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**Websites**

**Accreditation Council for Continuing Medical Education.** National organization that grants accreditation for entities producing CME. [www.accme.org](http://www.accme.org)

**Accreditation Council for Graduate Medical Education.** National organization that grants accreditation of post-MD medical training programs. [www.acgme.org](http://www.acgme.org)

**American Board of Internal Medicine.** Sets the standards and certifies the knowledge, skills, and attitudes of physicians who practice internal medicine. [www.abim.org](http://www.abim.org)

**American Board of Medical Specialties.** Assists medical specialty boards in the development and use of standards on the ongoing evaluation and certification of physicians. [www.abms.org](http://www.abms.org)

**American College of Physicians.** Website includes resources and articles on career development and continuing education. [www.acponline.org](http://www.acponline.org)

**The Annotated List of Online Continuing Medical Education.** Dr. Bernard Sklar’s comprehensive list of online CME activities. [www.cmelist.com](http://www.cmelist.com)

**Applied Management Systems, Inc.** Provides accounts receivable management, health information management, and systems engineering consulting for healthcare organizations. [www.aboutams.com](http://www.aboutams.com)

**Center for Professional and Personal Renewal.** Peter Moskowitz, MD, offers coaching for physicians. [www.cppr.com](http://www.cppr.com)

**Center for Spirituality and Healing at the University of Minnesota.** Offers workshops for physicians and other healthcare providers. [www.csh.umn.edu](http://www.csh.umn.edu)

**CompHealth.** Salt Lake City-based staffing firm that helps
physicians, nurses, and allied health professionals find both permanent and temporary jobs. www.comphealth.com

**Doctor Disability Insurance.** A service to assist physicians in locating and selecting disability insurance. www.doctordisability.com

**eHealthInsurance.** Get quotes and compare individual health insurance plans. www.ehealthinsurance.com

**The Entrepreneurial MD.** Philippa Kennealy, MD, MPH, CPCC, PCC, coaches physicians to become thriving entrepreneurs. www.entrepreneurialmd.com

**The Glowacki Group.** A financial planning group offering an array of insurance and investment products and network services. www.glowacki-group.com

**Health Futures, Inc.** Jeff Goldsmith speaks, writes, and consults about the future of health care. www.healthfutures.net

**Henry J. Kaiser Family Foundation.** Non-profit organization that focuses on health policy and communication. www.kff.org

**Imagine What If, Inc.** Futurist and change expert Joe Flower works with healthcare organizations. www.imaginewhatif.com

**The Inventure Group.** Richard Leider is “the purpose coach.” www.inventuregroup.com.

**Jack Valancy Consulting.** Healthcare consultant and speaker. www.valancy.com

**LocumLife.** Free magazine for physicians doing or interested in working locums. www.locumlife.com

**MDVIP.** Florida-based company helping physicians establish prevention-based practices. www.mdvip.com

**Medical Group Management Association.** A national organization representing the medical group practice profession and healthcare administrators. www.mgma.org

**Migrant Clinicians Network.** Resource for healthcare providers who care for migrant and seasonal farm workers. www.migrantclinician.org

**MomMD.** A resource for women physicians with children. www.mommd.com
Richard Moss, MD. Author, spiritual teacher, and workshop leader. www.richardmoss.com

The Motley Fool. Practical investment advice—with humor. www.fool.com

National Association of Locum Tenens Organizations. Find a list of companies that place physicians in locum positions. www.nalto.org

National Association of Professional Organizers. For expert help getting yourself organized. www.napo.net

Pharmaceutical Careers, Inc. Tom Bramswig helps physicians find jobs in the pharmaceutical industry. www.pharmaceuticalcareers.com

ProtectYourIncome.com. A source for information and guidance on disability insurance for professionals. www.protectyourincome.com

Shoulder to Shoulder, Inc. Provides primary care, public health, dental care, nutrition, and education to poor communities in Honduras. www.shouldertoshoulder.org


Today’s Hospitalist Magazine. For physicians practicing hospital medicine. www.todayshospitalist.com
INDICATIONS AND USAGE
Namenda (memantine hydrochloride) is indicated for the treatment of moderate to severe dementia of the Alzheimer's type.

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

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

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

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

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

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

Drug-Drug Interactions
N-methyl-D-aspartate (NMDA) antagonists: The combination of Namenda with other NMDA antagonists (amantadine, ketamine, and dextromethorphan) has not been systematically evaluated and such use should be approached with caution. Effects of Namenda on substrates of microsomal enzymes: In vitro studies conducted with marker substrates of CYP450 enzymes (CYP1A2, -2A6, -2C9, -2D6, -2E1, -3A4) showed minimal inhibition of these enzymes by memantine. In addition, in vitro studies indicate that at concentrations exceeding those associated with efficacy, memantine does not induce the cytochrome P450 isoenzyme CYP3A4. Interactions of memantine with drugs metabolized by these enzymes are expected. Effects of inhibitors and/or substrates of microsomal enzymes on Namenda: Memantine is predominantly renally eliminated, and drugs that are substrates of or inhibitors of the CYP450 system are not expected to alter the metabolism of memantine.

