SAFETY DATA SHEET

Prepared to U.S. OSHA, CMA, ANSI, Canadian WHMIS Standards, European Union CLP EC 1272/2008 and the Global Harmonization Standard

1. IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY UNDERTAKING

TRADE/MATERIAL NAME: Ipratropium Bromide and Albuterol Sulfate Inhaler .5MG/ 3mg 60x3ml; Inhalation Solution 0.5mg/ 3mg 60x3ml and 0.5mg/ 3mg 30x3ml

DESCRIPTION: Aqueous Ipratropium Bromide and Albuterol Sulfate Solution
OTHER DESIGNATIONS: NDC# 00591-3817-30, 00591-3817-60
CHEMICAL NAMES: α_1[(*tert*-Butylamino) methyl]-4-hydroxy-*m*-xylene-$\alpha_1\alpha$'-diol Sulfate (2:1) Salt and 8-azoniabicyclo[3.2.1]-octane,3-(3-hydroxy-1-oxo-2-phenylpropoxy)-8-methyl-8-(1-methylethyl)-, bromide, monohydrate (endo, syn)-,(±)-
CHEMICAL FAMILIES: Substituted Phenol and Quarternary Ammonium Compound
HOW SUPPLIED: 3 mL in unit-dose low-density polyethylene (LDPE) vials
FORMULA: $(C_{13}H_{21}NO_3)_2 \bullet H_2SO_4$ and $C_{20}H_{30}BrNO_3 \bullet H_2O$
SUPPLIER OF THE SAFETY DATA SHEET

RESPONSIBLE PARTY U.S.:	**ACTAVIS**
U.S. ADDRESS:	400 Interpace Parkway Parsippany, NJ 07054, USA
U.S. BUSINESS PHONE/GENERAL MSDS INFORMATION:	1-800-272-5525
RESPONSIBLE PARTY EUROPE:	
EUROPEAN ADDRESS:	
e-mail: SafetyDataSheets@Actavis.com	
EUROPEAN BUSINESS PHONE:	
EMERGENCY PHONE (U.S./NORTH AMERICA):	CHEMTREC: 1-800-424-9300 (24 hours) U.S., Canada, Puerto Rico
EMERGENCY PHONE (OUTSIDE U.S.):	CHEMTREC: +1-703-527-3887 (24 hours) Outside North America

NOTE: ALL United States Occupational Safety and Health Administration Standard (29 CFR 1910.1200), U.S. State equivalent Standards, Canadian WHMIS [Controlled Products Regulations], EU Directives through EC 1907: 2006, and European Union CLP EC 1272/2008, required information is included in appropriate sections based on the U.S. ANSI Z400.1-2010 format. This product has been classified in accordance with the hazard criteria of the countries listed above.

DATE OF PREPARATION: October 6, 2015 **DATE OF REVISION:**

2. HAZARD IDENTIFICATION

EU CLP REGULATION (EC) 1272/2008 LABELING AND CLASSIFICATION: According to Article 1, item 5 (a) of CLP Regulation (EC) 1272/2008, medicinal products in the finished state for human use, as defined in 2001/83/EC, are excepted from classification and other criteria of 1272/2008.
Classification: Not Applicable Signal Word: Not Applicable Hazard Statement Codes: Not Applicable

EU LABELING AND CLASSIFICATION 67/548/EEC: According to Article 1 of European Union Council Directive 92/32/EEC, medical products in the finished state for human use (as defined by European Union Council Directives 67/548/EEC and 87/21/EEC) are not subject to the regulations and administrative provisions of European Union Council Directive 92/32/EEC.
Classification: Not Applicable Risk Phrases: Not Applicable Safety Phrases: Not Applicable

See Section 16 for full EU classification information of product and components and full text of hazard and precautionary statements.

EMERGENCY OVERVIEW:

Product Description: This product is a clear, colorless, odorless liquid.
Health Hazards: The primary health hazard associated with occupational exposure to this product is the potential for irritation of contaminated eyes and mild irritation of contaminated skin, especially if contamination is repeated.
Flammability Hazards: When involved in a fire, this material may decompose and produce irritating vapors and toxic compounds (including carbon oxides, nitrogen oxides, sulfur oxides, and hydrogen bromide).
Reactivity Hazards: This product is not reactive.
Environmental Hazards: Large quantities released to the environment may have an adverse effect.
Emergency Considerations: Emergency responders should wear appropriate protection for situation to which they respond.

3. COMPOSITION and INFORMATION ON INGREDIENTS

CHEMICAL NAME	CAS #	EINECS #	% w/w	EU Classification (67/548/EEC) GHS & EU Classification (1272/2008 EC) Risk Phrases/Hazard Statements/Symbol
Ipratropium Bromide	22254-24-6	244-873-8	0.01–0.09	SELF CLASSIFICATION EU 67/548 Classification: Harmful, Irritant Risk Phrases: R20, R22, R36 Hazard Symbol:  EU/GHS 1272/2008 Signal word: Warning Classification: Acute Oral & Inhalation Toxicity, cat. 4; Eye Irritation, cat. 2 Hazard Statement Codes: H302, H319, H332 Hazard Symbol/Pictogram: 
Albuterol Sulfate	51022-70-9	256-916-8	0.09–0.5	SELF CLASSIFICATION EU 67/548 Classification: Harmful, Risk Phrases: R20, R21, R22 Hazard Symbol:  EU/GHS 1272/2008 Signal word: Warning Classification: Acute Oral, Dermal & Inhalation Toxicity, cat. 4; Hazard Statement Codes: H302, H312, H332 Hazard Symbol/Pictogram: 
Edetate Disodium	139-33-3	205-358-3	Proprietary	EU 67/548 Hazard Classification: Not Applicable EU/GHS 1272/2008 Classification: Not Applicable
Hydrochloric Acid	7647-01-0	231-595-7	Proprietary	SELF CLASSIFICATION EU 67/548 Hazard Classification: Corrosive Risk Phrases: R34, R37 Hazard Symbol:  EU/GHS 1272/2008 Classification: Skin Corrosion Cat. 1B, STOT Respiratory System Cat. 3 Hazard Classification Codes: H314, H335 Signal Word: Danger Hazard Symbol/Pictogram: 
Sodium Chloride	7647-14-5	231-598-3	Proprietary	EU 67/548 Hazard Classification: Not Applicable EU/GHS 1272/2008 Classification: Not Applicable
Water	7732-18-5	231-791-2	Balance	EU 67/548 Hazard Classification: Not Applicable EU/GHS 1272/2008 Classification: Not Applicable

See Section 16 for full EU classification information of components.

