SAFETY DATA SHEETS

This SDS packet was issued with item:

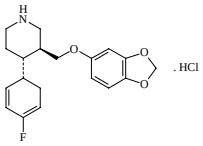
078726756

N/A

APOTEX
ADVANCING GENERICS

Material Safety Data Sheet

Section 1. Product Identification and Uses

Common/Trade name	**Paroxetine hydrochloride**	**DSL#**	Not on the DSL list.
Synonyms	Paroxetine hydrochloride hemihydrate	**CAS#**	78246-49-8
Chemical name	Piperidine, 3-((1,3-benzodioxol-5-yloxy)methyl)-4-(4-fluorophenyl)-, hydrochloride, (3S-trans)-	**Molecular weight**	365.83g/mole
Chemical family	Phenylpiperidine derivative	**Chemical formula**	$C_{19}H_{20}FNO_3$. HCl
Supplier	Brantford Chemicals Inc. Station Main, P.O. Box 1976, Brantford, Ontario N3T 5W5 Tel#: (519) 756-8942	**Chemical structure**	
Material uses	Pharmaceutical industry: Pharmaceutical ingredient. Therapeutic category: Antidepressant; SSRI	**Manufacturer**	Not available
Emergency phone	1- (416)-749-9300 ext. 5555 For general information call ext. 8483 (8 A.M.- 4 P.M.)	**DIN**	Not applicable

Section 2. Hazards Identification

Potential Acute Health Effects

Possible eye, skin, gastrointestinal and/or respiratory tract irritation.

Potential Chronic Health Effects

Possible hypersensitization.

WHMIS

CLASS D-1B: Material causing immediate and serious toxic effects (TOXIC).
CLASS D-2A: Material causing other toxic effects (VERY TOXIC).

Remark

Covered by Food & Drug Act and therefore not regulated under WHMIS

Apotex Hazard Classification (For Apotex internal practices only)

This material has been assigned hazard class: **2**

Section 3. First Aid Measures

Eye contact	IMMEDIATELY flush eyes with running water for at least 15 minutes, keeping eyelids open. Take care not to rinse contaminated water into the non-affected eye. Always seek medical attention for accidents involving the eyes.
Skin contact	Flush the contact area with lukewarm running water for at least 15 minutes. Seek medical attention if symptoms persists.
Hazardous skin contact	Flush the contact area with lukewarm running water for at least 15 minutes. Seek medical attention if symptoms persists.If contamination is extensive, remove clothing under running water. Discard or decontaminate clothing before reuse. Unless contact has been slight or if irritation persists see medical attention.
Slight inhalation	Allow the victim to rest in a well ventilated area. Seek immediate medical attention if irritation persists.
Hazardous inhalation	Take proper precautions to ensure your own safety before attempting rescue. Remove source of contamination or move victim to fresh air. If breathing is difficult, give oxygen. If breathing has stopped, trained personnel should begin artificial respiration, or if the heart has stopped, cardiopulmonary resuscitation (CPR) immediately. Seek medical attention.

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Slight ingestion	Flush out mouth with water. Seek medical attention if symptoms persists.
Hazardous ingestion	Never give anything by mouth if victim is rapidly losing consciousness, or is unconscious or convulsing. Rinse mouth thoroughly with water. If breathing has stopped, trained personnel should begin artificial respiration, or if the heart has stopped, cardiopulmonary resuscitation (CPR) immediately. Seek medical attention. Overdose treatment: Treatment should be symptomatic and supportive and may include the following: 1. Do not induce vomiting. 2. To decrease absorption, perform gastric lavage and administer activated charcoal as a slurry. 3. Monitor cardiac and central nervous system function; establish and monitor airway; monitor vital signs. 4. For hypotension, infuse isotonic fluid. If hypotension persists, administer dopamine or norepinephrine. 5. For seizures, administer an intravenous benzodiazepine. If seizures recur, consider phenobarbital or propofol. Monitor for hypotension, dysrhythmias, respiratory depression, and need for endotracheal intubation. Evaluate for hypoglycemia, electrolyte disturbances, and hypoxia. 6. For serotonin syndrome, administer cyproheptadine orally. 7. Due to the large volume distribution of paroxetine, forced diuresis, hemodialysis, hemoperfusion, or exchange transfusions are not likely to be of benefit. [Poisindex 2009; PDR 2009]

Section 4. Hazardous Ingredients

Name	CAS #	% (w/w)
Paroxetine hydrochloride	78246-49-8	100

Toxicity values of the hazardous ingredients

Refer to Sec. 11.

