

# SAFETY DATA SHEET

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## SECTION 1 - IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/ UNDERTAKING

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### Contact information

#### General



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<b>Product identifier</b>	Ferumoxytol Drug Product
<b>Synonyms</b>	Formulated polyglucose sorbitol carboxymethylether superparamagnetic iron oxide, Code 7228
<b>Trade names</b>	Feraheme™
<b>Chemical family</b>	Iron preparation, semi-synthetic carbohydrate coated superparamagnetic iron oxide nanoparticle
<b>Relevant identified uses of the substance or mixture and uses advised against</b>	Bulk formulated pharmaceutical mixture/Formulated pharmaceutical product/mixture packaged in final form for patient use for the treatment of Iron Deficiency Anemia in patients with chronic kidney disease.
<b>Note</b>	This SDS is written to address potential worker health and safety issues associated with the handling of the formulated product. Workers manufacturing this product should consult the SDSs of each hazardous ingredient for hazard information and handling recommendations.

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## SECTION 2 - HAZARDS IDENTIFICATION

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<b>Classification of the substance or mixture</b>	<b>Drugs in the finished state and intended for the final user are not subject to labeling in the US, EU or Canada.</b> Please consult the prescribing/packaging information. <b>The classification and labeling listed below is for bulk drug product.</b>
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**SECTION 2 - HAZARDS IDENTIFICATION ...continued**

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<b>Globally Harmonized System [GHS]</b>	Not classified
<b>Label elements</b>	
<b>GHS hazard pictogram</b>	None required
<b>GHS signal word</b>	None required
<b>GHS hazard statements</b>	None required
<b>GHS precautionary statements</b>	None required
<b>Other hazards</b>	<p>Ferumoxytol is indicated for the intravenous (IV) treatment of iron deficiency anemia in adult patients with chronic kidney disease. Adverse effects reported with high doses of ferumoxytol include gastrointestinal effects, dizziness, hypotension and peripheral edema. Severe allergic reactions have also been reported in some patients.</p> <p>Long-term inhalation exposure to high levels of iron oxide may cause effects on the respiratory system (pneumoconiosis, siderosis). It is unclear if similar effects would occur with inhalation exposure to ferumoxytol.</p>
<b>Note</b>	This mixture is not classified as hazardous according to Regulation EC No 1272/2008 (EU CLP) and Hazard Communication Standard No. 1910.1200 (US OSHA).

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**SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS**

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<u>Ingredient</u>	<u>CAS #</u>	<u>EINECS/ ELINCS#</u>	<u>Amount</u>	<u>GHS Classification</u>
Ferumoxytol	722492-56-0	N/A	1-10%	Not Classified

**Note** The ingredient(s) listed above are considered hazardous and/or are the active ingredient. The remaining components are non-hazardous and/or present at amounts below reportable limits. See Section 16 for full text of GHS classifications. The GHS classification is based on Regulation (EC) 1272/2008 and Hazard Communication Standard No. 1910.1200.

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**SECTION 4 - FIRST AID MEASURES**

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**Description of first aid measures**

<b>Immediate Medical Attention Needed</b>	Yes. If exposed or concerned: Get medical advice/attention.
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**SECTION 4 - FIRST AID MEASURES ...continued**

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<b>Eye Contact</b>	If easy to do, remove contact lenses, if worn. Immediately flush eyes with copious quantities of water for at least 15 minutes. If irritation occurs or persists, notify medical personnel and supervisor.
<b>Skin Contact</b>	Wash exposed area with soap and water and remove contaminated clothing/shoes. If irritation occurs or persists, notify medical personnel and supervisor.
<b>Inhalation</b>	Immediately move exposed subject to fresh air. If not breathing, give artificial respiration. If breathing is labored, administer oxygen. Immediately notify medical personnel and supervisor.
<b>Ingestion</b>	If swallowed, call a physician immediately. Do not induce vomiting unless directed by medical personnel. Do not give anything to drink unless directed by medical personnel. Never give anything by mouth to an unconscious person. Notify medical personnel and supervisor.
<b>Protection of first aid responders</b>	See Section 8 for Exposure Controls/Personal Protection recommendations.
<b>Most important symptoms and effects, both acute and delayed</b>	See Sections 2 and 11.
<b>Indication of immediate medical attention and special treatment needed, if necessary</b>	Medical conditions aggravated by exposure: None known or reported. Treat symptomatically and supportively. If accidental exposure occurs to an individual who is also taking one or more concomitant medications, consult the respective package or prescribing information for potential drug interactions.

