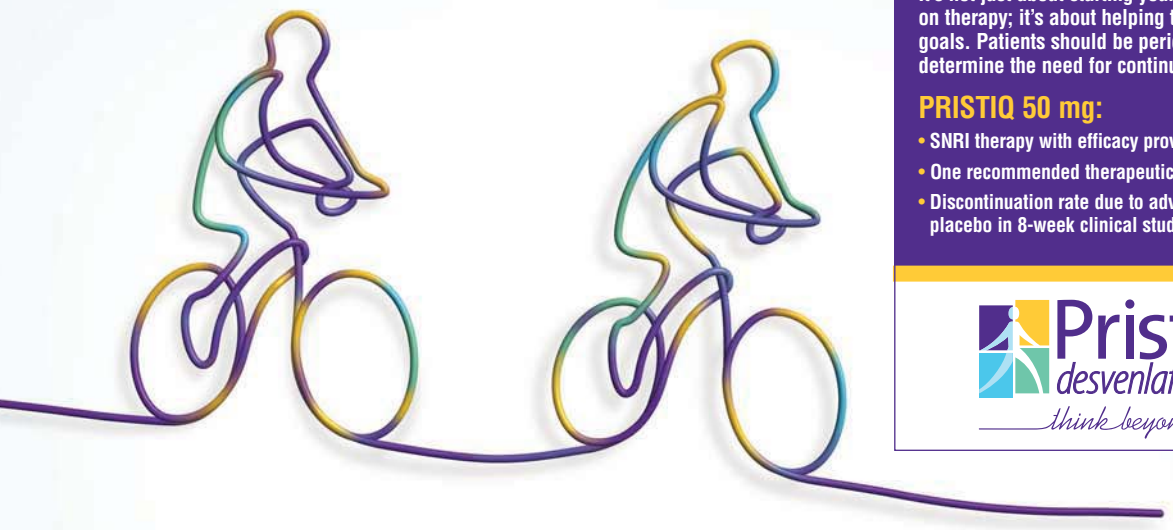
OVERDOSAGE: Human Experience with Overdosage- There is limited clinical experience with desvenlafaxine succinate overdosage in humans. In premarketing clinical studies, no cases of fatal acute overdose of desvenlafaxine were reported. The adverse reactions reported within 5 days of an overdose > 600 mg that were possibly related to Pristiq included headache, vomiting, agitation, dizziness, nausea, constipation, diarrhea, dry mouth, paresthesia, and tachycardia. Desvenlafaxine (Pristiq) is the major active metabolite of venlafaxine. Overdose experience reported with venlafaxine (the parent drug of Pristiq) is presented below; the identical information can be found in the *Overdosage* section of the venlafaxine package insert. In postmarketing experience, overdose with venlafaxine (the parent drug of Pristiq) has occurred predominantly in combination with alcohol and/or other drugs. The most commonly reported events in overdosage include tachycardia, changes in level of consciousness (ranging from somnolence to coma), mydriasis, seizures, and vomiting. Electrocardiogram changes (e.g., prolongation of QT interval, bundle branch block, QRS prolongation), sinus and ventricular tachycardia, bradycardia, hypotension, rhabdomyolysis, vertigo, liver necrosis, serotonin syndrome, and death have been reported. Published retrospective studies report that venlafaxine overdosage may be associated with an increased risk of fatal outcomes compared to that observed with SSRI antidepressant products, but lower than that for tricyclic antidepressants. Epidemiological studies have shown that venlafaxine-treated patients have a higher pre-existing burden of suicide risk factors than SSRI-treated patients. The extent to which the finding of an increased risk of fatal outcomes can be attributed to the toxicity of venlafaxine in overdosage, as opposed to some characteristic(s) of venlafaxine-treated patients, is not clear. Prescriptions for Pristiq should be written for the smallest quantity of capsules consistent with good patient management, in order to reduce the risk of overdose. **Management of Overdosage-**Treatment should consist of those general measures employed in the management of overdosage with any SSRI/SNRI. Ensure an adequate airway, oxygenation, and ventilation. Monitor cardiac rhythm and vital signs. General supportive and symptomatic measures are also recommended. Gastric lavage with a large-bore orogastric tube with appropriate airway protection, if needed, may be indicated if performed soon after ingestion or in symptomatic patients. Activated charcoal should be administered. Induction of emesis is not recommended. Because of the moderate volume of distribution of this drug, forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be of benefit. No specific antidotes for desvenlafaxine are known. In managing an overdose, consider the possibility of multiple drug involvement. The physician should consider contacting a poison control center for additional information on the treatment of any overdose. Telephone numbers for certified poison control centers are listed in the Physicians Desk Reference (PDR®).

This brief summary is based on Pristiq Prescribing Information W10529C002, revised April 2008.

