

MATERIAL SAFETY DATA SHEET

Boehringer Ingelheim Pharmaceuticals, Inc.

Alupent® Tablet

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P.O. Box 368
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(203) 798-5521 9AM - 4PM EST

DATE REVISED 03/28/03

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

1. SUBSTANCE IDENTIFICATION

CHEMICAL NAME: 1-(3-5-dihydroxyphenyl)-2-isopropylaminoethanol sulfate

CAS TYPE: 1

GENERIC NAME: Metaproterenol Sulfate

MOLECULAR FORMULA: $(C_{11}H_{17}NO_3)_2 \cdot H_2SO_4$

TRADEMARK: **Alupent® Tablet**

MOLECULAR WEIGHT: 520.59

PRODUCT USE: Bronchodilator³

CAS NUMBER:² 5874-97-5

SYNONYMS: Alotec, Metraprel, Orciprenaline Sulfate, Novasmasol, TH-152

2. COMPONENTS PER UNIT DOSE

MATERIAL	EXPOSURE LIMITS
Active Ingredient: Metaproterenol Sulfate	15 $\mu\text{g}/\text{m}^3$ BIEL**
Excipients: Colloidal Silicon Dioxide NF	10 mg/m^3 total dust
Dibasic Calcium Phosphate USP	No TLV established*
Starch, NF	10 mg/m^3 total dust
Lactose USP	No TLV established*
Magnesium Stearate NF	No TLV established*
	* As per 2002 ACGIH

**BIEL is the BI Exposure Control Level. Where governmentally imposed occupational exposure limits are lower, such limits should take precedence.

3. HAZARD IDENTIFICATION

EMERGENCY OVERVIEW

Round White Tablets containing white micronized powder.
Caution! Dusts may be harmful if inhaled. Danger! Dusts may form explosive clouds.

Use extinguishing media suitable for the material that is burning.

CONTRAINDICATIONS: This product should not be used by patients with a history of cardiac arrhythmias (irregular heart rhythm) associated with tachycardia (rapid heart beat).

Although rare, this product can cause immediate hypersensitivity in patients. Therefore, **Alupent Tablets**, should not be used by patients who have had a previous allergic reaction to any of the product's components.

ADVERSE REACTIONS TO PRODUCT: Nervousness, tachycardia, headache, cough, worsening of asthmatic symptoms, tremor, dizziness, fainting, gastrointestinal distress, diarrhea, nausea and vomiting, chattiness, chills, hives and flu-like symptoms.

For Active Ingredient:

ROUTES OF ENTRY: Ingestion, Inhalation, Skin and Eye contact.

ACUTE EXPOSURE: Eye, skin, and/or respiratory irritation.

SIGNS AND SYMPTOMS OF EXPOSURE: Possible allergic reaction if dust is inhaled (breathed), ingested (swallowed), or in contact with skin. Nervousness, tachycardia, headache, cough, worsening of asthmatic symptoms, tremor, dizziness, fainting, gastrointestinal distress, diarrhea, nausea and vomiting, chattiness, chills, hives and flu-like symptoms.

CHRONIC EXPOSURE: Possible hypersensitization (development of abnormal sensitivity).³

MEDICAL CONDITIONS POTENTIALLY AGGRAVATED BY EXPOSURE: Dust allergies, pre-existing respiratory conditions, heart and circulatory conditions, hypertension (high blood pressure), hyperthyroidism, diabetes, convulsive disorders.

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

4. EMERGENCY FIRST AID PROCEDURES

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

INGESTION: Rinse mouth out with large amounts of water. Do not induce vomiting or give anything by mouth to an unconscious or convulsing person. Seek medical attention.

INHALATION: Remove affected person to a well ventilated area and get immediate medical attention. If breathing becomes difficult, give oxygen. If breathing stops, start artificial respiration.

SKIN CONTACT: Remove contaminated clothing. Flush affected area with copious amounts of water. If irritation or rash develops, get medical attention.

EYE CONTACT: Flush eyes with large amounts of running water for 15 minutes. Get immediate medical attention.

NOTE TO PHYSICIAN: Treat symptomatically.

5. FIRE AND EXPLOSION HAZARD DATA

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

FIRE EXTINGUISHING 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. Use water spray to keep fire-exposed containers cool and protect against all exposures.

UNUSUAL FIRE AND EXPLOSION HAZARDS: None.

6. SPILL AND ACCIDENTAL RELEASE MEASURES

STEPS TO BE TAKEN IN THE EVENT OF A SPILL: Wear approved respirator and chemically compatible gloves if tablets have been compromised. Vacuum or sweep up spillage. Avoid creating dust. Place spillage in appropriate container for waste disposal. Wash contaminated clothing before reuse. Ventilate area, wash down spill site and control wash water.

7. PRECAUTIONS FOR SAFE HANDLING AND USE

HANDLING AND STORAGE PRECAUTIONS: Avoid contact with eyes, skin or clothing. Avoid generating dust. Store in airtight container. Protect from light and extreme heat.

