

MATERIAL SAFETY DATA SHEET

Boehringer Ingelheim Pharmaceuticals, Inc.
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877
(203) 798-4081 9AM - 4PM EST

Atrovent® Nasal Spray
0.06%

DATE ISSUED 04/95 REVISED: 05/98, 2/25/02,
7/17/02

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 Monohydrate

MOLECULAR FORMULA: C₂₀H₃₀BrNO₃•H₂O

TRADEMARK: **Atrovent® Nasal Spray 0.06%**

MOLECULAR WEIGHT: 430.4

PRODUCT USE: Bronchodilator

CAS NUMBER: 22254-24-6

SYNONYMS: Sch 1000, Itrop, Ipratropiumbromide (German)

2. COMPONENTS PER UNIT DOSE

MATERIAL	EXPOSURE LIMITS	% By Weight
Active Ingredient:		
Ipratropium bromide monohydrate	15 µg/m ³ **	< 1.0 %
Excipients:		
Benzalkonium chloride	No TLV established*	
Edetate disodium	No TLV established*	
Sodium chloride	No TLV established*	
Sodium hydroxide	2 mg/m ³ ceiling *	
Hydrochloric acid (for pH adjustment)	5 ppm (as HCl gas)*	
Purified water	No TLV established*	> 94%
	* As per 2000 ACGIH	

** BI Exposure Level (BIEL). Where governmentally imposed occupational exposure limits which are lower than the BIEL are in effect, such limits should take precedence.

3. HAZARD IDENTIFICATION

EMERGENCY OVERVIEW

Clear, colorless liquid.

Warning! May cause allergic reactions. May cause eye irritation.

Will not burn. Use extinguishing media suitable for the material that is burning.

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

TARGET ORGANS: Eyes, upper respiratory system.

CONTRAINDICATIONS: Although rare, this product can cause immediate hypersensitivity in patients. Therefore, **Atrovent Nasal Spray** should not be used by patients who have had a previous allergic reaction to atropine or its derivatives, or to any of the product's components.

SIGNS AND SYMPTOMS OF EXPOSURE/ADVERSE REACTIONS: Headache, swelling of lips and tongue, upper respiratory tract infection, epistaxis (nosebleed), rhinitis (nasal discharge/irritation), nasal dryness, blood tinged nasal mucous, pharyngitis (sore throat), nausea, blurred vision, and increased sensitivity to light.

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

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.

You should not use this drug if you have glaucoma or difficult urination due to an enlargement of the prostate, unless directed by a physician.

Atrovent® Nasal Spray 0.03% should not be used during pregnancy or breast feeding unless directed by a physician.

MEDICAL CONDITIONS POTENTIALLY AGGRAVATED BY EXPOSURE: Dust allergies, pre-existing hypersensitivity (allergic reaction) to any of the product's components, narrow angle glaucoma, prostatic hypertrophy, bladder neck obstruction, hepatic (liver) or renal (kidney) dysfunction.

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 immediate 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 soap and 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 at least 15 minutes. Seek medical attention if blurred vision or sensitivity to light occurs.

NOTE TO PHYSICIAN: Acute overdosage by intranasal administration is unlikely since ipratropium bromide is not well absorbed systemically after intranasal or oral administration. 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 known.

6. SPILL AND ACCIDENTAL RELEASE MEASURES

STEPS TO BE TAKEN IN THE EVENT OF A SPILL: Clean spill with absorbent material and place in an appropriate container for waste disposal. Wash contaminated clothing before reuse. For large spills of multiple containers: 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 freezing. Store in airtight container between 59°F (15°C) and 86°F (30°C). KEEP OUT OF REACH OF CHILDREN.

8. CONTROL MEASURES

ENGINEERING CONTROLS: None generally required for handling final product.

RESPIRATORY PROTECTION: None generally required. If needed, respiratory protection should be selected by a qualified person based on the exposure. NIOSH/MSHA approved respirators 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 for handling the final product. If there is a potential for eye or skin contact, safety glasses with side shields or goggles and disposable gloves are recommended.

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

9. PHYSICAL/CHEMICAL CHARACTERISTICS

For Product:

APPEARANCE AND ODOR: Clear colorless solution with little or no odor.

Boiling Point: N/A

Vapor Pressure (mmHg): N/A

Vapor Density: N/A

Water Solubility: Soluble

Specific Gravity: N/A

Melting Point: N/A

Evaporation Rate: N/A

pH: 4.7

10. REACTIVITY DATA

STABILITY: Stable.

CONDITIONS TO AVOID: None known.

INCOMPATIBLE MATERIALS: None known.

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

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

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 6mg/kg. Results of various mutagenicity studies were negative.

IMPAIRMENT OF FERTILITY: Fertility of male or female rats at oral doses up to approximately 50 mg/kg was unaffected by Atrovent administration. At doses above 500 mg/kg 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.

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

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

DOT Hazard Class: Not regulated.

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.

PREPARATION INFORMATION

Prepared by: Environmental Affairs & Safety.

Date Revised: 7/17/02

Replaces: 2/25/02

REVISION INFORMATION:

7/17/02

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1. Revised Section 2 – Components: Exposure Limits
2. Revised Section 3 – Hazard Identification: Emergency Overview
3. Revised 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. USAN, USP *Dictionary of International Drug Names*, 1994.
2. Investigator's Brochure for Atrovent®.
3. Physician's Desk Reference, 55th Edition, 2001.
4. MicroMedex Systems Integrated Index Copyright® 1974 - 2002