

MATERIAL SAFETY DATA SHEET

Boehringer Ingelheim Pharmaceuticals, Inc.

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Flomax™ Capsules

REVISED: 09/06/05

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

1. SUBSTANCE IDENTIFICATION

CHEMICAL NAME: (-)-(R)-5-[2-[[2-(o-ethoxyphenoxy) ethyl] amino] propyl]-2-methoxybenzenesulfonamide hydrochloride

CAS TYPE: 1

GENERIC NAME: Tamsulosin hydrochloride

MOLECULAR FORMULA: C₂₀H₂₈N₂O₅S • HCl

TRADEMARK: Flomax™ Capsules

MOLECULAR WEIGHT: 444.98

CHEMICAL FAMILY: Substituted benzene sulfonamide

CAS NUMBER: 106463-17-6

SYNONYMS: Harnal, Omnic, Omic

PRODUCT USE: Benign Prostatic Hyperplasia

2. HAZARD IDENTIFICATION

EMERGENCY OVERVIEW

For Product:

Physical State: Hard olive green opaque cap and orange opaque body gelatin capsule

WARNING!

May be harmful if swallowed.

Higher doses may cause elevated prolactin levels.

Flomax is an alpha-1 adrenergic antagonist, and may elicit effects common to this class of compounds (e.g. decreased blood pressure, dizziness, headache, drowsiness, weakness, palpitations, and nausea).

Potential Health Effects – Product:

CONTRAINDICATIONS: This product is contraindicated in patients known to be hypersensitive to tamsulosin or any component of Flomax™ therapeutic system.

ADVERSE REACTIONS TO PRODUCT: Postural hypotension, dizziness, vertigo, loss of consciousness, abnormal ejaculation, headache, flu-like symptoms and nasal congestion. If more than 0.2mg is taken, the patient may experience dizziness and collapse when standing up.

Overdosage of Flowmax™ can cause hypotension or severe headaches.

Potential Health Effects

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: Not expected to be a hazard to the skin. Hypersensitive reactions which can cause redness, itching and inflammation of the skin.

INGESTION: Not expected to be an ingestion hazard. 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, kidney

MEDICAL CONDITIONS POTENTIALLY AGGRAVATED BY EXPOSURE: Heart and circulatory conditions, and hypertension (high blood pressure).

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: Tamsulosin hydrochloride	No TLV established
Excipients: Methacrylic acid copolymer	20 ppm ACGIH 8-hr TLV-TWA (methacrylic acid) (irritation)
Microcrystalline cellulose	10 mg/m ³ ACGIH 8-hr TLV-TWA (irritation) 5 mg/m ³ OSHA Table Z-1 (cellulose, respirable fraction) 15 mg/m ³ OSHA Table Z-1 (cellulose, total dust)
Triacetin	No TLV established
Polysorbate 80	No TLV established
Sodium lauryl sulfate	No TLV established
Calcium stearate	10 mg/m ³ ACGIH 8-hr TLV-TWA (stearates, except stearates of toxic

Talc	metals) (irritation) 2 mg/m ³ ACGIH 8-hr TLV-TWA (talc) (lung)
FD&C Blue No.2	No TLV established
Titanium dioxide	10 mg/m ³ ACGIH 8-hr TLV-TWA (lung)
Ferric oxide	10 mg/m ³ ACGIH 8-hr TLV-TWA (ferric oxide dust / fume) (lung, siderosis, irritation)
	5 mg/m ³ ACGIH 8-hr TLV-TWA (iron oxide, respirable fraction) (pulmonary siderosis)
Gelatin	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.

For Product:

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.

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.

NOTE TO PHYSICIAN: Treat symptomatically.

5. FIRE AND EXPLOSION HAZARD DATA

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

FIRE EXTINGUISHING MEDIA: Water, multipurpose dry chemical, foam, CO₂.

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

6. SPILL AND ACCIDENTAL RELEASE MEASURES

STEPS TO BE TAKEN IF SIGNIFICANT QUANTITIES OF CAPSULES ARE BROKEN: Wear approved respirator, eye protection, personal protective coverings and gloves. Absorb spilled liquid and collect for disposal. Place spillage in appropriate container for waste disposal. Wash contaminated clothing before reuse.

7. PRECAUTIONS FOR SAFE HANDLING AND USE

HANDLING AND STORAGE PRECAUTIONS: Store in tight container. Store away from foodstuffs.

HANDLING SIGNIFICANT QUANTITIES OF BROKEN GELCAPS: Avoid contact with eyes, skin or clothing. Absorb liquid and collect for disposal. Wash hands thoroughly after handling.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Engineering Controls: Not generally required when handling containers or capsules. (See Section 3 for exposure limits).

