

# Texas Vendor Drug Program

## Drug Use Criteria: Memantine (Namenda®)

### Publication History

1. Developed April 2010.
2. Revised May 2019; May 2017; November 2015; March 2014; March 2012.

**Notes:** All criteria may be applied retrospectively. The information contained is for the convenience of the public. The Texas Health and Human Services Commission is not responsible for any errors in transmission or any errors or omissions in the document.

***Medications listed in the tables and non-FDA approved indications included in these retrospective criteria are not indicative of Vendor Drug Program formulary coverage.***

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**TEXAS**  
Health and Human  
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# 1 Dosage

## 1.1 Adults

Memantine, a non-competitive N-methyl D-aspartate (NMDA) receptor antagonist, is FDA-approved for use in the palliative management of moderate-to-severe Alzheimer's disease. Glutamate, the key excitatory neurotransmitter in the central nervous system, is released into synapses when certain neurons die and activates NMDA receptors, causing overexcitation, an influx of calcium ions and, ultimately, death of downstream neurons. NMDA receptor activation is thought to be one of the main causes of neurodegeneration in various types of dementia, including Alzheimer's-associated dementia. Memantine exerts pharmacologic effects by blocking glutamate activity. However, memantine has not been shown to delay or prevent neurodegeneration in Alzheimer's disease patients.<sup>1-13</sup>

Memantine is available as an immediate-release (IR) tablet and solution as well as extended-release (ER) capsule. Recently, a combination product containing donepezil and memantine extended-release (Namzaric®) has been FDA-approved for use in patients with moderate to severe Alzheimer's dementia stabilized on donepezil.<sup>7, 8, 16</sup> Acetylcholinesterase inhibitors like donepezil exert pharmacologic effects by increasing availability of intrasynaptic acetylcholine in the presence of intact cholinergic neurons.<sup>3-5</sup> Alzheimer's disease is associated with significant losses in cholinergic neurons and decreased concentrations of acetylcholine, a neurotransmitter significantly involved in learning and memory processes.<sup>17</sup>

Recommended memantine and memantine/donepezil dosages are summarized in Table 1. Patient profiles documenting dosages exceeding these recommendations will be reviewed.

In patients with severe renal impairment (creatinine clearance 5-29 mL/min, based on Cockcroft-Gault equation), the memantine target IR dose should be reduced to 5 mg orally twice daily, while memantine ER maximum dosages should not exceed 14 mg once daily.<sup>1-6</sup> Patients with severe renal impairment (CrCl 5-29 mL/min) stabilized on memantine 5 mg twice daily immediate-release or 14 mg daily extended-release and donepezil 10 mg daily may utilize memantine/donepezil combination therapy in doses not exceeding 14 mg/10 mg daily.<sup>3-7</sup>

**Table 1. Approved Memantine Adult Dosage Recommendations: Monotherapy<sup>1-6</sup>**

Drug Name	Dosage Form/ Strength	Titration Dose <sup>^</sup>	Maximum Recommended Dosage
memantine IR* (Namenda <sup>®</sup> )	5 mg, 10 mg tablets 2 mg/ml oral solution	Week 1: 5 mg orally once daily Week 2: 5 mg orally twice daily Week 3: 10 mg in am, 5 mg in pm Week 4: 10 mg orally twice daily	20 mg/day, in divided doses
memantine ER+ (Namenda XR <sup>®</sup> )	7 mg, 14 mg, 21 mg, 28 mg capsules	Week 1: 7 mg orally once daily Week 2: 14 mg orally once daily Week 3: 21 mg orally once daily Week 4: 28 mg orally once daily	28 mg/day as a single dose

\*IR = immediate-release; +ER = extended-release

<sup>^</sup>Titrate in weekly intervals to next dose, only if previous dose tolerated

**Table 2. Approved Memantine Adult Dosage Recommendations: Combination Therapy<sup>3-8</sup>**

Drug Name	Dosage Form/ Strength	Titration Dose <sup>^</sup>	Maximum Recommended Dosage
memantine extended- release/donepezil (Namzaric <sup>®</sup> )	7 mg/10 mg, 14 mg/ 10 mg, 21 mg/ 10 mg, 28 mg/ 10 mg capsules	---	28 mg/10 mg once daily

<sup>^</sup>Titrate in weekly intervals to next dose, only if previous dose tolerated

While Tariot et al.<sup>18</sup> have shown beneficial improvements in cognitive and behavioral performance when memantine is administered in combination with donepezil, a recent trial by Howard and cohorts<sup>19</sup> **and systematic review by Tricco et al.**<sup>20</sup> revealed that monotherapy with memantine or donepezil was significantly better than no therapy, but combined therapy did not produce significant improvements in cognitive and functional outcomes compared to donepezil alone. Although not FDA-approved, memantine therapy has demonstrated some efficacy in treating mild-to-moderate vascular dementia and Parkinson's disease dementia.<sup>6, 21, 22</sup> Memantine has been approved as an extended-release formulation to simplify the dosage regimen and improve compliance/adherence.<sup>23</sup>

## 1.2 Pediatrics

Memantine is not recommended for use in children and adolescents as safety and efficacy have not been established in the pediatric population.<sup>1-7</sup>

## 2 Duration of Therapy

Memantine may be prescribed chronically until the dementia associated with Alzheimer's disease becomes unresponsive to therapy.<sup>1-7</sup>

## 3 Duplicative Therapy

Adjunctive administration of memantine with other NMDA antagonists, such as amantadine and dextromethorphan, has not been clinically evaluated. Therefore, memantine should be prescribed cautiously, if at all, with other available NMDA antagonists.

## 4 Drug-Drug Interactions

Patient profiles will be assessed to identify those drug regimens which may result in clinically significant drug-drug interactions. Drug-drug interactions considered clinically relevant for memantine are summarized in **Table 3**. Only those drug-drug interactions identified as clinical significance level 1 or those considered life-threatening which have not yet been classified will be reviewed.

**Table 3. Memantine Drug-Drug Interactions<sup>1-7</sup>**

Target Drug	Interacting Drug	Interaction	Recommendation	Clinical Significance Level <sup>#</sup>
memantine, memantine/donepezil	alkalinizing agents (e.g., select carbonic anhydrase inhibitors, sodium bicarbonate)	memantine clearance reduced by about 80% in alkaline conditions (pH $\geq$ 8); adjunctive administration with alkalinizing agents may decrease memantine elimination and increase memantine serum levels and potential for increased pharmacologic/adverse effects	administer drug combination cautiously together; monitor patients for increased pharmacologic/adverse effects	moderate (DrugReax) 3-moderate (CP)

**Table 3. Memantine Drug-Drug Interactions<sup>1-7</sup>**

Target Drug	Interacting Drug	Interaction	Recommendation	Clinical Significance Level <sup>#</sup>
memantine, memantine/donepezil	other drugs excreted by renal tubular secretion (e.g., amiloride, cimetidine, dofetilide, nicotine, quinidine, ranitidine)	memantine eliminated by renal tubular cationic transport; combined administration may result in altered serum levels of both memantine and other drugs excreted by renal tubular secretion due to competition for transport system; elevated dofetilide levels may increase potential for arrhythmias, including torsades de pointes	monitor patient responses, observe for adverse effects or loss of efficacy, and adjust doses as necessary	moderate (DrugReax) dofetilide, procainamide, quinidine: 2-major; all other drugs: 3-moderate (CP)

<sup>#</sup>CP = Clinical Pharmacology

## 5 References

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