MATERIAL SAFETY DATA SHEET

Product Name: Atracurium Besylate Injection

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

Manufacturer Name And Address
Hospira Inc.
275 North Field Drive
Lake Forest, Illinois USA
60045

Hospira Australia Pty Ltd.
1 Lexia Place
Mulgrave VIC 3170
Australia

Emergency Telephone
CHEMTREC: North America: 800-424-9300;
International 1-703-527-3887; Australia (02) 8014 4880

Hospira, Inc., Non-Emergency 224-212-2000

Product Name
Atracurium Besylate Injection

Synonyms
2,2’-[1,5-pentanediylbis[oxy(3-oxo-3,1-propanediyl)]bis[1-[(3,4-
dimethoxyphenyl)methyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-2-
methylisoquinolinium] dibenzenesulfonate.

2. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name
Atracurium Besylate

Chemical Formula
C_{65}H_{82}N_{2}O_{18}S_{2}

Preparation
Non-hazardous ingredients include Water for Injection. Hazardous ingredients present at less than 1% include benzenesulfonic acid which is added as a buffer to adjust the pH.

<table>
<thead>
<tr>
<th>Component</th>
<th>Approximate Percent by Weight</th>
<th>CAS Number</th>
<th>RTECS Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atracurium Besylate</td>
<td>1</td>
<td>64228-81-5</td>
<td>NX5841000</td>
</tr>
</tbody>
</table>

3. HAZARD INFORMATION

Carcinogen List

<table>
<thead>
<tr>
<th>Substance</th>
<th>IARC</th>
<th>NTP</th>
<th>OSHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atracurium Besylate</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
</tr>
</tbody>
</table>

Emergency Overview
Atracurium Besylate Injection contains atracurium besylate, an intermediate-duration, nondepolarizing, skeletal muscle relaxant for intravenous administration. It is used as an adjunct to general anesthesia to facilitate endotracheal intubation and to provide skeletal muscle relaxation during surgery or mechanical ventilation. In the workplace, atracurium besylate should be considered a potent drug and possibly irritating to the eyes and respiratory tract. Possible target organs include the neuromuscular system, cardiovascular system, and respiratory system.
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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

No signs or symptoms from occupational exposure are known. In clinical use, adverse effects have included hypotension, slow irregular heart rate, hypersensitivity reactions such as rashes, wheezing, flushing, shortness of breath. The incidence of severe cardiovascular or allergic reactions is low. Atracurium can cause respiratory paralysis.

Medical Conditions Aggravated by Exposure

Hypersensitivity to atracurium besylate or similar materials, or to other ingredients in this product. Pre-existing neuromuscular or cardiovascular ailments.

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. Overdosage may increase the risk of histamine release and cardiovascular effects, especially hypotension. If cardiovascular support is necessary, this should include proper positioning, fluid administration, and the use of vasopressor agents if necessary. The patient’s airway should be assured, with manual or mechanical ventilation maintained as necessary. A longer duration of neuromuscular block may result from overdosage and a peripheral nerve stimulator may be used to monitor recovery. Recovery may be facilitated by administration of an anticholinesterase reversing agent such as neostigmine, edrophonium, or pyridostigmine, in conjunction with an anticholinergic agent such as atropine or glycopyrrolate. The package insert should be consulted for prescribing information.

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
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the applicable federal, state, or local regulations.

7. HANDLING AND STORAGE

Handling
No special handling required under conditions of normal product use. Protect from light.

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
Protect from freezing.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

<table>
<thead>
<tr>
<th>Exposure Guidelines</th>
<th>Exposure limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Component</td>
<td>Type</td>
</tr>
<tr>
<td>Atracurium Besylate</td>
<td>Hospira EEL</td>
</tr>
<tr>
<td>Atracurium Besylate</td>
<td>Hospira STEL</td>
</tr>
</tbody>
</table>

Respiratory protection
Respiratory protection is normally not needed during intended product use. However, if the generation of aerosols or vapors 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
Local exhaust ventilation is recommended to minimize employee exposure. The use of an enclosure, such as an approved ventilated cabinet designed to minimize airborne exposures, is also recommended.

