# Safety Data Sheet
*acc. to OSHA HCS*

Printing date 08/18/2016 Version 3 Reviewed on 08/18/2016

## 1 Identification

### Product identifier

***Sheet 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 in15 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).

### 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.

***Chemical Family:*** Gadolinium chelate.
***Molecular Formula:*** C17H29N4O7.Gd
***CAS Number:*** 120066-54-8

### 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

***Information department:***
B-Lands Consulting
WTC, 5 Place Robert Schuman, BP 1516
38025 Grenoble, FRANCE
Tel: +33 476 295 869
Fax: +33 476 295 870
Email: clients@reachteam.eu
www.reachteam.eu

### Emergency telephone number:
EMERGENCY CONTACT:
Health: 1-800-257-5181
U.S. Transport - Chemtrec: 1-800-424-9300
Intenational 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 Hazard(s) identification

### Classification of the substance or mixture
The product is not classified according to the Globally Harmonized System (GHS).

(Contd. on page 2)

# Safety Data Sheet
*acc. to OSHA HCS*

Printing date 08/18/2016 Version 3 Reviewed on 08/18/2016

**Trade name:** ProHance

(Contd. of page 1)

### Label elements
***GHS label elements*** Not applicable.

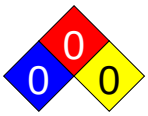
***Hazard pictograms*** Not applicable.

***Signal word*** Not applicable.

***Hazard statements*** Not applicable.

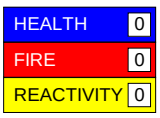
***Effects of Overexposure - Routes of Entry:***
***Inhalation:*** Under normal conditions, exposure to this material by inhalation is not expected to occur.
***Skin Contact:***
Exposure may occur via skin contact if gloves and protective clothing are not worn. The extent of systemic absorption of the 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.
***Additional Information:***
***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
***NFPA ratings (scale 0 - 4)***




Health = 0
Fire = 0
Reactivity = 0

***HMIS-ratings (scale 0 - 4)***




Health = 0
Fire = 0
Reactivity = 0

***Results of PBT and vPvB assessment***
***PBT:*** Not applicable.
***vPvB:*** Not applicable.

## 3 Composition/information on ingredients

### Chemical characterization: Substances

| ***Active Ingredient:*** | | |
|---|---|---|
| 120066-54-8 | (±)-[10-(2-hydroxypropyl)-1,4,7,10-tetraazacyclododecane-1,4,7-triacetate (3 -)] Gadolinium | 27.9% |

| ***Impurities and stabilising additives:*** | |
|---|---|
| CAS: 121915-83-1 | Calcium Calteridol |
| CAS: 77-86-1<br>EINECS: 201-064-4<br>RTECS: TY 2900000 | trometamol |

### Chemical characterization: Mixtures

***Description:*** Mixture: consisting of the following components.

(Contd. on page 3)

# Safety Data Sheet
*acc. to OSHA HCS*

Printing date 08/18/2016 Version 3 Reviewed on 08/18/2016

***Trade name:*** ProHance

(Contd. of page 2)

***Hazardous Components:*** Not applicable.

## 4 First-aid measures

### 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.

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

### 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.

## 5 Fire-fighting measures

### Extinguishing media

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

***For safety reasons unsuitable extinguishing agents:*** Unknown.

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

***Hazardous Combustion Products:***
Carbon Dioxide ($CO_2$)
In the absence of Oxygen: Carbon Monoxide (CO)
Nitrogen Oxides (NxOy)
Gadolinium Oxide ($Gd_2O_3$)
***Additional Information:*** Not Available

### 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.

(Contd. on page 4)

# Safety Data Sheet
*acc. to OSHA HCS*

Printing date 08/18/2016 Version 3 Reviewed on 08/18/2016

**Trade name:** ProHance

(Contd. of page 3)

***Protective Equipment:***
Firefighters should wear adequate personal protective equipment with protection of respiratory tract (selfcontained breathing apparatus) (SCBA).
Wear flame and chemicals resistant clothing, boots and gloves (see Section 8).

## 6 Accidental release measures

***Personal precautions, protective equipment and emergency procedures***
²Wear protective equipment appropriate to the circumstances (see Section 8)

***Environmental precautions:*** No special measures required.

***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.

***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

***Precautions for Safe Handling***
Do not break vials.
Avoid splashing of liquid product.
Avoid skin and eye contact.

***Conditions for Safe Storage, including any Incompatibilities***
***Requirements to be met by Storerooms and Receptacles:***
Store in a cool, dry place in tightly closed receptacles.
***Container Requirements:*** Single dose 15, 30 and 50 mL vials and 20 mL prefilled syringes.
***Storage Conditions:*** Store at 25 ÁC, excursions permitted to 15-30ÁC. Protect from light and do not freeze.
***Information about Storage in one Common Storage Facility:*** Not required.
***Further information about storage conditions:*** None.

***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.

***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***
***Appropriate Technical Controls:*** Provide adequate aspiration / ventilation in the workplace
***Additional information about Design of Technical Facilities:*** No further data (see Section 7).

