

MATERIAL SAFETY DATA SHEET

Boehringer Ingelheim Pharmaceuticals, Inc.

CATAPRES® Tablet

900 Ridgebury Road
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(203) 798-5521 9AM - 4PM EST

REVISED: 09/06/05

EMERGENCY TELEPHONE NUMBER
CHEMTREC - 24 hours
1-800-424-9300

1. SUBSTANCE IDENTIFICATION

CHEMICAL NAME: 2-(2, 6-Dichlorophenylamino)-2-imidazoline hydrochloride

CAS TYPE: 1

GENERIC NAME: Clonidine Hydrochloride

MOLECULAR FORMULA: C₉H₉Cl₂N₃ · HCl

TRADEMARK: CATAPRES ®

MOLECULAR WEIGHT: 266.56

CHEMICAL FAMILY: Antihypertensive

CAS NUMBER: 4205-91-8

SYNONYMS: Benzenamine, St 155, Clonidine, Catapresan, Dixarit, Isoglaucou

PRODUCT USE: Antihypertensive

2. HAZARD IDENTIFICATION

EMERGENCY OVERVIEW

For Product:

Physical State: 0.1 mg tablets – tan, oval, single scored with BI 6
0.2 mg tablets – orange, oval, single scored BI 7
0.3 mg tablets – peach, oval single scored BI 11

WARNING!

May be harmful or fatal if swallowed.

Potential Health Effects – Product:

CONTRAINDICATIONS: Hypersensitivity to Catapres® or to any other component of the therapeutic system.

Catapres® Tablets should be used with caution in patients with severe coronary insufficiency, conduction disturbances, recent myocardial infarction (heart attack), cerebrovascular disease, or chronic renal (kidney) failure.

ADVERSE REACTIONS TO PRODUCT: Dry mouth, drowsiness, fatigue, headache, lethargy (abnormal drowsiness), sedation, insomnia (inability to sleep), dizziness, impotence/sexual dysfunction, dry throat, constipation, nausea, change in taste and nervousness. Skin reactions including erythema (reddening), pruritus (itching), and contact dermatitis (inflammation) may occur.

WARNING

Patients should be instructed not to discontinue therapy without consulting their physician. Sudden cessation of clonidine treatment can cause nervousness, agitation, headache, and confusion accompanied or followed by a rapid rise in blood pressure and elevated catecholamine concentrations in the plasma.

Catapres® Tablets may increase the depression of the central nervous system caused by use of alcohol, barbiturates, or other sedating drugs.

Overdosage: With extreme overdoses profound hypotension (low blood pressure), weakness, drowsiness, diminished/absent reflexes and vomiting have been reported.

ROUTES OF ENTRY: Ingestion

ACUTE EXPOSURE:

INHALATION: Not expected to be an inhalation hazard.

EYE CONTACT: Not expected to be a hazard to the eye.

SKIN CONTACT: Can cause hypersensitive reactions. Exposure may cause redness, itching and inflammation.

INGESTION: May be harmful if ingested. Ingestion may cause dizziness, headache, drowsiness, weakness, nausea, palpitations, hyper- or hypotension, insomnia and other systemic effects.

CHRONIC EXPOSURE: Possible hypersensitization (development of abnormal sensitivity).

TARGET ORGANS: Cardiovascular system

MEDICAL CONDITIONS POTENTIALLY AGGRAVATED BY EXPOSURE: Cerebral, heart and heart circulatory conditions, Raynaud's disease, venous insufficiency, thromboangitis obliterans and depression.

OSHA REGULATORY STATUS: OSHA Exempt for product.

CARCINOGENICITY: Not listed as a carcinogen or potential carcinogen by NTP, IARC Monographs or OSHA.

3. COMPONENTS PER UNIT DOSE

MATERIAL	EXPOSURE LIMITS
Active Ingredient: Clonidine	190 ng/m ³ PECL*
Excipients: Colloidal Silicon Dioxide N.F.	10 mg/m ³ ACGIH 8-hr TLV-TWA (based on precipitated silica and silica gel) .8 mg/m ³ OSHA Z-3 8-hr TWA (silica: amorphous, including natural diatomaceous earth)
Lactose USP (Hydrous) Corn Starch N.F.	No TLV established 10 mg/m ³ ACGIH 8-hr TLV-TWA (dermatitis, lung) 5 mg/m ³ OSHA Z-1 PEL (starch, respirable fraction) 15 mg/m ³ OSHA Z-1 PEL (starch, total dust)

FD&C Blue # 1 (0.1mg)	No TLV established
FD&C Yellow # 6	No TLV established
FD& C Red #3 (0.1mg)	No TLV established
Gelatin	No TLV established
Glycerin	10 mg/m ³ ACGIH 8-hr TLV-TWA (glycerin mist) (irritation) 5 mg/m ³ OSHA Z-1 PEL (glycerin mist, respirable fraction) 15 mg/m ³ OSHA Z-1 PEL (glycerin mist, total dust) 5 mg/m ³ OSHA Z-1-A PEL (glycerin mist, respirable fraction) 10 mg/m ³ OSHA Z-1 PEL (glycerin mist, total dust)
Magnesium Stearate, NF	10 mg/m ³ ACGIH 8-hr TLV-TWA (stearates, except stearates of toxic metals) (irritation)
Methylparaben	No TLV established
Propylparaben	No TLV established
Dibasic Calcium Phosphate	No TLV established

*PECL is the BIPI Preliminary Exposure Control Level. Where governmentally imposed occupational exposure limits which are lower than the PECL are in effect, such limits should take precedence.

