SAFETY DATA SHEETS

This SDS packet was issued with item:

078946002

The safety data sheets (SDS) in this packet apply to the individual products listed below. Please refer to invoice for specific item number(s).

078946001

APOTEX
ADVANCING GENERICS

Material Safety Data Sheet

Section 1. Product Identification and Uses

Common/Trade name	**Pentoxifylline Extended-Release Tablets 400 mg**	**DSL#**	Not on the DSL list.
Synonyms	Pentoxyfylline Sustained Release Tablets Brand Name: Trental	**CAS#**	Not applicable.
Chemical name	Not applicable.	**Molecular weight**	Not applicable.
Chemical family	Methylxanthine derivative	**Chemical formula**	Not applicable.
Supplier	Apotex Corp. Weston, Florida 33326	**Chemical structure**	Not applicable.
Material uses	Pharmaceutical industry: Dosage form Therapeutic category: Vasoactive agent	**Manufacturer**	Apotex Inc. 150 Signet Drive Weston, Ontario M9L 1T9 416-749-9300
Emergency phone	**(416)-749-9300** ext. 5555 For general information call ext. 8483 (8 AM-4 PM)	**DIN**	Not available

Section 2. Hazards Identification

Potential Acute Health Effects

Not expected to be hazardous under normal handling conditions.

Potential Chronic Health Effects

Possible hypersensitization.

WHMIS

WHMIS CLASS D-2B: Material causing other toxic effects (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: **1**

Section 3. First Aid Measures

Eye contact	Flush with copious quantities of water. If irritation persists, obtain medical advice.
Skin contact	Not expected to result in hazardous effects.
Hazardous skin contact	Flush with copious amounts of water. Seek medical attention if irritation persist.
Slight inhalation	Not expected to result in hazardous effects.
Hazardous inhalation	Remove from exposure. Persons developing serious hypersensitivity reactions must receive immediate medical attention. If not breathing give artificial respiration (use protective mask with one-way valve). If breathing is difficult give oxygen.
Slight ingestion	Not expected to be hazardous. It is good practice to rinse mouth thoroughly with water and drink a cup of water to minimize discomfort.

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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 (use protective mask with one -way valve), or if the heart has stopped, cardiopulmonary resuscitation (CPR) immediately. Seek medical attention.
Treatment should be symptomatic and supportive and may include the following:
1. Perform early gastric lavage and/or administer activated charcoal slurry. DO NOT induce vomiting.
2. Monitor and correct electrolyte abnormalities.
3. Treat seizures with intravenous benzodiazepines. If seizures recur, treat with phenobarbital or propofol. Monitor for hypotension, dysrhythmias, respiratory depression, and need for endotracheal intubation. Evaluate for hypoglycemia, electrolyte imbalances, and hypoxia.
4. For hypotension, administer isotonic fluid. If hypotension persists, treat with dopamine or norepinephrine.
5. Hemodialysis and hemoperfusion are unlikely to be effective. [Poisindex 2010]

Section 4. Hazardous Ingredients

Name	CAS #	% (w/w)
Pentoxifylline	6493-05-6	70-90

Toxicity values of the hazardous ingredients

Refer to Sec. 11.

TLV Not established.

Section 5. Fire Fighting Measures

The product is: May be combustible at high temperature.

Autoignition temperature Not available.

Fire degradation products Decomposition products may include the following materials: carbon oxides (CO, CO_2), nitrogen oxides (NO, NO_2 etc.).

Flash points Not applicable.

Flammable limits Not available.

Fire extinguishing procedures Extinguisher media: 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: No.
Risks of explosion of the product in presence of static discharge: No.

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 Covering uniform. Gloves. Half facepiece Air Purifying Respirator with combination particulate/organic vapour cartridge. Splash goggles.

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Section 7. Handling and Storage

Precautions	In case of insufficient ventilation, wear suitable respiratory equipment. Avoid breathing dust. Wash thoroughly after handling.
Storage	Store at 20° to 25°C (68° to 77°F). Dispense in a tight, light-light resistant container.

Section 8. Exposure Controls/Personal Protection

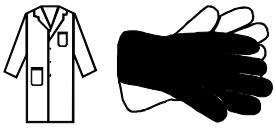
Engineering Controls

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

Covering uniform. Gloves.

Protective Clothing (Pictograms)



PERSONAL PROTECTIVE EQUIPMENT/RESPIRATORY PROTECTION GUIDELINES :
Under normal work conditions, the use of respiratory protective equipment is not expected to be required. However major spills should require the use of designated personal protective equipment. Have appropriate equipment available for use in emergencies such as spills or fire.
If the physical state of the finished product is altered by crushing, grinding or breakage, appropriate PPE may be required including half facepiece Air Purifying Respirator with combination particulate/organic vapour cartridges.
The respirator use limitations specified by the approving agency and the manufacturer must be observed.
EYE/FACE PROTECTION : Not required under normal working conditions.
SKIN PROTECTION : The use of nitrile gloves is required for Good Manufacturing Practices (GMP) compliance.
RESISTANCE OF MATERIALS FOR PROTECTIVE CLOTHING : Resistance of specific materials can vary from product to product. Evaluate resistance under conditions of use and maintain clothing carefully.
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.