4 FIRST-AID MEASURES

Persons developing hypersensitivity reactions should receive medical attention. If breathing is difficult, give oxygen. If not breathing, give artificial respiration. Take a copy of label and MSDS to physician or health professional with the contaminated individual.

SKIN EXPOSURE: If adverse skin effects occur, rinse affected area with soap and water. Seek medical attention.

EYE EXPOSURE: If this product contaminates the eyes, open eyes under gently running water. Use sufficient force to open eyelids and then "roll" while flushing eyes. Minimum flushing is for 15 minutes if the exposure has resulted in an adverse effect. The contaminated individual must seek medical attention if any adverse effect continues after rinsing.

INHALATION: If mists or sprays of this product are inhaled, remove the contaminated individual to fresh air. Seek medical attention if adverse effect occurs.

INGESTION: If this product is swallowed, CALL PHYSICIAN OR POISON CONTROL CENTER FOR MOST CURRENT INFORMATION. If professional advice is not available, do not induce vomiting. Never induce vomiting or give diluents (milk or water) to someone who is unconscious, having convulsions, or unable to swallow. If victim is convulsing, maintain an open airway and obtain immediate medical attention.

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: Cardiovascular conditions, diabetes mellitus, ketoacidosis, asthma, and hypersensitivity reaction to Albuterol Sulfate, Ipratropium Bromide, and Atropine and its derivatives may be aggravated by therapeutic use of this product. Regular visits to physician to check progress during therapy should be scheduled.

RECOMMENDATIONS TO PHYSICIANS: This product should only be given to patients by persons experienced in management of patients receiving the type of therapy intended for this product. Treat symptoms and eliminate exposure. The judicious use of a cardio-selective β-receptor blocker may be considered, bearing in mind that such medication can produce bronchospasm. There is insufficient evidence to determine if dialysis is beneficial for overdosage of Ipratropium Bromide and Albuterol Sulfate.

5. FIRE-FIGHTING MEASURES

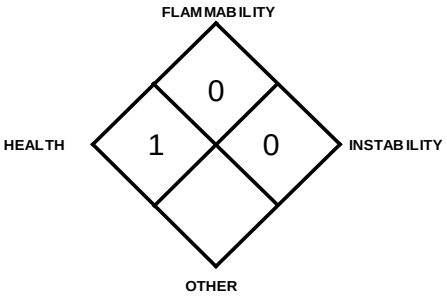
FLASH POINT: Not flammable.
AUTOIGNITION TEMPERATURE: Not established.
FLAMMABLE LIMITS (in air by volume, %):
Lower (LEL): Not established. Upper (UEL): Not established.

FIRE EXTINGUISHING MATERIALS: Use extinguishing media appropriate for surrounding fire.

Water Spray: OK
Carbon Dioxide: OK
Foam: OK
Dry Chemical: OK
Halon: OK
Other: Any "ABC" Class

FIRE EXTINGUISHING MATERIALS NOT TO BE USED: Non known.
UNUSUAL FIRE AND EXPLOSION HAZARDS: When involved in a fire, this material may decompose and produce irritating vapors and toxic compounds (including carbon oxides, nitrogen oxides, sulfur oxides, and hydrogen bromide).
Explosion Sensitivity to Mechanical Impact: Not sensitive.
Explosion Sensitivity to Static Discharge: Not sensitive.

NFPA RATING



Hazard Scale: **0** = Minimal **1** = Slight
2 = Moderate **3** = Serious **4** = Severe

SPECIAL FIRE-FIGHTING PROCEDURES: Incipient fire responders should wear eye protection. Structural firefighters must wear Self-Contained Breathing Apparatus (SCBA) and full protective equipment. If protective equipment is contaminated by this product, it should be thoroughly washed with soapy water prior to removal of SCBA respiratory protection. Firefighters whose protective equipment becomes contaminated should thoroughly shower with warm, soapy water and should receive medical evaluation if they experience any adverse effects.

6. ACCIDENTAL RELEASE MEASURES

SPILL AND LEAK RESPONSE: Proper protective equipment should be used. In the event of a spill, clear the area and protect people. The atmosphere must have levels of components lower than those listed in Section 8, (Exposure Controls and Personal Protective Equipment) if applicable, and have at least 19.5 percent oxygen before personnel can be allowed into the area without Self-Contained Breathing Apparatus (SCBA).

Small Spills: Small spills of this product (1 vial) outside a hood should be cleaned immediately by personnel wearing gowns and double latex or nitrile disposable gloves and eye protection. Wipe up spilled material carefully.

Large Spills: Trained personnel following pre-planned procedures should handle non-incidental releases. Access to the spill areas should be restricted. Protective apparel should be used with a respirator when there is any danger of airborne mists being generated. Minimum Personal Protective Equipment should be rubber gloves, rubber boots, face shield, and Tyvek suit**.** Minimum level of personal protective equipment for releases in which the level of oxygen is less than 19.5% or is unknown must be **Level B: triple-gloves (rubber gloves and nitrile gloves over latex gloves), chemical resistant suit and boots, hard hat, and Self-Contained Breathing Apparatus.** Wipe up spilled liquid, avoiding the generation of airborne mists or sprays. Prevent material from entering sewer or confined spaces, waterways, soil or public waters. Monitor area and confirm levels are bellow exposure limits given in Section 8 (Exposure Controls-Personal Protection), if applicable, before non-response personnel are allowed into the spill area. Decontaminate the area of the spill thoroughly using detergent and water. Place all spill residue in an appropriate container and seal. Dispose of in accordance with applicable Federal, State, and local procedures (see Section 13, Disposal Considerations).

7. HANDLING and USE

SAFE WORK AND HYGIENE PRACTICES: As with all chemicals, avoid getting this product ON YOU or IN YOU. Do not eat, drink, smoke, or apply cosmetics while handling this product. Wash hands thoroughly after handling this product or equipment and containers that contain this product. Particular care in working with this product must be practiced in pharmacies and other preparation areas, during manufacture of this compound, and during patient administration.

