

# Data Sheet

## DONEZIL

### *Donepezil hydrochloride 5 and 10mg tablets*

---

## Presentation

---

Donezil film-coated tablets for oral administration are supplied containing 5 mg or 10 mg donepezil hydrochloride equivalent to 4.56 mg or 9.12 mg donepezil free base, respectively. The inactive ingredients are lactose, maize starch, microcrystalline cellulose, hydroxypropyl cellulose and magnesium stearate. The film-coat contains hypromellose, titanium dioxide and polyethylene glycol.

Donezil 5 mg: 7mm white, film-coated, round tablets, embossed with "DL" scoreline "5" on one side and "G" on the reverse.

Donezil 10 mg: 9mm white, film-coated, round tablets, embossed with "DL" scoreline "10" on one side and "G" on the reverse.

---

## Uses

---

### **Actions**

It has been demonstrated that Alzheimer's disease is associated with a relative decrease in the activity of the cholinergic system in the cerebral cortex and other areas of the brain. Studies suggest that donepezil hydrochloride exerts its therapeutic effect by enhancing cholinergic function in the central nervous system. This is accomplished by increasing the concentration of acetylcholine through reversible inhibition of acetylcholinesterase.

Donepezil hydrochloride is a specific and reversible inhibitor of acetylcholinesterase, the predominant cholinesterase in the brain. Donepezil hydrochloride was found *in vitro* to be over 1000 times more potent an inhibitor of this enzyme than of butyrylcholinesterase, an enzyme which is present mainly outside the central nervous system.

### **Alzheimer's Disease**

In patients with Alzheimer's dementia participating in clinical trials, administration of single daily doses of 5 mg or 10 mg of donepezil hydrochloride produced steady-state inhibition of acetylcholinesterase activity (measured in erythrocyte membranes) of 63.6% and 77.3%, respectively when measured post dose. The inhibition of acetylcholinesterase (AChE) in red blood cells by donepezil hydrochloride has been shown to correspond closely to the effects in the cerebral cortex. In addition, significant correlation was demonstrated between plasma levels of donepezil hydrochloride, AChE inhibition and change in ADAS-cog, a sensitive and well validated scale which examines cognitive performance - including memory, orientation, attention, reason, language and praxis.

### **Pharmacokinetics**

#### **Absorption**

Donepezil is well absorbed with a relative oral bioavailability of 100% and reaches peak plasma concentrations in 3 to 4 hours. Oral administration of donepezil produces highly predictable plasma concentrations where plasma concentrations and area under the curve rise in proportion to the dose.

The terminal disposition half-life is approximately 70 hours, thus, administration of multiple single-daily doses results in gradual approach to steady state. Approximate steady-state is achieved within 3 weeks after initiation of therapy. Once at steady-state, plasma donepezil hydrochloride concentrations and the related pharmacodynamic activity show little variability

over the course of the day. Neither food nor time of administration (morning versus evening dose) affect the absorption of donepezil hydrochloride.

## **Distribution**

The steady state volume of distribution is 12 L/kg. Donepezil hydrochloride is approximately 96 % bound to human plasma proteins. The distribution of donepezil in various body tissues has not been definitively studied. However, in a mass balance study conducted in healthy male volunteers, 240 hours after the administration of a single 5 mg dose of <sup>14</sup>C-labeled donepezil hydrochloride, approximately 28% of the label remained un-recovered. This suggests that donepezil and/or its metabolites may persist in the body for more than 10 days. The average CSF: plasma ratio for both doses, expressed as a percent of the concentration in plasma, was 15.7%.

## **Metabolism/Excretion**

Donepezil is both excreted in the urine intact and extensively metabolized to four major metabolites, two of which are known to be active, and a number of minor metabolites, not all of which have been identified. Three of the human metabolites of donepezil have not undergone extensive safety tests in animals. These comprise two O-demethylated derivatives and an N-oxidation product. Donepezil is metabolised by CYP 450 isoenzymes 2D6 and 3A4 and undergoes glucuronidation. The rate of metabolism of donepezil is slow and does not appear to be saturable. These findings are consistent with the results from formal pharmacokinetic studies which showed that donepezil and/or its metabolites does not inhibit the metabolism of theophylline, warfarin, cimetidine, or digoxin in humans. Pharmacokinetic studies also demonstrated that the metabolism of donepezil is not affected by concurrent administration of digoxin or cimetidine (See **Interactions**).