Section 9. Physical and Chemical Properties

Physical state and appearance	White, oval, unscored, film-coated tablets, imprinted "APO 33" on one side and plain on the other side.		
pH	Not available.	**Taste**	Not available.
Odor threshold	Not available.	**Odor**	Not available.
Volatility	Not available.		
Melting point/ Freezing point	Not available.		
Boiling point	Not available.		
Specific gravity	Not available.		
Vapor density	Not applicable.		
Vapor pressure	Not applicable.		
Partition Coefficient:	Not available.		
Ionicity (surface active agent)	Not available.		
Critical temperature	Not available.		
Instability temperature	Not available.		

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Conditions of instability	No additional remark.
Dispersion properties	See solubility.
Evaporation rate	Not available.
Solubility	Not available.

Section 10. Stability and Reactivity

Stability	The product is stable.
Hazardous decomp. products	Not available.
Degradability	Not available.
Corrosivity	Not available.
	Remark No additional remark.
Reactivity/ Incompatibility	Not available.
	Remark No additional remark.

Section 11. Toxicological Information

Routes of entry	As the product is a solid dosage form, the major route of entry is ingestion. Other routes of entry, including inhalation, skin and eye contact may occur only under certain circumstances.
Toxicity data	**Pentoxifylline**: RTECS#: XH2475000 TDLo: 80 mg/kg (oral-woman): affects pulse rate LD50: 1170 mg/kg (oral-rat) LD50: 1225 mg/kg (oral-mouse)
Long-term effects	Possible hypersensitization. Target organ: blood. Carcinogenicity: Not listed by IARC, NTP, ACGIH, or OSHA. Studies in rats given pentoxifylline at doses up to 24 times the maximum recommended human dose for 18 months, with a 6 month drug-free period, showed an increase in benign mammary fibroadenomas in females at the highest dose. Mice given the same dose for 18 months showed no evidence of carcinogenicity. Reproductive Toxicity: Reproduction studies have been performed in rats, mice and rabbits at doses up to 23, 2 and 11 times the maximum recommended daily human dose and have revealed no evidence of impaired fertility or harm to the fetus due to pentoxifylline. Teratogenicity: Category C. Studies in rats and rabbits given oral doses up to 576 and 264 mg/kg, respectively, found an increased incidence of fetal resorptions in rats given the highest dose, but no fetal malformations were observed. Intravenous doses up to 25 mg/kg in rabbits and 50 mg in mice caused no adverse fetal effects. Mutagenicity: Pentoxifylline was negative in the Ames Salmonella typhimurium assay with and without activation and in the in vivo mouse micronucleus assay. It did not induce 6-TGr mutations in the HGPRT locus of V79 cells and did not cause morphological transformation of Syrian hamster embryo cells. It did induce chromosome aberrations and micronucleii in Chinese hamster V79 cells and human peripheral lymphocytes in vitro.
	Remark Medical conditions aggravated by exposure: Hypersensitivity to material, recent cerebral, retinal, or gastrointestinal bleeding, or any other condition in which there is a risk of bleeding; liver or kidney function impairment; cerebrovascular or coronary artery disease; hypotension. Individuals sensitive to methylxanthines such as caffeine, theophylline, or theobromine may be sensitive to this material also.
Short-term effects and Signs & Symptoms of overexposure	The usual oral adult dose of pentoxifylline is 400 mg three times a day. Adverse effects may include irregular heart beat, flushing, abdominal discomfort, gas, diarrhea, heartburn, nausea, vomiting, agitation, dizziness, drowsiness, headache, trouble sleeping, and blurred vision. Possible allergic reaction to material if inhaled, ingested, or in contact with skin. Overdose symptoms include gastrointestinal upset, flushing, lightheadedness, convulsions, drowsiness, fever, agitation, abnormal heart rate, and loss of consciousness. Symptoms usually occur 4 to 5 hours following ingestion and last about 12 hours.
	Remark

Continued on Next Page

The above adverse effects are based on clinical studies.

Section 12. Ecological Information

Ecological Information Not available.

Section 13. Disposal Considerations

Waste Disposal For internal Apotex waste disposal: Collect in sealed containers and place in appropriate labeled pharmaceutical solid waste class 261N.
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 (PIN and PG).

Special Provisions for Transport Not applicable.

Section 15. Other Regulatory Information and Pictograms

NATIONAL FIRE PROTECTION ASSOCIATION (NFPA) HAZARD INDEX

NFPA-HEALTH-blue :1-Slightly 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.)

Fire Hazard
Reactivity
Health
Specific Hazard

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

Health Hazard	1
Fire Hazard	1
Reactivity	0
Personal Protection	X

* - Chronic hazard indicator
X - See Section 8

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

Not an HCS controlled material in USA.

DOT (Department of Transportation) (U.S.A) (Pictograms) Not a DOT controlled material (United States).

EU Classification and Labelling Exempt from requirements of EU Dangerous Preparations directive - product regulated as a medicinal product, cosmetic product or medical device. R40- Possible risks of irreversible effects.

ADR (European Agreement of Dangerous goods by Road) (Pictograms) Not controlled under ADR (Europe).

Other Regulations

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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 HSDB & RTECS Database
PDR Electronic Library
The Merck Index, Fourteenth Edition

MSDS:	**Validation date: (year.month)**
U. S. Pharmacopeia	July 29, 2010

Revision date: 4/4/2011.

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Notice to Reader