STORAGE AND HANDLING PRACTICES: All employees who handle this material should be trained to handle it safely. Keep container tightly closed when not in use. Store containers in a cool, dry location, away from direct sunlight, sources of intense heat, or where freezing is possible. Store at 20–25°C (68–77°F). Protect from light. Material should be stored in secondary containers or in a diked area, as appropriate. Store containers away from incompatible chemicals (see Section 10, Stability and Reactivity). Post warning and “NO SMOKING” signs in storage and use areas as appropriate. Inspect all incoming containers before storage to ensure containers are properly labeled and not damaged. Empty containers may contain residual liquid or vapors; therefore, empty containers should be handled with care. Never perform any welding, cutting, soldering, drilling, or other hot work on an empty container or piping until all liquid, vapors, and residue have been cleared.

SPECIFIC USE(S): This product is for use as an inhaled treatment for bronchospasm. Follow all instructions from your physician and supplied with the product.

PRODUCT PREPARATION INSTRUCTIONS FOR MEDICAL PERSONNEL: Handle this product following standard medical practices and following the recommendations presented on the Package Insert.

PROTECTIVE PRACTICES DURING MAINTENANCE OF CONTAMINATED EQUIPMENT: When cleaning non-disposable equipment, wear appropriate gloves (double gloving is recommended), goggles, and lab coat. Wash equipment with soap and water. Wipe equipment down with damp sponge or polypad.

8. EXPOSURE CONTROLS - PERSONAL PROTECTION

VENTILATION, ENGINEERING, AND OCCUPATIONAL EXPOSURE CONTROLS: Use with adequate ventilation. Follow standard medical product handling procedures. During decontamination of work surfaces, workers should wear the same equipment recommended in Section 6 (Accidental Release Measures).

EXPOSURE LIMITS/GUIDELINES:

CHEMICAL NAME	CAS #	EXPOSURE LIMITS IN AIR							
		ACGIH-TLVs		OSHA-PELs		NIOSH-RELs		NIOSH	OTHER
		TWA	STEL	TWA	STEL	TWA	STEL	IDLH	
		ppm	ppm	ppm	ppm	ppm	ppm	ppm	µg/m^3
Ipratropium Bromide	22254-24-6	NE	NE	NE	NE	NE	NE	NE	NE
Albuterol Sulfate	51022-70-9	NE	NE	NE	NE	NE	NE	NE	NE
Edetate Disodium	139-33-3	NE	NE	NE	NE	NE	NE	NE	NE
Hydrochloric Acid	7647-01-0	NE	2 (ceiling)	NE	5 (ceiling)	NE	5 (ceiling)	50	DFG MAKs: TWA = 2 ceiling PEAK = 2•MAK 15 min., average value, 1 hour interval, 4 per shift Pregnancy Risk Group Classification: C
Sodium Chloride	7647-14-5	NE	NE	NE	NE	NE	NE	NE	NE

NE = Not Established. See Section 16 for Definitions of Terms Used.

INTERNATIONAL OCCUPATIONAL EXPOSURE LIMITS: In addition to the exposure limit values cited above, other exposure limits have been established by various countries for the components of this mixture. The limits given may not be the most current; individual country exposure limits may change and should be checked.

HYDROCHLORIC ACID:
Australia: TWA = 5 ppm (7 mg/m^3), JAN 1993
Belgium: STEL = 5 ppm (7.7 mg/m^3), JAN 1993
Denmark: CL 5 ppm (7 mg/m^3), OCT 2002
EC: TWA = 5 ppm (8 mg/m^3); STEL = 10 ppm (15 mg/m^3), FEB 2006
Germany: MAK = 3 mg/m^3 (2 mL/m^3), 2005
Finland: STEL = 5 ppm (7 mg/m^3), Skin, JAN 1999
France: VLE = 5 ppm (7.5 mg/m^3), JAN 1999
Hungary: STEL = 5 mg/m^3, JAN 1993
Mexico: Peak = 5 ppm (7 mg/m^3), 2004
The Netherlands: MAC-TGG = 8 mg/m^3, 2003
Norway: TWA = 5 ppm (7 mg/m^3), JAN1999

HYDROCHLORIC ACID (continued):
The Philippines: TWA = 5 ppm (7 mg/m^3), JAN 1993
Poland: MAC(TWA) = 5 mg/m^3, CEILING = 7 mg/m^3, JAN 1999
Russia: STEL = 5 mg/m^3, JUN 2003
Sweden: STEL = 5 ppm (8 mg/m^3) JAN 1999
Switzerland: MAK-W = 5 ppm (7.5 mg/m^3), KZG-W = 10 ppm (15 mg/m^3), JAN 1999
Thailand: TWA = 5 ppm (7 mg/m^3), JAN 1993
Turkey: TWA = 5 ppm (7 mg/m^3), JAN 1993
United Kingdom: TWA = 1 ppm (2 mg/m^3); STEL = 5 ppm (gas, mist), 2005
In Argentina, Bulgaria, Colombia, Jordan, Korea, New Zealand, Singapore, Vietnam, New Zealand, Singapore, Vietnam check ACGIH TLV

The following information on appropriate Personal Protective Equipment is provided to assist employers in complying with regulations found in U.S. OSHA 29 CFR Subpart I (beginning at 1910.132), equivalent standards of Canada (including CSA Standard Z94.4-02 and CSA Standard Z94.3-02), standards of EU member states (including EN 529:2005 for respiratory PPE, CEN/TR 15419:2006 for hand protection, and CR 13464:1999 for face/eye protection. Please reference applicable regulations and standards for relevant details.

RESPIRATORY PROTECTION: A respirator is not required for routine conditions of use of this product

EYE PROTECTION: For situations in which excessive splashes or sprays may be generated, wear chemical splash goggles, or regular splash goggles.

HAND PROTECTION: For situations in which prolonged skin contact is anticipated, double glove, using appropriate gloves. Check gloves for leaks. Wash hands before putting on gloves and after removing gloves. Gloves should cover the gown cuff.

BODY PROTECTION: Use appropriate protective clothing for the task (e.g., lab coat, etc.)