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**SECTION 5 - FIREFIGHTING MEASURES**

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<b>Extinguishing media</b>	Use water spray (fog), foam, dry powder, or carbon dioxide, as appropriate for surrounding fire and materials.
<b>Specific hazards arising from the substance or mixture</b>	None.
<b>Flammability/Explosivity</b>	As product is an aqueous solution, it is not expected to be flammable or explosive.
<b>Advice for firefighters</b>	Wear full protective clothing and a self-contained breathing apparatus with a full facepiece operated in the pressure demand or other positive pressure mode. Decontaminate all equipment after use.

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## SECTION 6 - ACCIDENTAL RELEASE MEASURES

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<b>Personal precautions, protective equipment and emergency procedures</b>	If product is released or spilled, take proper precautions to minimize exposure by using appropriate personal protective equipment (see Section 8). Area should be adequately ventilated. Do not breathe mist/vapors/spray.
<b>Environmental precautions</b>	No information identified.
<b>Methods and material for containment and cleaning up</b>	DO NOT CAUSE MATERIAL TO BECOME AIRBORNE. For small spills, soak up material with absorbent, e.g., paper towels. For large spills, cordon off spill area and minimize the spreading of spilled material. Soak up material with absorbent. Collect spilled material, absorbent, and rinse water into suitable containers for proper disposal in accordance with applicable waste disposal regulations (see Section 13). Decontaminate the area twice.
<b>Reference to other sections</b>	See Sections 8, 9 and 13 for more information.

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## SECTION 7 - HANDLING AND STORAGE

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<b>Precautions for safe handling</b>	Follow recommendations for handling pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed).
<b>Conditions for safe storage including any incompatibilities</b>	Store at controlled room temperature (20- 25°C) away from incompatible materials. Excursions are permitted to 15-30°C.
<b>Specific end use(s)</b>	No information identified.

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## SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

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### Control Parameters/ Occupational Exposure Limit Values

<u>Compound</u>	<u>Issuer</u>	<u>Type</u>	<u>OEL</u>
Ferumoxytol	AMAG	TWA-8 HR	5 mg/m <sup>3</sup> (measured as Fe)
	ACGIH	TWA-8 HR	5 mg/m <sup>3</sup> (respirable fraction) (Iron oxide)
	Austria	TWA-8 HR	5 mg/m <sup>3</sup> (respirable fraction); 10 mg/m <sup>3</sup> (inhalable fraction) (Iron oxide)
	Austria	STEL	10 mg/m <sup>3</sup> (respirable fraction, 2 X 60 min) (Iron oxide)

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**SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION ...continued**

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**Control Parameters/  
Occupational Exposure  
Limit Values**

...continued

<u>Compound</u>	<u>Issuer</u>	<u>Type</u>	<u>OEL</u>
	Belgium	TWA-8 HR	2 ppm (fume, as Fe); 5 mg/m <sup>3</sup> (fume, as Fe) (Iron oxide)
	Bulgaria, Finland	TWA-8 HR	5.0 mg/m <sup>3</sup> (as Fe) (Iron oxide)
	Denmark	TWA-8 HR	3.5 mg/m <sup>3</sup> (as Fe) (Iron oxide)
	Estonia, Sweden	TWA-8 HR	3.5 mg/m <sup>3</sup> (respirable dust, as Fe) (Iron oxide)
	France, Poland	TWA-8 HR	5 mg/m <sup>3</sup> (fume, as Fe) (Iron oxide)
	Germany	TWA-8 HR/STEL	1.5 mg/m <sup>3</sup> (respirable fraction)/10 mg/m <sup>3</sup> (as Fe) (Iron oxide)
	Greece	TWA-8 HR/STEL	10 mg/m <sup>3</sup> (as Fe) (Iron oxide)
	Hungary	TWA-8 HR	6 mg/m <sup>3</sup> (respirable dust) (Iron oxide)
	Ireland, United Kingdom	TWA-8 HR	5 mg/m <sup>3</sup> (fume, as Fe); 10 mg/m <sup>3</sup> (total inhalable dust, regulated under Rouge); 4 mg/m <sup>3</sup> (respirable dust, regulated under Rouge)
	Ireland	STEL	10 mg/m <sup>3</sup> (fume, as Fe) (Iron oxide)
	NIOSH	IDLH (Immediately dangerous to life or health)	2500 mg/m <sup>3</sup> (dust and fume, as Fe) (Iron oxide)
	NIOSH, Spain	TWA-8 HR	5 mg/m <sup>3</sup> (dust and fume, as Fe) (Iron oxide)
	Portugal	TWA-8 HR	5 mg/m <sup>3</sup> (respirable fraction, as Fe) (Iron oxide)
	Romania	TWA-8 HR/STEL	5/10 mg/m <sup>3</sup> (dust and fume) (Iron oxide)
	Slovak Republic	TWA-8 HR	1.5 mg/m <sup>3</sup> (Iron oxide)
	US OSHA	TWA-8 HR	10 mg/m <sup>3</sup> (fume) (Iron oxide)

**SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION ...continued**

**Control Parameters/  
Occupational Exposure  
Limit Values**

...continued

<u>Compound</u>	<u>Issuer</u>	<u>Type</u>	<u>OEL</u>
	United Kingdom	STEL	10 mg/m <sup>3</sup> (fume, as Fe); 30 mg/m <sup>3</sup> (total inhalable, regulated under Rouge); 12 mg/m <sup>3</sup> (respirable, regulated under Rouge)

**Exposure/Engineering controls**

Control exposures to below the OEL (if available). Otherwise, selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Use local exhaust and/or enclosure at dust-generating points. Emphasis is to be placed on closed material transfer systems and process containment, with limited open handling of powders. High-energy operations such as milling, particle sizing, spraying or fluidizing should be done within an approved emission control or containment system.

**Respiratory protection**

Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. For routine powder handling tasks, an approved and properly fitted air purifying respirator should provide ancillary protection based on the known or foreseeable limitations of existing engineering controls. Use a powered air-purifying respirator equipped with HEPA filters or combination filters or a positive-pressure air-supplied respirator if there is any potential for an uncontrolled release, when exposure levels are not known, or in any other circumstances where a lower level of respiratory protection may not provide adequate protection.

**Hand protection**

Wear nitrile or other impervious gloves if skin contact is possible. When the material is dissolved or suspended in an organic solvent, wear gloves that provide protection against the solvent.

**Skin protection**

Wear appropriate gloves, lab coat, or other protective overgarment if skin contact is likely. Base the choice of skin protection on the job activity, potential for skin contact and solvents and reagents in use.

**Eye/face protection**

Wear safety glasses with side shields, chemical splash goggles, or full face shield, if necessary. Base the choice of protection on the job activity and potential for contact with eyes or face. An emergency eye wash station should be available.

**Environmental Exposure Controls**

Avoid release to the environment and operate within closed systems wherever practicable. Air and liquid emissions should be directed to appropriate pollution control devices. In case of spill, do not release to drains. Implement appropriate and effective emergency response procedures to prevent release or spread of contamination and to prevent inadvertent contact by personnel.

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**SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION ...continued**

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<b>Other protective measures</b>	Wash hands in the event of contact with this substance, especially before eating, drinking or smoking. Protective equipment is not to be worn outside the work area (e.g., in common areas or out-of-doors).
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**SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES**

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**Information on basic physical and chemical properties**

<b>Appearance</b>	Black to reddish-brown aqueous liquid
<b>Color</b>	Black to reddish-brown
<b>Odor</b>	No information identified.
<b>Odor threshold</b>	No information identified.
<b>pH</b>	6-8
<b>Melting point/ freezing point</b>	No information identified.
<b>Initial boiling point and boiling range</b>	No information identified.
<b>Flash point</b>	No information identified.
<b>Evaporation rate</b>	No information identified.
<b>Flammability (solid, gas)</b>	No information identified.
<b>Upper/lower flammability or explosive limits</b>	No information identified.
<b>Vapor pressure</b>	No information identified.
<b>Vapor density</b>	No information identified.
<b>Relative density</b>	No information identified.
<b>Water solubility</b>	No information identified.
<b>Solvent solubility</b>	No information identified.
<b>Partition coefficient (<i>n</i>-octanol/water)</b>	No information identified.
<b>Auto-ignition temperature</b>	No information identified.

