1 Identification

Product identifier: Sheet code

Trade name: *ProHance*
Chemical Name: 10-(2-hydroxypropyl)-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid, monogadolinium salt
Synonyms: Gadoteridol Injection

Application of the substance / the mixture:
Intravenous injection contrast medium for magnetic resonance imaging.
We recommend that you use this product in a manner consistent with the listed use. If your intended use is not consistent with the stated use, please contact your sales or technical service representative. Packages of five single dose vials (5 mL fill in15 mL vial, and 10, 15, 20 mL fills in 30 mL vials, 50 mL, 100 mL). Packages of five single dose prefilled syringes (10 or 17 mL fills in a 20 mL syringes).

Details of the supplier of the safety data sheet

Manufacturer/Supplier:
Bracco Diagnostics Inc.
P.O. Box 5225
Princeton, NJ
08543
Phone number: 1-800-257-5181
Email: HSE@bracco.com (responsible for the SDS)

Emergency telephone number:
EMERGENCY CONTACT:
Health: 1-800-257-5181
U.S. Transport - Chemtrec: 1-800-424-9300
International Transport - Chemtrec: 1-703-527-3887

2 Hazard(s) identification

Classification of the substance or mixture
The product is not classified as hazardous, according to the Globally Harmonized System (GHS)

Label elements
GHS label elements: Not applicable

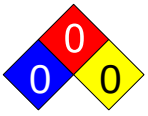
Hazard pictograms: Not applicable

Signal word: Not applicable

Hazard statements: Not applicable

Additional Information

Classification system:
NFPA ratings (scale 0 - 4)



Health = 0
Fire = 0
Reactivity = 0

HMIS-ratings (scale 0 - 4)

Health = 0
Fire = 0
Reactivity = 0

Other hazards:

Results of PBT and vPvB assessment

PBT: Not classified as PBT

vPvB: Not classified as vPvB

3 Composition/information on ingredients

Chemical characterization: Mixtures

Description: Mixture consisting of the following components

Information on components		
CAS No.	**Name**	**Qty.**
7732-18-5	Water USP	50 – 100 %
120066-54-8	(±)-[10-(2-hydroxypropyl)-1,4,7,10-tetraazacyclododecane-1,4,7-triacetate (3 -)] Gadolinium	27.9 %

4 First-aid measures

Description of first aid measures

General information: No special measures required.

After inhalation: Move patient to fresh air. If symptom arise consult a doctor. Supply fresh air. If required, provide artificial respiration. Consult a doctor if symptoms persist.

After skin contact: Immediately wash with water and soap and rinse thoroughly. If symptoms persist consult a doctor. Generally, the product does not irritate the skin.

After eye contact: Rinse opened eye for several minutes under running water. If irritation persist get medical attention.

After swallowing: immediately call a doctor. Vomiting may be induced only if a person is conscious and if ingestion has occurred within the past three hours. Never induce vomiting in a person who is unconscious or experiencing convulsions

Most important symptoms and effects, both acute and delayed

No further relevant information available

Indication of any immediate medical attention and special treatment needed

No further relevant information available

5 Fire-fighting measures

Extinguishing media

Suitable extinguishing agents: In case of fire, flood with water

Unsuitable extinguishing agents: Not applicable

Special hazards arising from the substance or mixture

In case of fire, the following can be released:
Carbon Dioxide (CO2);
In the absence of oxygen: Carbon Monoxide (CO);
Nitrogen Oxides (NxOy);
Gadolinium Oxide (Gd2O3)

Advice for firefighters

Protective equipment:
Firefighter should wear adequate personal protective equipment with protection of respiratory tract (SCBA).
In addition, firefighters should wear flame and chemicals resistant clothing, boots and gloves.

6 Accidental release measures

Personal precautions, protective equipment and emergency procedures
Keep away from ignition sources.
Wear protective equipment. Keep unprotected persons away.

Environmental precautions
Do not allow to enter sewers/surfaces or ground water.

Methods and material for containment and cleaning up
Absorb with liquid-binding material.
Absorb with liquid-binding material (sand, diatomite, vermiculite) or other non-combustible. absorbent material. Place spilt material in an appropriate container for disposal.
The spill area should be ventilated and decontaminated after material is collected.

