MATERIAL SAFETY DATA SHEET

Product Name: Codeine Phosphate Injection, USP

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
Codeine Phosphate Injection, USP

Synonyms
7,8-Didehydro-4,5 α-epoxy-3-methoxy-17-methylmorphinan-6α-ol phosphate

2. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name
Codeine Phosphate Hemihydrate

Chemical Formula
C_{18}H_{21}NO_{3} \cdot H_{3}PO_{4} \cdot 1/2H_{2}O

Preparation
Non-hazardous ingredients include Water for Injection. Hazardous ingredients present at less than 1% include sodium lactate, sodium metabisulfite, and sodium formaldehyde sulfoxylate. Sodium chloride is added to adjust isotonicity. The pH is adjusted between 3 and 6 with lactic acid or sodium hydroxide.

<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>Codeine Phosphate Hemihydrate</td>
<td>5</td>
<td>41444-62-6</td>
<td>NA</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>Codeine Phosphate Hemihydrate</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
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</tbody>
</table>

Emergency Overview
Codeine Phosphate Injection, USP is a solution containing codeine phosphate, an opioid analgesic. Clinically, codeine phosphate is given orally for the relief of cough, and for the relief of mild to moderate pain. In the U.S., codeine is a controlled substance and is regulated as a Schedule II, III, or V substance depending on the formulation. In the workplace, this material should be considered a potential sensitizer, potentially irritating to the eyes and respiratory tract, and a potential occupational reproductive hazard. Based on clinical use, potential target organs include the central nervous system, gastrointestinal system, respiratory system, cardiovascular system, and liver.

Occupational Exposure Potential
Information on the absorption of this product via inhalation or skin contact is not available. Avoid liquid aerosol generation and skin contact.

Signs and Symptoms
In the workplace, hypersensitivity reactions, including asthma, have been reported following occupational exposures to narcotic dusts during the processing of raw opiates. Based on clinical
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use, adverse effects may include nausea, vomiting, constipation, drowsiness, and confusion; micturition may be difficult and there may be ureteric or biliary spasm; the latter may be associated with alterations in liver enzyme values. Dry mouth, dizziness, sweating, facial flushing, headache, vertigo, bradycardia, tachycardia, palpitations, orthostatic hypotension, hypothermia, restlessness, changes of mood, decreased libido or potency, hallucinations, and miosis also occur. Large doses of codeine may produce respiratory depression and hypotension, with circulatory failure and deepening coma. Death may occur from respiratory failure. The triad of coma, pinpoint pupils, and respiratory depression is considered indicative of opioid overdosage.

Medical Conditions Aggravated by Exposure

Pre-existing hypersensitivity to codeine or related materials; pre-existing central nervous system ailments; pre-existing opiate dependency.

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 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. In the U.S., codeine is a controlled substance and is regulated as a Schedule II, III, or V substance depending on the formulation. Appropriate training and record-keeping procedures may be required during the routine handling of this
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>
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</thead>
<tbody>
<tr>
<td>Codeine Phosphate Hemihydrate</td>
<td>Hospira EEL</td>
<td>N/A</td>
<td>N/A</td>
<td>10</td>
<td>8hr TWA</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 (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. PHYSICAL/CHEMICAL PROPERTIES

Appearance/Physical State: Liquid
Color: Clear
Odor: NA
Odor Threshold: NA
pH: Between 3 and 6
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: NA
Partition coefficient: n-octanol/water: NA
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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 oxide of phosphorus.
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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<tbody>
<tr>
<td>Codeine Phosphate Hemihydrate</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<td>Codeine Phosphate, Anhydrous</td>
<td>100</td>
<td>LD50</td>
<td>Oral</td>
<td>85</td>
<td>mg/kg</td>
<td>Rat</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>237</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>654</td>
<td>mg/kg</td>
<td>Guinea Pig</td>
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<tr>
<td>Codeine Phosphate, Anhydrous</td>
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<td>LD50</td>
<td>Intravenous</td>
<td>54</td>
<td>mg/kg</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>62</td>
<td>mg/kg</td>
<td>Mouse</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>97.8</td>
<td>mg/kg</td>
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<td>Codeine Phosphate, Sesquihydrate</td>
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<td>LD50</td>
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<td></td>
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<td>Intravenous</td>
<td>70</td>
<td>mg/kg</td>
<td>Mouse</td>
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<tr>
<td>Codeine</td>
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<td>Codeine</td>
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<td>34</td>
<td>mg/kg</td>
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<td></td>
<td></td>
<td>69</td>
<td>mg/kg</td>
<td>Dog</td>
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</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. However, inadvertent contact of this product with eyes may produce irritation.
Dermal or Respiratory Sensitization None anticipated from normal handling of this product. However, hypersensitivity reactions, including asthma, have been reported following
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occupational exposures to narcotic dusts during the processing of raw opiates.

Reproductive Effects
A study in rats and rabbits reported no teratogenic effect of codeine after administration during organogenesis at dosages ranging from 5 to 120 mg/kg. In the rat, at a dosage of 120 mg/kg, a maternally toxic dosage, an increase in embryo resorption at the time of implantation was noted. In another study, a single 100 mg/kg dosage of codeine given to pregnant mice was reported to delay ossification in the offspring. In hamsters and mice, codeine produced developmental toxicity (as indicated by decreased fetal body weight) at doses below those producing maternal toxicity in both hamsters and mice. In the hamster, the more sensitive species to codeine developmental toxicity, effects were observed at a total daily dose of 100 mg/kg. Fetal physical dependence followed by withdrawal reported in women using opioids during pregnancy. Single report of cleft palate in fetus. Some reproductive effect data in bioassays. Codeine phosphate is known to the State of California to cause reproductive toxicity. FDA Pregnancy Category C.

Mutagenicity
Codeine phosphate was negative for mutagenicity in the Ames test, with and without metabolic activation.

Carcinogenicity
By analogy, codeine was negative for carcinogenicity in a 2-year dietary study in rats.

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

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. TRANSPORTATION INFORMATION

ADR/ADG/ DOT STATUS:
Not regulated
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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>
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<tbody>
<tr>
<td>Codeine Phosphate Hemihydrate</td>
<td>Not Listed</td>
<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
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
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 Codeine Phosphate Hemihydrate.

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: 09/09/2011
Obsolete Date: 10/21/2008

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