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**SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES ...continued**

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<b>Decomposition temperature</b>	No information identified.
<b>Viscosity</b>	2 CPS at 25°C
<b>Explosive properties</b>	No information identified.
<b>Oxidizing properties</b>	No information identified.
<b>Other information</b>	
<b>Molecular weight</b>	~750 kDa (ferumoxytol)
<b>Molecular formula</b>	Fe <sub>5874</sub> O <sub>8752</sub> · C <sub>11719</sub> H <sub>18682</sub> O <sub>9933</sub> Na <sub>414</sub> (ferumoxytol)

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**SECTION 10 - STABILITY AND REACTIVITY**

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<b>Reactivity</b>	No information identified.
<b>Chemical stability</b>	Stable at controlled room temperature for at least 24 months.
<b>Possibility of hazardous reactions</b>	Not expected to occur.
<b>Conditions to avoid</b>	Avoid extreme temperatures.
<b>Incompatible materials</b>	No information identified.
<b>Hazardous decomposition products</b>	No information identified.

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**SECTION 11 - TOXICOLOGICAL INFORMATION**

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**Note** No data were available for this mixture. The hazards may be similar to the hazards of the ingredient(s). In non-clinical studies, doses of ferumoxytol were measured as Fe.

**Information on toxicological effects**

**Route of entry** May be absorbed by inhalation, skin contact and ingestion.

**Acute toxicity**

<u>Compound</u>	<u>Type</u>	<u>Route</u>	<u>Species</u>	<u>Dose</u>
Ferumoxytol	LD <sub>50</sub>	IV	Rat/Dog	>450 mg/kg (measured as Fe)
	LD <sub>50</sub>	Oral	Rat/Mouse	>15 g/kg (FeO <sub>x</sub> )

**Irritation/Corrosion** No localized edema or tissue irritation occurred after intravenous, perivenous, or intraarterial administration for formulated ferumoxytol.



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**SECTION 11 - TOXICOLOGICAL INFORMATION ...continued**

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<b>Sensitization</b>	Ferumoxytol is a non-sensitizer in guinea pigs. Minimal potential for inducing anaphylactoid responses was observed in the rat paw edema model.
<b>STOT-single exposure</b>	No signs of toxicity were reported in rats or dogs following a single intravenous dose of 450 mg/kg.
<b>STOT-repeated exposure/Repeat-dose toxicity</b>	Repeat-dose toxicity studies with ferumoxytol at doses up to 12 mg(Fe)/kg/day for 13 weeks in rats and dogs demonstrated dose-dependent decreases in body weight gain and food consumption, and increases in pigmentation intensity. No systemic or immunological toxicity was observed at clinically relevant doses.
<b>Reproductive toxicity</b>	No adverse effects on fertility were observed in rats at intravenous doses as high as 18 mg (Fe)/kg/day ferumoxytol.
<b>Developmental toxicity</b>	Developmental toxicity was observed in rats and rabbits treated with ferumoxytol, but only at doses that were associated with maternal toxicity.
<b>Genotoxicity</b>	Non-genotoxic in the Ames bacterial mutagenicity assay, an <i>in vitro</i> chromosomal aberration assay, and an <i>in vivo</i> micronucleus test.
<b>Carcinogenicity</b>	No studies identified. None of the components of the mixture present at levels greater than or equal to 0.1% are listed by NTP, IARC, ACGIH or OSHA as a carcinogen.
<b>Aspiration hazard</b>	No data available.

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**SECTION 12 - ECOLOGICAL INFORMATION**

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<b>Toxicity</b>	<u>Compound</u>	<u>Type</u>	<u>Species</u>	<u>Concentration</u>
	Ferumoxytol	--	--	--
<b>Additional toxicity information</b>		No data available.		
<b>Persistence and Degradability</b>		No data available.		
<b>Bioaccumulative potential</b>		No data available.		
<b>Mobility in soil</b>		No data available.		
<b>Results of PBT and vPvB assessment</b>		Not performed.		
<b>Other adverse effects</b>		No data available.		

