MATERIAL SAFETY DATA SHEET

Fosphenytoin Sodium Injection, USP

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Section I – Chemical Product & Company Identification

Product Identification Fosphenytoin Sodium Injection, USP, 75mg/mL [50mg PE*/mL (PE = Phenytoin sodium equivalent)]			WHMIS classification
General Use Anti-convulsant, sodium channel inhibitor			Type of container Vials
Manufacturer's Name Hikma Farmacêutica, S.A.			Supplier's Information This material is intended for IV or IM injection under the supervision of physicians
Manufacturer's Address Estrada do Rio da Mó, 8, 8A, 8B, Fervença			
City Terrugem SINTRA	Postal Code 2705-906	Country Portugal	MSDS Preparer's name AMBR
Phone 351 219608410	E-mail geral@hikma.pt	Fax 351 21 961 51 02	Date of MSDS December 2009
Other useful information 5,5-diphenyl-3-[(phosphonooxy)methyl]-2,4- imidazolidinedione disodium salt			

Section II - Composition/Information on Ingredients

Hazardous Ingredients	% (by weight)	CAS identification	LD_{50} (species and route)	LC_{50} (species)
Fosphenytoin Sodium	7.5%	92134-98-0		

Tromethamine	1.2%	77-86-1		
Water for Injection USP	QS	7732-18-5		

Hydrochloric acid and/or sodium hydroxide added for pH adjustment

Section III - Hazards Identification & Emergency Overview

Route of entry

Skin ☒ Eye ☒ Inhalation ☒ Ingestion ☒

Emergency Overview

Harmful by inhalation, in contact with skin and if swallowed. May cause skin, eye, and respiratory tract irritation. May cause drowsiness and dizziness. May cause adverse cardiovascular effects. May cause central nervous system depression. May casuse adverse liver effects. May cause adverse effects on the bone marrow and blood-forming system. Contains a known or suspected reporductive toxin. May cause harm to the unborn child.

Potential Health Effects

Acute Toxicity

Eye – May cause irritation.

Skin – May cause irritation. May be absorbed through the skin in harmful amounts.

Inhalation – Not an expected route of exposure. Inhalation of vapour in high concentration may cause irritation of respiratory system. May cause additional effects as listed under “Ingestion”

Ingestion – Toxic if swallowed. Ingestion may cause gastrointestinal irritation. May cause adverse effects on bone marrow and blood-forming system. May cause adverse liver effects. May cause adverse kidney effects. May cause adverse cardiac effects.

Over Exposure by Injection

Chronic adverse effects may include bleeding, tender and enlarged gums, muscle pain, enlargement of facial features, swelling of breasts in males, excessive hair growth on body and face, and insomnia. Formate and phosphate metabolites of fosphenytoin may contribute to overdose toxicity. Formate toxicity is associated with severe anion-gap metabolic acidosis. Hypocalcemia may result from large increases in phosphate concentrations.

Medical Conditions Aggravated by Exposure

Allergies, neurological disorders, liver disorders, kidney disorders, blood disorders, and cardiovascular disease. Use of alcoholic beverages may enhance toxic effects.

Interactions with other Chemicals

Use of alcoholic beverages may enhance toxic effects. Note: Persons sensitive to hydantoin anticonvulsants, barbiturates, succinimides, or oxazolidinediones may experience cross-sensitivity to this material

Warning Symbols

Section IV - First Aid Measures

Skin Contact

For minor skin contact, avoid spreading material on unaffected skin. Wash with mild soap and water.

Eye Contact

In case of contact with substance, immediately flush skin or eyes with running water for at least 20 minutes.

Inhalation

Move victim to fresh air. Apply artificial respiration if victim is not breathing. Administer oxygen if breathing is difficult.

Ingestion

Call a physician or Poison Control Center immediately. Never give anything by mouth to an unconscious person. Do not induce vomiting without medical advice.

Antidotes	Other Measures
	Call 911 or emergency medical service. Remove and isolate contaminated clothing and shoes. Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves. Do not use mouth-to-mouth method if victim ingested or inhaled the substance; induce artificial respiration with the aid of a pocket mask with one way valve or other proper respiratory medical device. Use during pregnancy is contraindicated. Keep victim warm and quiet. Effects of exposure (inhalation, ingestion or skin contact) to substance may be delayed. See clinical drug insert information for treatment of overdose.

