



TEVA PARENTERAL MEDICINES

Material Safety Data Sheet

Pamidronate Disodium Injection

1. PRODUCT IDENTIFICATION

Product Name Pamidronate Disodium Injection
Product Use Medical Treatment; Chemotherapeutic Agent (bone resorption inhibitor)
Manufacturer Teva Parenteral Medicines, Inc.
Address 11 Hughes
 Irvine, CA 92618-1902

Chemtrec Emergency No. 1-800-424-9300 (United States)
 1-202-483-7617 (International Collect)

Business Phone 1-800-729-9991
Website Address <http://www.newsicor.com>

Common Names Aredia™
Chemical Name Phosphoric acid (3-amino-1-hydroxy-propylidene)bis-,disodium salt, penta-hydrate

Chemical Formula C₃H₉NO₇P₂Na₂ · 5H₂O
Chemical Family Bisphosphonates
How Supplied 30mg/10 mL vial; 90mg/10 mL vial

Date of Preparation: December 18, 2005

2. COMPOSITION AND INGREDIENTS

CHEMICAL NAME	CAS#	% by weight		EXPOSURE LIMITS IN AIR				
		3 mg/ mL	9 mg/ mL	ACGIH		OSHA		IDLH
				TLV	STEL	PEL	STEL	
Pamidronate Disodium	57248-88-1	0.3	0.9	NE	NE	NE	NE	NE
Mannitol	69-65-8	4.7	3.75	NE	NE	NE	NE	NE
Phosphoric Acid or	7664-38-2	Trace	Trace	1 mg/m ³	3 mg/m ³	1 mg/m ³	NE	1000 mg/m ³
Sodium Hydroxide	1310-73-2			NE	2 mg/m ³ - C	2 mg/m ³	NE	10 mg/m ³
Water for Injection	7732-18-5	Balance	Balance	NE	NE	NE	NE	NE

NE - Not Established C - Ceiling Limit

NOTE: All WHMIS required information is included. It is located in appropriate sections based on the ANSI Z400.1 format

CHEMTREC NUMBER: Use only in the event of a chemical emergency involving a spill, leak, fire, exposure or accident involving this drug.

3. HAZARD IDENTIFICATION

EMERGENCY OVERVIEW: Material is a clear, colorless liquid. May be harmful if swallowed. Harmful to the fetus. May cause damage to the reproductive system, bone and kidneys. Avoid breathing vapor. Avoid exposure during pregnancy and while breastfeeding. Avoid contact with eyes, skin and clothing. Do not taste or swallow. Wash thoroughly after handling.

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3. HAZARD IDENTIFICATION cont...

Symptoms of Overexposure by Route of Exposure: This material is intended for injection under the supervision of physicians.

Inhalation: Inhalation of significant amounts of the product is not anticipated to occur because of the small size of individual containers.

Contact with Skin or Eyes: Contact may cause irritation. Effects may include stinging, watering, and redness, and swelling of the eyes and redness, itching, burning and skin damage.

Ingestion: Although ingestion is not an anticipated route of occupational exposure, this material is moderately toxic and may be harmful if swallowed. Symptoms similar to those identified under injection may occur.

Injection: Local redness and pain are the primary symptoms of accidental injection in an occupational setting. Medical personnel are not anticipated to experience over-exposures to the therapeutic doses of this product. However, effects including fever, hypertension, abdominal pain, nausea, vomiting, constipation, phlebitis, headache, dizziness, bone pain, and fluctuation in serum calcium and mineral levels may occur. See package insert for adverse reactions associated with therapeutic doses of this product.

Health Effects or Risks From Exposure (An explanation in lay terms):

Acute: The primary health effects anticipated in an occupational setting include irritation of eyes and skin as well as redness and local swelling after accidental injection. In case of over-exposure by injection, effects such as fever, hypertension, abdominal pain, nausea, vomiting, constipation, phlebitis, headache, dizziness, bone pain, and fluctuation in serum calcium and mineral levels may occur.

Cancer: Animal studies suggest no carcinogenic potential (see Section 11).

Chronic: This product has caused developmental and reproductive effects in animals (see Section 11).

Target Organs: This product may produce adverse effects on the kidneys and bone (see Section 11).

Pre-Existing Medical Conditions: Conditions aggravated by exposure may include reproductive, kidney and bone disorders. This material is contraindicated in patients with clinically significant hypersensitivity to it or other bisphosphonates.

4. FIRST-AID MEASURES

Skin Exposure: Remove contaminated shoes and clothing and cleanse affected area(s) thoroughly by washing with mild soap and water. If irritation or redness develops and persists, seek medical attention.

Eye Exposure: If irritation or redness develops, move victim away from exposure and into fresh air. Flush eyes with clean water and seek medical attention. For direct contact, hold eyelids apart and flush the affected eye(s) with clean water for at least 15 minutes. Seek medical attention.

Inhalation: Immediately move victim away from exposure and into fresh air. If respiratory symptoms or other symptoms of exposure develop, seek immediate medical attention. If victim is not breathing, clear airway and immediately begin artificial respiration. If breathing difficulties develop, oxygen should be administered by qualified personnel. Seek immediate medical attention.