ENVIRONMENTAL EXPOSURE CONTROLS: Controls should be engineered to prevent release to the environment, including procedures to prevent spills, atmospheric release and release to waterways.

9. PHYSICAL and CHEMICAL PROPERTIES

MOLECULAR WEIGHT: 576.7 (pure Albuterol Sulfate)
MOLECULAR WEIGHT: 430.4 (pure Ipratropium Bromide)

BOILING POINT: Not available.
FREEZING/MELTING POINT: Not available.
FLASH POINT: Not applicable.
FLAMMABILITY: Not flammable.
EXPLOSIVE PROPERTIES: Not explosive.
OXIDIZING PROPERTIES: Not an oxidizer.
SOLUBILITY: Slightly soluble in ethanol.
SOLUBILITY IN WATER: Completely soluble.
VAPOR PRESSURE (air = 1): Not available.
SPECIFIC GRAVITY (water = 1): Not available
RELATIVE VAPOR DENSITY (air = 1): Not available.
VISCOSITY: Not available.
EVAPORATION RATE (nBuAc = 1): Not available.
ODOR THRESHOLD: Not available.
COEFFICIENT WATER/OIL DISTRIBUTION: Not available.
pH: 4

APPEARANCE AND COLOR: This product is a clear, colorless, odorless liquid.

HOW TO DETECT THIS SUBSTANCE: There are no distinguishing characteristics associated with this product to aid in identification in event of an accidental spill.

10. STABILITY and REACTIVITY

DECOMPOSITION CONDITIONS/STABILITY: This product is stable when properly stored (see Section 7, Handling and Storage).

DECOMPOSITION PRODUCTS: Combustion: Carbon oxides, nitrogen oxides, sulfur oxides, and hydrogen bromide. Hydrolysis: None known.

MATERIALS WITH WHICH SUBSTANCE IS INCOMPATIBLE: This product is generally compatible with other common materials in a medical facility. Strong oxidizers, acetaldehyde, chlorine, ethylene oxide, acids, isocyanates, and other chemicals that could affect its performance should be avoided.

10. STABILITY and REACTIVITY

HAZARDOUS POLYMERIZATION: Will not occur.

CONDITIONS TO AVOID: Heat may cause this product to decompose, destroying the product and producing irritating vapors and toxic gases. Avoid contact with incompatible chemicals.

11. TOXICOLOGICAL INFORMATION

GENERAL TOXICITY INFORMATION: Symptoms described in patients given therapeutic doses of this substance include the following.

For Males and Females: Body pain, chest pain, diarrhea, indigestion, nausea, leg cramps, bronchitis, lung disease, pharyngitis, pneumonia, urinary tract infection, constipation, voice alterations, skin rash, itching, hives, precipitation or worsening of narrow-angle glaucoma, acute eye pain, blurred vision, paradoxical bronchospasm, wheezing, exacerbation of chronic obstructive pulmonary disease symptoms, drowsiness, aching, flushing, upper respiratory tract infection, palpitations, taste perversion, elevated heart rate, sinusitis, back pain, and sore throat.

SYMPTOMS OF OVEREXPOSURE BY ROUTE OF EXPOSURE: The health hazard information provided below is pertinent to medical employees using this product in an occupational setting. This product is designed to be administered by inhalation using a nebulizer. The following paragraphs describe the symptoms of exposure by route of exposure.

INHALATION: Inhalation of mists or sprays of this product, especially in a poorly ventilated space, may cause excessive β-adrenergic stimulation, seizures, angina, high blood pressure, low blood pressure, rapid heartbeat, irregular heartbeat, nervousness, headache, tremor, dry mouth, palpitation, nausea, dizziness, fatigue, general body weakness or discomfort, insomnia, an abnormally low concentration of potassium in the blood, exaggeration of symptoms described under "General Toxicity Information", cardiac arrest, and death.

HAZARDOUS MATERIAL IDENTIFICATION SYSTEM

HEALTH HAZARD	(BLUE)	1
FLAMMABILITY HAZARD	(RED)	0
PHYSICAL HAZARD	(YELLOW)	0

PROTECTIVE EQUIPMENT

EYES	RESPIRATORY	HANDS	BODY
	SEE SECTION 8		SEE SECTION 8

For Routine Industrial Use and Handling Applications

Hazard Scale: **0** = Minimal **1** = Slight **2** = Moderate **3** = Serious **4** = Severe * = Chronic hazard

CONTACT WITH SKIN or EYES: Skin contact may cause mild irritation, which is alleviated upon rinsing with soap and water. Prolonged or repeated skin overexposures may cause dermatitis (dry red skin). Eye contact can cause irritation, stinging, redness, and tearing.

SKIN ABSORPTION: The components of this product are not known to be absorbed through intact skin.

INGESTION: Ingestion is not a significant route of occupational overexposure. Acute ingestion of large quantities of this product or chronic ingestion caused by poor hygiene practices may cause adverse symptoms. Symptoms of ingestion overexposure may include rapid heartbeat, widened pulse pressure, an abnormally high level of glucose in the blood, agitation, low serum carbon dioxide, vomiting, and an abnormally low concentration of potassium in the blood.

INJECTION: Though not anticipated to be a significant route of overexposure for this product, injection (via punctures or lacerations by contaminated objects) may cause redness at the site of injection. Symptoms may include those described for "Other Potential Health Effects" and "Inhalation".

HEALTH EFFECTS OR RISKS FROM EXPOSURE: An Explanation in Lay Terms. Overexposure to this product may cause the following health effects:

ACUTE: The primary health effects that may be experienced by medical personnel exposed to this product is irritation of contaminated skin. Accidental inhalation and ingestion may be harmful. Eye contact will cause irritation.

CHRONIC: Prolonged or repeated skin exposures can cause dermatitis (dry, red skin).

TARGET ORGANS: ACUTE: Industrial Exposure: Skin. Therapeutic Doses: Respiratory system, cardiopulmonary system. CHRONIC: Industrial Exposure: Skin. Therapeutic Doses: Respiratory system.

IRRITANCY OF PRODUCT: This product may irritate contaminated eyes and mildly irritate contaminated skin, especially if contamination is repeated.

SENSITIZATION OF PRODUCT: Individuals who have had allergic reactions to prescription as well as to over-the-counter products containing Albuterol Sulfate or any other components of this product may experience allergic reactions to this product.

