MATERIAL SAFETY DATA SHEET

Product Name: Midazolam Hydrochloride Injection, Solution

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

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

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
Midazolam Hydrochloride Injection, Solution

Synonyms
8-Chloro-6-(2-fluorophenyl)-1-methyl-4H-imidazo(1,5-a)(1,4)benzodiazepine hydrochloride

2. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name
Midazolam Hydrochloride

Chemical Formula
C\textsubscript{18}H\textsubscript{13}ClFN\textsubscript{3}•HCl

Preparation
Non-hazardous ingredients include Water for Injection. Hazardous ingredients present at less than 1% include sodium chloride; hydrochloric acid and/or sodium hydroxide are used 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>Midazolam Hydrochloride</td>
<td>≤ 0.5</td>
<td>59467-96-8</td>
<td>NI2922250</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>Midazolam Hydrochloride</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
</tr>
</tbody>
</table>

Emergency Overview
Midazolam Hydrochloride Injection, Solution contains midazolam hydrochloride, a short-acting benzodiazepine central nervous system depressant used to relieve anxiety and provide sedation. In the U.S., midazolam is subject to Schedule IV control under the Controlled Substances Act. In the workplace, midazolam hydrochloride should be considered a potent drug and a potential occupational reproductive hazard. Possible target organs include the central nervous system, gastrointestinal system, genitourinary system, cardiovascular system, and possibly the fetus.

Occupational Exposure Potential
Information on the absorption of this product via inhalation or skin contact is not available. Published reports have indicated that some benzodiazepines have the potential to be absorbed through intact skin or mucus membranes. Avoid liquid aerosol generation and skin contact.

Signs and Symptoms
During occupational use, this product should be considered potentially irritating to the eyes and respiratory tract. In clinical use, common adverse effects include drowsiness, sedation, muscle weakness, and ataxia. Less frequent adverse effects include vertigo, headache, confusion,
Product Name: Midazolam Hydrochloride Injection, Solution

depression, slurred speech, tremor, visual disturbances, urinary retention or incontinence, gastrointestinal disturbances, decreased blood pressure, changes in salivation, and amnesia. Death due to respiratory depression, hypotension, or cardiac arrest has been reported infrequently in patients given intravenous midazolam for conscious sedation.

Medical Conditions

Aggravated by Exposure
Pre-existing hypersensitivity to midazolam hydrochloride, related benzodiazepines, or other ingredients in this product. Pre-existing central nervous system, gastrointestinal system, genitourinary system, and cardiovascular system ailments; pregnancy.

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. Treatment of injectable midazolam overdosage is the same as that followed for overdosage with other benzodiazepines. Respiration, pulse rate and blood pressure should be monitored and general supportive measures should be employed. Attention should be given to the maintenance of a patent airway and support of ventilation, including administration of oxygen. An intravenous infusion should be started. Should hypotension develop, treatment may include intravenous fluid therapy, repositioning, judicious use of vasopressors appropriate to the clinical situation, if indicated, and other appropriate countermeasures. There is no information as to whether peritoneal dialysis, forced diuresis or hemodialysis are of any value in the treatment of midazolam overdosage. Flumazenil, a specific benzodiazepine-receptor antagonist, is indicated for the complete or partial reversal of the sedative effects of benzodiazepines and may be used in situations when an overdose with a benzodiazepine is known or suspected. There are anecdotal reports of reversal of adverse hemodynamic responses associated with midazolam hydrochloride following administration of flumazenil to pediatric patients. Prior to the administration of flumazenil, necessary measures should be instituted to secure the airway, assure adequate ventilation, and establish adequate intravenous access. Flumazenil is intended as an adjunct to, not as a substitute for, proper management of benzodiazepine overdose. Patients treated with flumazenil should be monitored for resedation, respiratory depression and other residual benzodiazepine effects for an appropriate period after treatment. Flumazenil will only reverse benzodiazepine-induced effects but will not reverse the effects of other concomitant medications. The reversal of benzodiazepine effects may be associated with the onset of seizures in certain high-risk patients. The prescriber should be aware of a risk of seizure in association with flumazenil treatment, particularly in longterm benzodiazepine users and in cyclic antidepressant overdose. The complete flumazenil package insert, including CONTRAINDICATIONS, WARNINGS and PRECAUTIONS, should be consulted prior to use.
5. FIRE FIGHTING MEASURES

Flammability
None anticipated from this aqueous product.