OTHER PRECAUTIONS: Wash thoroughly after handling material. Wear fresh clothing daily. Wash contaminated clothing before reuse.

8. CONTROL MEASURES

ENGINEERING CONTROLS: Minimize dust generation. Use closed equipment where possible. Use spot ventilation to remove dust from the work area. If operations generate dusts, use explosion-proof ventilation equipment to control airborne levels. (See section 2 for exposure limits.)

RESPIRATORY PROTECTION: Not generally required. The need for respiratory protection should be determined by an industrial hygiene survey. (See Section 2 for exposure limits.) NIOSH/MSHA approved respirators for protection should be used if respirators are found to be necessary.

VENTILATION: General ventilation should be adequate to maintain exposure levels below recommended established exposure limits. If general ventilation is not sufficient, local exhaust is recommended.

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

Eye Protection: Safety goggles
Protective Clothing: Laboratory coats

Hand Protection: Rubber gloves
Other: Eye wash

WORK/HYGIENIC PRACTICES: Do not permit eating, drinking or smoking near this material.

9. PHYSICAL/CHEMICAL CHARACTERISTICS

APPEARANCE AND ODOR: Scored round white tablets, odorless.

Boiling Point: N/A

Specific Gravity: N/A

Vapor Pressure (mmHg): N/A

Melting Point: 396-397° F (202°-203° C)

Vapor Density: N/A

Evaporation Rate: N/A

Water Solubility: Soluble

pH: N/A

10. REACTIVITY DATA

STABILITY: Stable.

CONDITIONS TO AVOID: None known.

INCOMPATIBLE MATERIALS: Alkalis, heavy metal ions, and oxidizing agents.

HAZARDOUS DECOMPOSITION OR BY-PRODUCTS: When heated to decomposition or under fire conditions, material emits toxic fumes.

HAZARDOUS POLYMERIZATION: Will not occur.

11. TOXICOLOGICAL INFORMATION

ACUTE TOXICITY: (Active Ingredient)

5538 mg/kg oral - rat LD₅₀

4800 mg/kg oral - mouse LD₅₀

455 mg/kg inhalation - dog LD₅₀

750 mg/kg inhalation - monkey LD₅₀

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 or nursing.

Teratogenic and embryotoxic in rabbits when given at 620 times the human inhalation dose and at 100 mg/kg or 62 times maximum recommended human oral dose. These effects include skeletal abnormalities (bone deformities), hydrocephalus (fluid on the brain), and skull bone separation.

Recent studies in laboratory animals (minipigs, rodents and dogs) recorded the occurrence of cardiac arrhythmias and sudden death when beta agonists and methylxanthines were administered concurrently. The significance of these findings when applied to humans is currently unknown.

CARCINOGENESIS/MUTAGENESIS/IMPAIRMENT OF FERTILITY: In an 18-month study in mice, Alupent produced a significant increase in benign ovarian tumors in females at doses corresponding to

31 and 62 times the maximum recommended dose (based on a 50kg, individual). The relevance of these findings to man are unknown. Mutagenic studies with Alupent have not been conducted.

12. ECOLOGICAL INFORMATION

None known.

13. DISPOSAL CONSIDERATIONS

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

14. TRANSPORT INFORMATION

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

DOT Proper Shipping Name: N/A
Hazard Class: Not regulated.
Identification Number: N/A
Packing Group: N/A
Label: N/A

15. REGULATORY INFORMATION

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.

16. OTHER INFORMATION

ABBREVIATIONS:

BIPI - Boehringer Ingelheim Pharmaceuticals, Inc.

N/A - Not applicable.

N/E - Not established.

PREPARATION INFORMATION

Prepared by: Environmental Affairs & Safety.

Date Revised: 03/28/03

Replaces: 04/20/98

REVISION INFORMATION:

Section 2:Components per Unit Dose	Section 7:Precautions for Safe Handling & Use
Section 3:Hazard Identification	Section 8:Control Measures
Section 5:Fire & Explosion Hazard Data	Section 11: Toxicological Information

The opinions expressed herein are those of qualified experts within Boehringer Ingelheim Pharmaceuticals, Inc. (BIPI). We believe that the information contained within this MSDS is current as of the date issued. Since the use of this information and these opinions and the conditions of use of this material are not within the control of BIPI, it is the user's obligation to determine the conditions of safe use of this material. BIPI urges the users of this product to study this MSDS and become aware of any hazards associated with this material. In the interests of safety, the information contained in this MSDS should be made available to your employees, agents and contractors who handle this material.

**SEE CURRENT PACKAGE INSERT FOR
FURTHER INFORMATION**

REFERENCES

1. NIOSH – RTECS® *Registry of Toxic Effects of Chemical Substances*, 1993-2003
2. BIPI – Material Safety Data Sheet for Alupent® Solution 5% , 4/98
3. Investigator's Brochure for Alupent® .
4. Physician's Desk Reference®, 1974-2003
5. REPROTOX® Reproductive Toxicology Center, 8/1/02
6. DRUGDEX® Drug Evaluations, 1974-2003