

SAFETY DATA SHEET

Product Name Atrovent® HFA (ipratropium bromide HFA) Inhalation Aerosol

Date Issued: March 31,2011

1. SUBSTANCE IDENTIFICATION

SUBSTANCE/MIXTURE NAME: Atrovent® HFA (ipratropium bromide HFA) Inhalation Aerosol

EMERGENCY CONTACT NUMBER: **(800) 424-9300 – Chemtrec**

SUPPLIER ROUTINE CONTACT NUMBER: (203) 798-5521

SUPPLIER NAME: **Boehringer-Ingelheim Pharmaceuticals, Incorporated**

900 Ridgebury Road
Ridgefield, Connecticut
06877-0368

RECOMMENDED USES: **Pharmaceutical Compound**

2. HAZARD IDENTIFICATION

HAZARD CLASSIFICATION: **WARNING - This is a medicinal compound, designed to be prescribed by a licensed health care professional. Should the patient observe any adverse symptoms or effects, they should contact their health care provider immediately. In addition, they should discontinue taking this medication. Should any employee, while handling or processing this compound, observe any adverse health effects, they should contact their health care provider immediately. In addition, they should evacuate the work environment. Follow all instructions and packaging labels.**

GHS HAZARD LABEL:

Product:

The product is a non-hazardous mixture of single components and need not be labeled according to EC-Directive 67/548, as amended.



OTHER NON GHS CLASSIFIABLE HAZARDS: This product is a pharmaceutical compound. All precautions for pharmaceutical compounds should be thoroughly observed.

3. COMPOSITION/INFORMATION ON INGREDIENTS

EMERGENCY OVERVIEW:

Volatile milky white liquid

Warning: May cause sensitization. May cause skin, eye 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

MATERIAL	Exposure Limits
Active Ingredient:	
Ipratropium Bromide	15 ug/m3 (BIEL*)
Inactive Ingredients:	
HFA-134a (1,1,1,2-tetrafluoroethane) as propellant	1000 PPM 8 Hour TWA (WEEL**)
Sterile Water	N/E
Dehydrated alcohol	1000 PPM 8 Hour TWA (OSHA as Ethyl Alcohol)
Anhydrous citric acid	N/E

* 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.

COMMON NAME: Atrovent® HFA Inhalation Aerosol	CAS NUMBER: 22254-24-6 (active ingredient)
SYNONYMS: Ipratropium Bromide	MOLECULAR FORMULA: C ₂₀ H ₃₀ BrNO ₃ ·H ₂ O (active ingredient)
MOLECULAR WEIGHT: 430.4 (active ingredient)	PRODUCT USE: Bronchodilator

4. FIRST AID MEASURES

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

IMMEDIATE EFFECTS: Hypersensitivity reactions including urticaria, angioedema, rash, bronchospasm, anaphylaxis, and oropharyngeal edema may occur after the administration of ATROVENT HFA.

DELAYED EFFECTS: May increase intraocular pressure, May cause urinary retention

BY EXPOSURE ROUTE

INHALATION: Remove from area to fresh air. Seek medical attention if respiratory irritation develops or if breathing becomes difficult.

INGESTION: Give 3-4 glasses of water, but **DO NOT** induce vomiting. If vomiting occurs, give fluids again. Get medical attention to determine whether vomiting or evacuation of stomach is necessary. Do not give anything by mouth to an unconscious or convulsing person.

SKIN CONTACT: Remove contaminated clothing. Wash affected areas with plenty of water, and soap if available, for several minutes. Seek medical attention if irritation or rash develops and persists.

INJECTION: In case of accidental injection, wash and thoroughly disinfect, get medical attention.

