



MATERIAL SAFETY DATA SHEET

Product Name: PAMIDRONATE DISODIUM - pamidronate disodium solution

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

| | | |
|---|---|--|
| Manufacturer Names And Addresses | 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: (02) 8014 4880 | |
| Hospira, Inc., Non-Emergency | 224-212-2055 | |
| Material Name | PAMIDRONATE DISODIUM - pamidronate disodium solution | |
| Synonyms | Phosphonic acid (3-amino-1-hydroxypropylidene)bis-, disodium salt; Disodium 3-amino-1-hydroxypropylidene-1,1-biphosphate; Disodium Pamidronate. | |

2. HAZARD INFORMATION

| | | | |
|--|---|------------------------|-------------------------|
| Emergency Overview | PAMIDRONATE DISODIUM - pamidronate disodium solution contains pamidronate disodium, a bisphosphonate which inhibits bone resorption. Clinically, pamidronate disodium is used to treat severe hypercalcemia associated with malignancy, osteolytic lesions and bone pain in multiple myeloma, or bone metastases associated with breast cancer. In the workplace, this material should be considered a potent drug, potentially irritating to the skin, eyes and respiratory tract, and a potential occupational reproductive hazard. Following an accidental over-exposure, possible target organs may include the eyes, skeletal system, gastrointestinal system, cardiovascular system, central nervous system, blood, kidneys and fetus. | | |
| Occupational Exposure Potential | Potential occupational routes of exposure may include the skin, eyes, and respiratory tract. Avoid the generation of aerosols, and inadvertent contact with the skin, eyes, or mucus membranes. Where possible, engineering controls should be utilized to control potential exposures to the aerosolized product. | | |
| Signs and Symptoms | None known from workplace exposures. This product may be irritating to the skin, eyes, respiratory tract, and mucus membranes. By analogy, in clinical use, pamidronate disodium may produce fever, gastrointestinal disturbances (abdominal pain, anorexia, constipation, nausea, vomiting) and hematological abnormalities (anemia, thrombocytopenia, and lymphocytopenia). Flu-like symptoms (malaise, rigors, fatigue, and flushes) are common during intravenous infusion of pamidronate but generally resolve spontaneously. Tenderness at the infusion site has also been reported. Like other bisphosphonates, pamidronate may cause nephrotoxicity. Central nervous system (CNS) effects may include agitation, confusion, dizziness, lethargy, insomnia, and somnolence. Atrial fibrillation, tachycardia, and both hypotension and hypertension have also been reported. Bronchospasm and interstitial pneumonitis have occurred rarely. | | |
| Medical Conditions Aggravated by Exposure | Pre-existing hypersensitivity to pamidronate disodium or other bisphosphonates. Pre-existing skeletal system, cardiovascular system, gastrointestinal system, central nervous system, blood, and kidney ailments; or pregnancy. | | |
| Carcinogen Lists: | IARC: Not listed | NTP: Not listed | OSHA: Not listed |

3. COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient Name Pamidronate Disodium
Chemical Formula C₃H₉NO₇P₂Na₂

| Component | Approximate Percent by Weight | CAS Number | RTECS Number |
|----------------------|-------------------------------|------------|--------------|
| Pamidronate Disodium | 0.3-0.9 | 57248-88-1 | SZ6525000 |

Non-hazardous ingredients include water and mannitol. Hazardous ingredients present at less than 1% include phosphoric acid and/or sodium hydroxide which are 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.

5. FIRE FIGHTING MEASURES

Flammability Not anticipated for this aqueous product.

Fire & Explosion Hazard Not anticipated for this aqueous product.

Extinguishing Media As with any fire, use extinguishing media appropriate for the primary cause of fire.

Special Fire Fighting Procedures No special requirements are needed for single units or packages. For larger amounts, self-contained breathing apparatus and protective equipment and clothing are recommended to minimize contact with respiratory tract, skin and eyes.

6. ACCIDENTAL RELEASE MEASURES

Spill Cleanup and Disposal Put on suitable protective clothing and equipment as specified by site spill procedures. Isolate and contain the area around the spill. Absorb spilled liquid with suitable material and clean affected area with soap and water. Dispose of materials according to the applicable federal, state, or local regulations.

