SDS: XOPENEX® (levalbuterol hydrochloride) Inhalation Solution

SAFETY DATA SHEET

1. Identification

Product Identifier: XOPENEX® (levalbuterol hydrochloride) Inhalation Solution

Synonyms: Levalbuterol; levalbuterol Hydrochloride, (R)-Albuterol hydrochloride; (R)-a-[[(1-Dimethylethyl)amino]methyl]-4-hydroxy-1,3-benzenedimethanol hydrochloride; R-a-[(tert-Butylamino)methyl]-4-hydroxy-m-xylene-a,a'-diol hydrochloride; Levosalbutamol hydrochloride; (R)-Salbutamol hydrochloride.

National Drug Code (NDC): 17478-172-24
17478-173-24
17478-174-24
17478-171-30

Recommended Use: Pharmaceutical.

Company: Oak Pharmaceuticals, Inc. (Subsidiary of Akorn, Inc.)
1925 West Field Court, Suite 300
Lake Forest, Illinois 60045

Contact Telephone: 1-800-932-5676

E mail: customer.service@akorn.com

Emergency Phone Number: CHEMTREC 1-800-424-9300 (U.S. and Canada)

2. Hazard(s) Identification

Physical Hazards: None required.
Health Hazards: None required.
Signal Word: None required.
Hazard Statement(s): None required.
Precautionary Statement(s): None required.
Hazards Not Otherwise Classified: None required.

Supplementary Information: Xopenex® Inhalation Solution contains levalbuterol hydrochloride, the (R)-enantiomer of albuterol, which is a highly potent and relatively selective b2- adrenergic agonist. It is used as a bronchodilator. Frequently reported adverse effects associated with use by inhalation are commonly seen with b2-agonists, and include dizziness, cardiovascular effects (changes in blood pressure or heart rate, and abnormal ECG patterns), metabolic imbalance, and sore nose and throat. There have also been occasional reports of anaphylactic reaction, hives, swelling, rash, and potentially life-threatening paradoxical bronchospasm.

3. Composition/Information on Ingredients

Chemical Name	CAS Number	Synonyms	Chemical Formula	Molecular Weight	Percentage
Levalbuterol Hydrochloride	50293-90-8	Levalbuterol; levalbuterol Hydrochloride, (R)-Albuterol hydrochloride; (R)-a-[[(1-Dimethylethyl)amino]methyl]-4-hydroxy-1,3-benzenedimethanol hydrochloride; R- a-[(tert-Butylamino) methyl]-4-hydroxy-m-xylene-a,a'-diol hydrochloride; Levosalbutamol hydrochloride; (R)-Salbutamol hydrochloride.	$C_{13}H_{21}NO_3$•HCl	275.8	0.01-0.05%

*The formula also contains Sodium Chloride to adjust tonicity, and Sulfuric Acid to adjust the pH to 4.0 (3.3 to 4.5).

Note: The ingredient(s) listed above are considered hazardous. The remaining components are non-hazardous and/or present at amounts below reportable limits. See Section 16 for full text of EU and GHS classifications. The EU classification is based on Directive 67/548/EEC and the GHS classification is based on Regulation (EC) 1272/2008.

4. First Aid Measures

Ingestion: If a person vomits place them in the recovery position so that vomit will not reenter the mouth and throat. Rinse mouth with water. If swallowed, seek medical advice immediately and show the container or label. Treat symptomatically and supportively. Ensure that medical personnel are aware of the material(s) involved and take precautions to protect themselves.

Eye Contact: Remove from source of exposure. Flush with copious amounts of water for at least 15 minutes. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Ensure that medical personnel are aware of the material(s) involved and are aware of precautions to protect themselves.

Skin Contact: Remove from source of exposure. Remove and isolate contaminated clothing and shoes. Flush with copious amounts of water for at least 20 minutes. Use soap. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Ensure that medical personnel are aware of the material(s) involved and are aware of precautions to protect themselves.