9. PHYSICAL/CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Appearance/Physical State</th>
<th>Liquid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color</td>
<td>Colorless or faint yellow sterile solution</td>
</tr>
<tr>
<td>Odor</td>
<td>NA</td>
</tr>
<tr>
<td>Odor Threshold:</td>
<td>NA</td>
</tr>
<tr>
<td>pH:</td>
<td>3.25 - 3.65</td>
</tr>
<tr>
<td>Melting point/Freezing point:</td>
<td>Approximately that of water (0 °C, 32 °F)</td>
</tr>
<tr>
<td>Initial Boiling Point/Boiling Point Range:</td>
<td>Approximately that of water (100 °C, 212 °F)</td>
</tr>
<tr>
<td>Evaporation Rate:</td>
<td>NA</td>
</tr>
</tbody>
</table>
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**Flammability (solid, gas):** NA
**Upper/Lower Flammability or Explosive Limits:** NA
**Vapor Pressure:** Approximately that of water (17.5 mm Hg at 20°C)
**Vapor Density:** NA
**Specific Gravity:** Approximately that of water (1.0)
**Solubility:** NA
**Partition coefficient: n-octanol/water:** NA
**Auto-ignition temperature:** NA
**Decomposition temperature:** NA

### 10. STABILITY AND REACTIVITY

**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:

<table>
<thead>
<tr>
<th>Ingredient(s)</th>
<th>Percent</th>
<th>Test Type</th>
<th>Route of Administration</th>
<th>Value</th>
<th>Units</th>
<th>Species</th>
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</thead>
<tbody>
<tr>
<td>Atracurium Besylate</td>
<td>100</td>
<td>LD50</td>
<td>Oral</td>
<td>&gt; 50 but</td>
<td>mg/kg</td>
<td>Rat</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt; 500</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atracurium Besylate</td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>2</td>
<td>mg/kg</td>
<td>Mouse</td>
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<tr>
<td>Atracurium Besylate</td>
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<td>LD50</td>
<td>Intravenous</td>
<td>1.31</td>
<td>mg/kg</td>
<td>Rat</td>
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<tr>
<td>Atracurium Besylate</td>
<td>100</td>
<td>LD50</td>
<td>Dermal</td>
<td>200</td>
<td>mg/kg</td>
<td>Rabbit</td>
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<tr>
<td>Atracurium Besylate</td>
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<td>LD50</td>
<td>Dermal</td>
<td>&gt; 2000</td>
<td>mg/kg</td>
<td>Rat</td>
</tr>
</tbody>
</table>

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

**Dermal Irritation/Corrosion**
None anticipated from normal handling of this product. The active ingredient was not irritating in a skin irritation test in rabbits.

**Ocular Irritation/Corrosion**
None anticipated from normal handling of this product. However, inadvertent contact of this product with eyes may produce irritation. The active ingredient produced transient mild to moderate conjunctival redness reversible in three
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days in an eye irritation test in rabbits.

Dermal or Respiratory Sensitization

None anticipated from normal handling of this product. The active ingredient was not a sensitizer in the maximization test in guinea pigs at challenge concentrations of 25 and 50% in petrolatum. Rarely, hypersensitivity reactions, including anaphylaxis, have been reported during the clinical use of this product.