Wyeth®

For the treatment of adults with major depressive disorder

The start is just the beginning



It's not just about starting your adult patients with MDD on therapy; it's about helping them toward their treatment goals. Patients should be periodically reassessed to determine the need for continued treatment.[1]

PRISTIQ 50 mg:

- SNRI therapy with efficacy proven in 8-week clinical studies
- One recommended therapeutic dose from the start
- Discontinuation rate due to adverse events comparable to placebo in 8-week clinical studies[1]

Pristiq® desvenlafaxine 50 mg

think beyond start™

IMPORTANT TREATMENT CONSIDERATIONS

PRISTIQ 50-mg Extended-Release Tablets are indicated for the treatment of major depressive disorder in adults.

WARNING: SUICIDALITY AND ANTIDEPRESSANT DRUGS

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

Contraindications

- PRISTIQ is contraindicated in patients with a known hypersensitivity to PRISTIQ or venlafaxine.
- PRISTIQ must not be used concomitantly with an MAOI or within 14 days of stopping an MAOI. Allow 7 days after stopping PRISTIQ before starting an MAOI.

Warnings and Precautions

- **All patients treated with antidepressants should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the first few months of treatment and when changing the dose.** Consider changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse or includes symptoms of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia, hypomania, mania, or suicidality that are severe, abrupt in onset, or were not part of the patient's presenting symptoms. **Families and caregivers of patients being treated with antidepressants should be alerted about the need to monitor patients.**
- Development of a potentially life-threatening serotonin syndrome may occur with SNRIs and SSRIs, including PRISTIQ, particularly with concomitant use of serotonergic drugs, including triptans, and with drugs that impair the metabolism of serotonin (including MAOIs). If concomitant use is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. Concomitant use of PRISTIQ with serotonin precursors is not recommended.
- Patients receiving PRISTIQ should have regular monitoring of blood pressure since sustained increases in blood pressure were observed in clinical studies. Pre-existing hypertension should be controlled before starting PRISTIQ. Caution should be exercised in treating patients with pre-existing hypertension or other underlying conditions that might be compromised by increases in blood pressure. Cases of elevated blood pressure requiring immediate treatment have been reported. For patients who experience a sustained increase in blood pressure, either dose reduction or discontinuation should be considered.
- SSRIs and SNRIs, including PRISTIQ, may increase the risk of bleeding events. Concomitant use of aspirin, NSAIDs, warfarin, and other anticoagulants may add to this risk.
- Mydriasis has been reported in association with PRISTIQ; therefore, patients with raised intraocular pressure or those at risk of acute narrow-angle glaucoma (angle-closure glaucoma) should be monitored.
- PRISTIQ is not approved for use in bipolar depression. Prior to initiating treatment with an antidepressant, patients should be adequately screened to determine the risk of bipolar disorder.
- As with all antidepressants, PRISTIQ should be used cautiously in patients with a history or family history of mania or hypomania, or with a history of seizure disorder.
- Caution is advised in administering PRISTIQ to patients with cardiovascular, cerebrovascular, or lipid metabolism disorders. Increases in blood pressure and small increases in heart rate were observed in clinical studies with PRISTIQ. PRISTIQ has not been evaluated systematically in patients with a recent history of myocardial infarction, unstable heart disease, uncontrolled hypertension, or cerebrovascular disease.
- Dose-related elevations in fasting serum total cholesterol, LDL (low density lipoprotein) cholesterol, and triglycerides were observed in clinical studies. Measurement of serum lipids should be considered during PRISTIQ treatment.
- On discontinuation, adverse events, some of which may be serious, have been reported with PRISTIQ and other SSRIs and SNRIs. Abrupt discontinuation of PRISTIQ has been associated with the appearance of new symptoms. Patients should be monitored for symptoms when discontinuing treatment. A gradual reduction in dose (by giving 50 mg of PRISTIQ less frequently) rather than abrupt cessation is recommended whenever possible.
- Dosage adjustment (50 mg every other day) is necessary in patients with severe renal impairment or end-stage renal disease (ESRD). The dose should not be escalated in patients with moderate or severe renal impairment or ESRD.
- Products containing desvenlafaxine and products containing venlafaxine should not be used concomitantly with PRISTIQ.
- Hyponatremia may occur as a result of treatment with SSRIs and SNRIs, including PRISTIQ. Discontinuation of PRISTIQ should be considered in patients with symptomatic hyponatremia.
- Interstitial lung disease and eosinophilic pneumonia associated with venlafaxine (the parent drug of PRISTIQ) therapy have been rarely reported.

Adverse Reactions

- The most commonly observed adverse reactions in patients taking PRISTIQ vs placebo for MDD in short-term fixed-dose premarketing studies (incidence ≥5% and twice the rate of placebo in the 50-mg dose group) were nausea (22% vs 10%), dizziness (13% vs 5%), hyperhidrosis (10% vs 4%), constipation (9% vs 4%), and decreased appetite (5% vs 2%).

Reference: 1. Pristiq® (desvenlafaxine) Prescribing Information, Wyeth Pharmaceuticals Inc.

Please see brief summary of Prescribing Information on adjacent pages.

Pristiq® desvenlafaxine EXTENDED-RELEASE TABLETS

Wyeth®