

Material Safety Data Sheet

1. PRODUCT AND COMPANY IDENTIFICATION

<i>Product Information</i>	
Product Name	Ablavar®
Version	1.0, 6/24/09
<i>Synonyms</i>	
MS-325 Injection, Gadofosveset Trisodium Injectable Solution	
Product Uses	This material is used as a medical imaging agent.
<i>Company Identification</i>	
Address	Lantheus Medical Imaging 331 Treble Cove Road Billerica, MA 01862 United States Of America 1-800-299-3431
Emergency Phone Number	CHEMTREC 1-800-424-9300. For all international transportation emergency call CHEMTREC at 1-703-527-3887. Collect calls accepted.

2. COMPOSITION INFORMATION ON INGREDIENTS

Components	Concentration	CAS No.
<i>Hazardous Components</i>		
Gadofosveset trisodium:	20 – 21%	211570-55-7
Fosveset	< 0.1 %	193901-91-6
<i>Other Ingredients</i>		
Water	> 79 - 80%	7732-18-5

3. HAZARDS IDENTIFICATION

<i>Emergency Overview</i>	
Appearance	Liquid: clear, colorless to slightly yellow
Signal Word	Caution!
Hazard Statements	May be harmful if inhaled, ingested or in contact with the skin. May cause allergic sensitization. Exposure poses increased risk for persons with severe kidney dysfunction. See Section 10.
Precautionary Measures	Avoid ingestion, inhalation, skin and eye contact. Wash hands after handling to minimize exposure.
<i>Potential Health Effects</i>	
Eyes	Not available.
Skin	Not available.
Ingestion	Not available.
Inhalation	Not available.
Target Organs	Kidneys, lungs, lymph nodes.
Signs and Symptoms	Acute: may cause itching, tingling or prickling sensation, salivation, nausea, vomiting, pupil dilation, convulsions, nose bleeds, tremors, prostration.
<i>Environmental Effects</i>	Not available

4. FIRST AID MEASURES

Eye contact	Rinse immediately with plenty of water for at least 15 minutes. Keep eye wide open while rinsing. Obtain medical attention.
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Skin contact	Wash off immediately with plenty of water for at least 15 minutes. If skin irritation occurs, get medical advice/attention.
Inhalation	Move to fresh air. Oxygen or artificial respiration if needed. Obtain medical attention.
Ingestion	Obtain medical attention. Do NOT induce vomiting. Never give anything by mouth to an unconscious person.
Notes to Physicians	This material is used as a medical imaging agent. This product, by intravenous doses in animals far above those used for medical imaging, itching, tingling or prickling sensation, salivation, nausea, vomiting, pupil dilation, convulsions, nose bleeds, tremors, prostration, death. Material not fully tested. Refer to Section 10.
Medical Surveillance	Employees, who are pregnant, are breast-feeding, or who are concerned with other reproductive issues should be encouraged to consult with the occupational health physician monitoring worker's health.

5. FIRE-FIGHTING MEASURES

Flammable Properties	Not available.
Extinguishing Media	Suitable extinguishing media: Dry chemical, Water spray, Foam Unsuitable extinguishing media: Do NOT use water jet.
Protection of Firefighters	Specific hazards: Not available Protective equipment: Use personal protective equipment. In the event of fire, wear self-contained breathing apparatus. Hazardous Combustion Products: Not available
Other Information	Decontaminate protective clothing and equipment before reuse.

6. ACCIDENTAL RELEASE MEASURES

Personal Precautions	Refer to protective measures listed in sections 7 and 8. Use personal protective equipment. Examples include tightly fitting safety goggles, lab coat and impervious gloves. Depending on the nature of the spill (quantity and extent of spill) additional protective clothing and equipment such as a self-contained breathing apparatus may be needed.
Environmental Precautions	Prevent release to drains and waterways. Prevent release to the environment.
Containment Methods	Contain spillage, and then collect with non-combustible absorbent material, (e.g. sand, earth, diatomaceous earth, vermiculite) and place in container for disposal according to local/national regulations (see section 12).
Cleanup Methods	Contain and collect spillage and place in container for disposal according to local regulations (see Section 12). Handle waste materials, including gloves, protective clothing, contaminated spill cleanup material, etc., as appropriate for chemically and pharmacologically similar materials.

