

Material Safety Data Sheet

acc. to ISO/DIS 11014

Printing date 11/07/2011

Version 1

Reviewed on 11/07/2011

1: Identification of the substance/mixture and of the company/undertaking

1.1 Product identifier

Sheets Code: 270

Trade name: ProHance

Chemical Name:

10-(2-hydroxypropyl)-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid, monogadolinium salt.

Synonyms: Gadoteridol Injection

How Supplied:

Packages of five single dose vials (5 mL fill in 15 mL vial, and 10, 15, or 20 mL fills in 30 mL vials).

Packages of five single dose prefilled syringes (10 or 17 mL fills in a 20 mL syringes).

1.2 Relevant identified uses of the substance or mixture and uses advised against

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.

Application of the substance / the preparation

Intravenous injection contrast medium for magnetic resonance imaging.

Chemical Family: Gadolinium chelate.

Molecular Formula: C₁₇H₂₉N₄O₇.Gd

CAS Number: 120066-54-8

1.3 Details of the supplier of the safety data sheet

Manufacturer/Supplier:

Bracco Diagnostics Inc.

P.O. Box 5225

Princeton, NJ 08543

Further Information Obtainable from:

B-Lands Consulting

WTC, 5 Place Robert Schuman, BP 1516

38025 Grenoble, FRANCE

Tel: +33 476 295 869

Fax: +33 476 295 870

services@reachteam.eu

www.reachteam.eu

1.4 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

Emergency Overview:

Colorless to slightly yellow aqueous solution containing gadoteridol, a diagnostic agent.

See Health Effects and Toxicology sections for additional information.

2: Hazards identification

2.1 Classification of the substance or mixture

Classification according to Regulation (EC) No 1272/2008

The product is not classified according to the CLP regulation.

Classification according to Directive 67/548/EEC or Directive 1999/45/EC Not applicable.

Information concerning particular hazards for human and environment:

The product does not have to be labelled due to the calculation procedure of international guidelines.

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Classification system:

The classification was made according to the latest editions of international substances lists, and expanded upon from company and literature data.

2.2 Label elements

Labelling according to Regulation (EC) No 1272/2008 Void

Hazard pictograms Void

Signal word Void

Hazard statements Void

Effects of Overexposure - Routes of Entry:

Inhalation: Under normal conditions, exposure to this material by inhalation is not expected to occur.

Skin Contact:

Exposure may occur via skin contact if gloves and protective clothing are not worn. The extent of systemic absorption of the material after skin contact is not known.

Ingestion:

Ingestion of large quantities of this material in an occupational setting would not be expected to occur. Ingestion of trace amounts of the material might occur if the material contacts hands and hands are not washed prior to eating, drinking or smoking. The extent of systemic absorption of gadoteridol after ingestion is not known.

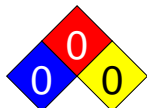
Information pertaining to particular dangers for man and environment:

Negative Effects on the Health: See also Sections 11

Negative Effects on the Environment: See also Section 12

Classification system:

NFPA ratings (scale 0 - 4)



Health = 0
Fire = 0
Reactivity = 0

HMIS-ratings (scale 0 - 4)



HEALTH 0 Health = 0
FIRE 0 Fire = 0
REACTIVITY 0 Reactivity = 0

Results of PBT and vPvB assessment

PBT: Not applicable.

vPvB: Not applicable.

3: Composition/information on ingredients

3.1 Substances

Active Ingredients:

120066-54-8	Gadoteridol
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Impurities and stabilising additives:

CAS: 121915-83-1	Calcium Cateridol
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CAS: 77-86-1 EINECS: 201-064-4 RTECS: TY 2900000	trometamol
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3.2 Mixtures

Description: Mixture: consisting of the following components.

Dangerous Components

CAS N°	Description	%
Void		

Not Dangerous Components

CAS N°	Description	%
CAS: 120066-54-8	Gadoteridol	27.9%
CAS: 7732-18-5 EINECS: 231-791-2 RTECS: ZC0110000	Water USP	≈72%
CAS: 77-86-1 EINECS: 201-064-4 RTECS: TY 2900000	frometamol	<1%
CAS: 121915-83-1	Calcium Cateridol	<1%

Additional information: For the wording of the listed risk phrases refer to section 16.

