Dementa-D

Memantine Hydrochloride USP Extended Release
& Donepezil Hydrochloride USP

Description
Dementa-D capsule contains Memantine, an orally active NMDA receptor antagonist, as the hydrochloride salt and Donepezil, a reversible inhibitor of the enzyme acetylcholinesterase, as the hydrochloride salt.

Composition
Dementa-D capsule 14/10 mg : Each capsule contains Memantine Hydrochloride USP 14 mg extended release & Donepezil Hydrochloride USP 10 mg.
Dementa-D capsule 28/10 mg : Each capsule contains Memantine Hydrochloride USP 28 mg extended release & Donepezil Hydrochloride USP 10 mg.

Mode of Action
Persistent activation of N-methyl-D-aspartate (NMDA) receptors in Central Nervous System by the excitatory amino acid glutamate has been hypothesized to contribute to the symptomatology of Alzheimer's disease. Memantine is postulated to exert its therapeutic effect through its action as a low to moderate affinity as an uncompetitive (open-channel) NMDA receptor antagonist which binds preferentially to the NMDA receptor-operated cation channels.
Current theories on the pathogenesis of the cognitive signs and symptoms of Alzheimer's disease attribute some of them to a deficiency of cholinergic neurotransmission. Donepezil is postulated to exert its therapeutic effect by enhancing cholinergic function. This is accomplished by increasing the concentration of acetylcholine in the central nervous system through reversible inhibition of its hydrolysis by acetylcholinesterase.

Pharmacokinetics
Memantine is well absorbed after oral administration and has linear pharmacokinetics over the therapeutic dose range. It is excreted predominantly unchanged in urine and has a terminal elimination half-life of about 60-80 hours.14 mg once-daily memantine hydrochloride extended-release Cmax and AUC0-24 values are 48%. The mean volume of distribution of Memantine is 9-11 L/kg and the plasma protein binding is low (45%).
Memantine undergoes partial hepatic metabolism. The hepatic microsomal CYP450 enzyme system does not play a significant role in the metabolism of memantine. Memantine is excreted predominantly in the urine, unchanged, and has a terminal elimination half-life of about 60-80 hours.
Donepezil is absorbed with a relative oral bioavailability of 100% and reaches peak plasma concentrations in 3 to 4 hours. Donepezil is metabolized by CYP 450 isoenzymes 2D6 and 3A4 and undergoes glucuronidation. The elimination half-life of donepezil is about 70 hours, and the mean apparent plasma clearance (Cl/F) is 0.13 – 0.19 L/hr/kg.

Indications
Dementa-D is indicated for the treatment of moderate to severe dementia of the Alzheimer's type.

Dosage and Administration
The recommended starting dose is 14/10 mg once daily in the evening. Dose should be increased to the maintenance dose of 28/10 mg once daily. The minimum recommended interval between dose increase is one week. It can be taken with or without food. For patients with severe renal impairment (Creatinine clearance 5-29 ml/min), the recommended dose is 14/10 mg taken once a day in the evening.

Side Effects
Most frequent side effects (frequency of 2% or less) include dizziness, headache & diarrhea. Occasional side effects include muscle problems if anesthesia needed, slow heartbeat & fainting, stomach acidity, nausea & vomiting, difficulty passing urine, seizures & worsening of lung problems.

Drug Interactions
Drugs that make the urine alkaline, NMDA antagonists, Anticholinergics, Cholinomimetics & other cholinesterase inhibitors.

Contraindications
Dementa-D is contraindicated in patients with known hypersensitivity to memantine hydrochloride, donepezil hydrochloride, piperidine derivatives, or to any excipients used in the formulation.

Precautions
Donepezil hydrochloride, as a cholinesterase inhibitor, is likely to exaggerate succinylcholine-type muscle relaxation during anesthesia. Patients treated with Dementa-D should be monitored closely for symptoms of active or occult gastrointestinal bleeding, especially those at increased risk for developing ulcers. Because of their pharmacological action, cholinesterase inhibitors may have vagotonic effects on the sinoatrial and atrioventricular nodes. This effect may manifest as bradycardia or heart block in patients both with and without known underlying cardiac conduction abnormalities. Although not observed in clinical trials of donepezil hydrochloride, cholinomimetics may cause bladder outflow obstruction. Cholinomimetics, including donepezil hydrochloride, are believed to have some potential to cause generalized convulsions. Because of their cholinomimetic actions, cholinesterase inhibitors should be prescribed with care to patients with a history of asthma or obstructive pulmonary disease.

Pregnancy and Lactation
Pregnancy Category C. There are no adequate and/or well-controlled studies of Dementa-D or its active ingredients (memantine hydrochloride and donepezil hydrochloride) in pregnant women. Dementa-D should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
It is not known whether memantine or donepezil are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Dementa-D is administered to a nursing woman.

Missed Dose
If any dose is missed, just wait and take the next dose at the usual time. Do not double the dose to compensate for the missed dose.

Storage Condition
Do not store above 30°C and keep in a dry place. Protect from light. Keep this medication out of reach of children.

Packaging
Dementa-D capsule 14/10 mg : Each carton contains 3x10's capsule in blister pack.
Dementa-D capsule 28/10 mg : Each carton contains 4x8's capsule in blister pack.

Manufactured by

ZISKA
PHARMA

Ziska Pharmaceuticals Ltd.
Kaliakoir, Gazipur, Bangladesh