TLV Industry : 40 micrograms/m^3 (hemihydrate)

Section 5. Fire Fighting Measures

The product is:	May be combustible.
Autoignition temperature	Not available.
Fire degradation products	These products are carbon oxides (CO, CO2), nitrogen oxides (NO, NO2...), halogenated compounds.
Flash points	Not applicable
Flammable limits	Not available.
Fire extinguishing procedures	Extinguisher media: water spray, dry chemical, carbon dioxide or foam as appropriate for surrounding fire and materials. Special fire fighting procedures: As with all fires, evacuate personnel to safe area. Firefighters should use self-contained breathing equipment and protective clothing.
Flammability	Emits toxic fumes under fire conditions.
	Remark No additional remark.
Risks of explosion	Risks of explosion of the product in presence of mechanical impact: Not available. Risks of explosion of the product in presence of static discharge: Fine airborne dust can be ignited by static discharge.
	Remark No additional remark.

Section 6. Accidental Release Measures

Spill and leak	Vacuum or sweep up spillage. Avoid dust. Place spillage into an appropriate labeled waste disposal container. Wash contaminated clothing before reuse. Ventilate area and wash spill site. Follow appropriate Safe Work Practices.

Protective Clothing Pictograms in case of large spill and/or high exposure levels

Protective clothing in case of large spill	Hooded Full suit -Tyvek coveralls or equivalent. Powered Air Purifying Respirator with combination particulate/organic vapour cartridge. Gloves.

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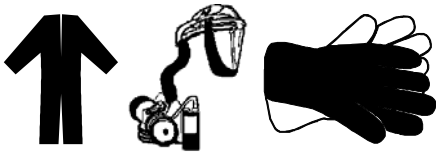


Section 7. Handling and Storage

Precautions

Use with adequate dust control. In case of insufficient ventilation, wear suitable respiratory equipment. Avoid inhalation, skin and eye contact. Wash thoroughly after handling. Pregnant women should avoid exposure to this product.

Storage

Keep in tight containers under Nitrogen. Store at 20°C to 25°C (68°F to 77°F).

Section 8. Exposure Controls/Personal Protection

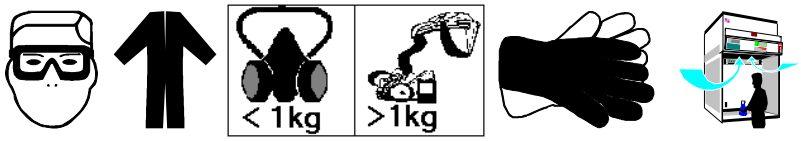
Engineering Controls

Exposure to this material can be controlled in many ways. The measures appropriate for a particular worksite depend on how this material is used and on the extent of exposure. This general information can be used to help develop specific control measures. Ensure that control systems are properly designed and maintained. Comply with occupational, environmental, fire, and other applicable regulations.
Engineering methods to control hazardous conditions are preferred. Methods include mechanical (local exhaust) ventilation, process or personnel enclosure and control of process conditions. Administrative controls and personal protective equipment may also be required. Supply sufficient replacement air to make up for air removed by exhaust system.

Personal Protection

Splash goggles. Full suit with hood, or disposable/washable coveralls. Half facepiece Air Purifying Respirator with combination particulate/organic vapour cartridge (less then 1 kg). Powered Air Purifying Respirator (PAPR) with combination particulate/organic vapour cartridge (greater then 1 kg). Nitrile gloves (impervious). Chemical fume hood.

Protective Clothing (Pictograms)



