MATERIAL SAFETY DATA SHEET

Product Name: Leucovorin Calcium Injection, USP

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

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

Hospira UK Limited
Queensway
Royal Leamington Spa
Warwickshire, England CV313RW

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
Leucovorin Calcium Injection, USP

Synonyms
Leucovorin Calcium; Calcium Folinate; Citrovorum Factor; Folinic Acid; L-glutamic acid, N-(4-((2-amino-5-formyl-1, 4, 5, 6, 7, 8- hexahydro- 4-oxo-6-pteridinyl)methyl)amino)benzoyl )-calcium salt (1:1); Calcium N-[p-[[6RS]-2-amino-5-formyl-5,6,7,8-tetrahydro-4-hydroxy-6-pteridinyl[methyl][amino]benzoyl]-L-glutamate (1:1).

2. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name
Leucovorin Calcium Pentahydrate

Chemical Formula
C_{20}H_{21}CaN_{7}O_{7} \cdot 5 \text{H}_{2}O

Preparation
Non-hazardous ingredients include Water for Injection. Hazardous ingredients present at less than 1% include sodium chloride; sodium hydroxide and/or hydrochloric acid are added 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>Leucovorin Calcium Pentahydrate</td>
<td>1</td>
<td>41927-89-3</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>Leucovorin Calcium Pentahydrate</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
</tr>
</tbody>
</table>

Emergency Overview
Leucovorin Calcium Injection, USP is a solution containing leucovorin calcium, the calcium salt of folic acid. Folinic acid is the 5-formyl derivative of tetrahydrofolic acid, the active metabolite of folic acid (a B-vitamin). Clinically, calcium folinate is used to minimize adverse effects in patients treated with folic acid antagonists such as methotrexate. In the workplace, this material should be considered potentially irritating to the eyes and respiratory tract. Based on clinical use, potential target organs include the gastrointestinal system and nervous system.
### 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
None known from occupational exposures. In clinical use, calcium folinate is well-tolerated. Adverse effects have included gastrointestinal distress and fever from parenteral administration. Occasionally, allergic sensitization, including anaphylactoid reactions and urticaria, has been reported following the administration of both oral and parenteral calcium folinate. Insomnia, agitation, and depression have been reported rarely, after high doses.

### Medical Conditions Aggravated by Exposure
Pre-existing hypersensitivity to folinic acid salts; pre-existing hematological disorders or anemias due to vitamin B12 deficiency.

## 4. FIRST AID MEASURES

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Eye contact</strong></td>
<td>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.</td>
</tr>
<tr>
<td><strong>Skin contact</strong></td>
<td>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.</td>
</tr>
<tr>
<td><strong>Inhalation</strong></td>
<td>Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.</td>
</tr>
<tr>
<td><strong>Ingestion</strong></td>
<td>Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.</td>
</tr>
</tbody>
</table>

## 5. FIRE FIGHTING MEASURES

<table>
<thead>
<tr>
<th>Description</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Flammability</strong></td>
<td>None anticipated for this aqueous product.</td>
</tr>
<tr>
<td><strong>Fire &amp; Explosion Hazard</strong></td>
<td>None anticipated for this aqueous product.</td>
</tr>
<tr>
<td><strong>Extinguishing media</strong></td>
<td>As with any fire, use extinguishing media appropriate for primary cause of fire.</td>
</tr>
<tr>
<td><strong>Special Fire Fighting Procedures</strong></td>
<td>No special provisions required beyond normal fire fighting equipment such as flame and chemical resistant clothing and self contained breathing apparatus.</td>
</tr>
</tbody>
</table>

## 6. ACCIDENTAL RELEASE MEASURES

<table>
<thead>
<tr>
<th>Description</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Spill Cleanup and Disposal</strong></td>
<td>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.</td>
</tr>
</tbody>
</table>

## 7. HANDLING AND STORAGE

<table>
<thead>
<tr>
<th>Description</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Handling</strong></td>
<td>No special handling required under conditions of normal product use.</td>
</tr>
<tr>
<td><strong>Storage</strong></td>
<td>No special storage required for hazard control. For product protection, follow storage recommendations noted on the product case label, the primary</td>
</tr>
</tbody>
</table>
8. EXPOSURE CONTROLS/PERSONAL PROTECTION

<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>Leucovorin Calcium Pentahydrate</td>
<td>Not Applicable</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>None Established</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. Since protection provided by air purifying respirators is limited, a powered air purifying respirator or supplied air should be considered during an uncontrolled release event, if exposure levels are not known, or during events where air-purifying respirators may not provide adequate protection. 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, colorless to pale yellow.

Odor
NA

Odor Threshold:
NA

pH:
7.5 to 8.5 for a 2.5% aqueous solution

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:
Leucovorin calcium occurs as a yellowish to beige, odorless powder, which is very soluble in water and practically insoluble in alcohol.

Partition coefficient: n-octanol/water:
NA

Auto-ignition temperature:
NA
Product Name: Leucovorin Calcium Injection, USP

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) and nitrogen oxides (NOx).

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>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium Folinate</td>
<td>100</td>
<td>LD50</td>
<td>Oral</td>
<td>&gt;8000</td>
<td>mg/kg</td>
<td>Rat</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&gt;7000</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td>Calcium Folinate</td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>732</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>991</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td>Calcium Folinate</td>
<td>100</td>
<td>LD50</td>
<td>Intraperitoneal</td>
<td>1063</td>
<td>mg/kg</td>
<td>Rat</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1036</td>
<td>mg/kg</td>
<td>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. However, inadvertent contact of this product with eyes may produce irritation with redness and discomfort.

Dermal or Respiratory Sensitization
None anticipated from normal handling of this product. However, allergic sensitization, including anaphylactoid reactions and urticaria, has been reported occasionally during the clinical use of this product.

Reproductive Effects
No studies have been conducted to evaluate the potential impairment of fertility by calcium folinate. Animal reproduction studies have not been conducted with calcium folinate.

Mutagenicity
No studies have been conducted to evaluate the mutagenic potential of calcium folinate.

Carcinogenicity
No studies have been conducted to evaluate the carcinogenic potential of
Product Name: Leucovorin Calcium Injection, USP

calcium folinate.

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

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

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>
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<tr>
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</tbody>
</table>

RCRA Status Not Listed

U.S. OSHA Target Organ Toxin

Classification 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
Product Name: Leucovorin Calcium Injection, USP

Hazard Category
Not Applicable

Signal Word
Not Applicable

Symbol
Not Applicable

Prevention
P260 - Do not breathe dust/fume/gas/mist/vapors/spray.

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 Leucovorin Calcium Pentahydrate.

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.
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
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
Product Name: Leucovorin Calcium Injection, USP

MSDS Coordinator: Hospira GEHS
Date Prepared: 10/21/2011
Obsolete Date: 07/06/2009

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