ProHance®

gadoteridol

# When Stability Matters

Committed **to Science,**
Committed **to You.**™

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# An **established safety** profile

## Low overall rates of undesirable effects[1-5]

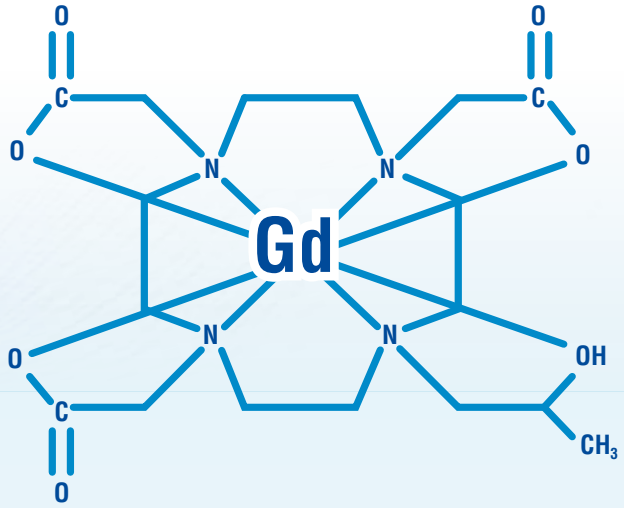
- In a large observational study in more than 28,000 patients, the overall adverse reaction rate was less than 0.75%[6]

## The lowest osmolality and viscosity among all Gd-based agents[7]

- A lower-viscosity contrast agent will require lower pressures to achieve rapid injection rates and, consequently, may be better tolerated[8]

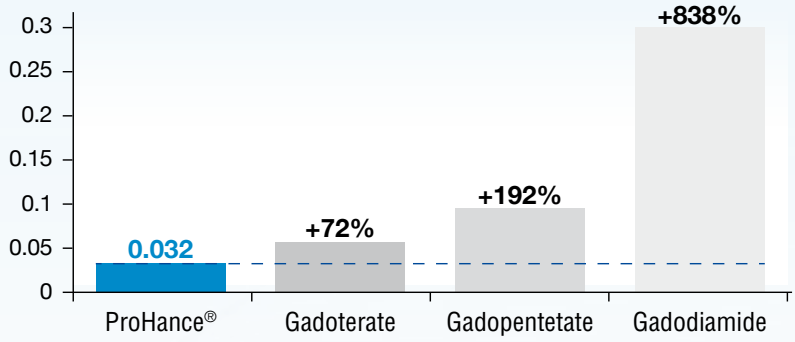
# By all measures, ProHance® is a **highly stable** Gd chelate

**ProHance® is a non-ionic molecule with a macrocyclic structure that cages Gd inside**[9]




***In-vivo* measurement of residual Gd remaining in the body after administration is clinically more relevant than *in-vitro* tests**[10]

**% of radiolabeled Gd remaining in the body (mice and rats) 14 days after injection**[11]




(Modified from Tweedle et al. 1995[11])

- 3-fold lower $Gd^{3+}$ deposition 14 days after IV administration vs. gadopentetate*[11]
- Even greater difference in favour of ProHance® vs. gadodiamide* in the amount of residual $Gd^{3+}$ found in animals[11]

**In a study of Gd retention in bone, Omniscan® left 2.5 times more Gd behind than did ProHance®**[12]

**ProHance® demonstrated a very high *in-vivo* stability**[9,11]

* The compounds tested were different from the commercial products.

# An easy-to-use contrast agent in a **wide range of indications**

**The clinical experience of ProHance® exceeds 15 million doses administered worldwide[13]**

## Approved for MRI in children from 6 months of age*

to visualize lesions with abnormal vascularity in the brain, spine, and associated tissues[5]

## Indicated in adults for CNS and whole body MRI

including head, neck, liver, breast, musculoskeletal system and soft tissue pathologies[5]

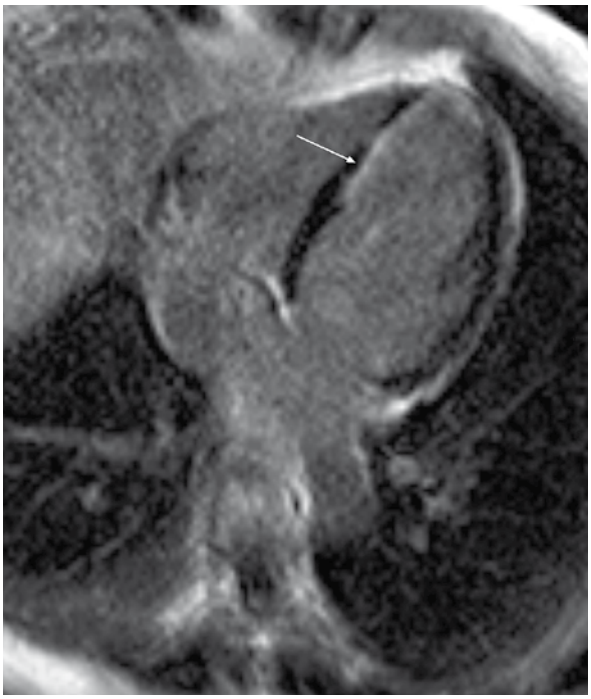
## No contraindication for use in patients with severe renal impairment or renal failure[5**]