Inhalation: Remove from source of exposure. Move individual(s) to fresh air. Give artificial respiration if individual(s) are not breathing and call emergency medical service. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Ensure that

	medical personnel are aware of the material(s) involved and are aware of precautions to protect themselves.
Protection of First-Aiders:	Use personal protective equipment (see section 8).
Signs and Symptoms:	See section 2 and 11.
Medical Conditions Aggravated by Exposure:	Levalbuterol HCl is a potent potent bronchodilator. Medical conditions aggravated by exposure: cardiovascular system conditions, vascular smooth muscle disorders, convulsive disorders, hyperthyroidism, diabetes mellitus. Treat symptomatically and supportively. If accidental exposure occurs to an individual who is also taking one or more concomitant medications, consult the respective package or prescribing information for potential drug-drug interactions.
Notes to Physician:	Treat supportively and symptomatically.

5. Firefighting Measures

Suitable Extinguishing Media:	Use water spray (fog), foam, dry powder, or carbon dioxide, as appropriate for surrounding fire and materials.
Unsuitable Extinguishing Media:	Not determined.

Specific Hazards Arising from the Chemical:

Hazardous Combustion Products:	No information identified. May emit carbon monoxide, carbon dioxide, oxides of nitrogen, hydrogen chloride and other chlorine-containing compounds.
Flammability/Explosivity:	No explosivity or flammability data identified. As product is an aqueous solution, it is not expected to be flammable or explosive.
Other Specific Hazards:	Not determined.
Special Protective Equipment/ Precautions for Firefighters:	Wear self-contained breathing apparatus and full and protective gear. Decontaminate all equipment after use.

6. Accidental Release Measures

Personal Precautions:	Keep unnecessary personnel away. Do not touch damaged containers or spilled material unless wearing appropriate personal protective equipment and clothing.
Personal Protective Equipment:	If product is released or spilled, take proper precautions to minimize exposure by using appropriate personal protective equipment (see Section 8). Area should be adequately ventilated. Do not breathe mist/vapors/spray.

Methods for Cleaning Up: DO NOT CAUSE MATERIAL TO BECOME AIRBORNE. For small spills, soak up material with absorbent, e.g., paper towels. For large spills, cordon off spill area and minimize the spreading of spilled material. Soak up material with absorbent. Collect spilled material, absorbent, and rinse water into suitable containers for proper disposal in accordance with applicable waste disposal regulations (see Section 13). Decontaminate the area twice with an appropriate solvent (see Section 9).

Environmental Precautions: Contain material and prevent release to basements, confined spaces, waterways or soil.

Reference to Other Sections: Refer to Sections 8, 12 and 13 for further information.

7. Handling and Storage

Precautions for Safe Handling: Handle in accordance with product label and/or product insert information. Handle in accordance with good industrial hygiene and safety practices.

Conditions for Safe Storage, Including Any Incompatibilities: Store at 20°– 25°C (68°– 77°F) away from incompatible materials. Keep out of reach of children. Avoid direct sunlight. Avoid extreme temperatures.

Specific End Use: Pharmaceuticals.

8. Exposure Controls/Personal Protection

Occupational Exposure Guidelines:

Common or Chemical Name	Employee Exposure Limits
Levalbuterol Hydrochloride	Sunovion OEL: 1 µg/m, 8 Hour TWA
Sulfuric Acid	ACGIH TLV: 0.2 mg/m³ TWA OSHA PEL: 1 mg/m³ TWA OSHA STEL: 3 mg/m³ TWA

Note: Wash hands, face and other potentially exposed areas immediately in the event of physical contact. Dispose of broken vials/syringes in a sharps container.

Engineering Controls: None required for normal handling of packaged product. If vials are crushed or broken: Control exposures to below the OEL of active pharmaceutical ingredient. Otherwise, selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Open handling should not be performed when handling potent substances, or substances of unknown toxicity. Material should be handled inside a closed process, ventilated enclosure, isolator or device of equivalent or better control that is suitable for dusts and/or aerosols.

Respiratory Protection:	None required for normal handling of packaged product. Where respirators are deemed necessary to reduce or control occupational exposures, use NIOSH-approved respiratory protection and have an effective respirator program in place (applicable U.S. regulation OSHA 29 CFR 1910.134).
Eyes Protection:	None required for the normal handling of packaged product. Safety glasses with side shields are recommended. Face shields or goggles may be required if splash potential exists or if corrosive materials are present. Approved eye protection (e.g., bearing the ANSI Z87 or CSA stamp) is preferred. Maintain eyewash facilities in the work area.
Hand Protection:	None required for the normal handling of packaged product. Chemically compatible gloves are recommended. For handling solutions, ensure that the glove material is protective against the solvent being used. Use handling practices that minimize direct hand contact. Employees who are sensitive to natural rubber (latex) should use nitrile or other synthetic non-latex gloves. Use of powdered latex gloves should be avoided due to the risk of latex allergy.
Skin Protection:	None required for the normal handling of packaged product. Wear protective laboratory coat, apron, or disposable garment when working with large quantities.