PERSONAL PROTECTIVE EQUIPMENT:
If engineering controls and work practices are not effective in controlling exposure to this material, then wear suitable personal protective equipment, including approved respiratory protection. Have appropriate equipment available for use in emergencies such as spills or fire. If respiratory protection is required, institute a complete respiratory protection program, including selection, fit testing, training, maintenance and inspection. Refer to the CSA Standard Z94, "Selection, Care, and Use of Respirators".
RESPIRATORY PROTECTION GUIDELINES:
Where Local Exhaust Ventilation (LEV) at dust generating process points exists, respiratory protection may not be required.
When working with quantities less than 1 kg and in the absence of appropriate Local Exhaust Ventilation (LEV) with dusty processes, a half facepiece Air Purifying Respirator with combination particulate/organic vapour cartridge and goggles is recommended.
When working with quantities greater than 1 kg and in the absence of Local Exhaust Ventilation (LEV) with dusty processes, a Powered Air Purifying Respirator (PAPR) with combination particulate/organic vapour cartridge and helmet/hood or Supplied Air Respirator (SAR) is recommended.
The specific respirator selected must be based on contamination levels found in the work place, the specific operation and not exceed the working limits of the respirator.
When performing cleaning activities refer to appropriate cleaning solution MSDS.
EYE/FACE PROTECTION: Splash goggles/safety glasses.
PROTECTIVE CLOTHING/SKIN PROTECTION: Glove selection must take into account any solvents and other hazards present. The selection of gloves for a specific activity must be based on the material's properties and on possible permeation and degradation that may occur under the circumstances of use. Potential allergic reactions can occur with certain glove materials (e.g. Latex) and therefore these should be avoided. Full environmental suit with hood. and/or other resistant protective clothing when working in dusty areas. Have a safety shower/eye-wash fountain readily available in the immediate work area.
EXPOSURE CONTROLS/PERSONAL PROTECTION COMMENTS: In the event clothing becomes contaminated, remove promptly. Launder before use. Inform laundry personnel of contaminant's hazards. Do not eat, drink or smoke in work areas. Wash hands thoroughly after handling this material. Maintain good housekeeping.
PREGNANCY PRECAUTION:
Pregnant women should avoid exposure to this product unless:
True Barrier Technology or appropriate engineering controls exists or:
When working with quantities less than 1 kg and in the absence of appropriate Local Exhaust Ventilation (LEV) with dusty processes, a full facepiece Air Purifying Respirator with combination particulate/organic vapour cartridge and goggles is worn.
When working with quantities greater than 1 kg and in the absence of Local Exhaust Ventilation (LEV) with dusty processes, a Powered Air Purifying Respirator (PAPR) with combination particulate/organic vapour cartridge and helmet/hood or Supplied Air Respirator (SAR) is worn.

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Section 9. Physical and Chemical Properties

Physical state and appearance	Solid. (Powder)	**Odor**	Odorless.
pH	6 - 7 (aqueous solution)	**Taste**	Not available.
Odor threshold	Not available.	**Color**	Off-white.
Volatility	Not available.		
Melting point/ Freezing point	120 - 145° C (hemihydrate); 115 - 126° C (anhydrous)		
Boiling point	Not available.		
Specific gravity	Not available.		
Vapor density	Not available.		
Vapor pressure	Not available.		
Partition Coefficient:	Log Pow = 1.3 (hemihydrate)		
Ionicity (surface active agent)	Not available.		
Critical temperature	Not available.		
Instability temperature	Not available.		
Conditions of instability	No additional remark.		
Dispersion properties	See solubility.		
Evaporation rate	Not available.		
Solubility	Slightly soluble in water. Soluble in ethanol and in methanol.		

Section 10. Stability and Reactivity

Stability	Normally stable.
Hazardous decomp. products	Toxic fumes of: carbon monoxide, carbon dioxide, nitrogen oxides.
Degradability	Not available.
Corrosivity	Not available.
	Remark No additional remark.
Reactivity/ Incompatibility	Strong oxidizing agents, strong bases. Avoid exposure to light and heat.
	Remark Not additional remark.

Section 11. Toxicological Information

Routes of entry	Eye contact. Ingestion. Inhalation. Skin contact.
Toxicity data	LD50: 374 mg/kg (hemihydrate); 415 mg/kg (anhydrous) (oral-rat) LD50: 378 mg/kg (anhydrous) (oral-mouse) Irritancy Data: Skin/Rabbit: non-irritant (intact skin); irritant (abraded skin) (hemihydrate) Eye/species not reported: severe