Following administration of <sup>14</sup>C-labeled donepezil, plasma radioactivity, expressed as a percent of the administered dose, was present primarily as intact donepezil (53 %), 6-O-desmethyl donepezil (11%), which has been reported to inhibit AChE to the same extent as donepezil *in vitro* and was found in the plasma at concentrations equal to about 20 % of donepezil. Approximately 57% of the total radioactivity was recovered in urine and faeces, respectively, over a period of 10 days, while 28% remained unrecovered, with about 17% of the donepezil dose recovered in the urine as unchanged drug. There is no evidence to suggest enterohepatic recirculation of donepezil and/or any of its metabolites. Plasma donepezil concentrations decline with a half-life of approximately 70 hours.

Sex, race and smoking history have no clinically significant influence on plasma concentrations of donepezil.

## **Pharmacokinetic/dynamic properties - Characteristics in patients**

As an inhibitor of AChE, donepezil augments cholinergic function in the central nervous system, thereby providing its therapeutic benefit. The enzyme AChE also occurs peripherally in red blood cells, therefore, measurement of AChE activity in erythrocyte membranes provides an index for donepezil pharmacodynamics. This surrogate marker has been evaluated in several human pharmacokinetic/pharmacodynamic trials and in controlled clinical trials.

The population plasma donepezil concentrations and red blood cell AChE inhibition measurements verified that patients in clinical trials experienced exposure to donepezil hydrochloride and its pharmacodynamic actions as predicted.

Results from therapeutic drug monitoring showed no apparent relationship between plasma concentration and adverse drug reactions.

## **Indications**

Donezil is indicated for the treatment of mild, moderate and severe Alzheimer's disease.

Donezil is indicated for the treatment of vascular dementia (dementia associated with cerebrovascular disease).

---

## Dosage and Administration

---

### ***Adults/Elderly***

Treatment should be initiated and supervised by a doctor experienced in the diagnosis and treatment of Alzheimer's Dementia. Individual response to donepezil can not be predicted. Treatment should be continued for as long as a therapeutic benefit for the patient exists. Discontinuation of therapy should be considered where there is no longer evidence of a therapeutic effect, which should be assessed by periodic evaluations by the physician using input from the patient and caregiver. The use of donepezil in patients with other types of dementia or other types of memory impairment (e.g., age-related cognitive decline) has not been established.

The dosages of donepezil hydrochloride shown to be effective in controlled clinical trials are 5 mg and 10 mg administered once daily. Although there is no statistically significant evidence that a greater treatment effect is obtained from the use of the 10 mg dose, there is a suggestion, based on analysis of group data, that some additional benefits may accrue to some patients from the use of the higher dose.

Treatment is initiated at 5 mg/day (once-a-day dosing). Donezil tablets should be taken orally, in the evening, just prior to retiring and can be taken with or without food.

The 5 mg/day dose should be maintained for at least one month in order to allow the earliest clinical responses to treatment to be assessed and to allow steady-state concentrations of donepezil to be achieved. Following a one-month clinical assessment of treatment at 5 mg/day, the dose of Donezil can be increased to 10 mg/day (once-a-day dosing).

The maximum recommended daily dose is 10 mg. Doses greater than 10 mg/day have not been studied in clinical trials.

Upon discontinuation of treatment, a gradual abatement of the beneficial effects of Donezil is seen. There is no evidence of a rebound effect after abrupt discontinuation of therapy.

### ***Renal & Hepatic Impairment***

A similar dose schedule can be followed for patients with renal or mild to moderate hepatic impairment as clearance of donepezil is not significantly affected by these conditions.

### ***Use in Children***

Donezil is not recommended for use in children (see **Precautions - Paediatric use**).

---

## Contraindications

---

Donezil is contraindicated in patients with a known hypersensitivity to donepezil hydrochloride, piperidine derivatives, or to any excipients used in the formulation.

---

## Precautions

---

**Anaesthesia:** Donepezil hydrochloride, as a cholinesterase inhibitor, may exaggerate succinylcholine-type muscle relaxation during anaesthesia.

**Cardiovascular Conditions:** Because of the pharmacological action, cholinesterase inhibitors may have vagotonic effects on heart rate (e.g., bradycardia). The potential for this action may be particularly important to patients with "sick sinus syndrome" or other supraventricular cardiac conduction conditions, such as sinoatrial or atrioventricular block.