9. Physical and Chemical Properties

Physical State/Color:	Clear, colorless liquid.
Odor:	No data available.
Odor Threshold:	No data available.
pH:	4.0.
Melting Point:	Not applicable.
Freezing Point:	Not applicable.
Boiling Point:	No data available.
Flash Point:	No data available.
Evaporation Rate:	No data available.
Flammability (solid, gas):	No data available.
Flammability Limit - Lower:	No data available.
Flammability Limit - Upper:	No data available.
Vapor Pressure:	No data available.
Vapor Density:	No data available.
Relative Density:	No data available.
Solubility(ies):	Soluble in water.
Partition Coefficient (n-octanol/water):	No data available.
Auto-Ignition Temperature:	No data available.
Decomposition Temperature:	No data available.
Viscosity:	No data available.

10. Stability and Reactivity

Reactivity: No data available.

Chemical Stability: Stable under recommended storage conditions.

Possibility of Hazardous Reactions: Not expected to occur.

Conditions to Avoid (e.g., static discharge, shock, or vibration): Avoid extreme temperatures.

Incompatible Materials: Strong oxidizing agents, strong acids and strong bases.

Hazardous Decomposition Products: No data available.

11. Toxicological Information

Information on the Likely Routes of Exposure:

Inhalation: May be absorbed by inhalation.

Ingestion: No data available
Skin Contact: No data available
Eye Contact: No data available

Symptoms Related to the Physical, Chemical and Toxicological Characteristics: See Section 4. To the best of our knowledge, the chemical, physical and toxicological properties have not been thoroughly investigated.

Delayed and Immediate Effects of Exposure: Hives, itching, bronchospasm, and anaphylaxis have been reported. Syncope and hypotension may occur. Cardiac arrest, basilar artery ischemia, severe shock and death may occur rarely.

Acute Toxicity:

Compound	Species	Route	Test Type	Dose
Levalbuterol HCl	Rat	Oral	LD_{50}	2,000 – 3,000 mg/kg
Levalbuterol HCl	Rat	Intravenous	LD_{50}	50 – 75 mg/kg
Sodium Chloride	Rat	Oral	LD_{50}	3,000 mg/kg
Sodium Chloride	Mouse	Oral	LD_{50}	4,000 mg/kg
Sodium Chloride	Rat	Inhalation	LC_{50}	>42 g/m³ (1-hr)
Sodium Chloride	Rabbit	Dermal	LD_{50}	>10,000 mg/kg
Sulfuric Acid	Rat	Oral	LD_{50}	2,140 mg/kg
Sulfuric Acid	Rat	Inhalation	LC_{50}	510 mg/m³
Sulfuric Acid	Mouse	Inhalation	LC_{50}	320 mg/m³

Corrosivity: Sulfuric acid is a corrosive substance and can cause severe skin/eye burns.

Dermal Irritation: No data available.
Eye Irritation: No data available.

