MATERIAL SAFETY DATA SHEET

Product Name: Isoproterenol Hydrochloride Injection, USP

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

Manufacturer Name And Address
Nexus Pharmaceuticals Inc.
175 Hawthorn Parkway
Vernon Hills, Illinois USA
60061

Emergency Telephone
CHEMTREC: North America: 800-424-9300;

Non-Emergency
847-996-3790

Product Name
Isoproterenol Hydrochloride Injection

Synonyms
3,4-Dihydroxy-α-[(isopropylamino)methyl] benzyl alcohol hydrochloride.

2. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name
Isoproterenol Hydrochloride

Chemical Formula
$C_{11}H_{17}NO_3 \bullet HCl$

Preparation
Non-hazardous ingredients include Water for Injection. Hazardous ingredients present at less than 1% include edetate disodium (EDTA), sodium citrate dihydrate, anhydrous citric acid, and sodium chloride. Hydrochloric acid is added to adjust the pH of the solution.

Component	Approximate Percent by Weight	CAS Number	RTECS Number
Isoproterenol Hydrochloride	0.02	51-30-9	DO1925000

3. HAZARD INFORMATION

Carcinogen List

Substance	IARC	NTP	OSHA
Isoproterenol Hydrochloride	Not Listed	Not Listed	Not Listed

Emergency Overview
Isoproterenol Hydrochloride Injection (Isuprel) is a solution containing isoproterenol hydrochloride, a sympathomimetic amine that acts on beta-adrenergic receptors. It stimulates the central nervous system and has stimulating action on the heart, resulting in increased cardiac output, excitability, and heart rate. It also causes peripheral vasodilatation and produces a fall in diastolic blood pressure; systolic blood pressure is usually maintained or slightly increased. In addition, isoproterenol has bronchodilating properties. Therapeutically, isoproterenol has been used to treat a variety of cardiac disorders, asthma, bronchospasm, carotid sinus hypersensitivity and shock. In the workplace, this material should be considered a potent drug, and potentially irritating to the skin, eyes, and respiratory tract. Based on clinical use, possible target organs include the central nervous system, respiratory system, cardiovascular system, and smooth muscle.

Occupational Exposure Potential	Clinically, isoproterenol hydrochloride is available as an inhalation medication for the treatment of asthma. It is systemically bioavailable via the pulmonary route. Other studies suggest that isoproterenol has some potential to be absorbed through the skin. Avoid dust or aerosol generation and avoid skin contact.
Signs and Symptoms	None known from workplace exposures. In clinical use, adverse reactions may include nervousness, increased heart rate, palpitations, flushing, chest pain, restlessness, insomnia, anxiety, tension, fear and excitement. Manifestations of acute over dosage include chest pain, dizziness, headache, irregular heartbeat, fast or pounding heartbeat, nausea or vomiting, restlessness, weakness, flushing, or decreased diastolic pressure. Direct application of isoproterenol to the eye can cause a decrease in intraocular pressure and even an increase in heart rate.
Medical Conditions Aggravated by Exposure	Pre-existing hypersensitivity to sympathomimetic amines; pre-existing central nervous system, respiratory system, or cardiovascular system disorders such as cardiac arrhythmias associated with tachycardia.

4. FIRST AID MEASURES

Eye contact	Remove from source of exposure. Flush with copious amounts of water. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.
Skin contact	Remove from source of exposure. Flush with copious amounts of water. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.
Inhalation	Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.
Ingestion	Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Notes to physician: Blood pressure and ECG may be monitored and the following treatment used, as appropriate: tachycardia in asthmatic patients may be treated with cardio-selective beta-blockers (metoprolol or atenolol, but used cautiously since cardio-selectivity may not be absolute). Non-asthmatics may be treated with propranolol; blood pressure may be regulated with rapid-acting vasodilators (nitrites, sodium nitroprusside) or alpha-blocking agents (quinidine, phentolamine).

5. FIRE FIGHTING MEASURES

Flammability	None anticipated for this aqueous product.
Fire & Explosion Hazard	None anticipated for this aqueous product.
Extinguishing media	As with any fire, use extinguishing media appropriate for primary cause of fire.
Special Fire Fighting Procedures	No special provisions required beyond normal firefighting equipment such as flame and chemical resistant clothing and self contained breathing apparatus.