**Gastrointestinal Conditions:** Through their primary action, cholinesterase inhibitors may be expected to increase gastric acid secretion due to increased cholinergic activity. Therefore, patients at increased risk for developing ulcers, e.g., those with a history of ulcer disease or those receiving concurrent nonsteroidal anti-inflammatory drugs (NSAIDs), should be monitored closely for symptoms of active or occult gastrointestinal bleeding. However, the clinical studies with donepezil hydrochloride showed no increase, relative to placebo, in the incidence of either peptic ulcer disease or gastrointestinal bleeding.

**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 generalised convulsions. However, seizure activity may also be a manifestation of Alzheimer's disease. Cholinomimetics have the potential to exacerbate or induce extrapyramidal symptoms.

**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.

The administration of donepezil hydrochloride concomitantly with other inhibitors of acetylcholinesterase, agonists or antagonists of the cholinergic system should be avoided.

## **Mortality in Subjects with Vascular Dementia**

Three clinical trials of 6 months duration were conducted studying individuals meeting the NINDS-AIREN criteria for probable or possible vascular dementia (VaD) and excluding patients with a diagnosis of Alzheimer's disease. In the first study, the mortality rates were 2/198 (1.0%) on donepezil hydrochloride 5 mg, 5/206 (2.4%) on donepezil hydrochloride 10 mg and 7/199 (3.5%) on placebo. In the second study, the mortality rates were 4/208 (1.9%) on donepezil hydrochloride 5 mg, 3/215 (1.4%) on donepezil hydrochloride 10 mg and 1/193 (0.5%) on placebo. In the third study, the mortality rates were 11/648 (1.7%) on donepezil hydrochloride 5 mg and 0/326 (0%) on placebo ( $p < 0.02$ ). The mortality rate for the three VaD studies combined in the donepezil hydrochloride group (1.7%) was numerically higher than in the placebo group (1.1%), however, this difference was not statistically significant. The majority of deaths in patients taking either donepezil hydrochloride or placebo appear to result from various vascular related causes, which could be expected in this elderly population with underlying vascular disease. An analysis of all serious non-fatal and fatal vascular events showed no difference in the rate of occurrence in the donepezil hydrochloride group relative to placebo.

When Alzheimer's disease studies were pooled ( $n=4146$ ), the mortality rate in the placebo group numerically exceeded that in the donepezil hydrochloride group. There is no evidence of an increased risk of mortality in the current approved indications of mild, moderate and severe Alzheimer's disease.

## **Preclinical Safety Data**

### ***Mutagenicity***

Donepezil hydrochloride was not mutagenic in bacterial or in the mouse lymphoma forward mutation assay *in vitro*. Donepezil did not induce unscheduled DNA synthesis in rat primary hepatocyte cultures following oral dosing of the animals. In the chromosome aberration test in cultures of Chinese hamster lung cells, some clastogenic effects were observed in the *in-vivo* mouse micronucleus model.

### ***Carcinogenicity***

No evidence of carcinogenicity was found in long-term studies in mice and rats with dietary dosing of donepezil resulting in peak plasma concentrations of up to 17 times and 6-19 times, respectively, that in humans at the recommended clinical dose of 10 mg/day.

### ***Fertility***

Donepezil hydrochloride had no effect on fertility in rats up to 10 mg/kg/day (a tissue exposure equivalent to approximately twice that in humans at the maximum recommended clinical dose of 10 mg/day) in male and female rats based on AUC (see ***Use in Pregnancy and Lactation***).

### **Use in Pregnancy and Lactation**

Teratology studies conducted in pregnant rats at doses up to 16 mg/kg/day and in pregnant rabbits at doses up to 10 mg/kg/day not disclose any evidence for teratogenic potential of donepezil. In rats this dose resulted in a systemic drug exposure in excess of human values. However, in rabbits the extent of systemic drug exposure is not known. Treatment of pregnant rats from late gestation to the end of lactation with an oral donepezil dose of 10 mg/kg/day resulted in a slight increase in incidence of stillborn pups, and slightly reduced pup survival through day 4 postpartum.

There are no adequate or well-controlled studies in pregnant women. Donepezil should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus.

It is not known whether donepezil hydrochloride is excreted in human breast milk and there are no studies in lactating women. Excretion of donepezil and/or its metabolites into milk occurred after oral treatment of nursing rats, with milk concentrations similar to those in plasma. Therefore, women on donepezil should not breast feed.

