MATERIAL SAFETY DATA SHEET

Product Name: Atracurium Besylate Injection

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

<table>
<thead>
<tr>
<th>Manufacturer Name And Address</th>
<th>Hospira, Inc.</th>
<th>Hospira Australia Pty Ltd</th>
</tr>
</thead>
<tbody>
<tr>
<td>Address</td>
<td>275 North Field Drive</td>
<td>1 Lexia Place</td>
</tr>
<tr>
<td></td>
<td>Lake Forest, Illinois 60045</td>
<td>Mulgrave VIC 3170</td>
</tr>
<tr>
<td></td>
<td>USA</td>
<td>AUSTRALIA</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Emergency Telephone #’s</th>
<th>CHEMTREC: North America: 800-424-9300; International 1-703-527-3887; Australia (02) 8014 4880</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospira, Inc., Non-Emergency</td>
<td>224 212-2055</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Atracurium Besylate Injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synonyms</td>
<td>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.</td>
</tr>
</tbody>
</table>

2. HAZARD INFORMATION

<table>
<thead>
<tr>
<th>Emergency Overview</th>
<th>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 and the cardiovascular system.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occupational Exposure Potential</td>
<td>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.</td>
</tr>
<tr>
<td>Signs and Symptoms</td>
<td>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.</td>
</tr>
<tr>
<td>Medical Conditions</td>
<td>Hypersensitivity to atracurium besylate or similar materials, or to other ingredients in this product. Pre-existing neuromuscular or cardiovascular ailments.</td>
</tr>
<tr>
<td>Aggravated by Exposure</td>
<td>IARC: Not listed NTP: Not listed OSHA: Not listed</td>
</tr>
</tbody>
</table>

3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Active Ingredient Name</th>
<th>Atracurium Besylate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical Formula</td>
<td>C_{65}H_{82}N_{2}O_{18}S_{2}</td>
</tr>
</tbody>
</table>

<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>

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

Fire & Explosion
None anticipated for this 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 fire fighting 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. Protect from light.

Storage
No special storage required for hazard control. For product protection, follow USP controlled room temperature 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

Exposure Guidelines

<table>
<thead>
<tr>
<th>Component</th>
<th>OSHA-PEL</th>
<th>ACGIH-TLV</th>
<th>AIHA WEEL</th>
<th>Hospira EEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atracurium Besylate</td>
<td>8 hr TWA: Not Established</td>
<td>8 hr TWA: Not Established</td>
<td>8-hr TWA: Not Established</td>
<td>8 hr TWA: 100 mcg/m3 STEL: 500 mcg/m3</td>
</tr>
</tbody>
</table>

Notes: OSHA PEL: US Occupational Safety and Health Administration – Permissible Exposure Limit
ACGIH TLV: American Conference of Governmental Industrial Hygienists – Threshold Limit Value.
AIHA WEEL: Workplace Environmental Exposure Level
EEL: Employee Exposure Limit.
TWA: 8 hour Time Weighted Average.
STEL: 15-minute Short Term Exposure Limit.

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
When handling this material, disposable gloves should be worn at all times. Further, the use of double gloves is recommended. Disposable gloves made from nitrile, neoprene, polyurethane or natural latex generally have low permeability to this material. Persons known to be allergic to latex rubber should select a non-latex glove. Gloves should be changed regularly, and removed immediately after known contamination. Care should be taken to minimize inadvertent contamination when removing and/or disposing of gloves.

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.
Product Name: Atracurium Besylate Injection

9. PHYSICAL/CHEMICAL PROPERTIES

Appearance/Physical State  Product is a clear, colorless or faint yellow, sterile solution
Odor  NA
Odor Threshold: NA
pH: 3.25 – 3.65
Melting point/Freezing point: Approximately that of water (0 °C, 32 °F).
Initial Boiling Point/Boiling Point Range Approximately that of water (100 °C, 212 °F).
Evaporation Rate: NA
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 (Air =1) NA
Evaporation Rate 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

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>
</tr>
</thead>
<tbody>
<tr>
<td>Atracurium Besylate</td>
<td>100</td>
<td>LD50</td>
<td>Oral</td>
<td>&gt; 50 but &lt; 500</td>
<td>mg/kg</td>
<td>Rat</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>
</tr>
<tr>
<td>Atracurium Besylate</td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>1.31</td>
<td>mg/kg</td>
<td>Rat</td>
</tr>
<tr>
<td>Atracurium Besylate</td>
<td>100</td>
<td>LD50</td>
<td>Dermal</td>
<td>200</td>
<td>mg/kg</td>
<td>Rabbit</td>
</tr>
<tr>
<td>Atracurium Besylate</td>
<td>100</td>
<td>LD50</td>
<td>Dermal</td>
<td>&gt; 2000</td>
<td>mg/kg</td>
<td>Rat</td>
</tr>
</tbody>
</table>