Sensitization:	No data available.
STOT-repeated exposure/ Repeat dose toxicity:	Inhalation studies of up to 3 months' duration were conducted with Levalbuteral using rats and dogs. No local signs of intolerance in respiratory tissue were seen at doses up to 6 and 0.28 mg/kg/day, respectively. These doses are considered NOAELs. Additional study details were not identified.
Toxicokinetics/Metabolism:	No data available.
Target Organ Effects:	Based on clinical use, possible target organs include the central and peripheral nervous systems and the cardiovascular system.
Reproductive Effects:	No studies identified for Levalbuterol HCl. However, racemic albuterol sulfate did not impair fertility in rats at doses up to 50 mg/kg/day (route not specified).
Developmental Toxicity:	Levalbuterol HCl was not teratogenic in rabbits at oral doses up to 25 mg/kg/day.
Genotoxicity:	Levalbuterol HCl was negative in the Ames bacterial mutagenicity assay, a forward mutation assay test in mammalian cells, and an in vivo mouse micronucleus test.
Carcinogenicity:	No studies identified for levalbuterol HCl. However, racemic albuterol sulfate given orally (diet) to rabbits caused benign tumors of the female reproductive organs starting at 2 mg/kg/day. In contrast, dietary studies of racemic albuterol sulfate in mice (18 months) and hamsters (22 months) were negative at up to 50 mg/kg/day. Overall, these data suggest that albuterol, and levalbuterol, are not likely to be carcinogenic. Levalbuterol is not listed by NTP, IARC, ACGIH or OSHA as a carcinogen. Sulfuric acid is labeled as a group 1 (carcinogenic to humans) by IARC, and as known to be a human carcinogen by NTP.
National Toxicology Program (NTP):	Not considered to be a carcinogen.
International Agency for Research on Cancer (IARC):	Not considered to be a carcinogen.
Occupational Safety and Health Administration (OSHA):	Not considered to be a carcinogen.
Mutagenicity:	No data available.
Aspiration Hazard:	No data available.

12. Ecological Information

Ecotoxicity

Aquatic:

Compound	Species	Test Type	Dose
Sodium Chloride	Fish (various species)	EC_{50}/96h	>4,700 mg/L
Sodium Chloride	Daphnia magna	EC_{50}/48h	340 – 1,000 mg/L
Sulfuric Acid	Brachydanio rerio (fresh water fish)	LC_{50}/24h	82 mg/L
Sulfuric Acid	Shrimp	LC_{50}/48h	80 – 90 mg/L
Sulfuric Acid	Carassius auratus (fresh water fish)	LC_{50}/96h	134 mg/L
Sulfuric Acid	Daphnia magna	LC_{50}/48h	>914 mg/L
Sulfuric Acid	Oncorhynchus mykiss (rainbow trout)	LC_{50}/48h	>952 mg/kg

Terrestrial: No data available.

Persistence and Degradability: Racemic albuterol is not readily biodegradable.

Bioaccumulative Potential: Racemic albuterol is not expected to bioaccumulate.

Mobility in Soil: Racemic albuterol is immobile in soil.

Mobility in Environment: No data available.
Other Adverse Effects: No data available.

Note: Ecological characteristics of this product/mixture were not available. The ecology data listed above are for specific ingredients, where applicable. Releases to the environment should be avoided.

13. Disposal Considerations

Dispose of all waste in accordance with Federal, State and Local regulations.

14. Transport Information

Transport: Based on the available data, this product/mixture is not regulated as a hazardous material/dangerous good under EU ADR/RID, US DOT, Canada TDG, IATA, or IMDG.

UN Number: Not applicable.
UN Proper Shipping Name: Not applicable.
Transport Hazard Class(es): Not applicable.
Packing Group: Not applicable.

Department of Transportation: Not regulated as a hazardous material.

International Air Transport Association (IATA): Not regulated as a dangerous good.

International Maritime Dangerous Good (IMDG):	Not regulated as a dangerous good.

15. Regulatory Information

US Federal Regulations:

Toxic Substance Control Act (TSCA):	Exempt.
CERCLA Hazardous Substance and Reportable Quantity:	Not listed.
SARA 313:	Not listed.
SARA 302:	Not listed.

State Regulations

Massachusetts:	Not listed.
New Jersey:	Not listed.
Pennsylvania:	Not listed.
California Proposition 65:	Not listed.

16. Other Information

Full text of R phrases and EU Classifications:	C - Corrosive. T - Toxic. R22 - Harmful if swallowed. R35 - Causes severe burns. R48/23 - Danger of serious damage to health by prolonged exposure by inhalation.
Full text of H phrases, P phrases and GHS classification:	ATO4 - Acute Toxicity (Oral) Category 4. H302 - Harmful if swallowed. SC1 - Skin corrosion Category 1. H314 - Causes severe skin burns and eye damage. EI1 - Eye corrosion Category 1. H318 - Causes serious eye damage. STOT-R1 – Specific Target Organ Toxicity Following Repeat Exposure Category 1. H372 - Causes damage to the cardiovascular and respiratory systems through prolonged or repeated exposure.

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