4: First aid measures

4.1 Description of first aid measures

General information: No special measures required.

After Inhalation:

Remove exposed person to fresh air.
If person is not breathing, give artificial respiration.
If breathing is difficult administer oxygen.
Get medical attention immediately.

After Skin Contact:

Remove contaminated clothing.
Wash skin with plenty of water for 5 minutes.
Seek medical attention if irritation (redness, itching or swelling) develops or persists.

After Eye Contact:

Hold eyelids apart and flush with plenty of water for 5 minutes.
Get medical attention if signs of irritation develop.

After Swallowing:

Get medical attention immediately.
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.

4.2 Most important symptoms and effects, both acute and delayed See also Section 2 and 11.

4.3 Indication of any immediate medical attention and special treatment needed:

No further relevant information available.

Means of Specific and Immediate Treatment to Keep at the Workplace: No special measures required.

Note to physicians: None.

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5: Firefighting measures

5.1 Extinguishing media

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

For safety reasons unsuitable extinguishing agents: Unknown.

5.2 Special hazards arising from the substance or mixture See also Section 10.

Hazardous Combustion Products:

Carbon Dioxide (CO₂)

In the absence of Oxygen: Carbon Monoxide (CO_x)

Nitrogen Oxides (N_xO_y)

Gadolinium Oxide (Gd₂O₃)

Additional Information: Not Available

5.3 Advice for Firefighters

Evacuate personnel to an upwind direction, remove unneeded material and cool container(s) with water from a maximum distance.

Move container from fire area if you can do it without risk.

Protective Equipment:

Firefighters should wear adequate personal protective equipment with protection of respiratory tract (self-contained breathing apparatus) (SCBA).

Besides they should wear flame and chemicals resistant clothing, boots and gloves (see Section 8).

6: Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures

Wear protective equipment appropriate to the circumstances (see Section 8)

6.2 Environmental precautions: No special measures required.

6.3 Methods and material for containment and cleaning up:

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.

6.4 Reference to other sections

See Section 7 for information on Safe Handling.

See Section 8 for information on Personal Protection Equipment.

See Section 13 for Disposal Information.

See Section 12 for Ecological Information.

7: Handling and storage

7.1 Precautions for Safe Handling

Do not break vials.

Avoid splashing of liquid product.

Avoid skin and eye contact.

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

7.2 Conditions for Safe Storage, including any Incompatibilities

Requirements to be Met by Storerooms and Receptacles:

Store in cool place. Keep container tightly closed in a dry and well-ventilated place.

Container Requirements: Single dose 15, 30 and 50 mL vials and 20 mL prefilled syringes.

Storage Conditions: Store at 20-25 degrees C. Protect from light and do not freeze.

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Information about Storage in one Common Storage Facility: Not required.

Further information about storage conditions: None.

7.3 Specific end use(s) No further relevant information available.

8: Exposure controls/personal protection

Additional information about design of technical systems: No further data; see item 7.

8.1 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.

8.2 Exposure controls

Appropriate Technical Controls: Provide adequate aspiration / ventilation in the workplace

Additional information about Design of Technical Facilities: No further data (see Section 7).

Personal protective equipment

General Protective and Hygienic Measures:

The usual precautionary measures for handling chemicals should be followed.

Wash hands before breaks and at the end of work.

Wear protective equipment (PPE) appropriate to the circumstances.



Do not eat, drink, smoke while working.

Provide appropriate ventilation

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:



Wear impervious gloves if the potential exists for dermal contact.

Material of Gloves:

Latex, Latex / Nitrile or Nitrile Gloves.

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.

Selection of the glove material on consideration of the penetration times, rates of diffusion and the degradation.

The glove material has to be impermeable and resistant to the product/ the substance/ the mixture.

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.