11. TOXICOLOGICAL INFORMATION (Continued)

TOXICITY DATA: This MSDS presents toxicity data currently available for the active components, Ipratropium Bromide and Albuterol Sulfate. Additional data are available for other components of this product, but are not presented in this MSDS. Contact Watson Pharmaceuticals for more information.

ALBUTEROL SULFATE:

LD_{50} (Oral-Rat) > 2500 mg/kg

ALBUTEROL SULFATE (continued):

LD_{50} (Oral-Mouse) 1950 mg/kg

ALBUTEROL SULFATE (continued):

LD_{50} (Intraperitoneal-Rat) 295 mg/kg: Eye: lacrymation; Respiration: respiratory depression

ALBUTEROL SULFATE (continued):

LD_{50} (Intraperitoneal-Mouse) 200 mg/kg

LD_{50} (Subcutaneous-Rat) > 2500 mg/kg: Lungs, Thorax, or Respiration: other changes Skin and Appendages: hair

LD_{50} (Subcutaneous-Mouse) 737 mg/kg: Eye: lacrymation; Behavioral: convulsions or effect on seizure threshold

LD_{50} (Intravenous-Rat) 59,100 µg/kg: Behavioral: altered sleep time (including change in righting reflex); Respiratory depression

LD_{50} (Intravenous-Mouse) 48,700 µg/kg: Behavioral: altered sleep time (including change in righting reflex); Lungs, Thorax, or Respiration: respiratory depression

TDLo (Oral-Rat) 4650 mg/kg/31 days-intermittent: Changes in heart weight; Lungs: changes in lung weight; Related to Chronic Data: death

TDLo (Oral-Rat) 35 g/kg/5 weeks-intermittent: Lungs, Thorax: structural or functional change in trachea or bronchi, other changes; Related to Chronic Data: death

TDLo (Oral-Rat) 1820 mg/kg/26 weeks-intermittent: Endocrine: other changes, changes in thyroid weight

TDLo (Oral-Rat) 13,300 mg/kg/95 weeks-continuous: Tumorigenic: equivocal tumorigenic agent by RTECS criteria; Reproductive: Tumorigenic effects: ovarian tumors, tumor types after systemic administration not seen spontaneously

TDLo (Oral-Rat) 1 g/kg: female 1 day(s) pre-mating: Reproductive: Maternal Effects: uterus, cervix, vagina

TDLo (Intravenous-Rat) 0.008 mg/kg: Cardiac: change in rate; Vascular: BP lowering not characterized in autonomic section; Lungs, Thorax, or Respiration: bronchiolar dilation

TDLo (Subcutaneous-Rat) 1750 mg/kg/5 weeks-intermittent: Cardiac: other changes, changes in heart weight Cardiac: other changes, changes in heart weight

TDLo (Subcutaneous-Rat) 1820 mg/kg/26 weeks-intermittent: Lungs, Thorax: structural or functional change in trachea or bronchi; Blood: hemorrhage Skin and Appendages: dermatitis, other (after systemic exposure)

IPRATROPIUM BROMIDE:

Standard Draize Test (Eye-Rabbit) 100 mg/24 hours: Moderate

TCLo (Inhalation-Man) 1 µg/kg: Gastrointestinal: other changes

LD_{50} (Oral-Rat) 1663 mg/kg: Behavioral: convulsions or effect on seizure threshold, ataxia; Lungs, Thorax, or Respiration: dyspnea

LD_{50} (Oral-Mouse) 1001 mg/kg: Behavioral: convulsions or effect on seizure threshold, ataxia; Lungs, Thorax, or Respiration: dyspnea

LD_{50} (Oral-Rabbit) 1557 mg/kg: Behavioral: tremor, ataxia; Lungs, Thorax, or Respiration: respiratory depression

LD_{50} (Oral-Dog) 1300 mg/kg: Behavioral: convulsions or effect on seizure threshold, ataxia; Lungs, Thorax, or Respiration: dyspnea

LD_{50} (Intraperitoneal-Rat) 113 mg/kg: Behavioral: ataxia, tetany; Lungs, Thorax, or Respiration: dyspnea

LD_{50} (Intraperitoneal-Mouse) 72 mg/kg: Behavioral: convulsions or effect on seizure threshold, coma; Respiratory depression

LD_{50} (Subcutaneous-Rat) 635 mg/kg: Behavioral: ataxia, tetany; Respiration: dyspnea

LD_{50} (Subcutaneous-Mouse) 300 mg/kg: Behavioral: convulsions or effect on seizure threshold, ataxia; Lungs, Thorax, or Respiration: dyspnea

LD_{50} (Intravenous-Rat) 15,700 µg/kg

LD_{50} (Intravenous-Mouse) 12,290 µg/kg: Behavioral: convulsions or effect on seizure threshold, ataxia; Lungs, Thorax, or Respiration: dyspnea

LD_{50} (Intravenous-Dog) 20 mg/kg: Behavioral: convulsions or effect on seizure threshold, ataxia; Lungs, Thorax, or Respiration: dyspnea

LD_{50} (Intravenous-Mammal-Species Unspecified) 10 mg/kg: Peripheral Nerve and Sensation: flaccid paralysis without anesthesia (usually neuromuscular blockage)

TDLo (Oral-Rat) 33,600 mg/kg/4 weeks-continuous: Behavioral: food intake (animal); Liver: changes in liver weight; Kidney/Ureter/Bladder: changes in bladder weight

TDLo (Oral-Rat) 91 g/kg/26 weeks-continuous: Kidney/Ureter/Bladder: other changes in urine composition, changes in bladder weight; Endocrine: changes in adrenal weight

IPRATROPIUM BROMIDE (continued):

TDLo (Oral-Rat) 35 g/kg/5 weeks-intermittent: Brain and Coverings: changes in brain weight; Cardiac: changes in heart weight; Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: phosphatases

TDLo (Oral-Rat) 11,200 mg/kg/4 weeks-continuous: Endocrine: other changes; Blood: changes in serum composition (e.g. TP, bilirubin, cholesterol); Nutritional and Gross Metabolic: weight loss or decreased weight gain