Acetylcholinesterase (AChE) inhibitors: Co-administration of Namenda with the AChE inhibitor donepezil HCl did not affect the pharmacokinetics of either compound. In a 24-week controlled clinical study in patients with moderate to severe Alzheimer's disease, donepezil, which was co-administered at the same dose as in the placebo group, did not differ. Table 1 lists treatment-emergent signs and symptoms that were reported in at least 2% of patients in placebo-controlled dementia trials and that were associated with the conditions of use, reporting behavior and the types of patients treated may differ. Table 1 lists treatment-emergent signs and symptoms that were reported in at least 2% of patients in placebo-controlled dementia trials and that were associated with the conditions of use, reporting behavior and the types of patients treated may differ. Table 1 lists treatment-emergent signs and symptoms that were reported in at least 2% of patients in placebo-controlled dementia trials and that were associated with the conditions of use, reporting behavior and the types of patients treated may differ.

Adverse Events Reported in Controlled Trials: The reported adverse events in Namenda (memantine hydrochloride) trials reflect experience gained under closely monitored conditions in a highly selected patient population. In actual practice or in other clinical trials, these frequency estimates may not apply, as the conditions of use, reporting behavior and the types of patients treated may differ. Table 1 lists treatment-emergent signs and symptoms that were reported in at least 2% of patients in placebo-controlled dementia trials and that were associated with the conditions of use, reporting behavior and the types of patients treated may differ. Table 1 lists treatment-emergent signs and symptoms that were reported in at least 2% of patients in placebo-controlled dementia trials and that were associated with the conditions of use, reporting behavior and the types of patients treated may differ.

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

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

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

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

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

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

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

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Table 1: Adverse Events Reported in at Least 2% of Patients in Placebo-Controlled Dementia Trials and in at Least 2% of Patients Receiving Namenda and at a Higher Frequency Than Placebo-Controlled Patients.

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

Body System Placebo Namenda % %

Body as a Whole

Fatigue

Pain

Cardiovascular System

Hypertension

Central and Peripheral Nervous System

Dizziness

Headache

Gastrointestinal System

Constipation

Vomiting

Musculoskeletal System

Back pain

Psychiatric Disorders

Confusion

Somnolence

Hallucination

Respiratory System

Coughing

Dyspnea

1

2

3

4

5

6

7
Other adverse events occurring with an incidence of at least 2% in Namenda-treated patients but at a greater or equal rate on placebo were agitation, fall, inflicted injury, urinary incontinence, diarrhea, bronchitis, insomnia, urinary tract infection, influenza-like symptoms, abnormal gait, depression, upper respiratory tract infection, anxiety, peripheral edema, nausea, anorexia, and arthralgia.

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

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

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

Other Adverse Events Observed During Clinical Trials

Namenda has been administered to approximately 1350 patients with dementia, of whom more than 1200 received the maximum recommended dose of 20 mg/day. Patients received Namenda treatment for periods of up to 884 days, with 862 patients receiving at least 24 weeks of treatment and 387 patients receiving 48 weeks or more of treatment. Treatment emergent signs and symptoms that occurred during 8 controlled clinical trials and 4 open-label trials were recorded as adverse events by the clinical investigators using terminology of their own choosing. To provide an overall estimate of the proportion of individuals having similar types of events, the events were grouped into a smaller number of standardized categories using WHO terminology, and event frequencies were calculated across all studies. All adverse events occurring in at least two patients are included, except for those already listed in Table 1, WHO terms too general to be informative, minor symptoms or events unlikely to be drug-caused, e.g., because they are common in the condition being treated. Events are grouped in relation to body system and listed and listed using the following definitions: frequent adverse events - those occurring in at least 10% of patients; infrequent adverse events- those occurring in 1-9% of patients; rare adverse events - those occurring in less than 1% of patients. Adverse events are not necessarily related to Namenda treatment and in most cases were observed at a similar frequency in placebo-treated patients in the controlled studies.

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

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


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

Psychiatric Disorders: Frequent: aggressive reaction. Infrequent: delusion, personality disorder, emotional lability, nervousness, sleep disorder, libido increased, psychosis, anemia, apathy, paranoid reaction, thinking abnormal, crying abnormal, appetite increased, paroxysm, delirium, depersonalization, neurosis, suicide attempt.


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

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


Events Reported Subsequent to the Marketing of Namenda, both US and Ex-US

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

ANIMAL TOXICOLOGY

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

DRUG ABUSE AND DEPENDENCE

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

OVERDOSE

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

Because strategies for the management of overdose are continually evolving, it is advisable to contact a poison control center to determine the latest recommendations for the management of an overdose of any drug. As in any cases of overdose, general supportive measures should be utilized, and treatment should be symptomatic. Elimination of memantine can be enhanced by acidification of urine.
Improves function, delays onset of behavioral symptoms, and provides benefits in cognition\textsuperscript{1,2}

Excellent safety and tolerability with low risk of unpleasant gastrointestinal side effects\textsuperscript{4,6}

May reduce care dependence and caregiver distress\textsuperscript{3,6}

Proven effective first-line and in combination with an acetylcholinesterase inhibitor\textsuperscript{1,2}

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**Preferred status on the majority of health plan and Medicare Part D formularies**

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

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


For more details, please visit [www.namenda.com](http://www.namenda.com).

Please see brief summary of Prescribing Information on the adjacent pages.