SAFETY DATA SHEET

Product Name: Atracurium Besylate Injection

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

Manufacturer Name And Address
Hospira, Inc.
275 North Field Drive
Lake Forest, Illinois 60045
USA
Hospira Australia Pty Ltd
1 Lexia Place
Mulgrave VIC 3170
AUSTRALIA

Emergency Telephone #’s
CHEMTREC: North America: 800-424-9300;
International 1-703-527-3887; Australia - 61-290372994; UK - 44-870-8200418

Product Name
Atracurium Besylate Injection

Synonyms
2,2’-[1,5-pentanediyl]bis[oxy(3-oxo-3,1-propanediyl)][bis[1-[(3,4-di(2-methylisoquinolinium) dibenzenesulfonate.

2. HAZARD(S) IDENTIFICATION

Emergency Overview
Atracurium Besylate Injection is a solution containing atracurium besylate, an intermediate-duration, nondepolarizing, skeletal muscle relaxant for intravenous administration. Clinically, 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.

U.S. OSHA GHS Classification

Physical Hazards
Not Classified

Health Hazards
STOT - RE
2

Label Element(s)

Pictogram

Signal Word
Warning

Hazard Statement(s)
May cause damage to organs through prolonged or repeated exposure

Precautionary Statement(s)

Prevention
Do not breathe vapor or spray.
Wash hands thoroughly after handling.

Response
Get medical attention if you feel unwell.

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.
Product Name: Atracurium Besylate Injection

3. COMPOSITION/INFORMATION ON INGREDIENTS

<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 for Injection. Hazardous ingredients present at less than 1% include benzenesulfonic acid which is added 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**
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 such as carbon dioxide, dry chemical extinguishing powder or foam.

**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 control 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 precautions required for hazard control.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

<table>
<thead>
<tr>
<th>Exposure Guidelines</th>
<th>Exposure Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Component</td>
<td>OSHA-PEL</td>
</tr>
<tr>
<td>Atracurium Besylate</td>
<td>8 hr TWA: Not Established</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.

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

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  
NA

Initial Boiling Point/Boiling Point Range  
NA

Flash Point  
NA

Evaporation Rate  
NA

Flammability (solid, gas)  
NA

Upper/Lower Flammability or Explosive Limits  
NA

Vapor Pressure  
NA

Vapor Density (Air =1)  
NA

Relative Density  
1.0

Solubility  
NA

Partition coefficient: n-octanol/water  
NA

Auto-ignition temperature  
NA

Decomposition temperature  
NA

Viscosity  
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 active ingredient 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 &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>
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<td>Intravenous</td>
<td>1.31</td>
<td>mg/kg</td>
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<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>
<td>100</td>
<td>LD50</td>
<td>Dermal</td>
<td>&gt; 2000</td>
<td>mg/kg</td>
<td>Rat</td>
</tr>
</tbody>
</table>

LD50: Dosage that produces 50% mortality. LD50(dermal) is the dosage that produces 50% mortality when applied to the skin.
Product Name: Atracurium Besylate Injection

11. TOXICOLOGICAL INFORMATION: continued

**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 anticipated from normal handling of this product. In clinical use, adverse effects have included hypotension, slow irregular heart rate, hypersensitivity reactions such as rashes, wheezing, flushing, and shortness of breath. The incidence of severe cardiovascular or allergic reactions is low. Atracurium can cause respiratory paralysis.

**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 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**

None anticipated from normal handling of this product. 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.

**Carcinogen Lists**

IARC: Not listed  NTP: Not listed  OSHA: Not listed

**Specific Target Organ Toxicity – Single Exposure**

NA

**Specific Target Organ Toxicity – Repeat Exposure**

Based on clinical use, possible target organs include the neuromuscular system, cardiovascular system, and respiratory system.
Product Name: Atracurium Besylate Injection

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 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 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. TRANSPORTATION INFORMATION

<table>
<thead>
<tr>
<th>ADR/ADG/ DOT STATUS</th>
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<tbody>
<tr>
<td>Proper Shipping Name</td>
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<tr>
<td>Hazard Class</td>
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<td>UN Number</td>
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<tr>
<td>Packing Group</td>
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<tr>
<td>Reportable Quantity</td>
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</table>

<table>
<thead>
<tr>
<th>ICAO/IATA STATUS</th>
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<tbody>
<tr>
<td>Proper Shipping Name</td>
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<table>
<thead>
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<th>IMDG STATUS</th>
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<td>Packing Group</td>
<td>NA</td>
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<tr>
<td>Reportable Quantity</td>
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</table>

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

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


GHS/CLP 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.

<table>
<thead>
<tr>
<th>Hazard Class</th>
<th>Hazard Category</th>
<th>Pictogram</th>
<th>Signal Word</th>
<th>Hazard Statement</th>
</tr>
</thead>
<tbody>
<tr>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Prevention
Do not breathe vapor or spray.
Wash hands thoroughly after handling.

Response
Get medical attention if you feel unwell.
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.

EU Classification* *Medicinal products are exempt from the requirements of the EU Dangerous Preparations Directive.

<table>
<thead>
<tr>
<th>Classification(s)</th>
<th>Symbol</th>
<th>Indication of Danger</th>
<th>Risk Phrases</th>
<th>Safety Phrases</th>
</tr>
</thead>
<tbody>
<tr>
<td>NA</td>
<td>NA</td>
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<td>S23: Do not breathe vapor/spray</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td>NA</td>
<td>S24: Avoid contact with the skin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td>NA</td>
<td>S25: Avoid contact with eyes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td>NA</td>
<td>S37/39 Wear suitable gloves and eye/face protection.</td>
<td></td>
</tr>
</tbody>
</table>
Product Name:  Atracurium Besylate Injection

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
STOT - SE  Specific Target Organ Toxicity – Single Exposure
STOT - RE  Specific Target Organ Toxicity – Repeated Exposure
TSCA  Toxic Substance Control Act
TWA  8-hour Time Weighted Average

MSDS Coordinator:  Hospira GEHS
Date Prepared:  October 17, 2012
Date Revised:  June 02, 2014

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