7. HANDLING AND STORAGE

- Handling** No special control measures are required during the normal use of this product. During handling, avoid aerosolization of the product solution.
- 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** Persons with a known allergy to pamidronate disodium or other bisphosphonates, women who are pregnant, or women who want to become pregnant, should consult a health or safety professional prior to handling this material.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Guidelines

| Component | Exposure limits | | | |
|----------------------|---------------------------|---------------------------|---------------------------|--------------|
| | OSHA-PEL | ACGIH-TLV | Hospira EEL | Other Limits |
| Pamidronate Disodium | 8-hr TWA: Not established | 8-hr TWA: Not established | 8-hr TWA: Not Established | NA |

Notes: OSHA PEL: US Occupational Safety and Health Administration – Permissible Exposure Limit
 ACGIH TLV: American Conference of Governmental Industrial Hygienists – Threshold Limit Value.
 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 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 oncolytic agents. 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** As a minimum, the use of chemical safety goggles is recommended when handling this material.
- Engineering Controls** If the generation of aerosols is likely, local exhaust ventilation is recommended to minimize employee exposure. If available, the use of an enclosure, such as an approved ventilated cabinet designed to minimize airborne exposures, is also recommended.

9. PHYSICAL/CHEMICAL PROPERTIES

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|--|--|
| Appearance/Physical State | A clear colorless aqueous solution. |
| Odor | NA |
| Odor Threshold: | NA |
| pH: | 6.0-7.0 |
| 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 |
| Evaporation Rate | NA |
| Specific Gravity | NA |
| Solubility | Pamidronate disodium is soluble in water and in 2N sodium hydroxide, sparingly soluble in 0.1N hydrochloric acid and in 0.1N acetic acid, and practically insoluble in organic solvents. |
| Partition coefficient: n-octanol/water: | NA |
| Auto-ignition temperature | NA |
| Decomposition temperature | NA |

10. STABILITY AND REACTIVITY

| | |
|---|--|
| Reactivity | NA |
| Chemical Stability | Stable under recommended storage conditions and use. |
| Hazardous Reactions | NA |
| Conditions to avoid | NA |
| 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 (CO _x), nitrogen oxides (NO _x), and phosphorus oxides (PO _x). |
| Hazardous Polymerization | Not anticipated to occur with this product. |

11. TOXICOLOGICAL INFORMATION

No data found for the formulated product. Information for the active ingredient follows.

Acute Toxicity

| Ingredient(s) | Percent | Test Type | Route of Administration | Value | Units | Species |
|-----------------------|----------------|------------------|--------------------------------|--------------|--------------|----------------|
| Pamidronate Disodium | 100 | LD50 | Oral | 625 | mg/kg | Mouse |
| *Pamidronate Disodium | 100 | LD50 | Oral | 1560 | mg/kg | Rat |
| *Pamidronate Disodium | 100 | LD50 | Oral | 680 | mg/kg | Mice, male |
| *Pamidronate Disodium | 100 | LD50 | Oral | 1000 | mg/kg | Mice, female |
| *Pamidronate Disodium | 100 | LD50 | Oral | 820 | mg/kg | Rabbit |
| Pamidronate Disodium | 100 | LD50 | Intravenous | 50 | mg/kg | Rat |
| Pamidronate Disodium | 100 | LD50 | Intravenous | 45 | mg/kg | Mouse |
| Pamidronate Disodium | 100 | LD50 | Intravenous | 190 | mg/kg | Mouse |

LD50 is the dosage producing 50% mortality.

* Bedford Laboratories MSDS

Aspiration Hazard

None anticipated from normal handling of this product.

Dermal Irritation/Corrosion

None anticipated from normal handling of this product. Pamidronate disodium is reported to be moderately irritating to the skin in a skin irritation study in animals. Inadvertent skin contact with this product may produce irritation and redness.

Ocular Irritation/Corrosion

None anticipated from normal handling of this product. Pamidronate disodium is reported to be severely irritating to the eyes in an eye irritation study in animals. Inadvertent eye contact with this product may produce irritation with redness and discomfort.

Dermal or Respiratory Sensitization

None anticipated from normal handling of this product. In clinical use, rare occurrences of allergic manifestations have been reported for pamidronate disodium, including hypotension, dyspnea, or angioedema, and, very rarely, anaphylactic shock.

Reproductive Effects

In rats, decreased fertility occurred in first-generation offspring of parental animals that were treated orally with 150 mg/kg/day of pamidronate. Bolus intravenous studies conducted in rats and rabbits resulted in maternal toxicity and embryo/fetal effects. Administration of pamidronate to rats and rabbits either orally at a dosage of 150 mg/kg, or intravenously at dosages of 6 to 15 mg/kg during organogenesis produced delayed ossification. Pamidronate given intravenously to rats produced a shortening of long bones at dosages of 12-15 mg/kg; other findings included dilated renal pelvices and ureters.

