Taj Pharmaceuticals Ltd.

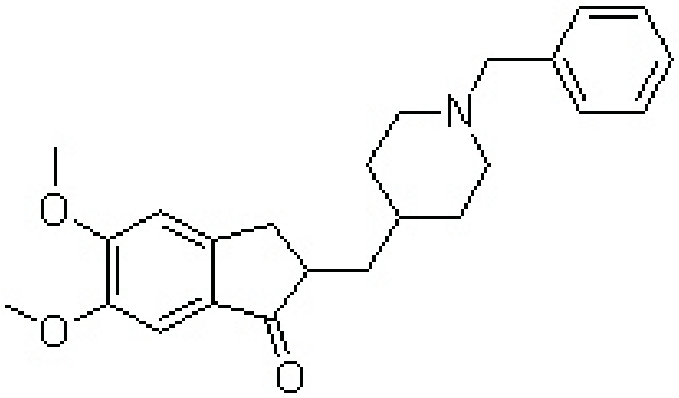
Donepezil

CAS No. : 120014-06-4

Synonyms

2-[(1-Benzyl-4-piperidyl)methyl]-5,6-dimethoxy-2,3-dihydroinden-1-one

Molecular Formula C24H29NO3
Molecular Weight 379.49
CAS Number 120014-06-4



Properties

Melting point 207 ºC
Water solubility 2.931 mg/L
CLINICAL 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. 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. There is no evidence that donepezil alters the course of the underlying dementing process.

DOSAGE

Donepezil is generally taken once daily at night prior to retiring. Its absorption is not affected by food so that it may be taken with or without food.

The dosages of Donepezil 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 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 Donepezil 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.
Severe Alzheimer's Disease

Donepezil has been shown to be effective in controlled clinical trials at a dose of 10 mg administered once daily.

Evidence from the controlled trials in mild to moderate Alzheimer's Disease 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, a dose of 10 mg should not be achieved until patients have been on a daily dose of 5 mg for 4 to 6 weeks.

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SIDE EFFECTS

Nausea, vomiting, diarrhea, loss of appetite, tiredness, drowsiness, trouble sleeping, or muscle cramps may occur as your body adjusts to the drug. These effects usually last 1-3 weeks and then subside. If any of these effects persist or worsen, notify your doctor or pharmacist promptly. Tell your doctor immediately if any of these unlikely but serious side effects occur: mental/mood changes (depression), slow/irregular heartbeat, fainting, vision problems, more frequent or trouble with urination, weight loss. Tell your doctor immediately if any of these highly unlikely but very serious side effects occur: black stools, vomit that looks like coffee grounds, severe stomach/abdominal pain, seizures. If you notice other effects not listed above, contact your doctor or pharmacist.

PRECAUTIONS

No evidence of a carcinogenic potential was obtained in an 88-week carcinogenicity study of donepezil hydrochloride conducted in CD-1 mice at doses up to 180 mg/kg/day (approximately 90 times the maximum recommended human dose on a mg/m² basis), or in a 104-week carcinogenicity study in Sprague-Dawley rats at doses up to 30mg/kg/day (approximately 30 times the maximum recommended human dose on a mg/m² basis).

Donepezil was not mutagenic in the Ames reverse mutation assay in bacteria, or in a mouse lymphoma forward mutation assay in vitro. In the chromosome aberration test in cultures of Chinese hamster lung (CHL) cells, some clastogenic effects were observed. Donepezil was not clastogenic in the in vivo mouse micronucleus test and was not genotoxic in an in vivo unscheduled DNA synthesis assay in rats.

Donepezil had no effect on fertility in rats at doses up to 10 mg/kg/day (approximately 8 times the maximum recommended human dose on a mg/m² basis).

Pregnancy

Pregnancy Category C: Teratology studies conducted in pregnant rats at doses up to 16 mg/kg/day (approximately 13 times the maximum recommended human dose on a mg/m² basis) and in pregnant rabbits at doses up to 10 mg/kg/day (approximately 16 times the maximum recommended human dose on a mg/m² basis) did not disclose any evidence for a teratogenic potential of donepezil. However, in a study in which pregnant rats were given up to 10 mg/kg/day (approximately 8 times the maximum recommended human dose on a mg/m² basis) from day 17 of gestation through day 20 postpartum, there was a slight increase in still births and a slight decrease in pup survival through day 4 postpartum at this dose; the next lower dose tested was 3 mg/kg/day. There are no adequate or well-controlled studies in pregnant women. ARICEPT® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Nursing Mothers

INTERACTION

Your healthcare professionals (e.g., doctor or pharmacist) may already be aware of any possible drug interactions and may be monitoring you for it. Do not start, stop or change the dosage of any medicine before checking with them first.

Before using this medication, tell your doctor or pharmacist of all prescription and nonprescription/herbal products you may use, especially of: anticholinergic medications (e.g., benztropine, diphenhydramine), aspirin (high doses used for arthritis), cholinergic drugs (e.g., bethanechol), cholinesterase inhibitors (e.g., neostigmine), long-term use of non-steroidal anti-inflammatory drugs (NSAIDs, such as ibuprofen, naproxen), drugs affecting the liver enzymes that remove donepezil from your body (such as carbamazepine, dexamethasone, phenobarbital, phenytoin, rifampin).

Check all prescription and nonprescription medicine labels carefully since many medications contain pain relievers/fever reducers (NSAIDs such as aspirin, ibuprofen, or naproxen) that if taken together with donepezil, may increase your risk for stomach/intestinal bleeding. Low-dose aspirin, as prescribed by your doctor for specific medical reasons such as heart attack or stroke prevention (usually at dosages of 81-325 milligrams per day), should be continued. Consult your doctor or pharmacist for more details.

This document does not contain all possible interactions. Therefore, before using this product, tell your doctor or pharmacist of all the products you use. Keep a list of all your medications with you, and share the list with your doctor and pharmacist.

DRUG DESCRIPTION

Donepezil is an oral medication used to treat Alzheimer's disease. It belongs to a class of drugs called cholinesterase inhibitors that also includes tacrine (Cognex). Scientists believe that Alzheimer's disease may result from a deficiency in chemicals (neurotransmitters) used by nerves in the brain to communicate with one another. Donepezil inhibits acetylcholinesterase, an enzyme responsible for the destruction of one neurotransmitter, acetylcholine. This leads to increased concentrations of acetylcholine in the brain, and the increased concentrations are believed to be responsible for the improvement seen during treatment with donepezil. Donepezil improves the symptoms but does not slow down the progression of Alzheimer's disease.donepezil hydrochloride is a reversible inhibitor of the enzyme acetylcholinesterase, known chemically as (±)-2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-1H-inden-1-one hydrochloride. Donepezil hydrochloride is commonly referred to in the pharmacological literature as E2020. It has an empirical formula of C24H29NO3HCl and a molecular weight of 415.96. Donepezil hydrochloride is a white crystalline powder and is freely soluble in chloroform, soluble in water and in glacial acetic acid, slightly soluble in ethanol and in acetonitrile and practically insoluble in ethyl acetate and in n-hexane.

Note /Government Notification: These chemicals are designated as those that are used in the manufacture of the controlled substances and are important to themanufacture of the substances. For any (Control Substance) products Import and Export *** subjected to your country government laws /control substance ACT.

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The Controlled Substances Act (CSA) was enacted into law by the Congress of the United States as Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970.[1] The CSA is the federal U.S. drug policy under which the manufacture, importation, possession, use and distribution of certain substances is regulated. The Act also served as the national implementing legislation for the Single Convention on Narcotic Drugs

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