6. ACCIDENTAL RELEASE MEASURES

Spill Cleanup and Disposal Isolate area around spill. Put on suitable protective clothing and equipment as specified by site spill procedures. Absorb the liquid with suitable material and clean affected area with soap and water. Dispose of spill materials according to the applicable federal, state, or local regulations.

7. HANDLING AND STORAGE

Handling No special handling required under conditions of normal product use. Do not breathe aerosol; avoid contact with skin and eyes.

Storage No special storage required for hazard control. For product protection, follow temperature storage recommendations noted on the product case label, the primary container label, or the product insert.

Special Precautions Protect from light, oxidizing materials, and extreme heat.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Guidelines

	Exposure limits				
Component	**Type**	**mg/m3**	**ppm**	**µg/m3**	**Note**
Isoproterenol Hydrochloride	Not Applicable	N/A	N/A	N/A	None Established

Respiratory protection Respiratory protection is normally not needed during intended product use. However, if the generation of aerosols is likely, and engineering controls are not considered adequate to control potential airborne exposures, the use of an approved air-purifying respirator with a HEPA cartridge (N95 or equivalent) is recommended under conditions where airborne aerosol concentrations are not expected to be excessive. For uncontrolled release events, or if exposure levels are not known, provide respirators that offer a high protection factor such as a powered air purifying respirator or supplied air. A respiratory protection program that meets OSHA's 29 CFR 1910.134 and ANSI Z88.2 requirements must be followed whenever workplace conditions require respirator use. Personnel who wear respirators should be fit tested and approved for respirator use as required.

Skin protection If skin contact with this material is likely, the use of latex or nitrile gloves is recommended.

Eye protection Eye protection is normally not required during intended use. However, if eye contact is likely to occur, the use of chemical safety goggles (as a minimum) is recommended.

Engineering Controls Engineering controls are normally not needed during the normal use of this product.

9. PHYSICAL/CHEMICAL PROPERTIES

Appearance/Physical State Liquid, aqueous
Color Clear, Colorless
Odor Odorless
Odor Threshold: NA
pH: 2.5 - 4.5
Melting point/Freezing point: NA

Initial Boiling Point/Boiling Point Range:	NA
Evaporation Rate:	NA
Flammability (solid, gas):	NA
Upper/Lower Flammability or Explosive Limits:	NA
Vapor Pressure:	NA
Vapor Density:	NA
Specific Gravity:	NA
Solubility:	Soluble in water and alcohol mixture; less soluble in absolute ethanol and practically insoluble in chloroform, ether, benzene.
Partition coefficient: n-octanol/water:	-2.69
Auto-ignition temperature:	NA
Decomposition temperature:	NA

10. STABILITY AND REACTIVITY

Reactivity	Not determined.
Chemical Stability	Stable under standard use and storage conditions. Solutions become pink to brownish-pink on standing exposed to air and almost immediately when made alkaline.
Hazardous Reactions	Not determined.
Conditions to avoid	To minimize decomposition, protect from light.
Incompatibilities	Not determined.
Hazardous decomposition products	Not determined. During thermal decomposition, it may be possible to generate irritating vapors and/or toxic fumes of carbon oxides (COx), nitrogen oxides (NOx), and hydrogen chloride.
Hazardous Polymerization	Not anticipated to occur with this material.

11. TOXICOLOGICAL INFORMATION

Acute Toxicity
Not determined for the product formulation. Information for the ingredients is as follows:

Ingredient(s)	Percent	Test Type	Route of Administration	Value	Units	Species
Isoproterenol Hydrochloride	100%	LD50	Oral	2221 1260 3070 600	mg/kg mg/kg mg/kg mg/kg;	Rat Mouse Rabbit Dog
Isoproterenol Hydrochloride	100%	LD50	Intravenous	26.9 77 27 50	mg/kg mg/kg mg/kg mg/kg	Rat Mouse Rabbit Dog