4. EMERGENCY FIRST AID PROCEDURES

Persons developing anaphylactic (life-threatening) reactions, such as difficulty in breathing or unconsciousness, must receive immediate medical attention.

Product:

INHALATION: Should not pose a hazard in final form. Move to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention immediately.

EYE CONTACT: Should not pose a hazard in final form. Any material that contacts the eye should be washed out immediately with water. If easy to do, remove contact lenses if worn. Get medical attention if irritation persists.

SKIN CONTACT: Should not pose a hazard in final form. Immediately flush with plenty of water for at least 15 minutes while removing contaminated clothing and shoes. Get medical attention.

INGESTION: Call a physician or poison control center immediately. Only induce vomiting at the instruction of medical personnel. Never give anything by mouth to an unconscious person.

NOTE TO PHYSICIAN: Clonidine overdose usually responds to symptomatic treatment with careful cardiac monitoring. Supportive care may include atropine sulfate for bradycardia, intravenous fluids and/or vasopressors agents for hypotension and vasodilators for hypertension. Naloxone may be a useful adjunct for the management of clonidine-induced respiratory depression, hypotension and/or coma. Blood pressure should be monitored since the administration of naloxone has occasionally resulted in paradoxical hypertension. Tolazoline administration has yielded inconsistent results and is not recommended as first-line therapy. Dialysis is not likely to significantly enhance the elimination of clonidine.

5. FIRE AND EXPLOSION HAZARD DATA

Flash Point	Flammable Limits	
N/A	Upper	Lower
	N/A	N/A

FIRE EXTINGUISHING MEDIA: Water spray dry chemical, carbon dioxide

SPECIAL FIRE FIGHTING PROCEDURES: Wear self-contained breathing apparatus and protective clothing. Cool fire exposed containers with water.

UNUSUAL FIRE AND EXPLOSION HAZARDS: None

HAZARDOUS COMBUSTION PRODUCTS: Carbon dioxide, carbon monoxide, nitroxides and hydrogen chloride

6. SPILL AND ACCIDENTAL RELEASE MEASURES

STEPS TO BE TAKEN IF SIGNIFICANT QUANTITIES OF TABLETS ARE BROKEN: Wear an approved respirator, eye protection, personal protective coverings and gloves. Use HEPA filtered vacuum or wet sweeping to clean up spillage. Avoid dust. Place spillage in appropriate container for waste disposal. Wash contaminated clothing before use.

7. PRECAUTIONS FOR SAFE HANDLING AND USE

HANDLING AND STORAGE PRECAUTIONS: Store in a tight, light resistant container. Store away from foodstuffs. Store below 86° F (30°C).

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Engineering Controls: Not generally required when handling containers or capsules. (See Section 3 for exposure limits). Good ventilation (typically 10 air changes per hour) should be used. Ventilation rates should be matched to conditions. If operations involve crushing or other processes that may release powder, use process enclosures, local exhaust ventilation, or other engineering controls to maintain airborne levels below recommended exposure limits.

Respiratory Protection: Not generally required when handling containers or capsules. The need for respiratory protection should be determined by an industrial hygiene survey. (See Section 3 for exposure limits). NIOSH/MSHA approved respirators for protection should be used if respirators are found to be necessary.

PERSONAL PROTECTIVE EQUIPMENT: Not generally required when handling containers. If containers are compromised or exposure to the active ingredient or mixture is likely wear:

Eye Protection: Safety goggles w/side shields (or goggles)	Hand Protection: Neoprene or nitrile gloves
Protective Clothing: Laboratory coats	Other: Eye wash

WORK/HYGIENIC PRACTICES: Keep away from foodstuffs, beverages and feed. Immediately remove all soiled and contaminated clothing. Wash hands before breaks and at the end of work.

9. PHYSICAL/CHEMICAL CHARACTERISTICS

For Product:

APPEARANCE AND ODOR: 0.1 mg tablets – tan, oval, single scored with BI 6, odorless
0.2 mg tablets – orange, oval, single scored BI 7, odorless
0.3 mg tablets – peach, oval single scored BI 11, odorless

Boiling Point: N/A

Vapor Pressure (mmHg): N/A

Vapor Density: N/A

Specific Gravity: N/A

Melting Point: 305 °C (581°F)

Evaporation Rate: N/A

Water Solubility: 1 g in 13 ml @ 20°C
Freezing Point: N/A
Flammable Limits: N/A
Flashpoint: N/A

Autoignition Temperature: N/A
Decomposition Temperature: N/A
Partition Coefficient (n-Octanol/water): N/A
Volatiles, %: N/A

10. REACTIVITY DATA

STABILITY: Stable to 60°C (140°F)

CONDITIONS TO AVOID: None known

INCOMPATIBLE MATERIALS: None known

HAZARDOUS DECOMPOSITION OR BY-PRODUCTS: When heated to decomposition or under fire conditions emit toxic fumes of nitroxides and hydrogen chloride.