Good general ventilations (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 gel, 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 with side shields (or goggles) Hand Protection: Latex 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: Hard olive green opaque cap and orange opaque body gelatin capsule,

Boiling Point: N/A

Vapor Pressure (mmHg): 2×10^{-5} Pascals at 25 °C

Vapor Density: N/A

Water Solubility: 11.8 mg/ml

Freezing Point: N/A

Flammable Limits: N/A

Flashpoint: N/A

Volatiles, %: N/A

Specific Gravity: N/A

Melting Point: 230 °C

Evaporation Rate: N/A

pH: 6.7 (0.9% solution)

Autoignition Temperature: N/A

Decomposition Temperature: N/A

Partition Coefficient (n-Octanol/water): N/A

10. REACTIVITY DATA

STABILITY: Stable

CONDITIONS TO AVOID: None

INCOMPATIBLE MATERIALS: None known

HAZARDOUS DECOMPOSITION OR BY-PRODUCTS: None known

HAZARDOUS POLYMERIZATION: Will not occur

11. TOXICOLOGICAL INFORMATION

ACUTE TOXICITY: The median lethal dose of Flomax when administered orally to rats was 650 mg/kg for males and 787 mg/kg for females. Signs of toxicity included decreased locomotor activity, ptosis, prone position, lateral position, hypothermia, lacrymation and piloerection. The median lethal dose in mice was 1023 mg/kg for males and 1220 mg/kg for females. Signs of toxicity were similar to those seen in rats.

Minimum lethal dose was over 1000 mg/kg in dogs administered orally. Toxicity signs were vomiting, diarrhea, decreased locomotor activity, body weight and food consumption, and elevated GOT, GPT, ALP and CPK.

Ocular exposure: Not irritating to rabbits eyes.

Subchronic exposure:

In a three month dietary study, rats received time weighted average daily dose of 68, 200, or 327 mg of Flomax per kg of body weight for males, 80, 229, or 378 mg/kg for females. Treatment related effects included dose related decreases in body weight gain, food consumption and efficiency of food utilization, decreases in mean erythrocyte count, hemoglobin, packed cell volume and leukocyte counts, increased reticulocyte counts and lymphocyte counts, increased asparatate transaminase values and increased specific gravity of the urine. Hepatic enzyme activity was increased at the middle and high doses. Uterine weights were decreased at all dosage groups. Hyperplasia of the glandular tissue of mammary gland in the middle and high dose was the only histopathologic finding. The low dose was considered to be a no-effect level.

In a three month study in dogs, all animals survived at daily oral doses of 2, 20, 200 mg/kg. Signs of toxicity included relaxed nictitating membranes, miosis, excessive salivation, hypoactivity, redness of eyes, excessive lacrimation, tremors, ataxia, lethargy and emesis. Treatment related effects were increased erythrocytes, hemoglobin, packed cell volume, reticulocytes and leukocytes, and

increased alanine transaminase and aspartate transaminase values. Ovarian and uterine weights were decreased at high dose. The no effect level was considered to be 2 mg/kg.

CARCINOGENICITY: In a study with rats and mice, there was no development of carcinogenesis in male rats or mice. However, in female rats and mice there was a modest increase in the incidence of mammary gland fibroadenomas. The rats were given 3 times the maximum therapeutic dose of that human men received. Mice were given 8 times the maximum therapeutic dosage.

MUTAGENICITY: Flomax was negative in the Ames test, the DNA repair assay in primary rat hepatocytes, the mouse lymphoma assay and micronucleus test in mice.

TERATOGENICITY: PREGNANCY CATEGORY B: No evidence of risk in humans. Administration of tamsulosin to pregnant female rats at dose levels up to 300 mg/kg/day (approximately 50 times the human therapeutic AUC exposure) revealed no evidence of harm to the fetus. Administration of tamsulosin to pregnant rabbits at dose levels up to 50 mg/kg/day produced no evidence of fetal harm.

REPRODUCTIVITY: Studies in rats revealed significantly reduced fertility in males dosed with single or multiple daily doses of 300 mg/kg/day of tamsulosin (AUC exposure in rats about 50 times the human exposure with the maximum therapeutic dose).

Studies in female rats revealed significant reductions in fertility after a single or multiple dosing with 300 mg/kg/day R-isomer or racemic mixture of tamsulosin, respectively. In female rats, the reductions in fertility were considered to be associated with impairments in fertilization.

CONCLUSION: Observed major effects of exposure to Flomax in animals have been consistent with the pharmacological activity of the compound. No Flomax related mutagenic effects have been observed.

Listed Carcinogens: None

12. ECOLOGICAL INFORMATION

ACUTE TOXICITY:	EC ₅₀ (Daphnia) = 37.9 mg/l
ACTIVATED SLUDGE INHIBITION	EC ₅₀ > 100 mg/ml
BIODEGRADABILITY:	Not ready biodegradable (only 4% after 28 days)

13. DISPOSAL CONSIDERATIONS

WASTE DISPOSAL CONSIDERATIONS: Dispose of in accordance with local, state and federal regulations. Recommended method is incineration or landfill.

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. It is regulated under the Food & Drugs Act in Canada.

16. OTHER INFORMATION

ABBREVIATIONS:

BIPI - Boehringer Ingelheim Pharmaceuticals, Inc.

N/A - Not applicable.

N/E - Not established.

PREPARATION INFORMATION

Prepared by: Ariel Research Corporation for BIPI . Environmental Affairs & Safety.

Date Revised: 09/05

Replaces: 06/98

REVISION INFORMATION: Section 2 –additional information ;added; Section 3 –Exposure limits updated, Updated Section 4: First Aid Measures, Section 9-additional physical properties added; Section 15-additional transportation added, 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, 6/98

7. Physician's Desk Reference, 2003.

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