MEMANTINE

THERAPEUTICS

Brands
- Namenda, Ebixa

Generic?
No

Class
- NMDA receptor antagonist

Commonly Prescribed for
(FDA approved in bold)
- Alzheimer dementia (AD) (moderate or severe)
- Vascular dementia
- Parkinson’s disease related dementia
- Dementia with Lewy bodies (DLB)
- HIV dementia
- Migraine prophylaxis
- Neuropathic pain
- Attention deficit hyperactivity disorder
- Binge-eating disorder

How the Drug Works
- Binds preferentially to NMDA receptors, preventing glutamate from activating these receptors. The excitatory effects of glutamate are postulated to contribute to the development of AD and lesions such as neurofibrillary tangles
- Although symptoms of AD can improve, memantine does not prevent disease progression

How Long Until It Works
- Weeks to months

If It Works
- Continue to use but symptoms of dementia usually continue to worsen

If It Doesn’t Work
- Non-pharmacologic measures are the basis of dementia treatment. Maintain regular schedules and routines. Avoid prolonged travel, unnecessary medical procedures or emergency room visits, crowds, and large social gatherings
- Limit drugs with sedative properties such as opioids, hypnotics, antiepileptic drugs and tricyclic antidepressants

Best Augmenting Combos for Partial Response or Treatment-Resistance
- Addition of cholinesterase inhibitors may be beneficial. In one study donepezil plus memantine reduced the rate of progression compared to those taking donepezil alone
- Treat depression, if present, with SSRIs. Avoid tricyclic antidepressants in demented patients due to risk of confusion
- For significant confusion and agitation avoid neuroleptics (especially in Lewy body dementia) to avoid the risk of neuroleptic malignant syndrome. Atypical antipsychotics (risperidone, quetiapine, olanzapine, clozapine) can be used instead

Tests
- None required

ADVERSE EFFECTS (AEs)

How Drug Causes AEs
- Direct effect on NMDA receptors

Notable AEs
- Hypertension, dizziness, constipation, coughing, dyspnea, fatigue, pain, ataxia, vertigo, confusion

Life-Threatening or Dangerous AEs
- Syncope or cardiac arrhythmias can occur although it is unclear that these events are related to memantine

Weight Gain
- Unusual

Sedation
- Unusual

What to Do About AEs
- In patients with dementia, determining if AEs are related to medication or another medical
MEMANTINE (continued)

condition can be difficult. For CNS side effects, discontinuation of non-essential centrally acting medications may help. If a bothersome AE is clearly drug-related then discontinue memantine

Best Augmenting Agents for AEs
• Most AEs do not respond to adding other medications

Metabolites have little clinical effect. Peak effect at 3–7 hours. Protein binding 45%

Drug Interactions
• Use with caution with other drugs which are NMDA antagonists (amantadine, ketamine, dextromethorphan)
• Use with caution with drugs that also utilize renal mechanisms of excretion such as ranitidine, cimetidine, hydrochlorothiazide or nicotine
• Drugs that make urine alkaline (carbonic anhydrase inhibitors, sodium bicarbonate) reduce memantine clearance. Use with caution

Do Not Use
• Hypersensitivity to the drug

DOSING AND USE

Usual Dosage Range
• 5–20 mg/daily

Dosage Forms
• Tablets: 5, 10 mg
• Oral Solution: 2 mg/mL

How to Dose
• Start at 5 mg in the evening. Increase by 5 mg per week until taking 10 mg twice daily or until reaching desired effect. Do not increase dose faster than intervals of 1 week. If AEs occur, titrate more slowly

Dosing Tips
• Slow titration can reduce AEs. Food does not affect absorption

Overdose
• Symptoms may include restlessness, psychosis, hallucinations, and stupor. Treatment: acidification of urine will enhance urinary excretion of memantine

Long-Term Use
• Safe for long-term use. Effectiveness may decrease over time as the dementing illness progresses

Habit Forming
• No

How to Stop
• Abrupt discontinuation is unlikely to produce AEs except worsening of dementia symptoms

Pharmacokinetics
• Most drug is secreted in urine unchanged with an elimination half-life of 60–80 hours. Minimal inhibition of CYP p450 enzymes.

Renal Impairment
• Drug is renally excreted. Consider dose reduction with moderate impairment and do not use in patients with severe renal insufficiency

Hepatic Impairment
• No known effects

Cardiac Impairment
• No significant change in ECG observed in trials compared to placebo. No known effects

Elderly
• There is reduced drug clearance, but no dose adjustment needed as the dose used is the lowest that provides clinical improvement

Children and Adolescents
• Not studied in children. AD does not occur in children

Pregnancy
• Category B. Decreased birth weight in animal studies. Use only if benefits of medication outweigh risks

Breast Feeding
• Unknown if excreted in breast milk. Use with caution
### THE ART OF NEUROPHARMACOLOGY

#### Potential Advantages
- Proven effectiveness for AD, even with severe dementia. Fewer cholinergic or GI AEs than cholinesterase inhibitors

#### Potential Disadvantages
- Cost and minimal effectiveness. Does not prevent progression of AD or other dementias. May be less effective for Lewy body dementia than cholinesterase inhibitors

#### Primary Target Symptoms
- Confusion, agitation, performing activities of daily living

#### Pearls
- May be used in combination with cholinesterase inhibitors with good effect
- Effective for migraine prophylaxis in open-label studies at doses of 10 mg/day or greater
- Structurally related to amantadine, a weak NMDA antagonist

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**Suggested Reading**