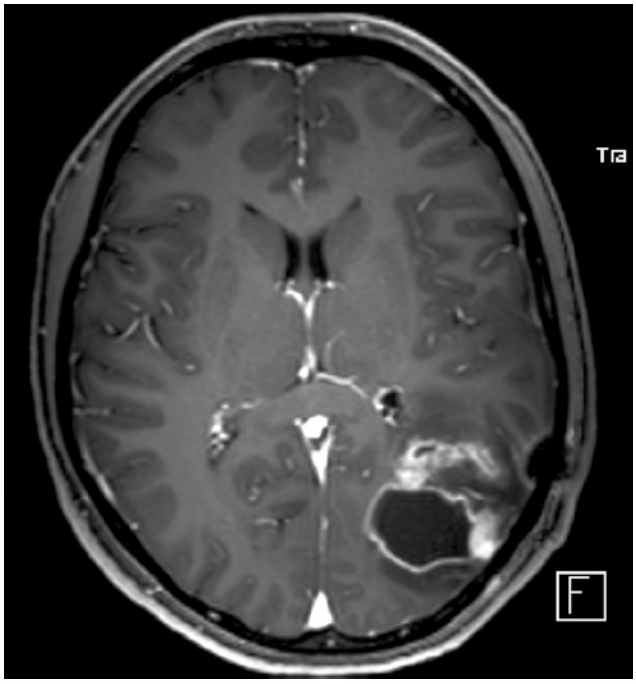
* This may not apply to all countries where the product is marketed. Please contact your local Bracco organisation for more information.

** Since nephrogenic systemic fibrosis (NSF) may occur with some Gd-containing contrast agents, ProHance® should only be used in patients with acute or severe chronic renal impairment and in patients in the perioperative liver transplantation period after careful risk/benefit assessment and if the diagnostic information is essential and not available with non-contrast enhanced MRI. Please refer to your local ProHance® SPC for more information.

# ProHance® provides additional information in a **wide range of examinations** of the body

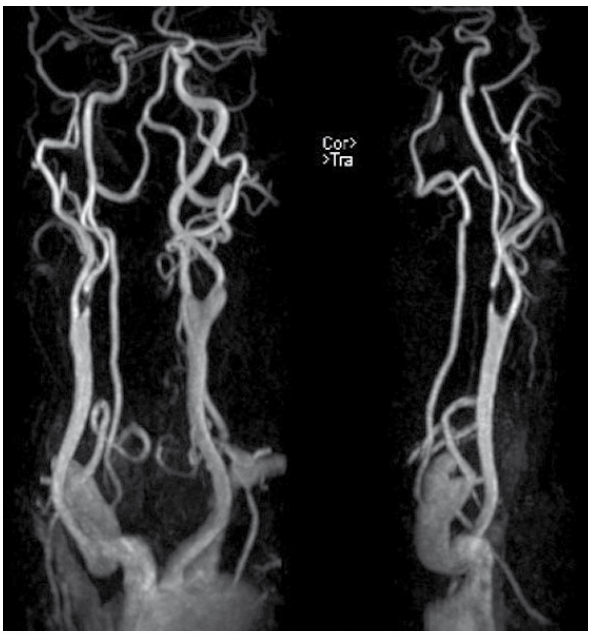
54-yo female patient with subendocardial infarct.
MRI with ProHance® shows a subendocardial delayed enhancement involving the mid and apical segment of the septum.






31-yo female patient with recurrent occipito-temporal glioblastoma after administration of ProHance® 0.1 mmol/kg at 3 Tesla.

83-yo male patient with filiform stenosis in the proximal right ICA. In addition, missing A1 segment of the anterior cerebral artery on the right (variant of the norm).



# When **stability matters** you can count on **ProHance®**

## Non-ionic macrocyclic chelate

Very high *in-vivo* stability
reducing the risk of Gd exposure[9,11]

## Broad-use contrast agent

Approved for paediatric patients from 6 months*
as well as CNS and whole body MRI in adults[5]

## Proven safety profile

Low overall rates of adverse events
in clinical trials and observational studies[5,6]

## Long global experience

More than 15 million doses
administered worldwide since 1992[13]

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Please contact your local Bracco organisation for more information.