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7. HANDLING and STORAGE

Work and Hygiene Practices: As with all chemicals, avoid getting this product ON YOU or IN YOU. Do not eat, drink, smoke or apply cosmetics while handling the product. Wash hands thoroughly after handling.

Particular care in working with this product must be practiced in pharmacies and other preparation areas, during manufacture of this product, and during patient administration. Precautions should be taken during the following activities:

- Withdrawal of needles from drug vials.
- Drug transfers using syringes and needles or filter straws.
- Expulsion of air from drug-filled syringes.

Storage and Handling Practices: Employees must be trained to properly use the product. Ensure vials are properly labeled. Store only in approved containers. Keep away from sources of ignition and any incompatible materials or conditions (see Section 10). Protect from light and do not store above 30°C (86°F).

Protective Practices During Maintenance of Contaminated Equipment: When cleaning non-disposable equipment, wear latex or nitrile gloves (double gloving is recommended), goggles, and lab coat. Wash equipment with soap and water. All needles, syringes, vials and other disposable items contaminated with this product should be disposed of properly.

8. EXPOSURE CONTROLS - PERSONAL PROTECTION

Ventilation and Engineering Controls: Use with adequate ventilation. Follow standard medical product handling procedures.

Respiratory Protection: Not normally required for routine, medical administration of this product. A NIOSH certified air-purifying respirator with a type 95 filter may be used under conditions where airborne concentrations are expected to be excessive. Protection provided by air purifying respirators is limited (see manufacturer's respirator selection guide). Use a positive pressure air supplied respirator if there is potential for uncontrolled release, exposure levels are not known, or any other circumstances 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 warrant a respirator's use.

Eye Protection: Approved eye protection to safeguard against potential eye contact, irritation or injury is recommended. Depending on conditions of use, a face shield may be necessary.

Hand Protection: Use latex, nitrile, or rubber gloves. Check gloves for leaks. Wash hands before and after using gloves.

Body Protection: No special body protection required for routine, medical administration of this product. Wear lab coat, gown, or smock, as appropriate for procedure.

Product Preparation Instructions for Medical Personnel: Follow standard procedure for handling pharmaceutical materials and recommendations presented on the Package Insert.

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9. PHYSICAL and CHEMICAL PROPERTIES

Relative Vapor Density (air = 1):	ND	Evaporation Rate (n-BuAc=1):	ND
Specific Gravity (water = 1):	ND	Melting/Freezing Point:	ND
Solubility in Water:	Soluble	Boiling Point:	ND
Vapor Pressure, mm Hg @ 25°C.	ND	pH:	6.0-7.4
Odor Threshold: Odorless			
Appearance and Color: Clear, colorless solution			

ND = No Data

10. STABILITY and REACTIVITY

Stability: Stable under normal conditions of storage and handling.

Materials With Which Substance is Incompatible: This product is generally compatible with other common materials in a medical facility.

Hazardous Polymerization: Will not occur.

Hazardous Combustion Products: Heat may cause product to decompose, destroying the product or producing toxic fumes.

11. TOXICOLOGICAL INFORMATION

Toxicity Data: The following information is for Pamidronate Disodium, the active ingredient:

Oral LD50(mouse) =625 mg/kg IP LD50 (mouse) = 45 mg/kg
 IV LD50 (rat) = 50 mg/kg IV LD50 (mouse) = 190 mg/kg

Suspected Cancer Agent: In a 104-week carcinogenicity study (daily oral administration) in rats, there was a positive dose response relationship for benign adrenal pheochromocytoma in males. Although this condition was also observed in females, the incidence was not statistically significant. When the dose calculations were adjusted to account for the limited oral bioavailability of pamidronate in rats, the lowest daily dose associated with adrenal pheochromocytoma was similar to the intended clinical dose. Adrenal pheochromocytoma was also observed in low numbers in the control animals and is considered a relatively common spontaneous neoplasm in the rat. Pamidronate (daily oral administration) was not carcinogenic in an 80-week study in mice. This product, as well as all components, has **NOT** been identified as carcinogens by NTP, IARC or OSHA.

Irritancy of Product: This product may be irritating to contaminated skin, eyes and other tissues. The active ingredient is severely irritating to the eyes and moderately irritating to the skin of albino rabbits.



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11. TOXICOLOGICAL INFORMATION cont...

Sensitization to the Product: Rare instances of allergic reaction have occurred from clinical use. No data on allergic sensitization potential from repeated skin contact.

Target Organ(s): Cats and dogs given one hour I.V. infusion of doses of 2-20 mg/kg once a week for 3 months demonstrated toxicity to the kidney including increased BUN and creatinine levels and tubular degeneration and necrosis. It has also demonstrated varying degrees of renal impairment in humans. Osteoclastic hyperactivity resulting in excessive bone resorption can occur.

Reproductive Toxicity Information: Listed below is information concerning the effects of Pamidronate Disodium on human and animal reproductive systems. This material is classified as a Pregnancy Category D (Positive Evidence of Risk):

Mutagenicity: Pamidronate was nonmutagenic in six mutagenicity assays: Ames test, Salmonella and Escherichia/liver- microsome test, nucleus-anomaly test, sister-chromatid-exchange study, point-mutation test, and micronucleus test in the rat.