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

GENERAL ADVICE

Seek medical attention after exposure to this compound; physician or health care provider should treat symptomatically. Wash contaminated clothing before reuse. First responders should wear personal protective equipment as defined in:

SECTION 5 for FIRE FIGHTING
SECTION 6 for ACCIDENTAL RELEASES, or
SECTION 8 for EXPOSURE CONTROL/PERSONAL PROTECTION

5. FIRE AND EXPLOSION HAZARD DATA

SUITABLE EXTINGUISHING MEDIA: Water spray, dry chemical, carbon dioxide or foam as appropriate for surrounding fire and materials.

SPECIFIC HAZARDS ARISING FROM THE CHEMICAL: Pressurized containers may explode when heated. When heated to decomposition, materials emit hydrofluoric acid

SPECIAL PROTECTIVE EQUIPMENT: Firefighters should use self-contained breathing equipment and protective clothing (Turn-out Gear).

PRECAUTIONS FOR FIRE FIGHTERS: As with all fires, evacuate personnel to safe area. Use water spray to keep fire-exposed containers cool and protect against all exposures.

6. ACCIDENTAL RELEASE MEASURES

PERSONAL PRECAUTIONS: For the final product form (to be used by patients with valid prescription for this material), personal protective equipment should not be necessary. Keep Atrovent® HFA (ipratropium bromide) Inhalation Aerosol canisters and/or meter dose inhalers out of reach of children. For manufacturing or processing facilities, a qualified person should determine the need for respiratory protection. NIOSH/MSHA approved respirators for protection should be used if respirators are found to be necessary.

PERSONAL PROTECTIVE EQUIPMENT	
Eye Protection: Safety glasses with side shields or goggles	Hand Protection: Gloves
Protective Clothing: Laboratory coats	Other: Eye wash & safety shower

Only trained employees should respond to any chemical release, review and act according to your companies' defined internal release or spill procedures. Employee's who have not been trained in appropriate spill response methods, should evacuate the area, closing all doors as they exit. If possible without endangering themselves, employees should remove any source of ignition.

ENVIRONMENTAL PRECAUTIONS: Whenever possible, employees should take all necessary steps to prevent components of this material from entering any catch basin, drain, ground water, sink, surface water, or toilet.

METHODS AND MATERIALS FOR CONTAINMENT AND CLEAN-UP: Wear approved respirator, eye protection and chemically compatible gloves if containers have been compromised. Ventilate the area. Dike spill and absorb with an inert material, then collect absorbed spillage. Avoid creating dust during spill clean-up. Place spillage in appropriate container for waste disposal. Wash contaminated clothing before reuse. Wash down spill site and control wash water.

7. HANDLING AND STORAGE

PRECAUTIONS FOR SAFE HANDLING: For final product, store in original container, keep out of reach of children, and store away from foodstuffs. This material should be handled and stored as per label and other instructions to ensure product integrity

PERSONAL HYGIENE In manufacturing or processing environments, employees should wear protective equipment, as defined in Section 8 – Exposure Control/Personal Protection. The required PPE should be removed before entering common area (cafeteria, hallway, or lavatory) or an office environment. Reusable PPE should be stored in an appropriate manner in the laboratory. Disposable PPE should be discarded just before exiting the laboratory. Employees using this substance should consult with their internal safety policies and procedures for chemical handling.

CONDITIONS FOR SAFE STORAGE: Store in original container at 25°C (77°F) within a temperature range of 15°C to 30°C (59°F to 86°F). Product must be stored away from any foodstuffs.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

MATERIAL	Exposure Limits
Active Ingredient:	
Ipratropium Bromide	15 ug/m3 (BIEL*)
Inactive Ingredients:	
HFA-134a (1,1,1,2-tetrafluoroethane) as propellant	1000 PPM 8 Hour TWA (WEEL**)
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Dehydrated alcohol	1000 PPM 8 Hour TWA (OSHA as Ethyl Alcohol)
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APPROPRIATE ENGINEERING CONTROLS: Not generally required when handling final product containers.

For manufacturing or processing environments, minimize droplet or mist generation. Use closed equipment where possible. Use spot ventilation to remove droplets or mists from the work area. If operations generate droplets or mists, use explosion-proof ventilation equipment to control airborne levels.

