Elzer®

Donepezil HCl

Composition:
Elzer® Tablet: Each film coated tablet contains Donepezil HCl INN 5 mg.

Pharmacology:
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. Elzer® (Donepezil hydrochloride) is postulated to exert its therapeutic effect by enhancing cholinergic function. This is accomplished by increasing the concentration of acetylcholine through reversible inhibition of its hydrolysis by acetylcholinesterase. If this proposed mechanism of action is correct, Donepezil's effect may lessen as the disease process advances and fewer cholinergic neurons remain functionally intact. There is no evidence that Donepezil alters the course of the underlying dementing process.

Indication:
Elzer® (Donepezil hydrochloride) is indicated for the treatment of mild to moderate dementia of the Alzheimer's type.

Dosage and administration:
The dosages of Elzer® (Donepezil hydrochloride) shown to be effective in controlled clinical trials are 5 mg and 10 mg administered once per day. The higher dose of 10 mg did not provide a statistically significantly greater clinical benefit than that of 5 mg. There is a suggestion, however, based upon order of group mean scores and dose trend analyses of data from these clinical trials, that a daily dose of 10 mg of Elzer® (Donepezil hydrochloride) might provide additional benefit for some patients. Accordingly, whether or not to employ a dose of 10 mg is a matter of prescriber and patient preference. Evidence from the controlled trials indicates that the 10 mg dose, with a one week titration, is likely to be associated with a higher incidence of cholinergic adverse events than the 5 mg dose. In open label trials using a 6 week titration, the frequency of these same adverse events was similar between the 5 mg and 10 mg dose groups. Therefore, because steady state is not achieved for 15 days and because the incidence of untoward effects may be influenced by the rate of dose escalation, treatment with a dose of 10 mg should not be contemplated until patients have been on a daily dose of 5 mg for 4 to 6 weeks.
Elzer® (Donepezil hydrochloride) should be taken in the evening, just prior to retiring. Elzer® (Donepezil hydrochloride) can be taken with or without food.

Contraindication and precaution:
It is contraindicated in patients with known hypersensitivity to Donepezil hydrochloride or to piperidine derivatives.

Anesthesia: Donepezil hydrochloride, as a cholinesterase inhibitor, is likely to exaggerate succinylcholine type muscle relaxation during anesthesia.

Cardiovascular Conditions: 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. Syncopal episodes have been reported in association with the use of Donepezil hydrochloride.

Gastrointestinal Conditions: Through their primary action, cholinesterase inhibitors may be expected to increase gastric acid secretion due to increased cholinergic activity. Therefore, patients should be monitored closely for symptoms of active or occult gastrointestinal bleeding, especially those at increased risk for developing ulcers, e.g., those with a history of ulcer disease or those receiving concurrent nonsteroidal anti-inflammatory drugs (NSAIDS). Clinical studies of Donepezil hydrochloride have shown no increase, relative to placebo, in the incidence of either peptic ulcer disease or gastrointestinal bleeding.
Donepezil hydrochloride, as a predictable consequence of its pharmacological properties, has been shown to produce diarrhea, nausea and vomiting. These effects, when they occur, appear more frequently with the 10 mg/day dose than with the 5 mg/day dose. In most cases, these effects have been mild and transient, sometimes lasting one to three weeks, and have resolved during continued use of Donepezil hydrochloride.
Genitourinary: Although not observed in clinical trials of Donepezil hydrochloride, cholinomimetics may cause bladder outflow obstruction.
Neurological Conditions: Seizures: Cholinomimetics are believed to have some potential to cause generalized convulsions. However, seizure activity also may be a manifestation of Alzheimer's Disease.
Pulmonary Conditions: Because of their cholinomimetic actions, cholinesterase inhibitors should be prescribed with care to patients with a history of asthma or obstructive pulmonary disease.

Side effect:
The most common adverse events, defined as those occurring at a frequency of at least 5% in patients receiving 10 mg/day and twice the placebo rate, are largely predicted by Donepezil's cholinomimetic effects. These include nausea, diarrhea, insomnia, vomiting, muscle cramp, fatigue and anorexia. These adverse events were often of mild intensity and transient, resolving during continued Donepezil treatment without the need for dose modification.
There is evidence to suggest that the frequency of these common adverse events may be affected by the rate of titration. An open-label study was conducted with 269 patients who received placebo in the 15 and 30-week studies. These patients were titrated to a dose of 10 mg/day over a 6-week period. The rates of common adverse events were lower than those seen in patients titrated to 10 mg/day over one week in the controlled clinical trials and were comparable to those seen in patients on 5 mg/day.

Drug interaction:
Formal pharmacokinetic studies evaluated the potential of Donepezil for interaction with theophylline, cimetidine, warfarin and digoxin. No significant effects on the pharmacokinetics of these drugs were observed.

Whether Donepezil has any potential for enzyme induction is not known.
Ketoconazole and quinidine, inhibitors of CYP450, 3A4 and 2D6, respectively, inhibit Donepezil metabolism in vitro. Whether there is a clinical effect of these inhibitors is not known. Inducers of CYP 2D6 and CYP 3A4 (e.g., phenytoin, carbamazepine, dexamethasone, rifampin, and phenobarbital) could increase the rate of elimination of Donepezil. Formal pharmacokinetic studies demonstrated that the metabolism of Donepezil is not significantly affected by concurrent administration of digoxin or cimetidine.

Use in pregnancy and lactation:
There are no adequate or well-controlled studies in pregnant women. Donepezil should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. It is not known whether Donepezil is excreted in human breast milk. Donepezil has no indication for use in nursing mothers.

Storage condition:
Store in a cool and dry place, protect from light and moisture. Keep all medication out of reach of children.

How supplied:
Elzer® Tablet: Each box contains 5x6's Tablet in blister pack.