Embryotoxicity/Teratogenicity/Reproductive Toxicity: In rats, decreased fertility occurred in first-generation offspring of parents who had received 150 mg/kg/day orally; however, this occurred only when animals were mated with members of the same dose group. Bolus intravenous studies conducted in rats and rabbits determined that pamidronate produces maternal toxicity and embryo/fetal effects when given during organogenesis at doses of 0.6 to 8.3 times the highest recommended human dose for a single intravenous infusion. Pamidronate given orally or intravenously to rats and rabbits during organogenesis and found at 150 mg per kg orally or 6-15 mg per kg intravenously delayed ossification. Shortening of long bones was found in rats after intravenous doses in rats of 12-15 mg per kg. Dilated renal pelvices and ureters were found in the offspring of dams treated intravenously. Delayed and prolonged parturition was also found in rats secondary to hypocalcemia.

ACGIH Biological Exposure Indices: Currently there are no Biological Exposure Indices (BEIs) associated with the components of this product.

12. ECOLOGICAL INFORMATION

All work practices must be aimed at eliminating environmental contamination.

Environmental Stability: This product will be relatively stable under ambient environmental conditions.

Acute Toxicity to Invertebrates: *Daphnia magna*, 48 hour static acute, NOEC = 15mg/L (active ingredient)

Microbial Growth Inhibition (active ingredient):



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12. ECOLOGICAL INFORMATION cont...

<u>Species</u>	<u>Minimum Inhibitory Concentration (mg/l)</u>
<i>Aspergillus niger</i>	>1000
<i>Trichoderma viride</i>	>1000
<i>Clostridium perfringens</i>	200
<i>Bacillus subtilis</i>	200
<i>Nostoc sp.</i>	>1000

Chemical Fate Information (for active ingredient):

Pamidronate disodium degrades significantly in activated sewage sludge over a period of 14 to 21 days. The estimated half-life is 9.90 days. This substance would not be expected to persist in the environment when the primary route of introduction is via domestic sewage treatment systems.

13. DISPOSAL CONSIDERATIONS

Preparing Wastes for Disposal: This material, if discarded as produced, is not a RCRA "listed" or "characteristic" hazardous waste. Use resulting in chemical or physical change or contamination may subject it to regulation as a hazardous waste. Along with properly characterizing all waste materials consult state and local regulations regarding the proper disposal of this material.

U.S. EPA Waste Number: None

14. TRANSPORTATION INFORMATION

This Materials is not Hazardous as Defined by 49 CFR 172.101 by the U. S. Department of Transportation

Proper Shipping Name: Not applicable

Hazard Class Number and Description: Not applicable

UN Identification Number: Not applicable

Packing Group: Not applicable

DOT Label(s) Required: Not applicable

North American Emergency Response Guidebook Number (1996): Not applicable.

MARINE POLLUTANT: No component of this product is listed as a Marine Pollutant (49 CFR 172.101, Appendix B)

Transport Canada Transportation of Dangerous Goods Regulations: Not applicable

15. REGULATORY INFORMATION

U.S. REGULATIONS

U.S. SARA Reporting Requirements: The components of this product are not subject to the reporting requirements of Sections 302, 304 and 313 of Title II of the Superfund Amendments and Reauthorization Act.

U.S. SARA Threshold Planning Quantity: Not applicable



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15. REGULATORY INFORMATION cont...

U.S. CERCLA Reportable Quantities (RQ): Not applicable

U.S. TSCA Inventory Status: Pamidronate Disodium is a "drug" as defined by the Federal Food, Drug and Cosmetic Act and is therefore not a chemical substance under TSCA.

California Safe Drinking Water and Toxic Enforcement Act (Proposition 65): This product does NOT contain a chemical known to the State of California to cause developmental and reproductive effects.

Other U.S. Federal Regulations: Based on this product's use, the requirements of the OSHA Bloodborne pathogen Standard (29 CFR 1910.1030) are applicable.

CANADIAN REGULATIONS

Canadian DSL/NDSL Status: Pamidronate Disodium is regulated by the Food and Drug Administration of Health Canada and is therefore exempt from the requirements of CEPA.

ANSI Labeling (Based on 129.1, Provided to Summarize Occupational Exposure Hazards): **CAUTION!** MAY BE HARMFUL IF SWALLOWED. HARMFUL TO THE FETUS. MAY CAUSE DAMAGE TO THE REPRODUCTIVE SYSTEM, KIDNEYS AND BONE. Pamidronate Disodium should be administered under the supervision of a qualified physician. Avoid exposure during pregnancy and while breastfeeding. Avoid over-exposure. Avoid breathing vapor. Avoid contact with eyes, skin and clothing. Do not eat, drink or smoke when handling Pamidronate Disodium. Do not taste or swallow. Wash thoroughly after handling. Clean up spills promptly.

16. OTHER INFORMATION

Issue Date: 5/25/07

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