SAFETY DATA SHEET

1. Identification

Product identifier
Donepezil Hydrochloride

Other means of identification

- Catalog number: 1224981
- Chemical name: (±)-2-[(1-Benzyl-4-piperidyl)methyl]-5,6-dimethoxy-1-indanone hydrochloride
- Synonym(s): E2020

Recommended use
Specified quality tests and assay use only.

Recommended restrictions
Not for use as a drug. Not for administration to humans or animals.

Manufacturer/Importer/Supplier/Distributor information

- Company name: U. S. Pharmacopeia
- Address: 12601 Twinbrook Parkway
- Rockville
- MD
- 20852-1790
- US
- Telephone: RS Technical Services 301-816-8129
- Website: www.usp.org
- E-mail: RSTECH@usp.org
- Emergency phone number: CHEMTREC within US & Canada 1-800-424-9300
- CHEMTREC outside US & Canada +1 703-527-3887

2. Hazard(s) identification

Physical hazards
Not classified.

Health hazards
- Acute toxicity, oral
- Category 2
- Serious eye damage/eye irritation
- Category 2A

OSHA hazard(s)
Not classified.

Label elements

Signal word: Danger

Hazard statement: Fatal if swallowed. Causes serious eye irritation.

Precautionary statement
- Prevention: Wash thoroughly after handling. Wear eye/face protection.
- Response: If swallowed: Immediately call a poison center/doctor. Rinse mouth. If in eyes: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists: Get medical advice/attention.
- Storage: Store locked up.
- Disposal: Dispose of contents/container in accordance with local/regional/national/international regulations.

Hazard(s) not otherwise classified (HNOC)
Not classified.

3. Composition/information on ingredients

Substance

Hazardous components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Common name and synonyms</th>
<th>CAS number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donepezil Hydrochloride</td>
<td>E2020</td>
<td>120011-70-3</td>
<td>100</td>
</tr>
</tbody>
</table>

4. First-aid measures

Inhalation
Move to fresh air. Call a physician if symptoms develop or persist.
Skin contact
Rinse skin with water/shower. Get medical attention if irritation develops and persists.

Eye contact
Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Get medical attention if irritation develops and persists.

Ingestion
Call a physician or poison control center immediately. Rinse mouth. Do not induce vomiting without advice from poison control center. If vomiting occurs, keep head low so that stomach content doesn't get into the lungs. Do not use mouth-to-mouth method if victim ingested the substance. Induce artificial respiration with the aid of a pocket mask equipped with a one-way valve or other proper respiratory medical device.

Most important symptoms/effects, acute and delayed
Irritation of eyes and mucous membranes. Gastrointestinal disturbances.

Indication of immediate medical attention and special treatment needed
Treatment of overdose should be symptomatic and supportive and may include the following:
1. Administer activated charcoal as a slurry. For substantial overdose, gastric lavage preceded by endotracheal intubation may be needed.
2. For cholinergic effects, administer atropine sulfate intravenously. Glycopyrrolate and methscopolamine bromide may be used as alternatives to atropine.
3. For hypotension, infuse isotonic fluid. If hypotension persists, administer dopamine or norepinephrine.
4. For seizures, administer a benzodiazepine intravenously. Consider phenobarbital if seizures recur. Monitor for hypotension, dysrhythmias, respiratory depression, and need for endotracheal intubation. Evaluate for hypoglycemia, electrolyte disturbances, and hypoxia.
5. For bronchospasm, administer albuterol. Epinephrine may be used to treat severe cardiovascular or bronchoconstrictor responses.
6. For acute lung injury, maintain adequate ventilation and oxygenation. Early use of PEEP and mechanical ventilation may be needed. [Meditext 2008]

General information
Remove from exposure. Remove contaminated clothing. For treatment advice, seek guidance from an occupational health physician or other licensed health-care provider familiar with workplace chemical exposures. In the United States, the national poison control center phone number is 1-800-222-1222. If person is not breathing, give artificial respiration. If breathing is difficult, give oxygen if available. Persons developing serious hypersensitivity (anaphylactic) reactions must receive immediate medical attention.

5. Fire-fighting measures
Suitable extinguishing media
Use fire-extinguishing media appropriate for surrounding materials. Water. Foam. Dry chemical or CO2.

Unsuitable extinguishing media
None known.