### **Paediatric Use**

Donezil is not recommended for use in children.

### **Driving, Use of Machinery**

Alzheimer's dementia and vascular dementia may cause impairment of driving performance or compromise the ability to use machinery. Furthermore, donepezil can cause fatigue, dizziness and muscle cramps, mainly when initiating or increasing the dose. The treating doctor should routinely evaluate the ability of patients on donepezil to continue driving or operating complex machines.

---

## **Adverse Effects**

---

### ***Mild to Moderately Severe Alzheimer's Disease Clinical Trials***

Most adverse events are mild in severity and transient in nature. The most common (incidence  $\geq$  5% and twice the frequency of placebo) were diarrhoea, muscle cramps, fatigue, nausea, vomiting and insomnia. Other common adverse events (incidence  $\geq$  5% and  $\geq$  placebo) were headache, pain, accident, common cold, abdominal disturbance and dizziness. Cases of syncope, bradycardia, sinoatrial block and atrioventricular block were observed. No notable abnormalities in laboratory values associated with treatment were observed except for minor increases in serum concentrations of creatinine kinase. Adverse events observed during long-term but not the short-term trials (incidence  $\geq$  5% and twice the frequency of placebo) included asthenia.

### **Adverse Events Leading to Discontinuation**

In trials of mild to moderate Alzheimer's disease, the rate of discontinuation for the donepezil hydrochloride 5 mg/day treatment group was comparable to that of placebo-treated patients

at approximately 5%. The rate of discontinuation of patients who received rapid dose escalations over 7 days from 5 mg/day to 10 mg/day, was higher at 13%. The most common signs and symptoms leading to discontinuation were nausea, diarrhoea and vomiting. For patients who did not discontinue, these signs and symptoms generally proved to be mild and transient, resolving in 1 to 2 days during continued use of the 10 mg/day dose. There is evidence to suggest that the frequency of these common adverse events may be affected by the rate of titration.

**Table 1: Adverse Events Reported in Controlled Clinical Trials in at Least 2% of Patients Receiving Donepezil Hydrochloride and at a Higher Frequency than Placebo-Treated Patients**

<b>Body System/Adverse Event</b>	<b>Placebo (n=355)</b>	<b>Donepezil (n=747)</b>
<b><i>Percent of Patients with any Adverse Event</i></b>	<b>72%</b>	<b>74%</b>
<b>Body as a Whole</b>		
Headache	9%	10%
Pain, various locations	8%	9%
Accident	6%	7%
Fatigue	3%	5%
<b>Cardiovascular</b>		
Syncope	1%	2%
<b>Digestive System</b>		
Nausea	6%	11%
Diarrhoea	5%	10%
Vomiting	3%	5%
Anorexia	2%	4%
<b>Haematological and Lymphatic System</b>		
Ecchymosis	3%	4%
<b>Metabolic and Nutritional</b>		
Weight Decrease	1%	3%
<b>Musculoskeletal System</b>		

<b>Body System/Adverse Event</b>	<b>Placebo (n=355)</b>	<b>Donepezil (n=747)</b>
Muscle Cramps	2%	6%
Arthritis	1%	2%
<b>Nervous System</b>		
Insomnia	6%	9%
Dizziness	6%	8%
Depression	<1%	3%
Abnormal Dreams	0%	3%
Somnolence	<1%	2%
<b>Urogenital</b>		
Frequent Urination	1%	2%

### **Other Adverse Events Observed During Clinical Trials**

Treatment emergent signs and symptoms that occurred during three controlled clinical trials were recorded as adverse events by the clinical investigators using terminology of their own choosing. All adverse events occurring at least twice and judged as possibly or definitely related to donepezil hydrochloride treatment are included, except for those already listed in Table 1. Events are classified by body system and include frequent adverse events - those occurring in at least 1/100 patients; infrequent adverse events - those occurring in 1/100 to 1/1000 patients.