INDIVIDUAL PROTECTION MEASURES:

RESPIRATORY PROTECTION: A qualified person should determine the need for respiratory protection. NIOSH/MSHA approved respirators for protection should be used if respirators are found to be necessary.

PERSONAL PROTECTIVE EQUIPMENT	
Eye Protection: Safety glasses with side shields or goggles	Hand Protection: Gloves
Protective Clothing: Laboratory coats	Other: Eye wash & safety shower

9. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AND ODOR: Milky White Liquid (in a metered dose inhaler)

Data (below) is for Active Ingredient

Auto-ignition temperature: N/D	Partition coefficient: n-octanol/water: P _{ow} 0.006
Boiling Point: N/D	pH: 5.0 to 6.7
Decomposition temperature: N/D	Relative density: N/D
Evaporation rate: N/D	Solubility: soluble 72.4 g/l
Flammability (solid, gas): N/D	Upper/lower explosive/flammable limits: N/D
Flash point: N/D	Vapor density: N/D
Initial boiling point and boiling range: N/D	Vapor pressure (mm Hg): N/D
Melting point/freezing point: 231°C	Viscosity: N/D
Odor threshold: N/D	Volatiles, %: N/D

10. STABILITY AND REACTIVITY

STABILITY: Stable

POSSIBILITY OF HAZARDOUS REACTIONS:

Potentially Hazardous Conditions	Conditions that may cause these Reactions
Polymerize: N/D	
Release excessive heat: N/D	
Release excessive pressure: N/D	
Other hazardous conditions: Explosion	Pressurized containers may explode when heated

CONDITIONS TO AVOID: Pressurized containers may explode when heated

INCOMPATIBLE MATERIALS: Acid or acid fumes

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

11. TOXICOLOGICAL INFORMATION

TOXICITY:

Acute toxicity:	Reproductive toxicity:
Aspiration hazard:	Serious eye damage/irritation:
Carcinogenicity: Not listed/listed as carcinogen or potential carcinogen by NTP, IARC Monographs or OSHA.	Skin corrosion/irritation:
Germ cell mutagenicity:	STOST-single exposure:
Respiratory or skin sensitization:	STOST-repeated exposure

MOST LIKELY ROUTE OF EXPOSURE: The most likely routes of exposure are via inhalation, dermal absorption, mucous membranes, or ingestion.

SYMPTOMS RELATED TO THE PHYSICAL, CHEMICAL AND TOXICOLOGICAL CHARACTERISTICS:

CONTRAINDICATIONS: ATROVENT HFA is contraindicated in the following conditions:
Hypersensitivity to ipratropium bromide or other ATROVENT HFA components and Hypersensitivity to atropine or any of its derivatives

PREGNANCY: There are no adequate and well-controlled studies of ATROVENT HFA (ipratropium bromide) in pregnant women. Because animal reproduction studies are not always predictive of human response, ATROVENT HFA should be used during pregnancy only if clearly needed.

No teratogenic effects occurred in oral reproduction studies in mice, rats or rabbits at approximately 200, 40,000, and 10,000 times the maximum recommended human daily inhalation dose (MRHDID) in adults on a mg/m² basis. Inhalation reproduction studies were conducted in rats and rabbits at approximately 60 and 140 times the MRHDID in adults on a mg/m² basis. Embryotoxicity was observed in rats as increased resorption at oral doses approximately 3600 times the MRHDID in adults on a mg/m² basis. This effect is not considered relevant to human use due to the large doses at which it was observed and the difference in route of administration

NURSING MOTHERS: It is not known whether the active component, ipratropium bromide, is excreted in human milk. Because lipid-insoluble quaternary cations pass into breast milk, caution should be exercised when ATROVENT HFA is administered to a nursing mother.

CARCINOGENESIS: Two-year oral carcinogenicity studies in rats and mice have revealed no carcinogenic activity at doses up to 6 mg/kg (approximately 240 and 120 times the maximum recommended human daily inhalation dose (MRHDID) in adults on a mg/m² basis).