Section V - Fire Fighting Measures

Flammable YES ☐ NO ☒	If yes, under which conditions?	
Means of Extinction Use water or a type ABC multi-purpose extinguisher.		
Flashpoint (ºC.) and Method Non-flamable	Upper flammable limit (% by volume) Not Applicable	Lower flammable limit (% by volume) Not Applicable
Auto ignition (ºC.) None	Explosion Data – Impact None	Explosion Data – Static Discharge None
Hazardous Combustion Products None		
Fire Fighting Recommendations (specific if necessary) As with any fire, evacuate personnel to a safe area. Fire-fighters should wear self-contained breathing apparatus to avoid smoke inhalation. Product is aqueous- based and is not expected to present a fire hazard concern.		

Section VI - Accidental Release Measures

Leak and Spill Procedures Prevent further leakage or spillage if safe to do so. Absorb with earth, sand or other non-combustible material and transfer to containers for later disposal.
General Precautions (Fire, Environmental and Personal) Use personal protective equipment. Do not touch damaged containers or spilled material unless wearing appropriate protective clothing
Decontamination Soak up with absorbent material. Keep in suitable and closed containers for disposal. Clean contaminated surface thoroughly. After cleaning, flush away traces with water

Section VII - Handling & Storage

Handling Procedures & Equipment Handle in accordance with good industrial hygiene and safety practices. Avoid contact with skin and eyes. Do not breathe vapors or spray mist.
Storage Requirements Store under refrigeration at 2ºC to 8ºC (36ºF to 46ºF). Keep away from heat. Protect from light. Keep out of the reach of children

Section VIII - Exposure Controls & Personal Protection

Exposure Limits ACGIH TLV ☐ OSHA PEL ☐ Other (specify) ☐
Specific Engineering Controls (ventilation, enclosed process, etc) Showers, eyewash stations, and ventilation systems.
Personal Protective Equipment Gloves ☒ Respirator ☒ Eye ☒ Footwear ☐ Clothing ☒ Other ☐
Specify type of checked equipment **Respiratory Protection:** If irritation is experienced, NIOSH/MSHA approved respiratory protection should be worn. Positive-pressure supplied air respirators may be required for high airborne contaminant concentrations. Respiratory protection must be provided in accordance with current local regulations. **Ventilation:** Handle product in a well-ventilated area. **Protective Gloves:** Impervious gloves **Eye Protection:** Safety glasses with side-shields. **Other Protective Clothing or Equipment:** Lab coat

Hygiene Measures
Handle in accordance with good industrial hygiene and safety practice. Avoid contact with skin, eyes and clothing.

Section IX - Physical & Chemical Properties

Physical State (STP) Liquid	Odour & Appearance Clear, colorless to yellow, odorless	Odour Threshold (ppm)
Specific Gravity Approximate to water	Vapour Density (air=1) Approximate to water	Vapour Pressure (mmHg) Approximate to water
Evaporation Rate Unknown	Boiling Point (ºC.) 100ºC/ 212ºF	Freezing Point (ºC.)
pH 8.3-9.3	Coefficient of Water/Oil distribution	Solubility in water Soluble in water

Section X - Stability & Reactivity Data

Chemical Stability YES ☒ NO ☐	If no, under which conditions?
Incompatibility with other substances YES ☒ NO ☐	If yes, which ones? Strong oxidizing agents, acids and bases
Reactivity and under what conditions	
Hazardous Decomposition Products None known based on information supplied.	
Hazardous Polymerization Hazardous polymerization does not occur.	
Conditions to Avoid Exposure to light. Excessive heat.	