Reference to other sections
No dangerous substances are released.
See section 7 for information on safe handling.
See section 8 for information on personal protection equipment.
See section 13 for disposal information.

Protective Action Criteria for Chemicals

PAC-1:		
77-86-1	trometamol	18 mg/m³

PAC-2:		
77-86-1	trometamol	190 mg/m³

PAC-3:		
77-86-1	trometamol	1,200 mg/m³

7 Handling and storage

Precautions for safe handling
Avoid splashes or spray in enclosed areas.
Avoid contact with the eyes and skin.
Do not break vials.

Information about protection against explosions and fires: No special measures required.

Conditions for safe storage, including any incompatibilities

Requirements to be met by storerooms and receptacles:
Store in a cool, dry place in a well-sealed receptacle.

Information about storage in one common storage facility: Not required.

Further information about storage conditions:
Container Requirements: Single dose 15-, 30- and 50-mL vials and 20 mL prefilled syringes.
Storage Conditions: Store at 25°C, excursions permitted to 15-30°C. Protect from light and do not freeze.

Specific end use(s)
No further relevant information available

8 Exposure controls/personal protection

Control parameters

Components with limit values that require monitoring at the workplace:
The product does not contain any relevant quantities of materials with critical values that have to be monitored at the workplace

Additional information:
The lists that were valid during the creation were used as basis.

Exposure controls

Personal protective equipment:

General protective and hygienic measures:
The usual precautionary measures for handling chemicals should be followed. Ensure good ventilation/exhaustion at the workplace.
Wash hands before breaks and at the end of work.

Do not eat, drink and smoke while working.

Breathing equipment:
Not anticipated for normal clinical environment. In non-routine exposure conditions, where risk assessment shows air-purifying respirators are appropriate, use respirators and components tested and approved under appropriate government standards such as NIOSH (US) or CEN (EU). Self-contained breathing apparatus should be available for emergency use

Protection of hands:

Protective gloves

The glove material must be impermeable and resistant to the product/ the substance/ the preparation. Due to missing tests no recommendation to the glove material can be given for the product/ the preparation/ the chemical mixture.
Selection of the glove material on consideration of the penetration times, rates of diffusion and the degradation

Material of gloves:
Natural rubber, NR Nitrile rubber, NBR
The selection of the suitable gloves does not only depend on the material, but also on further marks of quality and varies from manufacturer to manufacturer. As the product is a preparation of several substances, the resistance of the glove material cannot be calculated in advance and has therefore to be checked prior to the application

Penetration time of glove material:
The exact break through time has to be found out by the manufacturer of the protective gloves and has to be observed.

Eye protection:

Tightly sealed goggles

Body protection: Protective work clothing

9 Physical and chemical properties

Information on basic physical and chemical properties

General Information:

Appearance	
Form:	Liquid
Color:	Colorless – Slightly yellow
Odor:	Undistinguishable
Odor threshold:	Not determined
pH – Value:	6.5 – 8.0
Melting point/Melting range:	Ca 100 °C (~212 °F)
Boiling point/Boiling range:	Ca 0 °C (~32 °F)
Flash Point:	Not determined
Flammability (Solid, Gaseous)	Not applicable
Ignition temperature:	Not determined
Danger of explosion:	Product does not present an explosion hazard.
Flammability Limits	
Lower:	Not determined
Upper:	Not determined
Explosion Limits	
Lower:	Not determined
Upper:	Not determined
Oxidizing properties:	Not determined
Vapor pressure:	Gadoteridol: T = 26 °C, P° < 1.67 x 10-7 Torr
Density	(25 °C) 1.140 g/cm3
Relativity Density at 20° C (68° F):	Not determined
Vapor Density at 20° C (68° F):	Not determined
Evaporation rate:	As water
Solubility in / Miscibility with	
Water:	Not miscible or difficult to mix
Partition coefficient (n-octanol/water):	pH=7, logKow: -3.57 to -3.58 pH=9, logKow: -3.66 to -3.70

Viscosity	
Dynamic:	T=20 °C, n = 2.0 cP T=37 °C, n = 1.3 cP
Kinematic:	Not determined
Water:	71.9 %
VOC Content:	0.0 %
Solid Content:	0.0%

Other Information

No further relevant information available

10 Stability and Reactivity

Reactivity
No data available.
No further relevant information available.