MUTAGENICITY: Results of various mutagenicity studies (Ames test, mouse dominant lethal test, mouse micronucleus test and chromosome aberrations of bone marrow in Chinese hamsters) were negative.

IMPAIRMENT OF FERTILITY: Fertility of male or female rats at oral doses up to 50 mg/kg (approximately 2000 times the MRHDID in adults on a mg/m² basis) was unaffected by ipratropium bromide administration. At an oral dose of 500 mg/kg (approximately 20,000 times the MRHDID in adults on a mg/m² basis), ipratropium bromide produced a decrease in the conception rate.

OVERDOSAGE: Acute overdose by inhalation is unlikely since ipratropium bromide is not well absorbed systemically after inhalation or oral administration. Oral median lethal doses of ipratropium bromide were greater than 1001 mg/kg in mice (approximately 20,000 times the maximum recommended human daily inhalation dose (MRHDID) in adults on a mg/m² basis); 1663 mg/kg in rats (approximately 66,000 times the MRHDID in adults on a mg/m² basis); and 400 mg/kg in dogs (approximately 53,000 times the MRHDID in adults on a mg/m² basis).

RENAL IMPAIRMENT: The pharmacokinetics of ATROVENT HFA have not been studied in patients with renal insufficiency.

HEPATIC IMPAIRMENT: The pharmacokinetics of ATROVENT HFA have not been studied in patients with hepatic insufficiency

12. ECOLOGICAL INFORMATION

AQUATIC OR TERRESTRIAL TOXICITY:

Active Ingredient: Toxicity to Fish – No data available

Toxicity to Daphnia – NOEC (No observed effect concentration) = 3.16 mg/l (Daphnia magna) Exposition time: 21 d

Lowest observed effect concentration = 10.0 mg/l (Daphnia magna) Exposition time: 21 d

Toxicity to Algae – No data available

Toxicity to Bacteria - NOEC (No observed effect concentration) = 200.0 mg/l (activated sludge)

NOEC (No observed effect concentration) = 1,000.0 mg/l (activated sludge, industrial)

Chronic toxicity to aquatic invertebrates – No data available

PERSISTENCE AND DEGRADABILITY:

Active Ingredient: Biological degradation – Not readily biodegradable. Approximately 37%
Exposition time 47 d

Transport between environmental compartments – No data available

Bioaccumulation – Accumulation in organisms is not to be expected

PBT and vPvB Assessment – No data available

OTHER ADVERSE EFFECTS: Whenever possible, employees should take all necessary steps to prevent this material from entering any catch basin, drain, ground water, sink, surface water, or toilet.

13. DISPOSAL CONSIDERATIONS

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

14. TRANSPORT INFORMATION

D.O.T. Proper Shipping Name:	Not Regulated
Hazard Class:	N/A
Identification Number:	N/A
Packing Group:	N/A
Label:	N/A
Emergency Response Guide Book:	N/A

SPECIAL PRECAUTIONS FOR USERS: N/D

15. REGULATORY INFORMATION

SAFETY, HEALTH, AND ENVIRONMENTAL REGULATIONS SPECIFIC FOR THIS PRODUCT: 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.

The product is a non-hazardous mixture of single components and need not be labeled according to EC-Directive 67/548, as amended.

Active Ingredient	Water Hazard Class: VVWWS WGK 3 highly water contaminating Labeling No. 1.063
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16. OTHER INFORMATION

ABBREVIATIONS:

N/E: Not Established
N/A: Not Applicable
N/D: Not Determined
PPE: Personal Protective Equipment

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Date Prepared: March 31, 2011
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Sections Revised:

NOTICE:

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REFERENCES

Ipratropium Bromide MSDS BI (Europe) 12-20-2010
Ipratropium Bromide MSDS BI (USA) 12-22-2004
Highlights of Prescribing Information 12/2010