Section XI - Toxicological Information

Effects of acute exposure

Chemical Name	LD50 Oral	LD50 Dermal	LD50IV
Fosphenytoin	NA	NA	235 mg/kg (rat)
Tromethamine	59900 mg/kg (rat)	NA	NA

Effects of chronic exposure

Chronic Toxicity: Chronic adverse effects may include bleeding, tender and enlarged gums, muscle pain, enlargement of facial features, swelling of breasts in males, excessive hair growth on body and face, and insomnia. Formate and phosphate metabolites of fosphenytoin may contribute to overdose toxicity. Formate toxicity is associated with severe anion-gap metabolic acidosis. Hypocalcemia may result from large increases in phosphate concentrations.
Carcinogenicity: Phenytoin is the active metabolite of fosphenytoin. Phenytoin has been classified by the International Agency for Research on Cancer (IARC) as possibly carcinogenic to humans (Group 2B), and listed by the National Toxicology Program (NTP) as reasonably anticipated to be a human carcinogen.
Mutagenic Effects: None known
Reproductive Toxicity: Contains ingredients that are suspected reproductive hazards. It has been reported in the clinical literature that the use of hydantoin anticonvulsants during pregnancy may result in adverse effects on fetal growth and development.
Target Organ Effects: Kidney, liver, blood, central nervous system (CNS), and cardiovascular system.
Other Adverse Effects: Use during pregnancy is contraindicated. Use of hydantoin anticonvulsants prior to delivery may cause bleeding problems in the mother and newborn.
Endocrine Disruptor Information: This product does not contain any known or suspected endocrine disruptors.

Irritancy of Product	
Skin Sensitization	Respiratory Sensitization
Carcinogenicity IARC ☒ ACGIH ☐ Other☐	Explanation Phenytoin is the active metabolite of fosphenytoin. Phenytoin has been classified by the International Agency for Research on Cancer (IARC) as possibly carcinogenic to humans (Group 2B), and listed by the National Toxicology Program (NTP) as reasonably anticipated to be a human carcinogen.

Reproductive Toxicity Contains ingredients that are suspected reproductive hazards. It has been reported in the clinical literature that the use of hydantoin anticonvulsants during pregnancy may result in adverse effects on fetal growth and development.	Teratogenicity
Embriotoxicity	Mutagenicity None known
Name of synergistic Products/Effects	

Section XII - Ecological Information

Aquatic Toxicity & other Environmental Issues
Information is currently not available on the environmental impact of Fosphenytoin Sodium Injection. Handle in a manner to prevent spills or releases to the environment.

No component of this product is listed as a marine pollutant.

Section XIII - Disposal Considerations

Waste Disposal
This material, as supplied, is not a hazardous waste according to Federal regulations (40 CFR 261). This material could become a hazardous waste if it is mixed with or otherwise comes in contact with a hazardous waste, if chemical additions are made to this material, or if the material is processed or otherwise altered. Consult 40 CFR 261 to determine whether the altered material is a hazardous waste. Consult the appropriate state, or local regulations for additional requirements.

Contaminated Packaging
Dispose of in accordance with local regulations.

Section XIV - Transport Information

Special Shipping Information (general)
Fosphenytoin Sodium Injection, USP is not a DOT hazardous material.
Not regulated by TDG, MEX, ICAO, IATA, IMDG/IMO, RID, ADR, ADN

Specific Local Transport Information or Classifications

Section XV - Regulatory Information

General Regulatory Information
SARA 313 listed?: NO
CERCLA listed?: NO
RCRA listed?: NO

Specific Local Regulatory Information or Classification

This product has been classified in accordance with the hazard criteria of the Controlled Products Regulations (CPR) and the MSDS contains all the information required by CPR.

Section XVI - Other Information

1. Use of this product should be through or under the direction of a physician.
This MSDS does not address the therapeutic use of this material.

2. Persons administering this drug to patients must be careful to avoid needle sticks from syringes and other sharp used in the administration. All needle sticks must be reported to your company management.

3. Fosphenytoin Sodium Injection may be considered a Hazardous Drug as described in the NIOSH Alert: Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. Employees who prepare or administer hazardous drugs or who work in areas where these drugs are used should follow specific handling guidelines in order to prevent exposure to these agents in the air or on work surfaces, clothing, or equipment.

4. **Published guidance on the handling and transport of cytotoxic drugs:**
NIOSH Alert – Preventing occupational exposures to antineoplastic and other hazardous drugs in health care settings
http://www.cdc.gov/niosh/docs/2004-165/
National Study Commission on Cytotoxic Exposure: Recommendation for handling Cytotoxic Agents:
http://www.nih.gov/od/ors/ds/pubs/cyto/index.htm

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