Specific hazards arising from the chemical
No unusual fire or explosion hazards noted.

Special protective equipment and precautions for firefighters
Wear suitable protective equipment.

Fire-fighting equipment/instructions
Use water spray to cool unopened containers. As with all fires, evacuate personnel to a safe area. Firefighters should use self-contained breathing equipment and protective clothing.

Specific methods
Use standard firefighting procedures and consider the hazards of other involved materials.

6. Accidental release measures
Personal precautions, protective equipment and emergency procedures
Keep unnecessary personnel away. Do not touch damaged containers or spilled material unless wearing appropriate protective clothing. Ensure adequate ventilation. Avoid inhalation of dust from the spilled material. Wear appropriate personal protective equipment.

Methods and materials for containment and cleaning up
Sweep up or vacuum up spillage and collect in suitable container for disposal. Avoid the generation of dusts during clean-up. For waste disposal, see section 13 of the SDS. Clean surface thoroughly to remove residual contamination.

7. Handling and storage
Precautions for safe handling
As a general rule, when handling USP Reference Standards, avoid all contact and inhalation of dust, mists, and/or vapors associated with the material. Clean equipment and work surfaces with suitable detergent or solvent after use. After removing gloves, wash hands and other exposed skin thoroughly.

Conditions for safe storage, including any incompatibilities
Store in tight container as defined in the USP-NF. This material should be handled and stored per label instructions to ensure product integrity.
8. Exposure controls/personal protection

Exposure limit values

<table>
<thead>
<tr>
<th>Material</th>
<th>Type</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donepezil Hydrochloride</td>
<td>TWA</td>
<td>0.15 mg/m³</td>
</tr>
</tbody>
</table>

Industrial Use

No biological exposure limits noted for the ingredient(s).

Appropriate engineering controls

Airborne exposure should be controlled primarily by engineering controls such as general dilution ventilation, local exhaust ventilation, or process enclosure. Local exhaust ventilation is generally preferred to general exhaust because it can control the contaminant at its source, preventing dispersion into the work area. An industrial hygiene survey involving air monitoring may be used to determine the effectiveness of engineering controls. Effectiveness of engineering controls intended for use with highly potent materials should be assessed by use of nontoxic surrogate materials. Local exhaust ventilation such as a laboratory fume hood or other vented enclosure is recommended, particularly for grinding, crushing, weighing, or other dust-generating procedures.

Individual protection measures, such as personal protective equipment

Eye/face protection

Safety glasses with sideshields are recommended. Face shields or goggles may be required if splash potential exists or if corrosive materials are present. Approved eye protection (e.g., bearing the ANSI Z87 or CSA stamp) is preferred. Maintain eyewash facilities in the work area.

Skin protection

Hand protection

Chemically compatible gloves. For handling solutions, ensure that the glove material is protective against the solvent being used. Use handling practices that minimize direct hand contact.

Employees who are sensitive to natural rubber (latex) should use nitrile or other synthetic nonlatex gloves. Use of powdered latex gloves should be avoided due to the risk of latex allergy.

Other

For handling of laboratory scale quantities, a cloth lab coat is recommended. Where significant quantities are handled, work clothing may be necessary to prevent take-home contamination.

Respiratory protection

Where respirators are deemed necessary to reduce or control occupational exposures, use NIOSH-approved respiratory protection and have an effective respirator program in place (applicable U.S. regulation OSHA 29 CFR 1910.134).

General hygiene considerations

Handle in accordance with good industrial hygiene and safety practice.

9. Physical and chemical properties

Appearance

White to off-white crystalline powder.

Physical state

Solid.

Form

Powder.

Odor

Not available.

Odor threshold

Not available.

pH

Not available.

Melting point/freezing point

411.8 - 413.6 °F (211 - 212 °C) (decomposes)

Initial boiling point and boiling range

Not available.

Flash point

Not available.

Evaporation rate

Not available.

Flammability (solid, gas)

Not applicable.

Upper/lower flammability or explosive limits

Flammability limit - lower (%)

Not available.

Flammability limit - upper (%)

Not available.

Explosive limit - lower (%)

Not available.

Explosive limit - upper (%)

Not available.

Vapor pressure

Not available.

Vapor density

Not available.

Relative density

Not available.

Solubility in water

Soluble.