TDLo (Oral-Rat) 5500 mg/kg: female 7-17 day(s) after conception: Reproductive: Effects on Newborn: behavioral

TDLo (Oral-Rat) 13,500 mg/kg: female 17-22 day(s) after conception lactating female 21 day(s) post-birth: Reproductive: Effects on Newborn: live birth index (measured after birth), weaning or lactation index (e.g., # alive at weaning per # alive at day 4), growth statistics (e.g.%, reduced weight gain)

TDLo (Oral-Rat) 30 g/kg: male 60 day(s) pre-mating: Reproductive: Paternal Effects: testes, epididymis, sperm duct, prostate, seminal vesicle, Cowper's gland, accessory glands

TDLo (Oral-Rat) 55 mg/kg: female 7-17 day(s) after conception: Reproductive: Fertility: pre-implantation mortality (e.g. reduction in number of implants per female; total number of implants per corpora lutea); Specific Developmental Abnormalities: musculoskeletal system

TDLo (Oral-Rat) 550 mg/kg: female 7-17 day(s) after conception: Reproductive: Maternal Effects: parturition; Effects on Newborn: viability index (e.g., # alive at day 4 per # born alive)

TDLo (Oral-Rabbit) 65 mg/kg: female 6-18 day(s) after conception: Reproductive: Fertility: litter size (e.g. # fetuses per litter; measured before birth)

TDLo (Oral-Rabbit) 1120 mg/kg: male 28 day(s) pre-mating: Reproductive: Paternal Effects: prostate, seminal vesicle, Cowper's gland, accessory glands

CARCINOGENICITY INFORMATION:

ALBUTEROL SULFATE: In a 2-year study in Sprague-Dawley rats, Albuterol Sulfate caused a significant dose-related increase in the incidence of benign leiomyomas of the mesovarium at and above dietary doses of 2 mg/kg (approximately equal to the maximum recommended daily inhalation dose for adults on a mg/m^2 basis). In another study, this effect was blocked by the co-administration of propranolol, a non-selective β-adrenergic antagonist.

In an 18-month study in CD-1 mice, Albuterol Sulfate showed no evidence of tumorigenicity at dietary doses up to 500 mg/kg (approximately 140 times the maximum recommended daily inhalation dose for adults on a mg/m^2 basis). In a 22-month study in Golden hamsters, Albuterol Sulfate showed no evidence of tumorigenicity at dietary doses up to 50 mg/kg (approximately 20 times the maximum recommended daily inhalation dose for adults on a mg/m^2 basis).

IPRATROPIUM BROMIDE: In 2-year studies in Sprague-Dawley rats and CD-1 mice, Ipratropium Bromide showed no evidence of tumorigenicity at oral doses up to 6 mg/kg (approximately 15 times and 8 times the maximum recommended daily inhalation dose for adults in rats and mice respectively, on a mg/m^2 basis).

Ipratropium Bromide was not clastogenic in a mouse micronucleus assay.

The excipient components of this product are listed by agencies tracking the carcinogenic potential of chemical compounds, as follows:

HYDROCHLORIC ACID: IARC-3 Unclassifiable as to Carcinogenicity in Humans; **TLV-A4** Not Classifiable as a Human Carcinogen.

The remaining components of this product are not found on the following lists: U.S. EPA, U.S. NTP, U.S. OSHA, U.S. NIOSH, GERMAN MAK, IARC, or ACGIH and therefore are neither considered to be nor suspected to be cancer-causing agents by these agencies.

REPRODUCTIVE TOXICITY INFORMATION: An active component of this product, Albuterol Sulfate, is rated as Pregnancy Category C (RISK CANNOT BE RULED OUT, Human evidence is lacking, but animal evidence is positive.). The other active component of this product, Ipratropium Bromide, is rated as Pregnancy Category B (NO EVIDENCE OF RISK, Human evidence is negative, but animal evidence is positive). Listed below is information concerning the effects of Albuterol Sulfate and Ipratropium Bromide on human and animal reproductive systems.

11. TOXICOLOGICAL INFORMATION (Continued)

Mutagenicity: Albuterol Sulfate was not mutagenic in the Ames test or a mutation test in yeast. Albuterol Sulfate was not clastogenic in a human peripheral lymphocyte assay or in an AH1 strain mouse micronucleus assay. Ipratropium Bromide was not mutagenic in the Ames test and mouse dominant lethal test.

Embryotoxicity: This product is not reported to cause human embryotoxic effects.

Teratogenicity: During worldwide marketing experience, various congenital anomalies, including cleft palate and limb defects, have been reported in the offspring of patients being treated with Albuterol. Some of the mothers were taking multiple medications during their pregnancies. Because no consistent pattern of defects can be discerned, a relationship between Albuterol use and congenital anomalies has not been established.

A study in CD-1 mice given Albuterol subcutaneously showed cleft palate formation in 5 of 111 (4.5%) fetuses at 0.25 mg/kg (less than the maximum recommended daily inhalation dose of Albuterol Sulfate on a mg/m2 basis) and cleft palate formation in 10 of 108 (9.3%) fetuses at 2.5 mg/kg (approximately equal to the maximum recommended daily inhalation dose of Albuterol Sulfate on a mg/m2 basis). The drug did not induce cleft palate formation when administered subcutaneously at a dose of 0.025 mg/kg (less than the maximum recommended daily inhalation dose of Albuterol Sulfate on a mg/m2 basis). Cleft palate formation also occurred in 23 of 72 (30.5%) fetuses from females treated subcutaneously with 2.5 mg/kg isoproterenol (positive control). A reproduction study in Stride rabbits revealed cranioschisis in 7 of 19 (37%) fetuses when Albuterol Sulfate was administered orally at 50 mg/kg (approximately 60 times the maximum recommended daily inhalation dose of Albuterol Sulfate on a mg/m^2 basis).

Reproduction studies in CD-1 mice, Sprague-Dawley rats and New Zealand rabbits demonstrated no evidence of teratogenicity at oral doses of Ipratropium Bromide up to 10, 100, and 125 mg/kg, respectively (approximately 15, 270, and 680 times the maximum recommended daily inhalation dose for adults on a mg/m^2 basis). Reproduction studies in rats and rabbits demonstrated no evidence of teratogenicity at inhalation doses up to 1.5 and 1.8 mg/kg, respectively (approximately 4 and 10 times the maximum recommended daily inhalation dose for adults on a mg/m^2 basis).