HAZARDOUS POLYMERIZATION: Will not occur.

11. TOXICOLOGICAL INFORMATION

ACUTE TOXICITY

Active Ingredient:

LD₅₀ Oral (mouse) - 217 mg/kg

LD₅₀ Oral (rabbit) - 80 mg/kg

LD₅₀ Oral (rat) - 150 mg/kg

TDLo Oral (man) - 69 ug/kg

TDLo Oral (woman) – 376 ug/kg

EYE IRRITATION: No data

SKIN IRRITATION: Rabbit 500mg – mild irritant

TERATOGENICITY: - PREGNANCY CATEGORY C: **Risk to human fetuses cannot be ruled out.** Human studies are lacking, however, animal studies are positive for fetal damage. Consult physician before using if you suspect you are pregnant, pregnant or nursing.

Reproduction studies performed in rabbits at doses up to approximately 3 times the oral maximum recommended daily human dose (MRDHD) of **Catapres** (clonidine hydrochloride) produced no evidence of teratogenic or embryotoxic potential in rabbits. In rats, however, doses as low as 1/3 the oral MRDHD of clonidine were associated with increased resorptions in a study in which dams were treated continuously from 2 months prior to mating.

CARCINOGENESIS/MUTAGENESIS/IMPAIRMENT OF FERTILITY: Chronic dietary administration of clonidine was not carcinogenic to rats (132 weeks) or mice (78 weeks) dosed, respectively, at up to 46 to 70 times the maximum recommended daily human dose as mg/kg. There was no evidence to genotoxicity in the Ames test for mutagenicity or mouse micronucleus test for clastogenicity.

Fertility of male and female rats was unaffected by clonidine doses as high as 150 mcg/kg (approximately 3 times the MRDHD.) In a separate experiment, fertility of male rats appeared to be affected at dose levels of 500 to 20000 mcg/kg (10 to 40 times the oral MRDHD on a mg/kg basis; 2 to 8 times the MRDHD on a mg/m² basis).

12. ECOLOGICAL INFORMATION

Active ingredient: 2, 6-Dichloro-N-2-imidazolidinylidenebenzenamine: slightly water endangering.

13. DISPOSAL CONSIDERATIONS

WASTE DISPOSAL CONSIDERATIONS: Dispose of in accordance with local, state and federal regulations. This product falls under hazardous chemical / pharmaceutical waste based on toxicity data. Recommended method is incineration.

For Product: (At Home):

Discard away from children's reach.

14. TRANSPORT INFORMATION

Product:

This product is not subject to the regulations for the safe transport of hazardous materials.

DOT: Not regulated	TDG: Not regulated
IATA: Not regulated	IMDG: Not regulated

15. REGULATORY INFORMATION

CANADIAN CONTROLLED PRODUCTS REGULATIONS: This product has been classified in according to the hazard criteria of the Canadian Controlled Products Regulations, Section 33, and the MSDS contains all required information.

WHMIS CLASSIFICATION FOR ACTIVE INGREDIENT: Controlled. D1B, D2B

WHMIS CLASSIFICATION FOR PRODUCT: Noncontrolled.

INVENTORY STATUS:

This material is **not** listed on the US TSCA Inventory. Therefore, it can only be used for TSCA exempt purposes such as R&D or drug use.

This material is **not** listed on the DSL Inventory.

16. OTHER INFORMATION

ABBREVIATIONS:

BIPI - Boehringer Ingelheim Pharmaceuticals, Inc.

N/A - Not applicable.

N/E - Not established.

PREPARATION INFORMATION

Prepared by: BIPI Environmental Affairs & Safety.

Date Revised: 09/05

Replaces: 4/98

REVISION INFORMATION: Section 2 –additional information; added; Section 3- Exposure limits updated, Section 4: First Aid Measures, Section 6- updated, Section 7 – updated, Section 8 – updated, Section 12- information added; Section 14 additional information added, Section 15- Canadian Regulations added.

**SEE CURRENT PACKAGE INSERT FOR
FURTHER INFORMATION**

REFERENCES

1. Ariel Research ChemExpert: Registry of Toxic Effects of Chemical Substances.
2. Ariel Research, ChemExpert: Hazardous Substance Bank.
3. Ariel Research, Global Regulatory Database.
4. National Library of Medicine, Toxline.
5. American Hospital Formulary Service, 2003.
6. BIPI MSDS, 1998.
7. Physician's Desk Reference, 2003.

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