Partition coefficient (n-octanol/water)

Not available.
Auto-ignition temperature Not available.
Decomposition temperature Not available.
Viscosity Not available.
Other information

- Chemical family: Piperidine derivative.
- Molecular formula: C24H29NO3.HCl
- Molecular weight: 415.95
- Solubility (other): Freely soluble in chloroform; sparingly soluble in methanol; soluble in acetic acid; slightly soluble in ethanol and in acetonitrile; practically insoluble in ethyl acetate and in n-hexane.

10. Stability and reactivity

Reactivity: No reactivity hazards known.
Chemical stability: Stable at normal conditions.
Possibility of hazardous reactions: No dangerous reaction known under conditions of normal use.
Conditions to avoid: None known.
Hazardous decomposition products: NOx, Cl-. Irritating and/or toxic fumes or gases. Emits toxic fumes under fire conditions.

11. Toxicological information

Information on likely routes of exposure

- Ingestion: Fatal if swallowed.
- Inhalation: Due to lack of data the classification is not possible.
- Skin contact: Due to lack of data the classification is not possible.
- Eye contact: Causes serious eye irritation.

Symptoms related to the physical, chemical, and toxicological characteristics:


Cross sensitivity: Persons sensitive to piperidine derivatives may be sensitive to this material as well.


Acute toxicity: Fatal if swallowed.

<table>
<thead>
<tr>
<th>Product</th>
<th>Species</th>
<th>Test Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donepezil Hydrochloride (CAS 120011-70-3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral</td>
<td>Mouse</td>
<td>45.2 mg/kg</td>
</tr>
<tr>
<td>LD50</td>
<td>Rat</td>
<td>32.6 mg/kg</td>
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<tr>
<td>Skin corrosion/irritation</td>
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<tr>
<td>Based on available data, the classification criteria are not met.</td>
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<td></td>
</tr>
<tr>
<td>Serious eye damage/eye irritation</td>
<td>Causes serious eye irritation.</td>
<td></td>
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<tr>
<td>Local effects</td>
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<tr>
<td>Eye irritancy test</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Result: Irritating.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Species: Rabbit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin irritancy test</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Result: Non-irritating.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Species: Rabbit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory sensitization</td>
<td></td>
<td></td>
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<tr>
<td>Due to lack of data the classification is not possible.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin sensitization</td>
<td></td>
<td></td>
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<tr>
<td>Due to lack of data the classification is not possible.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Germ cell mutagenicity</td>
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<td></td>
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<tr>
<td>Due to lack of data the classification is not possible.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Data from germ cell mutagenicity tests were not found.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Mutagenicity
Ames test in S. typhimurium and E. coli
Result: Negative.
Chromosomal aberration assay in Chinese hamster lung cell cultures
Result: Positive.
In vitro mouse lymphoma forward mutation assay
Result: Negative.
In vivo mouse micronucleus test
Result: Negative.
Unscheduled DNA synthesis in rats
Result: Negative.

Carcinogenicity
Based on available data, the classification criteria are not met.
This material is not considered to be a carcinogen by IARC, NTP, or OSHA.

180 mg/kg/day Long-term carcinogenicity study, administered orally.
Result: No carcinogenic potential.
Species: Mouse
Test Duration: 88 weeks
30 mg/kg/day Long-term carcinogenicity study, administered orally.
Result: No carcinogenic potential.
Species: Rat
Test Duration: 104 weeks

Reproductive toxicity
Based on available data, the classification criteria are not met.

Reproductivity
1 - 10 mg/kg/day Reproductivity and development study, administered orally during late gestation.
Result: Fetotoxicity.
10 mg/kg/day Fertility study
Result: No adverse effects on fertility.
Species: Rat
10 mg/kg/day Reproductivity and development study, administered orally during organogenesis.
Result: No teratogenicity.
Species: Rabbit
16 mg/kg/day Reproductivity and development study, administered orally during organogenesis.
Result: No teratogenicity.
Species: Rat

Specific target organ toxicity - single exposure
Based on available data, the classification criteria are not met.

Specific target organ toxicity - repeated exposure
Based on available data, the classification criteria are not met.

Aspiration hazard
Based on available data, the classification criteria are not met.

