# Safety Data Sheet

Claris Lifesciences Inc.

**SDS No. CLI/SDS/MTP/01/00**

# METOPROLOL TARTRATE INJECTION, USP

## 1. PRODUCT IDENTIFICATION

| | |
|---|---|
| **Common/Trade Name:** | **Metoprolol Tartrate Injection, USP** |
| **How Supplied** | Glass Vial |
| **Strength** | 1 mg/mL |
| **Chemical Class** | Thiazide |
| **Chemical Name** | (±)-1-(Isopropylamino)-3-[p- (2-methoxyethyl)phenoxy]-2- propanol L- (+)-tartrate (2:1) (salt) |
| **Formula** | $(C_{15}H_{25}NO_3)_2 \cdot C_4H_6O_6$ |
| **Product Type** | Prescription Drug |
| **Product Use** | Pharmaceutical, Injectable |
| **Distributor Name** | CLARIS LIFESCIENCES INC. |
| **Distributor Address** | 1445 US HIGHWAY 130, North Brusnwick, NJ 08902 |
| **Manufacturer's Name** | CLARIS INJECTABLES LIMITED |
| **Address** | CHACHARWADI-VASANA,<br>AHMEDABAD - 382 213,<br>INDIA. |
| **Telephone Number For Information/ Medical Emergency** | 1-877-7CLARIS (1-877-725-2747) |
| **Date Prepared** | 28 April 2016 |

## 2. HAZARDOUS IDENTIFICATION

**Emergency Overview**

Metoprolol Tartrate Injection, Solution contains metoprolol tartrate, a selective inhibitor of beta-adrenergic receptors that is used in the management of hypertension and angina. In the workplace, this material should be considered potentially irritating to the eyes and respiratory tract. Based on clinical use, potential target organs include the cardiovascular system, respiratory system, and central nervous system.

**Occupational Exposure Potential**

Information on the absorption of this compound via ingestion, inhalation or skin contact is not available. Avoid liquid aerosol generation and skin contact with solution.

**Signs and Symptoms**

None known from occupational exposures. In clinical use, adverse effects of metoprolol are generally mild and transient. The most common adverse effects are dizziness, sedation, tiredness, insomnia and gastric upset. Shortness of breath, bradycardia, hypotension, angina, palpitation, insomnia, nausea, headache, skin rash, hepatitis and non-specific hepatic dysfunction muscle pain, alopecia, mental confusion, short-term memory loss, reversible psychosis and depression, and cold extremities have also been reported. Bronchoconstriction, wheezing and dyspnea have occurred in patients with a history of asthma that received doses of 100 mg or more. Congestive heart failure can be precipitated by administration of beta-blockers in patients with inadequate myocardial function. Overdose caused bradycardia, hypotension, bronchospasm, acute cardiac failure and death.

**Medical Conditions Aggravated by Exposure**

Pre-existing respiratory, central nervous system and cardiovascular ailments.

## 3. COMPOSITION INFORMATION

| Component | Content mg/ml | CAS |
|---|---|---|
| Metoprolol Tartrate | 1.0 | [56392-17-7] |
| Sodium Chloride | 9.0 | [7647-14-5] |
| Water for Injection | q.s.to 1.0 mL | [7732-18-5] |

q.s.: Quantity Sufficient

## 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.

## 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 for hazard control under conditions of normal product use.

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

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

## 8. EXPOSURE CONTROLS / PERSONAL PROTECTION INFORMATION

| | Exposure Limits | | | | |
|---|---|---|---|---|---|
| **Component** | **Type** | $mg/m^3$ | **ppm** | $\mu g/m^3$ | **Note** |
| **Metoprolol Tartrate** | **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 the product formulation is likely, the use of latex or nitrile gloves is recommended.

**Eye protection**
Eye protection is normally not required during intended product 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.

## 9.0 PHYSICAL AND CHEMICAL DATA

| | |
|---|---|
| **Appearance/Physical State** | : Liquid |
| **Color** | : Clear and colorless |
| **Odor** | : NA |
| **Odor Threshold** | : NA |
| **pH** | : 5.0-8.0 |
| **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** | : Metoprolol tartrate is very soluble in water; freely soluble in methylene chloride, in chloroform, and in alcohol; slightly soluble in acetone; and insoluble in ether. |
| **Partition coefficient: n-octanol/water** | : NA |
| **Auto-ignition temperature** | : NA |
| **Decomposition temperature** | : NA |

## 10.0 STABILITY AND REACTAVITY

| | |
|---|---|
| **Reactivity** | : Not determined. |
| **Chemical Stability** | : Stable under standard use and storage conditions. |
| **Hazardous Reactions** | : Not determined. |
| **Conditions to avoid** | : Not determined. |
| **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 sulfur oxides (SOx). |
| **Hazardous Polymerization** | : Not anticipated to occur with this product. |

