

MATERIAL SAFETY DATA SHEET

Boehringer Ingelheim Pharmaceuticals, Inc.
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Atrovent® HFA Inhalation Aerosol

DATE ISSUED: 12/22/04

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

1. SUBSTANCE IDENTIFICATION

CHEMICAL NAME: 8-Azoniabicyclo (3.2.1)-octane, 3-(3-hydroxy-1-oxo-2-phenylpropoxy)-8-methyl-8-(1-methylethyl)-,bromide, monohydrate (endo,syn)-,(±).

CAS TYPE: 1

GENERIC NAME: Ipratropium Bromide
MOLECULAR FORMULA: C₂₀H₃₀BrNO₃•H₂O

TRADEMARK: **Atrovent® HFA Inhalation Aerosol** MOLECULAR WEIGHT: 430.4 (active ingredient)
PRODUCT USE: Bronchodilator CAS NUMBER: 22254-24-6 (active ingredient)

2. COMPONENTS PER UNIT DOSE

MATERIAL	EXPOSURE LIMITS
Active Ingredient: Ipratropium Bromide	15 ug/m ³ BIEL**
Excipients: Hydrofluoroalkane (1,1,1,2 tetrafluoroethane) Citric acid Ethanol Water	1,000 ppm 8 hour TWA (WEEL)***

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

*** WEEL is the Workplace Environmental Exposure Level published by the American Industrial Hygiene Association

3. HAZARD IDENTIFICATION

EMERGENCY OVERVIEW

Volatile milky white liquid.

Warning: May cause sensitization. May cause eye, skin or respiratory irritation

Will not burn. If involved in a fire, material emits toxic fumes. Use extinguishing media suitable for the material that is burning.

Pressurized containers may explode when heated.

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

TARGET ORGANS: Liver, GI tract, adrenals, male reproductive organs and eyes.

CONTRAINDICATIONS: Although rare, this product can cause immediate hypersensitivity in patients. Therefore, **Atrovent® HFA Inhalation Aerosol** should not be used by patients who have had a previous allergic reaction to soya lecithin or related food products such as soybean and peanuts.

This product should also not be taken by individuals who have a history of sensitivity to atropine, its derivatives, or any of the product's components.

ADVERSE REACTIONS/SIGNS AND SYMPTOMS OF EXPOSURE TO PRODUCT: Rhinitis, headache, coughing, bronchitis, COPD exacerbation and bitter taste after inhalation. Other potential effects include: Palpitations, tachycardia, nervousness, dizziness, dry mouth, constipation, urine retention, rash, acute eye pain and glaucoma.

WARNING:

Do not spray in eyes. Direct eye contact with product may cause temporary blurring of vision, precipitation or worsening of narrow-angle glaucoma or eye pain. If these symptoms occur, contact your physician.

Immediate hypersensitivity (allergic) reactions may occur after use such as urticaria (hives), angioedema (giant hives), bronchospasm (spasms of the lung's bronchial tubes), oropharyngeal edema (swelling of the lips, tongue and throat) and rash.

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

MEDICAL CONDITIONS POTENTIALLY AGGRAVATED BY EXPOSURE: Dust allergies, pre-existing hypersensitivity (allergic reaction) to any of the product's components. Ipratropium bromide should be used with caution in patients with narrow angle glaucoma, prostatic hypertrophy, or bladder neck obstruction.

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: Remove contact lenses if necessary. Flush eyes with large amounts of running water for several minutes. Get immediate medical attention.

5. FIRE AND EXPLOSION HAZARD DATA

Flash Point
N/A

Upper
N/A

Lower
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:
Pressurized containers may explode when heated. When heated to decomposition, material emits hydrofluoric.

6. SPILL AND ACCIDENTAL RELEASE MEASURES

STEPS TO BE TAKEN IN THE EVENT OF A SPILL: Wear approved respirator and chemically compatible gloves if containers have been compromised. Use absorbent material to clean-up spills. Place material 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:

WARNING - CONTENTS UNDER PRESSURE

Do not puncture or incinerate container except at a facility capable of handling pressurized canisters. Store between 59°F (15°C) and 77°F (30°C) KEEP OUT OF THE REACH OF CHILDREN.

Avoid contact with eyes, skin or clothing. Avoid breathing aerosol. Store in airtight container and protect from light.

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

8. CONTROL MEASURES

VENTILATION: General ventilation should be adequate. Local exhaust ventilation not generally required when handling containers. (See section 2 for exposure limits.)

RESPIRATORY PROTECTION: Respiratory protection is not generally needed when handling final product. 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.

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

Eye Protection: Safety glasses w/ sideshields or goggles
Protective Clothing: Laboratory coats

Hand Protection: Neoprene gloves
Other: Eye wash

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

9. PHYSICAL/CHEMICAL CHARACTERISTICS

APPEARANCE AND ODOR: Milky white liquid
Boiling Point: N/A
Vapor Pressure (mmHg): N/A
Vapor Density: N/A
Water Solubility: Partially Soluble

Specific Gravity: N/A
Melting Point: N/A
Evaporation Rate: N/D
pH: N/A

10. REACTIVITY DATA

STABILITY: Stable.

CONDITIONS TO AVOID: None known.

INCOMPATIBLE MATERIALS: Acid or acid fumes.

HAZARDOUS DECOMPOSITION OR BY-PRODUCTS: When heated to decomposition, material emits toxic fumes of bromide, acid gases and phosgene.