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**SECTION 13 - DISPOSAL CONSIDERATIONS**

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**Waste treatment methods**                      Used product should be disposed of according to local, state, and federal regulations. Do not send down the drain or flush down the toilet. All wastes containing the material should be properly labeled. Dispose of wastes in accordance to prescribed federal, state, and local guidelines, e.g., appropriately permitted chemical waste incinerator. Rinse waters resulting from spill cleanups should be discharged in an environmentally safe manner, e.g., appropriately permitted municipal or on-site wastewater treatment facility.

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**SECTION 14 - TRANSPORT INFORMATION**

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**Transport**                                      This product/mixture is not regulated as a hazardous material/dangerous good under EU ADR/RID, US DOT, Canada TDG, IATA, or IMDG.

**UN number**                                      None assigned.

**UN proper shipping name**                      None assigned.

**Transport hazard classes and packing group**                      None assigned.

**Environmental hazards**                      Based on the available data, this mixture is not regulated as an environmental hazard or a marine pollutant.

**Special precautions for users**                      Avoid release to the environment.

**Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code**                      Not applicable.

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**SECTION 15 - REGULATORY INFORMATION**

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**Safety, health and environmental regulations/legislation specific for the substance or mixture**                      This SDS generally complies with the requirements listed under current guidelines in the US, EU and Canada.

**Chemical safety assessment**                      Not conducted.

**WHMIS classification**                      Not classified.

**TSCA status**                                      Drugs are exempt from TSCA.

**SARA section 313**                                      Not listed.

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**SECTION 15 - REGULATORY INFORMATION** ...continued

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**California proposition 65** Not listed.  
**Additional information** No other information identified.

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**SECTION 16 - OTHER INFORMATION**

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**Full text of H phrases and GHS classifications** Not applicable.

**Sources of data** Information from published literature and internal company data.

**Abbreviations** ACGIH - American Conference of Governmental Industrial Hygienists; ADR/RID - European Agreement Concerning the International Carriage of Dangerous Goods by Road/Rail; AIHA - American Industrial Hygiene Association; CAS# - Chemical Abstract Services Number; CLP - Classification, Labelling, and Packaging of Substances and Mixtures; DNEL - Derived No Effect Level; DOT - Department of Transportation; EINECS - European Inventory of New and Existing Chemical Substances; ELINCS - European List of Notified Chemical Substances; EU - European Union; GHS - Globally Harmonized System of Classification and Labeling of Chemicals; IARC - International Agency for Research on Cancer; IDLH - Immediately Dangerous to Life or Health; IATA - International Air Transport Association; IMDG - International Maritime Dangerous Goods; LOEL - Lowest Observed Effect Level; LOAEL - Lowest Observed Adverse Effect Level; NIOSH - The National Institute for Occupational Safety and Health; NOEL - No Observed Effect Level; NOAEL - No Observed Adverse Effect Level; NTP - National Toxicology Program; OEL - Occupational Exposure Limit; OSHA - Occupational Safety and Health Administration; PNEC - Predicted No Effect Concentration; SARA - Superfund Amendments and Reauthorization Act; STOT - Specific Target Organ Toxicity; STEL - Short Term Exposure Limit; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act; TWA - Time Weighted Average; WHMIS - Workplace Hazardous Materials Information System

**Issue Date** 27 July 2015

**Revisions** Updated format throughout and added information in section 2 and 11.

**Disclaimer** The above information is based on data available to us and is believed to be correct. Since the information may be applied under conditions beyond our control and with which we may be unfamiliar, we do not assume any responsibility for the results of its use and all persons receiving it must make their own determination of the effects, properties and protections which pertain to their particular conditions.

No representation, warranty, or guarantee, express or implied (including a warranty of fitness or merchantability for a particular purpose), is made with respect to the materials, the accuracy of this information, the results to be obtained from the use thereof, or the hazards connected with the use of the material. Caution should be used in the handling and use of the material because it is a pharmaceutical product.

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**SECTION 16 - OTHER INFORMATION ...continued**

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**Disclaimer ...continued**

The above information is offered in good faith and with the belief that it is accurate. As of the date of issuance, we are providing all information relevant to the foreseeable handling of the material. However, in the event of an adverse incident associated with this product, this Safety Data Sheet is not, and is not intended to be, a substitute for consultation with appropriately trained personnel.