Chemical stability

Thermal decomposition / conditions to be avoided:
No decomposition if used according to specifications.

Possibility of hazardous reactions
No dangerous reactions known

Conditions to avoid.
No further relevant information available.

Incompatible materials
No further relevant information available.

Hazardous decomposition products
No dangerous decompositions products known.

11 Toxicological Information

Information on toxicological effects

Acute toxicity:

LD/LC50 values that are relevant for classification:		
120066-54-8 (±)-[10-(2-hydroxypropyl)-1,4,7,10-tetraazacyclododecane-1,4,7-triacetate (3 -)] Gadolinium		
	LD50 iv	7,598 mg/kg (Female Mouse) 5,978 mg/kg (Male Mouse) 3,906 mg/kg (Mouse) 5,880 mg/kg (Rat)
77-86-1 trometamol		
Oral	LD50	5,900 mg/kg (Rat)
121915-83-1 Calcium Calteridol		
	LD50 iv	1,200 mg/kg (Mouse)

Primary irritant effect:

on the skin:
No irritant effect.
Material contains low concentration of components that are mild irritants or possible irritants. It may have potential to cause mild irritation, however, moderate or severe irritation is not expected.

on the eye:
No irritating effect.
No irritation effects reported. However, the product should be considered as a potential irritant.

Sensitization:
No sensitizing effects known.
The product can cause inflammation in people allergic to gadolinium and its compounds.

Other information (about experimental toxicology):
By Inhalation: Inhaling small doses of aerosolized material would not be expected to result in symptoms.
By Ingestion: Inadvertent ingestion of trace amounts of this material would not be expected to result in symptoms.
Germ Cell Mutagenicity: GADOTERIDOL has not demonstrated a genotoxic activity in reverse mutation test up performed using Salmonella bacteria T. and E. C., in a mutation assay on mouse lymphoma, in an in vitro cytogenetic assay measuring chromosomal aberrations in ovarian cells hamster, nor in the in vivo micronucleus assay on mice at doses of 5 mmol / kg.
Carcinogenicity: The GADOTERIDOL is not tested for carcinogenic properties.

Reproductive Toxicity: The GADOTERIDOL didn't show teratogenic activity in rats when administered for 12-day gestation period at doses 20 times higher than recommended for Human. An increase in spontaneous motor activity was observed in infants. At high doses, the product has caused maternal toxicity and there was an increase of post implantation loss. In rabbits, There was no evidence of teratogenic activity in rabbits at doses tested up to 1.5 mmol/kg or 840 mg/kg In rabbits, doses 20 times higher than the maximum doses recommended for humans, and administered intravenously for 13 days during gestation, have increased the incidence of miscarriages and premature births, while, there was no evidence of reproductive effects in rats at doses up to 1.5 mmol/kg or 840 mg/kg.

Subacute to Chronic Toxicity: Human data are not available. In studies with rats and dogs performed over a period of one month to doses approximately 3 times higher than therapeutic effects were evident in kidney (eg, vacuolation of renal tubular epithelium). These effects are reversible. The product does not is mutagenic. Other health effects have not been fully evaluated.

Additional toxicological information:
The product is not subject to classification according to internally approved calculation methods for preparations. When used and handled according to specifications, the product does not have any harmful effects to our experience and the information provided to us. When this product is used clinically, patients with a history of renal or hepatic disease, seizure, asthma or allergic respiratory diseases, and pregnant or breast-feeding women are asked to inform their physician of these conditions. The GADOTERIDOL was classified by the FDA in the "Pregnancy Category C" because of the effects observed in animals treated with very high doses intravenously. We recommended the clinical use during pregnancy only when the benefit prevails over potential risk to the fetus. It must be borne in mind that the doses administered for medical reasons are much higher than those due to exposure in the workplace

Carcinogenic categories

IARC (International Agency for Research on Cancer)
None of the ingredients are listed

NTP (National Toxicology Program)
None of the ingredients are listed

OSHA-Ca (Occupational Safety & Health Administration)
None of the ingredients are listed

12 Ecological information

Toxicity

Aquatic toxicity:	
120066-54-8 (±)-[10-(2-hydroxypropyl)-1,4,7,10-tetraazacyclododecane-1,4,7-triacetate (3 -)] Gadolinium	
IC50	>1,000 mg/L (Activated Sludge)
EC50	>920 mg/L (Daphnia)

Persistence and degradability

Half-life (hydrolysis: < 10 % after 5-days at 50 degrees C at all pH levels tested; half-life determined to be greater than 28 days

Bio accumulative potential

No further relevant information available

Mobility in soil

No further relevant information available

Additional ecological information

General notes: Avoid transfer into the environment.

