SAFETY DATA SHEET

Product Name: Zoledronic Acid Injection Concentrate for Intravenous Infusion

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

Manufacturer Name And Address	Hospira, Inc. 275 North Field Drive Lake Forest, Illinois 60045 USA
Emergency Telephone	CHEMTREC: North America: 800-424-9300; International 1-703-527-3887; Australia - 61-290372994; UK - 44-870-8200418
Hospira, Inc., Non-Emergency	224 212-2000
ProductName	Zoledronic Acid Injection Concentrate for Intravenous Infusion
Synonyms	(1-Hydroxy-2-imidazol-1-yl-phosphonoethyl) phosphonic acid monohydrate; Phosphonic acid, (1-hydroxy-2-(1H-imidazol-1-yl)ethylidene)bis-, hydrate (1:1); (1-Hydroxy-2-imidazol-1-yl-phosphonoethyl) phosphonic acid monohydrate.

2. HAZARD(S) IDENTIFICATION

Emergency Overview

Zoledronic Acid Injection Concentrate for Intravenous Infusion is a solution containing zoledronic acid, a bone resorption inhibitor used clinically to treat patients with advanced bone malignancies. In the workplace, this material should be considered a potential reproductive hazard, and a potent drug. Based on clinical use, possible target organs include the skeletal system, kidneys, gastrointestinal system, and blood.

U.S. OSHA GHS Classification

Physical Hazards	**Hazard Class**	**Hazard Category**
	Not Classified	Not Classified

Health Hazards	**Hazard Class**	**Hazard Category**
	Toxic to Reproduction	2
	STOT - RE	2

Label Element(s)

Pictogram

Signal Word: Warning

Hazard Statement(s)

Suspected of damaging fertility or the unborn child
May cause damage to organs through prolonged or repeated exposure

Precautionary Statement(s)

Prevention

Obtain special instructions before use
Do not handle until all safety precautions have been read and understood
Wear protective gloves/protective clothing/eye protection/face protection
Do not breathe vapor or spray
Wash hands thoroughly after handling

Response

Get medical attention if you feel unwell.

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.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient Name Zoledronic Acid Monohydrate
Chemical Formula $C_5H_{10}N_2O_7P_2 \bullet H_2O$

Component	Approximate Percent by Weight	CAS Number	RTECS Number
Zoledronic Acid Monohydrate	<0.1	165800-06-6	NA

Non-hazardous ingredients include mannitol and Water for Injection. Hazardous ingredients present at less than 1% may include sodium citrate dihydrate.

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 such as carbon dioxide, dry chemical extinguishing powder or foam.

Special Fire Fighting Procedures No special provisions required beyond normal firefighting 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 control 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 for hazard control under conditions of normal product use.

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

	Exposure Limits			
Component	**OSHA-PEL**	**ACGIH-TLV**	**AIHA WEEL**	**Hospira EEL**
Zoledronic Acid Monohydrate	8-hr TWA: Not Established	8-hr TWA: Not Established	8-hr TWA: Not Established	8-hr TWA: Not Established

Notes: OSHA PEL: US Occupational Safety and Health Administration – Permissible Exposure Limit
ACGIH TLV: American Conference of Governmental Industrial Hygienists – Threshold Limit Value.
AIHA WEEL: Workplace Environmental Exposure Level
EEL: Employee Exposure Limit.
TWA: 8-hour Time Weighted Average.

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 material formulation is likely, the use of latex or nitrile gloves is recommended.

Eye Protection 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 clinical use of this product.

9. PHYSICAL/CHEMICAL PROPERTIES

Appearance/Physical State	A clear colorless solution
Odor	NA
Odor Threshold	NA
pH	The pH of various formulations ranges from 5.5 to 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
Relative Density	NA
Solubility	Highly soluble in 0.1N sodium hydroxide solution, sparingly soluble in water and 0.1N hydrochloric acid, and practically insoluble in organic solvents.
Partition Coefficient: n-octanol/water	NA
Auto-ignition Temperature	NA
Decomposition Temperature	NA
Viscosity	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 phosphorus oxides (POx).

Hazardous Polymerization Not anticipated to occur with this material.

11. TOXICOLOGICAL INFORMATION

Acute Toxicity - Not determined for the product formulation. Information for the ingredients is as follows:

Ingredient(s)	Percent	Test Type	Route of Administration	Value	Units	Species
Zoledronic Acid	100	LD50	Intravenous	13	mg/kg	Rat
Zoledronic Acid	100	LD50	Oral	> 200	mg/kg	Rat

LD50 is the dosage producing 50% mortality.

Occupational Exposure Potential Information on the absorption of this product via inhalation or skin contact is not available. Avoid the generation of aerosols and inadvertent contact with the skin, eyes, or mucus membranes.

Signs and Symptoms None anticipated from normal handling of this product. This material should be considered a potential reproductive hazard, and a potent drug. In clinical use, common adverse events include fever, fatigue, and flu-like symptoms including chills, bone pain and/or arthralgias, and myalgias. Headache, nausea and vomiting have been reported as well. Renal insufficiency and renal failure have occurred after single dose. Anemia and thrombocytopenia may also occur. In some patients, treatment has produced severe hypocalcemia with tetany and paresthesia. Rare cases of rash, pruritus, and chest pain have been reported. As with other bisphosphonates, occurrences of conjunctivitis and hypomagnesemia have been reported following treatment.