## 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 |
|---|---|---|---|---|---|---|
| Metoprolol Tartrate | 100 | LD50 | Oral | 5500<br>3090-4670<br>1500<br>1158-2460<br>604<br>1090 | mg/kg<br>mg/kg<br>mg/kg<br>mg/kg<br>mg/kg<br>mg/kg | Rat<br>Rat<br>Mouse<br>Mouse<br>Rabbit<br>Dog |
| Metoprolol Tartrate | 100 | LD50 | Intravenous | 90<br>84<br>28.7 | mg/kg<br>mg/kg<br>mg/kg | Rat<br>Mouse<br>Dog |

**Aspiration Hazard** : None anticipated from normal handling of this product.

**Dermal Irritation/Corrosion** : None anticipated from normal handling of this product. However, inadvertent contact of this product with the skin may produce skin irritation.

**Ocular Irritation/Corrosion** : None anticipated from normal handling of this product. However, inadvertent contact of this product with the eyes may produce eye irritation.

**Dermal or Respiratory Sensitization**
None anticipated from normal handling of this product. In clinical use, broncho-constriction, wheezing and dyspnea have occurred in patients with a history of asthma that received doses of 100 mg or more.

**Reproductive Effects:**
No evidence of impaired fertility due to metoprolol was observed in a study performed in rats at doses up to 55.5 times the maximum daily human dose of 450 mg. Metoprolol has been shown to increase postimplantation loss and decrease neonatal survival in rats at doses up to 55.5 times the maximum daily human dose of 450 mg. Distribution studies in mice confirm exposure of the fetus when metoprolol is administered to the pregnant animal. These studies have revealed no evidence of impaired fertility or teratogenicity.

**Mutagenicity:**
All mutagenicity tests performed (a dominant lethal study in mice, chromosome studies in somatic cells, a Salmonella/mammalianmicrosome mutagenicity test, and a nucleus anomaly test in somatic interphase nuclei) were negative.

**Carcinogenicity:**
Long-term studies in animals have been conducted to evaluate carcinogenic potential. In a 2-year study in rats at three oral dosage levels of up to 800 mg/kg per day, there was no increase in the development of spontaneously occurring benign or malignant neoplasms of any type. The only histologic changes that appeared to be drug related were an increased incidence of generally mild focal accumulation of foamy macrophages in pulmonary alveoli and a slight increase in biliary hyperplasia. In a 21-month study in Swiss albino mice at three oral dosage levels of up to 750 mg/kg per day, benign lung tumors (small adenomas) occurred more frequently in female mice receiving the highest dose than in untreated control animals. There was no increase in malignant or total (benign plus malignant) lung tumors, nor in the overall incidence of tumors or malignant tumors. This 21-month study was repeated in CD-1 mice, and no statistically or biologically significant differences were observed between treated and control mice of either sex for any type of tumor.

**Target Organ Effects:**
Based on clinical use, potential target organs include the cardiovascular system, respiratory system, and central nervous system.

## 12. ECOLOGICAL INFORMATION

| | |
|---|---|
| **Aquatic Toxicity** | **:** Not determined for product |
| **Persistence/Biodegradability** | **:** Not determined for product |
| **Bioaccumulation** | **:** Not determined for product |
| **Mobility in Soil** | **:** Not determined for product |

## 13. DISPOSAL CONSIDERATIONS

**Waste Disposal**
All waste materials must be properly characterized. Further, disposal 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. TRANSPORT INFORMATION

| | |
|---|---|
| **ADR/ADG/ DOT STATUS** | **:** Not regulated |
| **IMDG STATUS** | **:** Not regulated |
| **ICAO/IATA STATUS** | **:** Not regulated |
| **Transport Comments** | : None |

## 15. REGULATORY INFORMATION

**USA Regulations**

| | |
|---|---|
| **RCRA Status** | Not Listed |
| **U.S. OSHA Classification** | Target Organ Toxin Possible Reproductive 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** | 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 Metoprolol Tartrate

| | |
|---|---|
| **Classification(s):** | Not Applicable |
| **Symbol:** | Not Applicable |
| **Indication of Danger:** | Not Applicable |
| **Risk Phrases:** | Not Applicable |
| **Safety Phrases:** | S23 - Do not breathe vapor.<br>S24 - Avoid contact with skin.<br>S25 - Avoid contact with eyes.<br>S37/39 - Wear suitable gloves and eye/face protection. |

## 16. OTHER INFORMATION

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|---|---|
| **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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