Water hazard class 1 (self-assessment): Slightly hazardous for water.

Do not allow undiluted product or large quantities of it to reach ground water, water course or sewage system.

Results of PBT and vPvB assessment

PBT: Not applicable
vPvB: Not applicable

Other adverse effects

No further relevant information available

13 Disposal considerations

Waste treatment methods

Recommendation:
Must not be disposed of together with household garbage. Do not allow product to reach sewage system. Reutilise if possible or contact a waste processors for recycling or safe disposal

Uncleaned packaging:

Recommendation:
Disposal must be made according to official regulations.
Packagings that cannot be cleansed are to be disposed of in the same manner as the product.

14 Transport information

UN Number	
DOT, ADR, ADN, IMDG, IATA	Not applicable
UN proper shipping name:	
DOT, ADR, ADN, IMDG, IATA	Not applicable
Transport hazard class(es)	
DOT, ADR, ADN, IMDG, IATA Class:	Not applicable
Packing Group	
DOT, ADR, IMDG, IATA	Not applicable
Environmental Hazards:	
Marine pollutant:	Not applicable
Special precautions for user	Not applicable
Transport in bulk according to Annex II of MARPOL 73/78 and the IBC code	Not applicable

15 Regulatory Information

Safety, health and environmental regulations/legislation specific for the substance or mixture

Sara

Section 355 (extremely hazardous substances):
Not listed
Section 313 (Specific toxic chemical listings):
Not listed

Proposition 65

Chemicals known to cause cancer:
Not listed
Chemicals known to cause reproductive toxicity for females:
Not listed
Chemicals known to cause reproductive toxicity for males:
Not listed
Chemicals known to cause developmental toxicity:
Not listed

Carcinogenic categories

EPA (Environmental Protection Agency)
Not listed
TLV (Threshold Limit Value established by ACGIH)
Not listed

NIOSH-Ca (National Institute for Occupational Safety and Health)
Not listed

GHS label elements: Not applicable
Hazard pictograms: Not applicable
Signal word: Not applicable
Hazard statements: Not applicable

16 Other information

This information is based on our present knowledge. However, this shall not constitute a guarantee for any specific product features and shall not establish a legally valid contractual relationship. Training Hints: All persons handling this product should be informed on the existence of the hazard, on any possible risk they might be subjected to and about all required protective measures to prevent such a damage or to reduce the exposition.

Contact:

Bracco Diagnostics Inc.
P.O. Box 5225
Princeton, NJ 08543

Date of preparation / last revision: 13/04/2023, Revision 07
Changes: Format update

Abbreviations and acronyms:
RID: Règlement international concernant le transport des marchandises dangereuses par chemin de fer (Regulations Concerning the International Transport of Dangerous Goods by Rail)
ICAO: International Civil Aviation Organisation
ADR: Accord européen sur le transport des marchandises dangereuses par Route (European Agreement concerning the International Carriage of Dangerous Goods by Road)
IMDG: International Maritime Code for Dangerous
Goods DOT: US Department of Transportation
IATA: International Air Transport Association
ACGIH: American Conference of Governmental Industrial Hygienists
EINECS: European Inventory of Existing Commercial Chemical
Substances ELINCS: European List of Notified Chemical Substances
CAS: Chemical Abstracts Service (division of the American Chemical Society) NFPA: National Fire Protection Association (USA)
HMIS: Hazardous Materials Identification System (USA)
VOC: Volatile Organic Compounds (USA, EU)
LC50: Lethal concentration, 50 percent
LD50: Lethal dose, 50 percent
Acute Tox. 3: Acute toxicity – Category 3