Fire & Explosion Hazard
None required from this aqueous product.

Extinguishing media
Carbon Dioxide, Foam, 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. However, in the U.S., midazolam is subject to Schedule IV control under the Controlled Substances Act.

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

Exposure Guidelines

<table>
<thead>
<tr>
<th>Component</th>
<th>Type</th>
<th>mg/m3</th>
<th>ppm</th>
<th>µg/m3</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam Hydrochloride</td>
<td>Hospira EEL</td>
<td>N/A</td>
<td>N/A</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

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 (N99 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.
Product Name: Midazolam Hydrochloride Injection, Solution

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 anticipated use of this product.

9. PHYSICAL/CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance/Physical State</td>
<td>Liquid</td>
</tr>
<tr>
<td>Color</td>
<td>Midazolam is a white to light yellow crystalline compound, insoluble in water. Midazolam Injection is a 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 (2.5 to 3.5)</td>
</tr>
<tr>
<td>Melting point/Freezing point:</td>
<td>NA</td>
</tr>
<tr>
<td>Initial Boiling Point/Boiling Point Range:</td>
<td>Not Determined</td>
</tr>
<tr>
<td>Evaporation Rate:</td>
<td>NA</td>
</tr>
<tr>
<td>Flammability (solid, gas):</td>
<td>NA</td>
</tr>
<tr>
<td>Upper/Lower Flammability or Explosive Limits:</td>
<td>NA</td>
</tr>
<tr>
<td>Vapor Pressure:</td>
<td>Not Determined</td>
</tr>
<tr>
<td>Vapor Density:</td>
<td>Not Determined</td>
</tr>
<tr>
<td>Specific Gravity:</td>
<td>Not Determined</td>
</tr>
<tr>
<td>Solubility:</td>
<td>The hydrochloride salt of midazolam, which is formed in situ, is soluble in aqueous solutions.</td>
</tr>
<tr>
<td>Partition coefficient: n-octanol/water:</td>
<td>NA</td>
</tr>
<tr>
<td>Auto-ignition temperature:</td>
<td>NA</td>
</tr>
<tr>
<td>Decomposition temperature:</td>
<td>NA</td>
</tr>
</tbody>
</table>

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), hydrogen chloride, and/or hydrogen fluoride.

Hazardous Polymerization  Not anticipated to occur with this product.
Product Name: Midazolam Hydrochloride Injection, Solution

11. TOXICOLOGICAL INFORMATION

Acute Toxicity
Not determined for the product formulation. Information for 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>Midazolam</td>
<td>100</td>
<td>LD50</td>
<td>Oral</td>
<td>215</td>
<td>mg/kg</td>
<td>Rat</td>
</tr>
<tr>
<td>Midazolam</td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>75, 357</td>
<td>mg/kg</td>
<td>Rat</td>
</tr>
<tr>
<td>Midazolam</td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>50</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td>Midazolam</td>
<td>100</td>
<td>LD50</td>
<td>Intramuscular</td>
<td>&gt; 50</td>
<td>mg/kg</td>
<td>Rat, Mouse</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.

Ocular Irritation/Corrosion
None anticipated from normal handling of this product. Midazolam produced minimal eye irritation in a study in animals. Inadvertent contact of this product with eyes may produce redness and discomfort.

Dermal or Respiratory Sensitization
None anticipated from normal handling of this product. In clinical use, allergic reactions including anaphylactoid reactions, hives, rash, pruritus have been reported infrequently.

Reproductive Effects
A reproduction study in male and female rats did not show any impairment of fertility at dosages up to 10 times the human intravenous dose of 0.35 mg/kg. Teratology studies conducted with midazolam maleate injectable in rabbits and rats at doses that were 5 and 10 times the human dose of 0.35 mg/kg did not show evidence of teratogenicity. Studies in rats showed no adverse effects on reproductive parameters during gestation and lactation. Dosages tested were approximately 10 times the human dose of 0.35 mg/kg.

Mutagenicity
Midazolam was not mutagenic in Salmonella typhimurium (5 bacterial strains), Chinese hamster lung cells (V79), human lymphocytes or in the micronucleus test in mice.