12. Ecological information

Ecotoxicity
No ecotoxicity data noted for the ingredient(s).
Persistence and degradability
No data is available on the degradability of this product.
Bioaccumulative potential
Not available.
Mobility in soil
Not available.
Other adverse effects
Not available.

13. Disposal considerations

Disposal instructions
Dispose in accordance with all applicable regulations. Under RCRA, it is the responsibility of the user of the product to determine, at the time of disposal, whether the product meets RCRA criteria for hazardous waste.

Local disposal regulations
Not available.

Hazardous waste code
Not available.

Waste from residues / unused products
Dispose of in accordance with local regulations. Empty containers or liners may retain some product residues. This material and its container must be disposed of in a safe manner (see: Disposal instructions).

Contaminated packaging
Empty containers should be taken to an approved waste handling site for recycling or disposal. Since emptied containers may retain product residue, follow label warnings even after container is emptied.
14. Transport information

DOT

<table>
<thead>
<tr>
<th>DOT</th>
<th>IATA</th>
</tr>
</thead>
<tbody>
<tr>
<td>UN number</td>
<td>UN2811</td>
</tr>
<tr>
<td>UN proper shipping name</td>
<td>Toxic solid, organic, n.o.s. (Donepezil Hydrochloride)</td>
</tr>
<tr>
<td>Transport hazard class(es)</td>
<td>6.1</td>
</tr>
<tr>
<td>Subsidiary class(es)</td>
<td>Not available.</td>
</tr>
<tr>
<td>Packing group</td>
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</tbody>
</table>

IATA

<table>
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<td>-</td>
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<tr>
<td>Packaging group</td>
<td>II</td>
</tr>
</tbody>
</table>

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code

No information available.

DOT; IATA

15. Regulatory information

US federal regulations

CERCLA/SARA Hazardous Substances - Not applicable.

One or more components are not listed on TSCA.

Superfund Amendments and Reauthorization Act of 1986 (SARA)

Hazard categories

Immediate Hazard - Yes
Delayed Hazard - No
Fire Hazard - No
Pressure Hazard - No
Reactivity Hazard - No

SARA 302 Extremely hazardous substance No

SARA 311/312 Hazardous chemical No

Other federal regulations

Safe Drinking Water Act (SDWA) Not regulated.

Food and Drug Administration (FDA) Not regulated.

US state regulations

California Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65): This material is not known to contain any chemicals currently listed as carcinogens or reproductive toxins.

International Inventories

<table>
<thead>
<tr>
<th>Country(s) or region</th>
<th>Inventory name</th>
<th>On inventory (yes/no)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>Australian Inventory of Chemical Substances (AICS)</td>
<td>No</td>
</tr>
<tr>
<td>Canada</td>
<td>Domestic Substances List (DSL)</td>
<td>No</td>
</tr>
<tr>
<td>Canada</td>
<td>Non-Domestic Substances List (NDSL)</td>
<td>No</td>
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<tr>
<td>China</td>
<td>Inventory of Existing Chemical Substances in China (IECSC)</td>
<td>No</td>
</tr>
<tr>
<td>Europe</td>
<td>European Inventory of Existing Commercial Chemical Substances (EINECS)</td>
<td>No</td>
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<tr>
<td>Europe</td>
<td>European List of Notified Chemical Substances (ELINCS)</td>
<td>No</td>
</tr>
<tr>
<td>Japan</td>
<td>Inventory of Existing and New Chemical Substances (ENCS)</td>
<td>No</td>
</tr>
<tr>
<td>Korea</td>
<td>Existing Chemicals List (ECL)</td>
<td>No</td>
</tr>
<tr>
<td>New Zealand</td>
<td>New Zealand Inventory</td>
<td>No</td>
</tr>
</tbody>
</table>
Country(s) or region: Philippines
Inventory name: Philippine Inventory of Chemicals and Chemical Substances (PICCS)
On inventory: No

Country(s) or region: United States & Puerto Rico
Inventory name: Toxic Substances Control Act (TSCA) Inventory
On inventory: No

*A “Yes” indicates that all components of this product comply with the inventory requirements administered by the governing country(s)

16. Other information, including date of preparation or last revision

Issue date: 06-03-2008
Revision date: 10-30-2014
Version #: 02
Further information: Not available.

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Revision Information: This document has undergone significant changes and should be reviewed in its entirety.