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Eye Protection:



Wear safety glasses (ANSI Z87.1)

Body Protection:

If the risk assessment deems it necessary, wear protective coveralls to prevent contact with the body, due to the splashing and spraying of liquid.

Limitation and Supervision of Exposure into the Environment: See also Section 7.

Additional Information about Design of Technical Systems: No further data; see Section 7.

9: Physical and chemical properties

9.1 Information on basic physical and chemical properties

General Information

Appearance:

Form:	Liquid
Color:	Colorless - Slightly Yellow
Odor:	Undistinguishable
Odour threshold:	Not determined.

pH-value: 6.5 - 8.0

Melting point/Melting range: $\approx 0\text{ }^{\circ}\text{C}$

Boiling point/Boiling range: $\approx 100\text{ }^{\circ}\text{C}$

Flash point: Not applicable.

Flammability (solid, gaseous): Not applicable.

Ignition temperature:

Decomposition temperature: Not determined.

Auto igniting: Product is not selfigniting.

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.

Vapor pressure:

Gadoteridol:
T = 26°C, P° < 1.67 x 10⁻⁷ Torr

Density: (25°C) 1.140 g/cm³

Relative density: Not determined.

Vapour density: Not determined.

Evaporation rate: \approx as water

Solubility in / Miscibility with

Water: Not miscible or difficult to mix.

Segregation coefficient (n-octanol/water): pH = 7, logKow: -3.57 to -3.58
pH = 9, logKow: -3.66 to -3.70

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Viscosity:

Dynamic:

T = 20 °C, η = 2.0 cP

T = 37 °C, η = 1.3 cP

Kinematic:

Not determined.

9.2 Other information

No further relevant information available.

10: Stability and reactivity

10.1 Reactivity:

There are not particular dangerous reactions with other substances in normal conditions of use

10.2 Chemical stability: Stable under normal conditions.

10.3 Possibility of hazardous reactions: No dangerous reactions known.

10.4 Conditions to avoid: No further relevant information available.

10.5 Incompatible materials: No further relevant information available.

10.6 Hazardous decomposition products: No further relevant information available (See Section 5)

11: Toxicological information

11.1 Information on toxicological effects

Acute toxicity:

LD/LC50 values that are relevant for classification:

120066-54-8 Gadoteridol

LD50 ivn	7598 mg/kg (female mouse)
	5978 mg/kg (male mouse)
	5880 mg/kg (rat)

77-86-1 trometamol

Oral LD50	5900 mg/kg (rat)
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121915-83-1 Calcium Cateridol

LD50 ivn	1200 mg/kg (mouse)
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Toxicological Information for Active Ingredients:

In laboratory animals, GADOTERIDOL has practically showed to be non-toxic for intravenous via.

At doses about 100 times higher than therapeutic, the animals showed ataxia, convulsions, collapse, irregular breathing. There were no dose-effect pathological changes in the surviving animals.

In studies with rats and dogs, for a month and at doses three times higher than therapeutic, there were obvious effects on your kidneys (eg, vacuolation of renal tubular), even if these effects were reversible.

Primary irritant effect:

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.

on the skin:

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 eyes: No irritation effects reported. However, the product should be considered as a potential irritant.

Sensitization: The product can cause inflammation in people allergic to gadolinium and its compounds.

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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 ProHance 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 postimplantation 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.

Specific Target Organ Toxicity

Single Exposure (STOT - SE): No further relevant information available

Repeated Exposure (STOT - RE): No further relevant information available

Aspiration Hazard: No further relevant information available

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.

Nausea and altered sense of taste are reported for 1, 4% of the patients to whom the product was injected.

Effects on the cardiovascular system, digestive system and central nervous system have been detected on less than 1% of patients. Clinical doses may exacerbate hemolytic anemia.

When this product is taken for clinical use, the patients suffering from hepato-renal disorders, asthma attacks and other respiratory diseases should inform your doctor.

It must be borne in mind, however, that the doses administered for medical reasons are much higher than those due to the exposure in the workplace.

Additional toxicological information:

Contact with small quantities of material for short periods is not expected to result in pharmacologic or toxic effects.