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.

Dermal or Respiratory Sensitization None anticipated from normal handling of this product. In clinical use, rare cases of rash, pruritus, and chest pain have been reported.

Reproductive Effects None anticipated from normal handling of this product. Female rats were given zoledronic acid subcutaneously at dosages of 0.01, 0.03, or 0.1 mg/kg/day beginning 15 days before mating and continuing through gestation. In the high-dosage group, adverse effects included inhibition of ovulation and a decrease in the number of pregnant rats. Effects in both the mid- and high-dosage groups included an increase in pre-implantation losses and a decrease in the number of implantations and live fetuses.

11. TOXICOLOGICAL INFORMATION: continued

Reproductive Effects: continued	Zoledronic acid was given subcutaneously to female rats at dosages of 0.01, 0.03, or 0.1 mg/kg/day beginning 15 days before mating and continuing through gestation. In the mid- and high-dosage groups, the number of stillbirths was increased and survival of neonates was decreased. Adverse maternal effects were noted in all dosage groups and may have been related to drug-induced periparturient hypocalcemia. In pregnant rats given zoledronic acid subcutaneously at dosages of 0.1, 0.2, or 0.4 mg/kg/day during gestation, adverse fetal effects noted in the mid- and high-dose groups included increases in pre- and post-implantation losses, decreases in viable fetuses, and fetal skeletal, visceral, and external malformations. Skeletal variations were also observed in the low-dose group. Signs of maternal toxicity were observed in the high-dosage group indicating that maximal exposure levels were achieved in this study. When pregnant rabbits given zoledronic acid subcutaneously at dosages of 0.01, 0.03, or 0.1 mg/kg/day during gestation, no adverse fetal effects were observed. However, maternal mortality and abortion occurred in all treatment groups and may have been caused by drug-induced hypocalcemia. US FDA Pregnancy Category D.
Mutagenicity	Zoledronic acid was not genotoxic in the Ames bacterial mutagenicity assay, in the Chinese hamster ovary cell assay, or in the Chinese hamster gene mutation assay, with or without metabolic activation. Zoledronic acid was also not genotoxic in the *in vivo* rat micronucleus assay.
Carcinogenicity	Standard lifetime carcinogenicity bioassays were conducted in mice and rats. Mice were given zoledronic acid orally at dosages of 0.1, 0.5, or 2.0 mg/kg/day. There was an increased incidence of Harderian gland adenomas in males and females in all treatment groups. In a similar study, rats were given zoledronic acid orally at dosages of 0.1, 0.5, or 2.0 mg/kg/day. No increased incidence of tumors was observed.
Carcinogen Lists	**IARC:** Not listed **NTP:** Not listed **OSHA:** Not listed
Specific Target Organ Toxicity – Single Exposure	NA
Specific Target Organ Toxicity – Repeat Exposure	Based on clinical use, possible target organs include the skeletal system, kidneys, gastrointestinal system, and blood.

12. ECOLOGICAL INFORMATION

***Aquatic Toxicity**	Not determined for product. Information for the active ingredient is as follows: EC50(48hr) > 18 mg/L in Daphnia magna for zoledronic acid. EbC50(72hr) = 5 mg/L Selenastrum capricornutum (green algae) for zoledronic acid. ErC50(72hr) = 15 mg/L in Selenastrum capricornutum (green algae) for zoledronic acid. EC50(30 min) = 100 mg/L for bacterial respiration inhibition in activated sludge for zoledronic acid.
***Persistence/Biodegradability**	Not determined for product. Information for the active ingredient is as follows: Aerobic Degradation ≤ 3% after 28 days for zoledronic acid. Not readily biodegradable
Bioaccumulation	Not determined for product.
Mobility in Soil	Not determined for product.

*Novartis SDS for Zometa

Notes:

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
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

US TSCA Status	Exempt.
US CERCLA Status	Not listed
US SARA 302 Status	Not listed
US SARA 313 Status	Not listed
US RCRA Status	Not listed
US 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

GHS/CLP 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	Hazard Category	Pictogram	Signal Word	Hazard Statement
NA	NA	NA	NA	NA

Prevention

Obtain special instructions before use
Do not handle until all safety precautions have been read and understood
Wear protective gloves/protective clothing/eye protection/face protection
Do not breathe vapor or spray
Wash hands thoroughly after handling

Response

Get medical attention if you feel unwell.

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.

15. REGULATORY INFORMATION: continued

EU Classification*	*Medicinal products are exempt from the requirements of the EU Dangerous Preparations Directive.
Classification(s)	NA
Symbol	NA
Indication of Danger	NA
Risk Phrases	NA
Safety Phrases	S23: Do not breathe vapor/spray S24: Avoid contact with the skin S25: Avoid contact with 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
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
STOT - SE	Specific Target Organ Toxicity – Single Exposure
STOT - RE	Specific Target Organ Toxicity – Repeated Exposure
TSCA	Toxic Substance Control Act
TWA	8-hour Time Weighted Average

MSDS Coordinator: Hospira GEHS
Date Prepared: June 04, 2013
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