**Body as a Whole:** generalised weakness, infection, influenza, assault

**Cardiovascular System:** vasodilation, hot flashes, hypotension, angina pectoris, hypertension

**Digestive System:** abdominal disturbance, constipation, faecal incontinence, bloating, stomach upset epigastric pain, eructation, gastrointestinal bleeding, increased appetite, flatulence, drooling, dry mouth, increased transaminases

**Metabolic and Nutritional Disorders:** dehydration, oedema of extremities

**Musculoskeletal System:** muscle weakness

**Nervous System:** agitation, anxiety, confusion, delusions, hallucinations, tremor, irritability, aggression, vertigo, ataxia, increased libido, restlessness, abnormal crying, aphasia, coldness (localised), muscle spasm, hypokinesia, nervousness, paraesthesia, paranoia, wandering

**Respiratory System:** rhinitis, coughing, dyspnoea

**Skin and Appendages:** rash, abrasion, diaphoresis, pruritus

**Special Senses:** cataract, ear disorder, vision blurred

**Urogenital System:** urinary incontinence, urinary tract infection, nocturia

### **Severe Alzheimer's Disease Clinical Trials**

A total of 573 patients with severe Alzheimer's disease were treated in controlled clinical studies with donepezil hydrochloride. Of these patients, 441 (77%) completed the studies. The mean duration of treatment for all donepezil hydrochloride groups was 148.4 days (range 1-231 days).

The incidence profile for adverse events for severe Alzheimer's disease was similar to that of mild to moderate Alzheimer's disease.

In controlled clinical trials in severe Alzheimer's disease, the rate of discontinuation due to adverse events was 11.3% in patients treated with donepezil hydrochloride compared to 6.7% in the placebo group. There were no adverse events occurring in at least 2% of patients and twice the incidence seen in placebo patients. Other less common adverse events leading to discontinuation included diarrhoea, nausea, vomiting, urinary tract infection, decreased appetite, and aggression.

The most common adverse events, defined as those occurring at a frequency of at least 5% in patients and twice the placebo rate, were diarrhoea, nausea, and aggression. Overall, the majority of adverse events were judged by the investigators to be mild or moderate in intensity.

### **Vascular Dementia Clinical Trials**

A comparison of the Alzheimer's disease and vascular dementia studies shows that the types of and relative proportions of adverse events associated with donepezil were similar in the two populations. In the combined vascular dementia studies the mortality rate in the donepezil hydrochloride group (1.7%) was numerically higher than in the placebo group (1.1%). (see **Precautions - Mortality in Subjects with Vascular Dementia**)

### **Post-marketing Experience**

There have been post-marketing reports of hallucinations, agitation, aggressive behaviour, seizure, abdominal pain, cholecystitis, hepatitis, gastric ulcer, duodenal ulcer, gastrointestinal haemorrhage, heart block, haemolytic anaemia, hyponatraemia, neuroleptic malignant syndrome and pancreatitis. However, there is inadequate data to determine the causal relationship with donepezil hydrochloride.

---

## **Interactions**

---

**Drugs Highly Bound to Plasma Proteins:** Drug displacement studies have been performed *in vitro* between this highly bound drug (96%) and other drugs such as frusemide, digoxin, and warfarin. Donepezil hydrochloride at concentrations of 0.3-10 µg/mL did not affect the binding of frusemide (5 µg/mL), digoxin (2 ng/mL) and warfarin (3 µg/mL) to human albumin. Similarly, the binding of donepezil hydrochloride to human albumin was not affected by frusemide, digoxin and warfarin.

**Effect of Donepezil Hydrochloride on the Metabolism of Other Drugs:** No *in vivo* clinical trials have investigated the effect of donepezil hydrochloride on the clearance of drugs metabolised by CYP 3A4 (e.g. cisapride, terfenadine) or by CYP 2D6 (e.g. imipramine). However, *in vitro* studies show a low rate of binding to these enzymes (mean  $K_i$  about 50-130 µM), that, given the therapeutic plasma concentrations of donepezil (164 nM), indicates little likelihood of interference.

Whether donepezil hydrochloride has any potential for enzyme induction is not known.

Formal pharmacokinetic studies evaluated the potential of donepezil hydrochloride for interaction with theophylline, cimetidine, warfarin and digoxin. No significant effects on the pharmacokinetics of these drugs were observed. Donepezil hydrochloride and/or any of its metabolites does not inhibit the metabolism of thioridazine, risperidone or sertraline in humans.

In a study of Parkinson's disease patients on optimal treatment with L-dopa/carbidopa, administration of donepezil hydrochloride for 21 days had no effect on L-dopa or carbidopa blood levels. In this study, no effects on motor activity were observed.