7. HANDLING AND STORAGE

Handling Precautions	Avoid exposure - obtain special instructions before use. Avoid inhalation. Keep away from heat and sources of ignition. Prevent release to drains and waterways.
Storage Conditions	Keep in a tightly closed container, stored in a cool, dry, ventilated area. Protect against physical damage. Containers of this material may be hazardous when empty since they retain product residues (dust, solids); observe all warnings and precautions listed for the product.
Container Requirements	Store in original container. Keep away from heat, sparks and flames.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION				
Exposure Limit(s)	Company Guideline	ACGIH	OSHA	NIOSH
Gadofosveset trisodium:	0.15 mg/m ³	---	---	---
Fosveset:	---	---	---	---
Lantheus Medical Imaging Exposure Guidelines Summary	Control exposures to Gadofosveset trisodium below 0.15 mg/m ³ 8 hr TWA			
Recommended Industrial Hygiene Monitoring Methods	Non-available.			
Engineering Controls and Ventilation	When handling small quantities in a clinical setting, good room ventilation is desirable. Specific engineering controls should not be needed. When handling larger quantities, such as in a manufacturing setting, ensure worker exposure is below the recommended exposure limit. If significant aerosol (dust) is generated, use local exhaust ventilation, process enclosures, containment technology, or other engineering controls to keep airborne levels below recommended exposure limit.			
Respiratory Protection	Respiratory protection is not required for normal use of this material. If the occupational exposure control limit (ECL) is exceeded, wear an appropriate respirator with a protection factor sufficient to control exposures to below the ECL.			
Eye Protection	Follow good chemical hygiene practices when using clinical or consumer presentations. Glasses or goggles are recommended if eye contact is possible.			
Hand Protection	Follow good chemical hygiene practices when using clinical or consumer presentations. Wear gloves when working with large quantities.			
Skin and Body Protection	Follow good chemical hygiene practices when using clinical or consumer presentations. It is recommended that a laboratory coat be worn when handling product.			
Hygiene	Wash hands and face before breaks and immediately after handling the product.			

9. PHYSICAL AND CHEMICAL PROPERTIES	
<i>Appearance</i>	
Physical State	Liquid
Color	Clear, colorless to slightly yellow
<i>Descriptive Properties</i>	
Molecular Weight	975.88, 957.86 (anhydrous form)
Odor	Odorless
pH	6.5 – 8.0

9. STABILITY AND REACTIVITY	
Chemical Stability	Stable under normal conditions.
Conditions to Avoid	Not available
Incompatible Products	Not available
Hazardous Decomposition Products	Hazardous decomposition products formed under fire conditions: Not available
Hazardous Reactions	None known. Stable under normal conditions. Hazardous polymerization does not occur.

10. TOXICOLOGICAL INFORMATION	
Routes of Entry	Ingestion, Inhalation, Eye Contact, Skin Contact
Eye Irritation	Not available
Skin Irritation	Not available
Respiratory Irritation	Not available
Sensitization	May cause sensitization in susceptible individuals.
Acute Toxicity Study	Acute toxicity (other routes of administration) Gadofosveset trisodium: LD ₅₀ (rat, intravenous): 2.9 g/kg
Repeated Dose Toxicity	Gadofosveset trisodium: 1 months intravenous (daily) rat study : NOEL = 9.76 mg/kg, NOAEL = 97.6 mg/kg Effects included vacuolation of the kidney cortical tubular epithelial cells of the proximal convoluted tubules, pale kidneys, and increased kidney weights, accumulation of vacuolated macrophages in the lungs, vacuolated reticuloendothelial cells in several tissues and vacuolated odontoblasts in the incisors. Histopathological changes persisted in the kidneys, lymph nodes, and adrenal medulla. 1 months intravenous (daily) monkey study: NOAEL: 97.6 mg/kg. Effects included: increased sialorrhea and vomiting (the latter only observed once in one male); tubular vacuolation of the proximal part (slight to moderate in male animals, minimal in female animals) In the high dose of 2.0 mmol/kg: frequent vomiting in both sexes and with high incidence followed by a decrease in food consumption and decrease in body weight gain and body weight loss; increase in monocyte count in males and females on day 24; increase in aspartate aminotransferase (AST) in males and females on days 2 and 24; increases in alpha- and beta-globulins in males and females on day 24; decrease in albumin in males and females on day 24; vacuolation of proximal renal tubules (massive), bladder urothel, lymph nodes (accompanied by histiocytosis), pancreatic islet, periportal hepatocytes and lung alveolar macrophages; further histological changes in the liver. The reported clinical observations and the changes in hematology and clinical chemistry were no longer visible after the 12 weeks recovery period. Findings which persisted after the 12 week recovery period were a minimal tubular vacuolation of the kidneys (proximal part) and minimal histiocytosis accompanied by vacuolation in some lymph nodes.
Genetic Toxicity	Gadofosveset trisodium: The mutagenicity potential of Gadofosveset trisodium was evaluated using two <i>in vitro</i> assays (the reverse mutation assay and chromosomal aberrations in CHO cells) and one <i>in vivo</i> assay (mouse bone marrow micronucleus assay). In all studies, Gadofosveset trisodium was not mutagenic under the conditions of these studies.