Reproductive Effects

Fertility studies have not been performed. Atracurium besylate was administered subcutaneously on days 6 through 18 of gestation to non-ventilated Dutch rabbits. Treatment groups were given either 0.15 mg/kg once daily or 0.10 mg/kg twice daily. Lethal respiratory distress occurred in two 0.15 mg/kg animals and in one 0.10 mg/kg animal, with transient respiratory distress or other evidence of neuromuscular block occurring in 10 of 19 and in 4 of 20 of the 0.15 mg/kg and 0.10 mg/kg animals, respectively. There was an increased incidence of certain spontaneously occurring visceral and skeletal anomalies or variations in one or both treated groups when compared to non-treated controls. The percentage of male fetuses was lower (41% vs. 51%) and the post-implantation losses were increased (15% vs. 8%) in the group given 0.15 mg/kg once daily when compared to the controls; the mean numbers of implants (6.5 vs. 4.4) and normal live fetuses (5.4 vs. 3.8) were greater in this group when compared to the control group.

Mutagenicity

Atracurium was evaluated in a battery of three short-term mutagenicity tests. It was non-mutagenic in both the Ames Salmonella assay at concentrations up to 1000 mcg/plate, and in a rat bone marrow cytogenicity assay at up to paralyzing doses. A positive response was observed in the mouse lymphoma assay under conditions (80 and 100 mcg/mL, in the absence of metabolic activation) which killed over 80% of the treated cells; there was no mutagenicity at 60 mcg/mL and lower, concentrations which killed up to half of the treated cells. A far weaker response was observed in the presence of metabolic activation at concentrations (1200 mcg/mL and higher) which also killed over 80% of the treated cells.

Carcinogenicity

The carcinogenic potential of atracurium besylate has not been fully evaluated in long-term studies in animals.

Target Organ Effects

This material should be considered potentially irritating to the eyes and respiratory tract. Following an accidental over-exposure, possible target organs include the neuromuscular system, cardiovascular system, and respiratory system.

12. ECOLOGICAL INFORMATION

Aquatic Toxicity

Not determined for this product. By analogy, information for cis-atracurium besylate, a closely related material, is presented below: Cis-atracurium besylate is not toxic to activated sludge microorganisms. *IC50 > 4000 mg/L, 3 hr, activated sludge. Cis-atracurium besylate is not toxic to a battery of microorganisms. *MIC > 300 mg/L in a battery of microorganisms. Cis-atracurium besylate may be harmful to daphnids. *EC50 (48 hr) = 14 mg/L in Daphnia magna.

Persistence/Biodegradability

Not determined for product. By analogy, information for cis-atracurium besylate is presented below: *Cis-atracurium besylate is hydrolyzed in water with half-lives ranging from < 4 minutes under basic conditions, about 6 hours under neutral conditions, to 19-days under acidic conditions. *Cis-atracurium
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besylate is unstable in water when exposed to light with a half-life of 2.45 days at pH 5. *Cis-atracurium besylate degraded 82% in a 28-day aerobic biodegradation assay (Modified Sturm test) and is considered readily biodegradable. It is not anticipated to persist in the environment.

Bioaccumulation 
Not determined for product.

Mobility in Soil
Not determined for product.

13. DISPOSAL CONSIDERATIONS

Waste Disposal
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. TRANSPORTATION INFORMATION

ADR/ADG/ DOT STATUS:
Not regulated

IMDG STATUS:
Not regulated

ICAO/IATA STATUS:
Not regulated

Transport Comments:
None

15. REGULATORY INFORMATION

USA Regulations

<table>
<thead>
<tr>
<th>Substance</th>
<th>TSCA Status</th>
<th>CERCLA Status</th>
<th>SARA 302 Status</th>
<th>SARA 313 Status</th>
<th>PROP 65 Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atracurium Besylate</td>
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<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
</tr>
</tbody>
</table>

RCRA Status
Not Listed

U.S. OSHA Classification
Target Organ Toxin

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
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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 Atracurium Besylate.

Classification(s): Not Applicable

Symbol: Not Applicable

Indication of Danger: Not Applicable

Risk Phrases: Not Applicable

Safety Phrases: S23 - Do not breathe vapor.
               S24/25 - Avoid contact with skin and eyes.

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

MSDS Coordinator: Hospira GEHS
Date Prepared: 09/01/2011
Obsolete Date: 11/09/2009
Product Name: Atracurium Besylate Injection

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