Reproductive Toxicity: Reproduction studies in rats demonstrated no evidence of impaired fertility at oral doses of Albuterol Sulfate up to 50 mg/kg (approximately 30 times the maximum recommended daily inhalation dose of Albuterol Sulfate on a mg/m^2 basis). A reproduction study in rats demonstrated decreased conception and increased resorptions when Ipratropium Bromide was administered orally at a dose of 90 mg/kg (approximately 240 times the maximum recommended daily inhalation dose for adults on a mg/m^2 basis). These effects were not seen with a dose of 50 mg/kg (approximately 140 times the maximum recommended daily inhalation dose for adults on a mg/m^2 basis)..

ACGIH BIOLOGICAL EXPOSURE INDICES (BEIs): Currently, there are no ACGIH Biological Exposure Indices (BEIs) determined for components of this product.

12. ECOLOGICAL INFORMATION

ALL WORK PRACTICES MUST BE AIMED AT ELIMINATING ENVIRONMENTAL CONTAMINATION.

MOBILITY: This product has not been tested for mobility in soil. Information for an active ingredient in this product, Albuterol Sulfate, is available as follows:

ALBUTEROL SULFATE:

Soil Adsorption/Mobility: The K_{OC} of Albuterol is estimated as 23, using a water solubility of 1.41X10+4 mg/L(1) and a regression-derived equation. According to a classification scheme, this estimated K_{OC} value suggests that Albuterol is expected to have very high mobility in soil. However, the estimated pKa1 and pKa2 values for Albuterol are 9.2 and 10.7, respectively, indicating that this compound may partially exist in the protonated form in the environment. Cations generally adsorb more strongly to organic carbon and clay than their neutral counterparts, suggesting that mobility may be much lower in some soils.

PERSISTENCE AND BIODEGRADABILITY: This product has not been tested for persistence or biodegradability. It is expected that the components will slowly degrade in the environment and form a variety of organic and inorganic materials; however, no specific information is known. Information for an active ingredient in this product, Albuterol Sulfate, is available as follows:

ALBUTEROL SULFATE:

Persistence and Biodegradability: Based on a classification scheme, an estimated Koc value of 23, determined from a water solubility of 1.41X10+4 mg/L and a regression-derived equation, indicates that Albuterol is expected to have very high mobility in soil. However, the estimated kPa of Albuterol is 10, indicating that this compound may partially exist in the protonated form in the environment. Cations generally adsorb more strongly to organic carbon and clay than their neutral counterparts, suggesting that mobility may be much lower in some soils. Volatilization of Albuterol from moist soil surfaces is not expected to be an important fate process given an estimated Henry's Law constant of 6.4X10-16 atm-cu m/mole, using a fragment constant estimation method. Albuterol is not expected to volatilize from dry soil surfaces based upon an estimated vapor pressure of 8.9X10-9 mmHg, determined from a fragment constant method. Albuterol is not expected to adsorb to suspended solids and sediment. Volatilization from water surfaces is not expected based upon the estimated Henry's Law constant. The pKa1 and pKa2 of Albuterol are 9.2 and 10.7, respectively, indicating that this compound will partially exist in the protonated in the environment and cations generally adsorb more strongly to suspended solids and sediment than their neutral counterparts. According to a model of gas/particle partitioning of semi-volatile organic compounds in the atmosphere, Albuterol, which has an estimated vapor pressure of 8.9X10-9 mm Hg at 25∞C, determined from a fragment constant method, is expected to exist solely in the particulate phase in the ambient atmosphere. Particulate-phase Albuterol may be removed from the air by wet and dry deposition.

12. ECOLOGICAL INFORMATION (Continued)

BIO-ACCUMULATION POTENTIAL: This product has not been tested for bio-accumulation potential. Information for an active ingredient in this product, Albuterol Sulfate, is available as follows:

ALBUTEROL SULFATE:

Bioconcentration: An estimated BCF of 3 was calculated for Albuterol, using a water solubility of 1.41X10+4 mg/L and a regression-derived equation. According to a classification scheme, this BCF suggests the potential for bioconcentration in aquatic organisms is low.

ECOTOXICITY: All releases to terrestrial, atmospheric and aquatic environments should be avoided. No specific data is available for this product.

OTHER ADVERSE EFFECTS: This product does not contain any component with known ozone depletion potential.

13. DISPOSAL CONSIDERATIONS

DISPOSAL METHODS: It is the responsibility of the generator to determine at the time of disposal whether the product meets the criteria of a hazardous waste per regulations of the area in which the waste is generated and/or disposed of. Waste disposal must be in accordance with appropriate Federal, State, and local regulations. This product, if unaltered by use, may be disposed of by treatment at a permitted facility or as advised by your local hazardous waste regulatory authority. Shipment of wastes must be done with appropriately permitted and registered transporters.

DISPOSAL CONTAINERS: Waste materials must be placed in and shipped in appropriate 5-gallon or 55-gallon poly or metal waste pails or drums. Permeable cardboard containers are not appropriate and should not be used. Ensure that any required marking or labeling of the containers be done to all applicable regulations.

PRECAUTIONS TO BE FOLLOWED DURING WASTE HANDLING: Wear proper protective equipment when handling waste materials.

U.S. EPA WASTE NUMBER: Not applicable.

EWC WASTE CODE: Wastes from natal care, diagnosis, treatment, or prevention of disease in humans: chemicals consisting of or containing dangerous substances, 18-01-06

14. TRANSPORTATION INFORMATION

U.S. DEPARTMENT OF TRANSPORTATION REGULATIONS: This product is not classified as dangerous goods, per U.S. DOT regulations, under 49 CFR 172.101.

TRANSPORT CANADA TRANSPORTATION OF DANGEROUS GOODS REGULATIONS: This product is not classified as Dangerous Goods, per regulations of Transport Canada.

INTERNATIONAL AIR TRANSPORT ASSOCIATION (IATA): This product is not classified as dangerous goods under rules of IATA.

INTERNATIONAL MARITIME ORGANIZATION (IMO) DESIGNATION: This product is not classified as Dangerous Goods by the International Maritime Organization.