(Contd. on page 5)

# Safety Data Sheet
*acc. to OSHA HCS*

Printing date 08/18/2016 Version 3 Reviewed on 08/18/2016

***Trade name:*** ProHance

(Contd. of page 4)

***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.
***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

| ***Information on basic physical and chemical properties*** | |
|---|---|
| ***General Information*** | |
| ***Appearance:*** | |
| ***Form:*** | Liquid |
| ***Color:*** | Colorless - Slightly Yellow |
| ***Odor:*** | Undistinguishable |

(Contd. on page 6)

**Safety Data Sheet**
*acc. to OSHA HCS*

Printing date 08/18/2016 Version 3 Reviewed on 08/18/2016

***Trade name:*** ProHance

(Contd. of page 5)

| | |
|---|---|
| ***Odour threshold:*** | Not determined. |
| ***pH-value:*** | 6.5 - 8.0 |
| ***Melting point/Melting range:*** | ca. 100 °C |
| ***Boiling point/Boiling range:*** | ca. 0 °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. |
| ***Density:*** | (25 °C) 1.140 g/cm3 |
| ***Bulk density:*** | (25 °C) 1.140 g/cm3 |
| ***Relative density*** | Not determined. |
| ***Vapour density*** | Not determined. |
| ***Solubility in / Miscibility with*** | |
| ***Water:*** | Not miscible or difficult to mix. |
| ***Partition coefficient (n-octanol/water):*** | pH=7, logKow: -3.57 to -3.58<br>pH=9, logKow: -3.66 to -3.70 |
| ***Viscosity:*** | |
| ***Dynamic:*** | T = 20 °C, η = 2.0 cP<br>T = 37 °C, η = 1.3 cP |
| ***Kinematic:*** | Not determined. |
| ***Water:*** | 71.9 % |
| ***Other information*** | No further relevant information available. |

## *10 Stability and reactivity*

***Reactivity:*** There are not particular dangerous reactions with other substances in normal conditions of use.

***Chemical stability:*** Stable under normal conditions.

***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 further relevant information available ( See Section 5)



(Contd. on page 7)

# Safety Data Sheet
*acc. to OSHA HCS*

Printing date 08/18/2016 Version 3 Reviewed on 08/18/2016

***Trade name:*** ProHance

(Contd. of page 6)

## *11 Toxicological information*

### *Information on toxicological effects*

***Acute toxicity:***
***Toxicological Information for Active Ingredients:***

| ***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 ivn | 7598 mg/kg (Female Mouse)<br>5978 mg/kg (Male Mouse)<br>5880 mg/kg (rat) |
| **77-86-1 trometamol** | | |
| Oral | LD50 | 5900 mg/kg (rat) |
| **121915-83-1 Calcium Calteridol** | | |
| | LD50 ivn | 1200 mg/kg (Mouse) |

***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.

***CMR effects (carcinogenity, mutagenicity and toxicity for reproduction):***
***Sensitization:*** The product can cause inflammation in people allergic to gadolinium and its compounds.
***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 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:***

(Contd. on page 8)

(Contd. of page 7)

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.

***Carcinogenic categories***

| ***IARC (International Agency for Research on Cancer)*** |
|---|
| None of the ingredients is listed. |

| ***NTP (National Toxicology Program)*** |
|---|
| None of the ingredients is listed. |

| ***OSHA-Ca (Occupational Safety & Health Administration)*** |
|---|
| None of the ingredients is listed. |

***Additional toxicological information:***
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.
***Any Eventual Delayed Effect after Prolonged Exposure:***
Repeated and prolonged exposure to skin may cause skin irritation

## *12 Ecological information*

***Toxicity***

| ***Aquatic toxicity:*** | |
|---|---|
| **120066-54-8 (±)-[10-(2-hydroxypropyl)-1,4,7,10-tetraazacyclododecane-1,4,7-triacetate (3 -)] Gadolinium** | |
| EC50 | >920 mg/l (Daphnia) |
| IC50 | >1000 mg/l (Activated Sludge) |

***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.

***Bioaccumulative potential*** No further relevant information available.

***Mobility in soil:*** No further relevant information available.

***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.

***Results of PBT and vPvB assessment***
***PBT:*** Not applicable.
***vPvB:*** Not applicable.

***Other adverse effects*** No further relevant information available.
***Additional Information:*** Use according to good working pratice.



(Contd. on page 9)

# Safety Data Sheet
*acc. to OSHA HCS*

Printing date 08/18/2016 Version 3 Reviewed on 08/18/2016

**Trade name:** ProHance

(Contd. of page 8)

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

## 14 Transport information

| | |
|---|---|
| ***UN-Number***<br>***DOT, ADR, ADN, IMDG, IATA*** | Void |
| ***UN proper shipping name***<br>***DOT, ADR, ADN, IMDG, IATA*** | Void |
| ***Transport hazard class(es)***<br>***ADR, ADN, IMDG, IATA***<br>***Class*** | Void |
| ***Packing group***<br>***DOT, ADR, IMDG, IATA*** | Void |
| ***Environmental hazards:***<br>***Marine pollutant:*** | No |
| ***Special precautions for user*** | Not applicable. |
| ***Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code*** | Not applicable. |
| ***UN "Model Regulation":*** | - |

## 15 Regulatory information

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

(Contd. on page 10)

# Safety Data Sheet
*acc. to OSHA HCS*

Printing date 08/18/2016 Version 3 Reviewed on 08/18/2016

***Trade name:*** ProHance

(Contd. of page 9)

***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.

***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.

***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.

***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 SDS:***
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
***Date of preparation / last revision:*** 08/18/2016

***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
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)
LC50: Lethal concentration, 50 percent

(Contd. on page 11)

# Safety Data Sheet
*acc. to OSHA HCS*

Printing date 08/18/2016 Version 3 Reviewed on 08/18/2016

***Trade name:*** ProHance

(Contd. of page 10)

LD50: Lethal dose, 50 percent

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

- data updating on the basis of the latest amendments.