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Long-term effects

Possible hypersensitization.
Carcinogenicity: Not listed by IARC, NTP, ACGIH, or OSHA.
In a two-year carcinogenicity study, a significantly greater number of male rats receiving high doses of paroxetine exhibited reticulum cell sarcomas than did rats receiving lower doses. There was also an increased linear trend for occurrence of lymphoreticular tumors in male rats. Female rats were not
affected. In mice, there was a dose-related increase in the number of tumors, but no drug-related increase in the number of mice with tumors. The relevance of these findings to humans is not known.
Reproductive Toxicity: Rats receiving paroxetine in fertility studies showed reduced pregnancy rates. Irreversible lesions occurred in the reproductive tract of male rats in toxicity studies.
Teratogenicity: Pregnanacy Category: D. Rats receiving paroxetine at doses of 15 mg/kg/day in fertility studies showed reduced pregnancy rates. Irreversible lesions occurred in the reproductive tract of male rats (at doses of 25 and 50 mg/kg/day for 2 to 52 weeks) in toxicity studies. Studies in rats (at doses up to 50 mg/kg/day) and rabbits (6 mg/kg/day) showed no birth defects, however, there was an increase in pup deaths in rats receiving paroxetine during the last trimester of pregnancy and continuing through lactation. Therapeutic use of paroxetine in the first trimester has been associated with increased risk of congenital and cardiovascular malformations in the newborn. Some newborns whose mothers took paroxetine in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. These may result from toxic effects of the drug, withdrawal effects, or serotonin syndrome. A study showed that babies born to mothers who took SSRIs in late pregnancy have a greater risk of persistent pulmonary hypertension of the newborn than babies whose mothers did not take antidepressants during pregnancy.
Mutagenicity: Paroxetine produced no genotoxic effects in a battery of five in vitro and two in vivo assays that included the following: bacterial mutation assay, mouse lymphoma mutation assay, unscheduled DNA synthesis assay, and tests for cytogenetic aberrations in vivo in mouse bone marrow and in vitro in human lymphocytes and in a dominant lethal test in rats.

Remark

Medical conditions aggravated by exposure: Hypersensitivity to material, bipolar disorder, major depressive disorder, seizure disorder, and severe liver or kidney function impairment.

Short-term effects and Signs & Symptoms of overexposure

Possible eye, skin, gastrointestinal and/or respiratory tract irritation.
The usual adult oral dose of Paroxetine is 20 to 50 mg/day.
Adverse effects may include agitation, chest pain, fever, chills, confusion, congestion, trouble breathing, abdominal pain, flatulence, muscle pain or weakness, fast or irregular heartbeat, skin rash, unusual tiredness or weakness, constipation, diarrhea, dizziness, dry mouth, headache, sweating, insomnia, nausea, decreased sexual ability or desire, tremor, problems urinating, vomiting, anxiety, and appetite changes. Possible allergic reaction to material if inhaled, ingested, or in contact with skin.
Overdose effects include large pupils, dizziness, sleepiness, confusion, nausea, racing heartbeat, trembling, vomiting, and coma.

Remark

The above adverse effects are based on clinical studies.

Section 12. Ecological Information

Ecological Information

Harmful to activated sludge microorganisms; toxic to daphnids and fish.

Section 13. Disposal Considerations

Waste Disposal

For internal Apotex waste disposal: Collect in sealed containers and place in appropriate labeled pharmaceutical solid waste class 261A.
For external waste disposal: Follow all appropriate safe work procedures and federal, provincial and local regulations for disposal. Use only licensed disposal and waste hauling companies.

Section 14. Transport Information TDG, IATA, IMDG

Not controlled under TDG (Canada).

UN

Not applicable.

Special Provisions for Transport

No additional remark.

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Section 15. Other Regulatory Information and Pictograms

NATIONAL FIRE PROTECTION ASSOCIATION (NFPA) HAZARD INDEX

NFPA-HEALTH-blue :2-Hazardous to health.
NFPA-FLAMMABILITY-red :1-Materials that must be preheated before ignition can occur.
NFPA-REACTIVITY-yellow :0-Normally stable.

National Fire Protection Association (U.S.A.)

Hazardous Material Information System (U.S.A.)

Health Hazard	2
Fire Hazard	1
Reactivity	0
Personal Protection	X

* - Chronic hazard indicator
X - See Section 8

HCS (Hazardous Communication System) (OHSA, U.S.A.)

Class: Toxic.

DOT (Department of Transportation) (U.S.A) (Pictograms)

Not a DOT controlled material (United States).

EU Classification and Labelling

R22- Harmful if ingested. R36/37/38- Irritating to eyes, respiratory system and skin. R40- Possible risks of irreversible effects. R63- Possible risk of harm to the unborn child. S36- Wear suitable protective clothing.

ADR (European Agreement of Dangerous goods by Road) (Pictograms)

Not controlled under ADR (Europe).

Other Regulations

This product has been classified in accordance with the hazard criteria of the Controlled Products Regulations (CPR) and the MSDS contains all of the information required by the CPR.

Section 16. Other Information

References

The Merck Index
HSBD & RTECS Database
RxList Monographs

MSDS:

U. S. Pharmacopeia

Validation date: (year.month)

October 20, 2010

Revision date: 7/4/2012.

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Notice to Reader

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