Section 1 - Chemical Product and Company

Distributor:
Sagent Pharmaceuticals, Inc.
1901 N. Roselle Rd, Suite 700
Schaumburg, IL 60195
847-908-1600

Emergency Telephone: 866-625-1618

Product Identifier: Pamidronate Disodium Injection, USP
Product Code: NDC 25021-802-10
NDC 25021-803-10
Common/Trade Name: Aredia®
Chemical Name: Phosphoric acid (3-amino-1-hydroxy-propylidene)bis-disodium salt, penta-hydrate
Chemical Family: Biphosphonate
Product Use: Pharmaceutical
Product Type: Regulated Prescription Drug
Container Information: Vials

Section 2 - Composition / Information on Ingredients

Ingredient	CAS No.	Weight %		Exposure Limits In Air				
		3 mg/ mL	9 mg/ mL	ACHIH		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 and/or Sodium Hydroxide	7664-38-2 1310-73-2	Trace	Trace	1 mg/m^3 NE	3 mg/m^3 2mg/m^3-C	1 mg/m^3 2 mg/m^3	NE NE	1000 mg/m^3 10mg/m^3
Water for Injection	7732-18-5	Balance	Balance	NE	NE	NE	NE	NE

NE - Not Established C – Ceiling Limit

Section 3 - Hazards Identification

Primary Physical and Health Hazards: 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.

Routes of Entry: Skin, inhalation, ingestion and injection

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

Chemical Listed as Carcinogen: **NTP:** No **IARC:** No **OSHA:** No

Medical Conditions Generally Aggravated by Exposure: 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 biphosphonates.

Section 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.

Ingestion: If swallowed, seek emergency medical attention. If victim is drowsy or unconscious and vomiting, place on the left side with the head down and DO NOT give anything by mouth. If not vomiting and professional advice is not available, DO NOT induce vomiting. If possible, do not leave victim unattended and observe closely for adequacy of breathing.

Inhalation: If respiratory symptoms develop, move victim away from source of exposure and into fresh air. If symptoms persist, seek 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.

Injection Local redness and pain are the primary symptoms of accidental injection in an occupational setting. Medical personnel are not anticipated to experience over-exposure 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.

Notes to Physician: See patient package insert in shipping carton for complete information.

Section 5 - Fire Fighting Measures

Flash Point: Non-flammable

Autoignition Temperature: Not applicable

Flammable Limits in Air: Lower %: Not established
Upper %: Not established

Flammable Limits: Not established

Extinguishing Media: Use extinguishing agent suitable for type of surrounding fire.

Special Fire Fighting Procedures: For fires beyond the incipient stage, emergency responders in the immediate hazard area should wear bunker gear. When the potential chemical hazard is unknown, in enclosed or confined spaces, or when explicitly required by DOT, a self-contained breathing apparatus should be worn. In addition, wear other appropriate protective equipment as conditions warrant (see Section 8). Isolate immediate hazard area and keep unauthorized personnel out. Contain spill if it can be done with minimal risk. Move undamaged containers from immediate hazard area if it can be done with minimal risk. Cool equipment exposed to fire with water, if it can be done with minimal risk.

Unusual Fire/Explosion Hazards: No unusual fire or explosion hazards are expected.

Section 6 - Accidental Release Measures

Spill: For small releases of this material, wear latex or nitrile gloves and safety glasses. Absorb spilled liquid and rinse area thoroughly with soap and water.

Release to Air: Wear appropriate protective equipment including respiratory protection as conditions warrant (see Section 8).

Release to Water: Refer to local water authority. Drain disposal is not recommended; refer to local, state, and federal disposal guidelines.

Section 7 - Handling and Storage

General Handling: As with all chemicals, avoid getting this material 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 withdrawal of needles from drug vials, drug transfer using syringes and needles or filter straws and expulsion of air from drug-filled syringes.

Waste Disposal Method: 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 material should be disposed of properly.

Storage Conditions: Protect from light and store at controlled room temperature 20°-25°C (68°-77°F). Follow instructions provided in packaging. Keep away from sources of ignition and any incompatible materials or conditions.

Section 8 - Exposure Controls / Personal Protection

Respiratory Protection: Not normally required for routine, medical administration or this material. 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 29 CFR 1910.467 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.

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

Skin Protection: Use latex, nitrile, or rubber gloves. Check gloves for leaks. Wash hands before and after using gloves. No special body protection required for routine, medical administration of this product. Wear lab coat, gown, or smock, as appropriate for procedure.

Other Protective Equipment: Not applicable

Additional Exposure Precautions: Follow standard procedure for handling pharmaceutical materials and recommendations presented on the Package Insert.