**Effect of Other Drugs on the Metabolism of Donepezil Hydrochloride:** *In vitro* studies have shown that the cytochrome P450 isoenzymes 3A4 and to a minor extent 2D6 are involved in the metabolism of donepezil. Ketoconazole and quinidine, inhibitors of CYP450, 3A4 and 2D6, respectively, inhibit donepezil metabolism *in vitro*. Therefore these and other CYP3A4 inhibitors, such as itraconazole and erythromycin, and CYP2D6 inhibitors, such as fluoxetine could inhibit the metabolism of donepezil. Whether there is a clinical effect of these inhibitors is not known. In two studies in healthy volunteers, ketoconazole increased mean donepezil concentrations by about 30%. These increases are smaller than those produced by ketoconazole for other agents sharing the CYP-3A4 pathway and are not likely to be clinically relevant. Administration of donepezil had no effect on the pharmacokinetics of ketoconazole.

Inducers of CYP 2D6 and CYP 3A4 (e.g., phenytoin, carbamazepine, dexamethasone, rifampicin, phenobarbital and alcohol) could increase the rate of elimination of donepezil. Since the magnitude of an inhibiting or inducing effect is unknown, such drug combinations should be used with care.

Formal pharmacokinetic studies demonstrated that the metabolism of donepezil is not significantly affected by concurrent administration of digoxin, cimetidine, thioridazine, risperidone or sertraline.

Donepezil hydrochloride has the potential to interfere with medications having anticholinergic activity. There is also the potential for synergistic activity with concomitant treatment involving such medications as succinylcholine, other neuro-muscular blocking agents or cholinergic agonists or beta blocking agents which have effects on cardiac conduction, but an *in vitro* study showed that donepezil hydrochloride had minimal effects on hydrolysis of succinylcholine.

---

## Overdosage

---

### Animal Study Data

The estimated median lethal dose of donepezil hydrochloride following administration of a single oral dose in mice, rats and dogs is 45, 32 and 15 mg/kg, respectively, or approximately 225, 160 and 75 times the maximum recommended human dose of 10 mg per day. Dose-related signs of cholinergic stimulation were observed in animals and included reduced spontaneous movement, prone position, staggering gait, lacrimation, clonic convulsions, depressed respiration, salivation, miosis, fasciculation and lower body surface temperature.

### Cholinergic Crisis

Overdosage with cholinesterase inhibitors can result in cholinergic crisis characterised by severe nausea, vomiting, salivation, sweating, bradycardia, hypotension, respiratory depression, collapse and convulsions. Increasing muscle weakness is a possibility and may result in death if respiratory muscles are involved.

### Treatment

As in any case of overdosage, general supportive measures should be utilised. Tertiary anticholinergics such as atropine may be used as an antidote for donepezil hydrochloride

overdosage. Intravenous atropine sulfate titrated to effect is recommended: an initial dose of 1.0 to 2.0 mg IV with subsequent doses based upon clinical response. Atypical responses in blood pressure and heart rate have been reported with other cholinomimetics when co-administered with quaternary anticholinergics such as glycopyrrolate. It is not known whether donepezil hydrochloride and/or its metabolites can be removed by dialysis (haemodialysis, peritoneal dialysis, or haemofiltration).

---

## Pharmaceutical Precautions

---

Store at or below 25°C

---

## Medicine Classification

---

Prescription Medicine

---

## Package Quantities

---

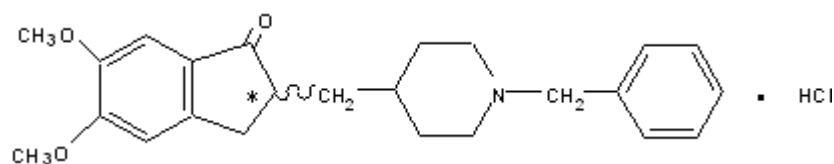
Donezil 5mg and 10mg tablets are available in blisters of 28 tablets

---

## Further Information

---

Donepezil hydrochloride is a specific and reversible inhibitor of the enzyme acetylcholinesterase, known chemically as (RS)-1-benzyl-4-[5,6-dimethoxy-1-indanon)-2-yl]-methylpiperidine hydrochloride. The CAS reference number for donepezil hydrochloride is 120011-70-3. Donepezil hydrochloride has an empirical formula of  $C_{24}H_{29}NO_3HCl$  and a molecular weight of 415.96 and is represented by the following structural formula:



MW415.96

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.

---

## Name and Address

---

Mylan New Zealand Ltd  
PO Box 11-183  
Ellerslie  
AUCKLAND  
Telephone: 09-579-2792

---

## Date of Preparation

---

2 February 2009