Mutagenicity

Pamidronate was nonmutagenic in a battery of mutagenicity assays including the Ames test, *Salmonella* and *Escherichia*/liver-microsome test, nucleus-anomaly test, sister-chromatid-exchange study, point-mutation test, and a micronucleus test in the rat.

Carcinogenicity

Pamidronate disodium produced a dose-related increase in benign adrenal pheochromocytoma in male rats in a 104-week oral-dose carcinogenicity study in rats. Similar, but not statistically significant findings were noted in females. Adrenal pheochromocytoma was also observed in low numbers in the control animals and is considered a relatively common spontaneous neoplasm in the rat. In a similar study, daily oral administration of pamidronate was not carcinogenic in an 80-week study in mice.

Target Organ Effects

Based on clinical use, possible target organs include the eyes, skeletal system, gastrointestinal system, cardiovascular system, central nervous system, blood, kidneys, and the fetus.

12. ECOLOGICAL INFORMATION

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|-------------------------------------|--|
| Aquatic Toxicity | **For pamidronate disodium, the no-observed-effect concentration (NOEC) = 15 mg/L in <i>Daphnia magna</i> (48-hour acute, static exposure). **MIC > 200 mg/L in a battery of microbial organisms. |
| Persistence/Biodegradability | **This material is not anticipated to persist in the aquatic environment. Pamidronate disodium degraded significantly in activated sewage sludge over a period of 14-21 days, with an estimated half-life is 9.9 days. |
| Bioaccumulation | Not determined. |
| Mobility in Soil | None |

**Teva Sicor MSDS

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 Number: | 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

| | |
|-------------------------|------------|
| TSCA Status | Exempt |
| CERCLA Status | Not listed |
| SARA 302 Status | Not listed |
| SARA 313 Status | Not listed |
| RCRA Status | Not listed |
| PROP 65 (Calif.) | Not listed |

Notes: TSCA, Toxic Substance Control Act; CERCLA, US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act; SARA, Superfund Amendments and Reauthorization Act; RCRA, US EPA, Resource Conservation and Recovery Act; Prop 65, California Proposition 65

U.S. OSHA Classification Possible Skin, Eye and Respiratory Irritant
 Reproductive Toxin
 Target Organ Toxin

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

| Hazard Class | Acute Oral Toxicity | Eye Irritation | Skin Irritation | Toxic to Reproduction | Target Organ Toxicity |
|-------------------------|---------------------|-----------------------|---|---|---|
| Hazard Category | Unclassified | 2B | 2 | 2 | 2 |
| Hazard Symbol | | |  |  |  |
| Signal Word | | Warning | Warning | Warning | Warning |
| Hazard Statement | | Causes eye irritation | Causes skin irritation | Suspected of damaging the unborn child | May cause damage to the eyes, skeletal system, gastrointestinal system, cardiovascular system, central nervous system, blood, and kidneys through prolonged or repeated exposure. |

GHS Precautionary Statements:




Prevention: Obtain special instructions before use.
 Do not handle until all safety precautions have been read and understood.
 Use personal protective equipment as required.
 Avoid breathing vapor or spray.
 In case of inadequate ventilation wear respiratory protection.
 Wear eye/face protection
 Wear protective gloves.
 Contaminated work clothing should not be allowed out of the workplace.
 Do not eat, drink or smoke when using this product.
 Wash hands thoroughly after handling.

Response: IF SWALLOWED: Immediately call a POISON CENTER or doctor. Rinse mouth.
 IF INHALED: If breathing is difficult, remove to fresh air and keep at rest in a position comfortable for breathing. If experiencing respiratory symptoms call a POISON CENTER or a doctor.
 IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs, seek medical attention. Take off contaminated clothing and wash before reuse. If skin irritation occurs, seek medical attention.
 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses if present and easy to do. Continue rinsing. Immediately call a POISON CENTER or doctor.

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 pamidronate disodium.

| | | | |
|------------------------------|--|---|---|
| Classification(s): | Harmful | Irritant | Toxic for Reproduction Category 2 |
| Symbol: |  |  |  |
| Indication of Danger: | Xn | Xi | T |
| Risk Phrases: | R22 - Harmful if swallowed R36/37/38 - Irritating to the eyes, respiratory system and skin R41 - Risk of serious damage to eyes R61 - May cause harm to the unborn child | | |
| Safety Phrases: | S23 - Do not breathe vapor or spray S24 - Avoid contact with the skin S25 - Avoid contact with eyes S26 - In case of contact with eyes, rinse immediately with plenty of water and seek medical advice. S36/37/39 - Wear suitable protective clothing, 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 ₅₀ | 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
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Disclaimer:

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