Carcinogenicity
Midazolam maleate was administered with diet in mice and rats for 2 years at dosages of 1, 9 and 80 mg/kg/day. In female mice in the highest dose group there was a marked increase in the incidence of hepatic tumors. In high-dose male rats there was a small but statistically significant increase in benign thyroid follicular cell tumors. Dosages of 9 mg/kg/day of midazolam maleate (25 times a human dose of 0.35 mg/kg) do not increase the incidence of tumors. The pathogenesis of induction of these tumors is not known. These tumors were found after chronic administration, whereas human use will ordinarily be of single or several doses.

Target Organ Effects
Based on clinical use, possible target organs include the central nervous system, gastrointestinal system, genitourinary system, cardiovascular system, and possibly the fetus.

12. ECOLOGICAL INFORMATION

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

LC50(48hr) = 7.1 mg/l in Daphnia LC50 = 4.3 mg/l in rainbow trout
EbC50(72hr) = 11.4 mg/l in algae (the no-observable biological effect concentration on growth (72hr) was 3.7 mg/l).
Product Name: Midazolam Hydrochloride Injection, Solution

Persistence/Biodegradability
Not determined for the product. Information for ingredients is as follows:
Midazolam was only 6% biodegraded in 28 days in the Sturm test. The EC50 (3h) for inhibition of microbial respiration was greater than 100 mg/l indicating that this material was non-inhibitory to microorganisms in the activated sludge respiration inhibition test.

Bioaccumulation
Not determined for product.

Mobility in Soil
Not determined for the 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. TRANSPORTATION INFORMATION

DOT STATUS
Not regulated

ICAO/IATA STATUS:
Not regulated

IMDG STATUS:
Not regulated

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>Midazolam Hydrochloride</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Listed</td>
</tr>
</tbody>
</table>

US RCRA Status
Not Listed

U.S. OSHA Classification
Target Organ Toxin
Reproductive 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
**Product Name: Midazolam Hydrochloride Injection, Solution**

**Prevention**
- P201 - Obtain special instructions before use.
- P202 - Do not handle until all safety precautions have been read and understood.
- P280.2 - Wear protective gloves and eye/face protection.
- P281 - Use personal protective equipment as required.

**Hazard Statement**
- Not Applicable

**Response:**
- If exposed or concerned: Get medical attention.

   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.

**EU Classification**
*Medicinal products are exempt from the requirements of the EU Dangerous Preparations Directive. Information provided below is for the pure drug substance Midazolam Hydrochloride.*

- **Classification(s):** Not Applicable
- **Symbol:** Not Applicable
- **Indication of Danger:** Not Applicable
- **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:**

<table>
<thead>
<tr>
<th>Notes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACGIH TLV</td>
</tr>
<tr>
<td>CAS</td>
</tr>
<tr>
<td>CERCLA</td>
</tr>
<tr>
<td>DOT</td>
</tr>
<tr>
<td>EEL</td>
</tr>
<tr>
<td>IATA</td>
</tr>
<tr>
<td>LD50</td>
</tr>
<tr>
<td>NA</td>
</tr>
<tr>
<td>NE</td>
</tr>
<tr>
<td>NIOSH</td>
</tr>
<tr>
<td>OSHA PEL</td>
</tr>
<tr>
<td>Prop 65</td>
</tr>
<tr>
<td>RCRA</td>
</tr>
<tr>
<td>RTECS</td>
</tr>
<tr>
<td>SARA</td>
</tr>
<tr>
<td>STEL</td>
</tr>
<tr>
<td>TSCA</td>
</tr>
<tr>
<td>TWA</td>
</tr>
</tbody>
</table>

MSDS Coordinator: Hospira GEHS
Date Prepared: 10/19/2011
Obsolete Date: 08/13/2010

**Disclaimer:**
The information and recommendations contained herein are based upon tests believed to be reliable. However, Hospira does not guarantee their accuracy or completeness NOR SHALL ANY OF THIS INFORMATION CONSTITUTE A WARRANTY, WHETHER EXPRESSED OR IMPLIED, AS TO THE SAFETY OF THE GOODS, THE MERCHANTABILITY OF THE GOODS, OR THE FITNESS OF THE GOODS FOR A PARTICULAR PURPOSE. Adjustment to conform to actual conditions of usage may be required. Hospira assumes no responsibility for results obtained or for incidental or consequential damages, including lost profits, arising from the use of these data. No warranty against infringement of any patent, copyright or trademark is made or implied.