Carcinogenicity		Not available			
		ACGIH	OSHA	NTP	IARC
Gadofosveset trisodium		---	---	---	---
Fosveset		---	---	---	---
Reproductive/Developmental Toxicity		<p>Gadofosveset trisodium:</p> <p>At 1.5 mmol/kg/day (4 weeks in males, 2 weeks in females) in Sprague-Dawley rats, the number of spermatids per gram of testicular tissue was reduced and reduced epididymides weight. Fertility was not reduced at this dose. This same dose caused some deaths, pale kidneys and in one case, enlarged kidneys in the test animals. The NOAEL for this study was 0.21 mmol/kg.</p> <p>In rat embryotoxicity studies, Gadofosveset trisodium at 2.0 mmol/kg/day for 11 days caused embryotoxicity in the form of an increased rate of skeletal variations and retardations. This dose also produced signs of maternal toxicity in the form of a slight reduction in food intake, a marginal body weight reduction, reduced body weight gain, reduced carcass weight, pale and heavier kidneys. The NOAEL for this study was 0.45 mmol/kg.</p> <p>In rabbits, an increased mean incidence of post-implantation loss caused by an increased number of early resorptions was observed in dams treated with Gadofosveset trisodium at 2 mmol/kg/day. Maternal toxicity was also noted at this dose in the form of increase kidney weight. The post-implantation loss was associated with a decrease in the number of fetuses and a decrease in the gravid uterus weight.</p>			
Conditions that may be aggravated by exposure to this material:		<p>The US FDA has requested that a boxed warning be added to the labeling of all gadolinium-based MRI contrast agents marketed in the US; the boxed warning describes the risk for nephrogenic systemic fibrosis (NSF) in patients receiving these agents with renal dysfunction that meets one of the following two conditions:</p> <ul style="list-style-type: none"> • acute or chronic severe renal insufficiency (glomerular filtration rate < 30 mL/min/1.73m²); • acute renal dysfunction due to the hepato-renal syndrome or in the perioperative liver transplantation period of any severity. <p>In patients with renal insufficiency, acute renal failure has occurred with the use of other gadolinium agents. The risk of renal failure may increase with increasing dose of gadolinium</p>			

	contrast. <i>Persons with these conditions should not be exposed to this material at any level except as recommended by a physician.</i>
	Clinical Trials Gadofosveset trisodium: At the proposed clinical dose (0.03 mmol/kg), 36.0% patients experienced at least one AE, and 23.6% experienced at least one treatment-related AE. The adverse effects profile of Gadofosveset trisodium Injection is one of generally mild, rapid onset, short duration events. The treatment related events were pruritus NOS, paresthesia, nausea, vasodilatation, and burning sensation NOS. With the exception of pruritus, these events are similar to those commonly associated with gadolinium-based contrast media. In clinical trials, a QTc change of 30 to 60 msec from baseline was observed in 6% of patients at 45 minutes post injection. This prolongation was not associated with arrhythmias or other symptoms. In clinical trials, anaphylactoid and/or anaphylactic reactions occurred in two of 1676 subjects.
Target Organs	Gadofosveset trisodium: Kidneys, lungs, lymph nodes
Symptoms	Gadofosveset trisodium: See "Clinical Trials".
Other Toxicity Information	<u>Not available</u>

11. ECOLOGICAL INFORMATION

Ecotoxicological Information (Aquatic)	Not available
Ecotoxicological Information (Terrestrial)	Not available
Chemical Fate	Not available.

12. DISPOSAL CONSIDERATIONS

Advice on Disposal and Packaging	Disposal should be in accordance with applicable regional, national, and local laws and regulations. Local regulations may be more stringent than regional or national requirements.
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13. TRANSPORT INFORMATION

<i>Transportation Classification for All Modes:</i>	
This material is not a dangerous good for the purpose of transportation.	

14. REGULATORY INFORMATION

United States of America	
OSHA Hazard Classification	Hazardous, Target Organs
313 Toxic Release Inventory. Listed Chemicals/Compounds	No components listed on the SARA 313 inventory.
TSCA Inventory	No
International	
Canada	

WHMIS	This MSDS has been prepared according to the hazard criteria of the Controlled Products Regulations (CPR) and the MSDS contains all of the information required by the CPR.
DSL/NDSL	No
Mexico	
Mexico Classification	Health classification - Minimal hazard - 0 - Substances that do not pose a hazard under emergency conditions other than that of ordinary combustible materials.

15. OTHER INFORMATION	
MSDS preparation information	
Prepared by	Environment, Health and Safety 1-978-671-8673
Prepared on	6/24/09
The information contained in this MSDS is believed to be accurate and represents the best information reasonably available at the time of preparation. However, we make no warranty, express or implied, with respect to such information. and we assume no liability from its use.	