EUROPEAN AGREEMENT CONCERNING THE INTERNATIONAL CARRIAGE OF DANGEROUS GOODS BY ROAD (ADR): This product is not classified by the United Nations Economic Commission for Europe to be dangerous goods.

15. REGULATORY INFORMATION

ADDITIONAL UNITED STATES REGULATIONS:

U.S. SARA REPORTING REQUIREMENTS: Components of this product are not subject to the reporting requirements of Sections 302, 304, and 313 of Title III of the Superfund Amendments and Reauthorization.

U.S. SARA THRESHOLD PLANNING QUANTITY: Not applicable.

U.S. CERCLA REPORTABLE QUANTITIES (RQ): Hydrochloric Acid = 5000 lb (2270 kg)

U.S. TSCA INVENTORY STATUS: This product is regulated by the Food and Drug Administration; it is not subject to requirements of TSCA.

CALIFORNIA SAFE DRINKING WATER AND TOXIC ENFORCEMENT ACT (PROPOSITION 65): Components of this product are not listed on the California Proposition 65 lists.

OTHER U.S. FEDERAL REGULATIONS: Regulatory information for components of this product is as follows:

ALBUTEROL SULFATE:

FDA: The Approved Drug Products with Therapeutic Equivalence Evaluations List identifies currently marketed prescription drug products, including Albuterol, approved on the basis of safety and effectiveness by FDA under sections 505 of the Federal Food, Drug, and Cosmetic Act. Certain other dosage form new animal drugs. Albuterol. Indications for use: for the immediate relief of bronchospasm and broncho-constriction associated with reversible airway obstruction in horses. Limitations: Not for use in horses intended for food.

ADDITIONALCANADIAN REGULATIONS:

CANADIAN DSL INVENTORY STATUS: This product regulated by the Therapeutic Products Programme (TPP) of Health Canada and so it exempt from requirements of the DSL/NDSL Inventory.

CANADIAN ENVIRONMENTAL PROTECTION ACT (CEPA) PRIORITIES SUBSTANCES LISTS: The components of this product are not on the CEPA Priorities Substances Lists.

OTHER CANADIAN REGULATIONS: Not applicable.

CANADIAN WHMIS CLASSIFICATION AND SYMBOL: Not applicable.

16. OTHER INFORMATION

ANSI LABELING (Based on 129.1, Provided to Summarize Occupational Exposure Hazards): CAUTION! CAUSES EYE IRRITATION. MAY CAUSE SKIN IRRITATION. MAY CAUSE CARDIO-PULMONARY EFFECTS. Avoid contact with skin or clothing. Avoid breathing mists or sprays. Do not taste or swallow. Keep container closed. Use only with adequate ventilation. Wash thoroughly after handling. Wear gloves, goggles, and appropriate body protection during handling or administration. FIRST-AID: In case of contact, flush eyes with plenty of water. If mists or sprays are inhaled, remove to fresh air. If adverse respiratory reaction occurs from allergic reaction, give oxygen and seek immediate medical attention. If ingested, DO NOT induce vomiting-seek immediate medical attention. In case of fire: Use water fog, dry chemical, CO2, or alcohol foam. IN CASE OF SPILL: Wipe up spilled product. Place residual in appropriate container and seal. Dispose of according to applicable regulations. Consult Data Sheet for additional information.

EU CLP REGULATION (EC) 1272/2008 LABELING AND CLASSIFICATION: According to Article 1, item 5 (a) of CLP Regulation (EC) 1272/2008, medicinal products in the finished state for human use, as defined in 2001/83/EC, are excepted from classification and other criteria of 1272/2008.

EU LABELING AND CLASSIFICATION 67/548/EEC: According to Article 1 of European Union Council Directive 92/32/EEC, medical products in the finished state for human use (as defined by European Union Council Directives 67/548/EEC and 87/21/EEC) are not subject to the regulations and administrative provisions of European Union Council Directive 92/32/EEC.

COMPONENT GLOBAL HARMONIZATION, EU CLP REGULATION (EC) 1272/2008 LABELING AND CLASSIFICATION FULL TEXT:

Ipratropium Bromide:

Classification: Acute Oral & Inhalation Toxicity, cat. 4; Eye Irritation, cat. 2.
Signal Word: Warning
Hazard Statements: H302, H319, H332
Precautionary Statements: P280: Wear protective gloves/protective clothing/eye protection/face protection; P260: Do not breathe dust; P262: Do not get in eyes, on skin, or on clothing

Hazard Symbol/Pictograms: 

Albuterol Sulfate:

Classification: Acute Oral, Dermal, & Inhalation Toxicity, cat. 4.
Signal Word: Warning
Hazard Statements: H302, H312, H332
Precautionary Statements: P280: Wear protective gloves/protective clothing/eye protection/face protection; P260: Do not breathe dust; P262: Do not get in eyes, on skin, or on clothing

Hazard Symbol/Pictograms: 

Hydrochloric Acid:

Classification: Skin Corrosion Category 1B, Specific Target Organ Toxicity Respiratory System Category 3
Signal Word: Danger
Hazard Statements: H314: Causes severe skin burns and eye damage. H335: May cause respiratory irritation.

Hazard Symbol/Pictograms: 

ALL OTHER COMPONENTS:

These components do not meet the criteria for classification of hazardous.

COMPONENT EU 67/548/EEC LABELING AND CLASSIFICATION FULL TEXT:

Ipratropium Bromide

Hazard Classification: Harmful, Irritant
Risk Phrases: R20, R22, R36

Hazard Symbol: 

Albuterol Sulfate:

Hazard Classification: Harmful
Risk Phrases: R20, R21, R22

Hazard Symbol: 

Hydrochloric Acid:

Hazard Classification: Corrosive
Risk Phrases: R35: Causes severe burns. R37: Irritating to respiratory system.

Hazard Symbols: 

16. OTHER INFORMATION (Continued)

ALL OTHER COMPONENTS:

EU Classification: An official classification for these substances has not been published in Commission Directives.

REFERENCES AND DATA SOURCES: Contact the supplier for information.

METHODS OF EVALUATING INFORMATION FOR THE PURPOSE OF CLASSIFICATION: Bridging principles were used to classify this product.

REVISION DETAILS: Updated with GHS

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