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. Clinical doses of this material may possibly aggravate hemolytic anemias.

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.

Any Eventual Delayed Effect after Prolonged Exposure:

Repeated and prolonged exposure to skin may cause skin irritation

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12: Ecological information

12.1 Toxicity

Aquatic toxicity:

120066-54-8 Gadoteridol

EC50 >920 mg/l (daphnia)

IC50 >1000 mg/l (activated sludge)

12.2 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.

12.3 Bioaccumulative potential No further relevant information available.

12.4 Mobility in soil: No further relevant information available.

Additional ecological information

General notes:

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.

Avoid transfer into the environment.

12.5 Results of PBT and vPvB assessment

PBT: Not applicable.

vPvB: Not applicable.

12.6 Other adverse effects No further relevant information available.

Additional Information: Use according to good working practice.

13: Disposal considerations

13.1 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 packagings:

Recommendation: Dispose in accordance with national, state, local or applicable country regulations.

14: Transport information

14.1 UN-Number

DOT, ADR, ADN, IMDG, IATA

Void

14.2 UN proper shipping name

DOT, ADR, ADN, IMDG, IATA

Void

14.3 Transport hazard class(es)

ADR, ADN, IMDG, IATA

Class

Void

14.4 Packing group

DOT, ADR, IMDG, IATA

Void

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14.5 Environmental hazards:

Marine pollutant: No

14.6 Special precautions for user Not applicable.

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

UN "Model Regulation": -

15: Regulatory information

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

This safety data sheet complies with the requirements of Regulation (EC) No. 1907/2006.

Sara

Section 355 (extremely hazardous substances):

None of the ingredients is listed.

Section 313 (Specific toxic chemical listings):

None of the ingredients is listed.

TSCA (Toxic Substances Control Act):

7732-18-5 Water USP

77-86-1 trometamol

Proposition 65

Chemicals known to cause cancer:

None of the ingredients is listed.

Chemicals known to cause reproductive toxicity for females:

None of the ingredients is listed.

Chemicals known to cause reproductive toxicity for males:

None of the ingredients is listed.

Chemicals known to cause developmental toxicity:

None of the ingredients is listed.

Carcinogenic categories

EPA (Environmental Protection Agency)

None of the ingredients is listed.

IARC (International Agency for Research on Cancer)

None of the ingredients is listed.

NTP (National Toxicology Program)

None of the ingredients is listed.

TLV (Threshold Limit Value established by ACGIH)

None of the ingredients is listed.

NIOSH-Ca (National Institute for Occupational Safety and Health)

None of the ingredients is listed.

OSHA-Ca (Occupational Safety & Health Administration)

None of the ingredients is listed.

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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.

Significant Dangers:

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.

WARNINGS:

Diagnostic agents are intended for use under direction of a physician and/or under the conditions of use described on the label and in the product's package insert. As a general precaution, personnel who handle drug substances should avoid contact (ingestion, inhalation, skin and eye contact) with these substances.

Department issuing MSDS:

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38025 Grenoble, FRANCE
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Contact:

HSE Department - Bracco Group
hse@bracco.com

Abbreviations and acronyms:

ADR: Accord européen sur le transport des marchandises dangereuses par Route (European Agreement concerning the International Carriage of Dangerous Goods by Road)
RID: Règlement international concernant le transport des marchandises dangereuses par chemin de fer (Regulations Concerning the International Transport of Dangerous Goods by Rail)
IMDG: International Maritime Code for Dangerous Goods
IATA: International Air Transport Association
ICAO: International Civil Aviation Organization
GHS: Globally Harmonized System of Classification and Labelling of Chemicals
ACGIH: American Conference of Governmental Industrial Hygienists
CAS: Chemical Abstracts Service (division of the American Chemical Society)
NFPA: National Fire Protection Association (USA)
HMIS: Hazardous Materials Identification System (USA)
LC50: Lethal concentration, 50 percent
LD50: Lethal dose, 50 percent

*** Data compared to the previous version altered.**

- data updating on the basis of the latest amendments.
- adaptation of the form according to Regulation 1907/2006/CE.