Aspiration Hazard	None anticipated from normal handling of this material.
Dermal Irritation/Corrosion	Inadvertent contact with skin may produce irritation with redness and discomfort. This material has some potential to be absorbed through skin and mucus membranes.
Ocular Irritation/Corrosion	Inadvertent contact with the eyes may produce irritation with redness, tearing and pain.
Dermal or Respiratory Sensitization	Not anticipated from normal handling of this product.
Reproductive Effects	Reproduction studies have been performed in rats and rabbits with isoproterenol at aerosol doses (30 minutes per day for 12 days) up to 15 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to isoproterenol. In another study, pregnant rats were given isoproterenol hydrochloride intraperitoneally at dosages of 0, 20, 40 or 80 mg/kg/day in sterile 0.9% saline on gestational days 6 through 15. Although these dosages produced some evidence of fetal and maternal toxicity, there was no evidence for teratogenicity in this study.
Mutagenicity	Isoproterenol was negative in the Ames test for mutagenicity in the presence and absence of metabolic activation. In an in vitro chromosomal aberration assay, isoproterenol hydrochloride was negative in the absence of metabolic activation but positive in the presence of metabolic activation.
Carcinogenicity	Long-term studies in animals to evaluate the carcinogenic potential of isoproterenol hydrochloride have not been conducted.
Target Organ Effects	Based on clinical use, possible target organs include the central nervous system, respiratory system, cardiovascular system, and smooth muscle.

12. ECOLOGICAL INFORMATION

Aquatic Toxicity	Not determined.
Persistence/Biodegradability	Not determined.
Bioaccumulation	Not determined.
Mobility in Soil	Not determined.

13. DISPOSAL CONSIDERATIONS

Waste Disposal	All waste materials must be properly characterized by the waste generator. Disposal of all pharmaceuticals should be performed in accordance with the federal, state or local regulatory requirements.
Container Handling and Disposal	Dispose of container and unused contents in accordance with federal, state and local regulations.

14. TRANSPORTATION INFORMATION

DOT STATUS Not regulated

ICAO/IATA STATUS: Not regulated

IMDG STATUS: Not regulated

15. REGULATORY INFORMATION

USA Regulations

Substance	TSCA Status	CERCLA Status	SARA 302 Status	SARA 313 Status	PROP 65 Status
Isoproterenol Hydrochloride	Not Listed	Not Listed	Not Listed	Not Listed	Not Listed

US RCRA Status Not Listed

U.S. OSHA Classification Target Organ Toxin
Possible Irritant

GHS Classification *In the EU, classification under GHS/CLP does not apply to certain substances and mixtures, such as medicinal products as defined in Directive 2001/83/EC, which are in the finished state, intended for the final user.

Hazard Class Not Applicable

Hazard Category Not Applicable

Signal Word Not Applicable

Symbol Not Applicable

Prevention P260 - Do not breathe dust/fume/gas/mist/vapors/spray.

Hazard Statement HNA - Not Applicable

Response: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists, get medical attention. Wash hands after handling.

Get medical attention if you feel unwell.

EU Classification*
*Medicinal products are exempt from the requirements of the EU Dangerous Preparations Directive. Information provided below is for the pure drug substance Isoproterenol Hydrochloride
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Classification(s): Not Applicable

Symbol: Not Applicable

Indication of Danger: Not Applicable

Product Name: Isoproterenol Hydrochloride Injection, USP

Risk Phrases: Not Applicable

Safety Phrases:
S23 - Do not breathe vapor.
S24 - Avoid contact with skin.
S25 - Avoid contact with eyes.
S37/39 - Wear suitable gloves and eye/face protection.

16. OTHER INFORMATION:

Notes:

ACGIH TLV	American Conference of Governmental Industrial Hygienists – Threshold Limit Value
CAS	Chemical Abstracts Service Number
CERCLA	US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act
DOT	US Department of Transportation Regulations
EEL	Employee Exposure Limit
IATA	International Air Transport Association
LD50	Dosage producing 50% mortality
NA	Not applicable/Not available
NE	Not established
NIOSH	National Institute for Occupational Safety and Health
OSHA PEL	US Occupational Safety and Health Administration – Permissible Exposure Limit
Prop 65	California Proposition 65
RCRA	US EPA, Resource Conservation and Recovery Act
RTECS	Registry of Toxic Effects of Chemical Substances
SARA	Superfund Amendments and Reauthorization Act
STEL	15-minute Short Term Exposure Limit
TSCA	Toxic Substance Control Act
TWA	8-hour Time Weighted Average

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