Section 9 - Physical and Chemical Properties

Physical State:	Liquid	**Specific Gravity:**	Approx to water
Appearance and Odor:	Clear, odorless	**Evaporation Rate:**	Approx to water
Boiling Point:	Not available	**Solubility in Water:**	Miscible
Vapor Pressure:	Not available	**pH:**	6.0-7.4
Vapor Density:	Not available	**Molecular Weight:**	369.1

Section 10 - Stability and Reactivity

Stability: Stable under normal conditions of storage and handling.

Incompatibility (Materials to avoid): This product is generally compatible with other common materials in a medical facility.

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

Hazardous Polymerization: Will not occur

Section 11 - Toxicological Information

Acute Toxicity

Component	Type	Route	Species	Dosage
Pamidronate Disodium	LD_{50}	Oral	Mouse	625 mg/kg
Pamidronate Disodium	LD_{50}	IV	Rat	50 mg/kg
Pamidronate Disodium	LD_{50}	Oral	Rat	1560 mg/kg
Pamidronate Disodium	LD_{50}	IP	Mouse	45 mg/kg
Pamidronate Disodium	LD_{50}	IV	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 therat. 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.

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, nuclesu-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 150mg/kg/day orally; this occurred only when animals were mated with members of the same dose group. Bouls 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.

Section 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):

Species	Minimum Inhibitory Concentration (mg/l)
Aspergillus niger	> 1000
Trichoderma viride	> 1000
Clostidium perfringens	200
Bacillus subtilis	200
Nostoc sp.	> 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 introdcution is via domestic sewage treatment systems.

Section 13 - Disposal Considerations

Waste 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.

Section 14 - Transport Information

Regulatory Organizations:
DOT: Not Regulated
ICAO/IATA: Not Regulated
IMO: Not Regulated

Section 15 - Regulatory Information

Below is selected regulatory information chosen primarily for possible Sagent usage. This section is not a complete analysis or reference to all applicable regulatory information. Please consider all applicable laws and regulations for your country/state.
U.S. Regulations
TSCA - *No*
CERCLA - *Not on this list*

SARA 302, 304 - *Not on this list*
SARA 313 - *Not on this list*
OSHA Substance Specific – *Bloodborne pathogen Standard (29 CFR 1910.1030)*

Section 16 - Other Information

As of the date of issuance, we are providing available information relevant to the handling of this material in the workplace. All information contained herein is offered with the good faith belief that it is accurate. THIS MATERIAL SAFETY DATA SHEET SHALL NOT BE DEEMED TO CREATE ANY WARRANTY OF ANY KIND (INCLUDING WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE). In the event of an adverse incident associated with this material, this safety data sheet is not intended to be a substitute for consultation with appropriately trained personnel. Nor is this safety data sheet intended to be a substitute for product literature which may accompany the finished product.

For additional information contact:
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Glossary: This glossary contains definitions of general terms used in MSDSs. Not all of these Glossary Terms will apply to this MSDS.

ACGIH	American Conference of Governmental Industrial Hygienists
AIHA	American Industrial Hygiene Association
CAS Number	Chemical Abstract Service Registry Number
CERCLA	Comprehensive Environmental Response Compensation and Liability Act (of 1980)
CHAN	Chemical Hazard Alert Notice
CHEMTREC	Chemical Transportation Emergency Center
DOT	Department of Transportation
EPA	Environmental Protection Agency
HEPA	High Efficiency Particulate Air (Filter)
IARC	International Agency for Research on Cancer
ICAO/IATA	International Civil Aviation Organization/International Air Transport Association
IMO	International Maritime Organization
KOW	Octanol/Water Partition Coefficient
LEL	Lower Explosive Limit
MSDS	Material Safety Data Sheet
MSHA	Mine Safety and Health Administration
NA	Not Applicable, except in Section 14 where NA = North America
NE	Not Established
NADA	New Animal Drug Application
NAIF	No Applicable Information Found
NCI	National Cancer Institute
NIOSH	National Institute for Occupational Safety and Health
NOS	Not Otherwise Specified
NTP	National Toxicology Program
OSHA	Occupational Safety and Health Administration
OEL	Occupational Exposure Limit
PEL	Permissible Exposure Limit (OSHA)
RCRA	Resource Conservation and Recovery Act
RQ	Reportable Quantity
RTECS	Registry of Toxic Effects of Chemical Substances
SARA	Superfund Amendments and Reauthorization Act
STEL	Short Term Exposure Limit
TLV	Threshold Limit Value (ACGIH)
TPQ	Threshold Planning Quantity
TSCA	Toxic Substances Control Act
TWA	Time Weighted Average/8 Hours Unless Otherwise Noted
UEL	Upper Explosive Limit
UN	United Nations
USP	United States Pharmacopeia
WEEL	Workplace Environmental Exposure Level (AIHA)