LD50(dermal) is the dosage that produces 50% mortality when applied to the skin.
### 11. TOXICOLOGICAL INFORMATION: continued

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aspiration Hazard</strong></td>
<td>None anticipated from normal handling of this product.</td>
</tr>
<tr>
<td><strong>Dermal Irritation/Corrosion</strong></td>
<td>None anticipated from normal handling of this product. The active ingredient was not irritating in a skin irritation test in rabbits.</td>
</tr>
<tr>
<td><strong>Ocular Irritation/Corrosion</strong></td>
<td>None anticipated from normal handling of this product. Inadvertent contact of this product with eyes may produce irritation. The active ingredient produced transient mild to moderate conjunctival redness reversible in three days in an eye irritation test in rabbits.</td>
</tr>
<tr>
<td><strong>Dermal or Respiratory Sensitization</strong></td>
<td>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.</td>
</tr>
<tr>
<td><strong>Reproductive Effects</strong></td>
<td>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.</td>
</tr>
<tr>
<td><strong>Mutagenicity</strong></td>
<td>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.</td>
</tr>
<tr>
<td><strong>Carcinogenicity</strong></td>
<td>The carcinogenic potential of atracurium besylate has not been fully evaluated in long-term studies in animals.</td>
</tr>
<tr>
<td><strong>Target Organ Effects</strong></td>
<td>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 and the cardiovascular system.</td>
</tr>
</tbody>
</table>


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 is 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 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.

*GlaxoSmithKline MSDS for Nimbex®

Notes: EC50: Concentration in water that produces 50% mortality in Daphnia sp; LC50: Concentration in water that produces 50% mortality in fish; EC50: Concentration in water that produces 50% inhibition of growth in algae.

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

DOT STATUS:  Not regulated
Proper Shipping Name:  NA
Hazard class:  NA
Un number:  NA
Packing group:  NA
Reportable quantity:  NA

ICAO/IATA STATUS:  Not regulated
Proper shipping name:  NA
Hazard class:  NA
Un:  NA
Packing group:  NA
Reportable quantity:  NA

IMDG STATUS:  Not regulated
Proper shipping name:  NA
Hazard class:  NA
Un number:  NA
Packing group:  NA
Reportable quantity:  NA

Notes:  DOT – US Department of Transportation Regulations
# 15. REGULATORY INFORMATION

<table>
<thead>
<tr>
<th>TSCA Status</th>
<th>Exempt.</th>
</tr>
</thead>
<tbody>
<tr>
<td>CERCLA Status</td>
<td>Not listed</td>
</tr>
<tr>
<td>SARA 302 Status</td>
<td>Not listed</td>
</tr>
<tr>
<td>SARA 313 Status</td>
<td>Not listed</td>
</tr>
<tr>
<td>RCRA Status</td>
<td>Not listed</td>
</tr>
<tr>
<td>PROP 65 (Calif.)</td>
<td>Not listed</td>
</tr>
</tbody>
</table>


**U.S. OSHA Classification**
- Possible Irritant
- Target Organ Toxin

**GHS Classification***

*Where medicinal products are not exempt, the recommended GHS workplace classification for this product is as follows:

<table>
<thead>
<tr>
<th>Hazard Class</th>
<th>Acute Oral Toxicity</th>
<th>Eye Irritation</th>
<th>Target Organ Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hazard Category</td>
<td>Unclassified</td>
<td>2B</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Symbol</th>
<th>NA</th>
<th>NA</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Signal Word</th>
<th>NA</th>
<th>Warning</th>
<th>Warning</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Hazard Statement</th>
<th>NA</th>
<th>Causes eye irritation</th>
<th>May cause damage to the neuromuscular system and cardiovascular system through prolonged or repeated exposure.</th>
</tr>
</thead>
</table>

**Prevention:**
- Do not eat, drink or smoke when using this product.
- Wash hands thoroughly after handling.
- Do not breathe mist/spray.

**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.

- Call a POISON CENTER or doctor/physician if exposed or you feel unwell.
15. REGULATORY INFORMATION: continued

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):   Irritant

Symbol:   

Indication of Danger   Xi

Risk Phrases:   R36/37 - Irritating to eyes and respiratory system

Safety Phrases:   S24 - Avoid contact with the 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
LD<sub>50</sub>   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:   Global Occupational Toxicology
Date Prepared:   September 15, 2005
Revision Date:   October 23, 2009
Revision Date:   November 9, 2009

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