HAZARDOUS POLYMERIZATION: Will not occur.

11. TOXICOLOGICAL INFORMATION

ACUTE TOXICITY for Active Ingredient:

Rat LD50 - Oral; **DOSE:** 1663 mg/kg **TOXIC EFFECTS:** *Behavioral* - Convulsions or effect on seizure threshold. *Behavioral* – Ataxia. *Lung, Thorax, or Respiration* - Dyspnea

Mouse LD50 - Oral; **DOSE:** 1001 mg/kg **TOXIC EFFECTS:** *Behavioral* - Convulsions or effect on seizure threshold. *Behavioral* – Ataxia *Lung, Thorax, or Respiration* – Dyspnea

Dog LD50 -Oral; **DOSE:** 1300 mg/kg **TOXIC EFFECTS:** *Behavioral* - Convulsions or effect on seizure threshold *Behavioral* – Ataxia *Lung, Thorax, or Respiration* – Dyspnea

Human TDLO: Inhalation; **Dose:** 1 ug/kg **TOXIC EFFECTS:** Gastrointestinal –other changes

ACUTE TOXICITY for Excipients:

LD50/LC50

Rat LC50 - ROUTE: Inhalation; DOSE: 1500 gm/m³/4H

Mouse LC50 - ROUTE: Inhalation; DOSE: 1700 gm/m³/2H

Dog LC - ROUTE: Inhalation; DOSE: >32 pph/1H

ANIMAL/PLANT STUDIES: A reduction in maternal weight gain in rabbits exposed to 40,000 ppm (166,800 mg/m³) 1,1,1,2-tetrafluoroethane and signs of delayed fetal development in rats following exposure of the dams to 50,000 ppm (208,500 mg/cu m). In other toxicological studies, adverse health effects have not been observed following exposure to concentrations up to 10,000 ppm (41,700 mg/m³).

TERATOGENICITY: PREGNANCY CATEGORY B: No evidence of teratogenic effects have been reported following oral administration or inhalation of Ipratropium bromide in animals (Pakes et al, 1980; Massey & Gotz, 1985). A slight reduction in weight of rat fetuses fed 500 mg/kg of Ipratropium bromide during organogenesis was reported by Nishimura et al (1978). Consult physician if you suspect you are pregnant, pregnant or nursing.

CARCINOGENESIS/MUTAGENESIS: Two-year oral carcinogenicity studies in rats and mice have revealed no carcinogenic potential at doses of Ipratropium Bromide up to 1,250 times the maximum recommended human daily dose for Atrovent. Results of various mutagenicity studies were negative. For 1,1,1,2 tetrafluoroethane carcinogenicity testing is limited to an increased incidence of Leydig cell adenomas following exposure to 50,000 ppm (208,500 mg/cu m). It has not been found to be genotoxic in studies conducted to date.

IMPAIRMENT OF FERTILITY: Fertility of male or female rats at oral doses up to approximately 10,000 times the maximum recommended human daily dose was unaffected by Atrovent administration. At doses above 18,000 times the maximum recommended human daily dose, increased resorption and decreased conception rates were observed.

12. ECOLOGICAL INFORMATION

The active ingredient was shown to exhibit moderate break down in biological degradation testing. After 47 days of testing, 37 % of the material had been broken down to CO₂. Octanol-water partition studies indicate the K_{ow} is less than one at the three pH levels studied. The active ingredient did not inhibit the growth of 5 commonly studied microorganisms at concentrations of 1000 mg/L.

If released to soil, 1,1,1,2-tetrafluoroethane will rapidly volatilize from either moist or dry soil to the atmosphere. It will display moderate to high mobility in soil. If released to water, it will rapidly volatilize to the atmosphere. The estimated half-life for volatilization from a model river is 3.0 hrs. 1,1,1,2-tetrafluoroethane will not bioconcentrate in fish and aquatic organisms nor will it adsorb to sediment and suspended organic matter. If released to the atmosphere, 1,1,1,2-tetrafluoroethane will undergo a very slow gas-phase reaction with photochemically produced hydroxyl radicals with an estimated half-life of 187 days. The atmospheric lifetime of 1,1,1,2-tetrafluoroethane has been estimated to range from 12.5 to 24 years.

13. DISPOSAL CONSIDERATIONS

WASTE DISPOSAL CONSIDERATIONS: Dispose of in accordance with local, state and federal regulations. Recommended method is incineration at a facility capable of handling pressurized canisters.

14. TRANSPORT INFORMATION

D.O.T. Proper Shipping Name: Exempt for all DOT rules
Hazard Class: N/A
Identification Number: N/A
Packing Group: N/A
Label: N/A
Emergency Response Guidebook - N/D

15. REGULATORY INFORMATION

This product contains 1,1,1,2 tetrafluoroethane. Medical aerosols are excluded from the definition of a "controlled product" under 40 CFR Part 82 - Protection of Stratospheric Ozone.

16. OTHER INFORMATION

ABBREVIATIONS:

BIPI - Boehringer Ingelheim Pharmaceuticals, Inc.

N/A - Not applicable.

N/D - Not determined

PREPARATION INFORMATION

Prepared by: Environmental Affairs & Safety.

Date Prepared: 12/22/04

Replaces: New

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SEE CURRENT PACKAGE INSERT FOR FURTHER INFORMATION

REFERENCES

1. Investigator's Brochure for Ipratropium Bromide HFA 4/2000.
2. MICROMEDEX Systems Integrated Index Copyright® 1974 - 2002