# A full line of **packaging options** to optimize dosing protocols

**ProHance® presentations offering dosing versatility and minimization of contrast waste**


*Available presentations**

| | |
|---|---|
| **Single-dose vials** | 5, 10, 15, 20 ml |
| **Prefilled syringes** | 10, 15, 17 ml |

**The only MR contrast agent in a 17 ml prefilled syringe**

## Recommended doses in MRI[5]

| | BRAIN AND SPINE | WHOLE BODY |
|---|---|---|
| **ADULTS** | 0.1 mmol/kg + 0.2 mmol/kg[a] | 0.1 mmol/kg[a] |
| **CHILDREN** (6 months and above)[b] | 0.1 mmol/kg | – |

[a] In patients suspected of having poorly enhancing lesions, in the presence of negative or equivocal scans, a second dose of 0.2 mmol/kg may be given up to 30 minutes after the first dose. Doses of 0.3 mmol/kg have been shown to be useful in patients suspected of having cerebral metastases or other poorly enhancing lesions.

[b] This may not apply to all countries where the product is marketed. Please contact your local Bracco organisation for more information.

* Please refer to the locally approved SPC for information on the presentations available in your country.

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## SUMMARY OF PRODUCT CHARACTERISTICS

**ProHance, 0.5 M solution for injection** **Composition** 1 ml of solution for injection contains: gadoteridol 279.3mg/ml (0.5M). **Excipients** Calteridol Calcium, Tromethamine USP, Hydrochloric Acid Ph Eur, Sodium Hydroxide Ph Eur, Water for Injections Ph Eur. **Therapeutic indications** Using Magnetic Resonance Imaging (MRI), ProHance provides contrast enhancement of the brain, spine and surrounding tissues resulting in improved visualization (compared with unenhanced MRI) of lesions with abnormal vascularity or those thought to cause a disruption of the normal blood-brain barrier. ProHance can also be used for whole body MRI including the head, neck, liver, breast, muscoloskeletal system and soft tissue pathologies. **Posology** *Adults* The recommended dose of ProHance for imaging most brain and spinal pathologies is 0.1 mmol/kg. However, doses of 0.3 mmol/kg have been shown to be useful in patients suspected of having cerebral metastases or other poorly enhancing lesions. The recommended dose for whole body MRI is 0.1 mmol/kg. *Children* In children aged 2 years and above, the recommended dose of ProHance for brain imaging and spine pathologies is 0.1 mmol/kg (0.2 ml/kg). ProHance has been used in only a limited number of children aged between 6 months and 2 years. If an MRI procedure must be performed in this group, particular caution should be exercised. **Contra-indications** ProHance is contra-indicated in patients with hypersensitivity to the active substance gadoteridol or any of its constituents or other gadolinium-based contrast. **Special warnings and special precaution for use** Patients with a history of allergy, drug reactions, or other hypersensitivity-like disorders should be closely observed during the procedure and the contrast medium administration, as well as for the time the physician deems useful given the patient condition. As with other gadolinium chelates, there have been reports of anaphylactic/anaphylactoid/ hypersensitivity reactions with gadoteridol. These reactions manifested with various degrees of severity, including anaphylactic shock or death. They involved one or more body systems, mostly respiratory, cardiovascular and/or mucocutaneous systems. Anaphylactic shock has been very rarely been reported with the use of gadoteridol. Appropriate drugs and instruments for emergency measures must be readily available. Transitory changes in serum iron (within normal range in the majority of cases) have been observed in some patients after administration of ProHance and these changes were shown not to be clinically significant. Since Gadoteridol is renally cleared from the body, caution should be exercised in patients with severely impaired renal function. **Undesirable effects** The accepted safety considerations and procedures that are required for Magnetic Resonance Imaging are applicable when ProHance is used for contrast enhancement. The following adverse reactions have been reported with ProHance. Adverse reactions from clinical trials have been included with an indication of the frequency. Adverse reactions from spontaneous reporting are included with the frequency "not known". There were no adverse reactions with an incidence greater than 2%. Common (≥1/100, <1/10): *Gastrointestinal disorders;* Nausea. Uncommon (≥1/1,000, <1/100): *Immune system disorders;* Anaphylactic/anaphylactoid reactions. *Nervous system disorders;* headache, paraesthesia, dizziness, taste disturbance. Eye disorders; increased lacrimation. *Vascular disorders;* flushing, hypotension. *Gastrointestinal disorders;* dry mouth, vomiting. *Skin and subcutaneous tissue disorders;* pruritus, rash, urticaria. *General disorders and administration site conditions;* injection site pain, asthenia. *Investigations;* heart rate increased. Rare (1/10,000, <1/1,000): *Psychiatric disorders;* anxiety. *Nervous system disorders;* mental impairment, abnormal coordination, convulsion. *Ear and labyrinth disorders;* tinnitus. *Cardiac disorders;* nodal arrhythmia. *Respiratory, thoracic and mediastinal disorders;* laryngospasm, dyspnoea, rhinitis, cough, apnea, wheezing. *Gastrointestinal disorders;* abdominal pain, tongue oedema, oral pruritus, gingivitis, loose stools. *Skin and subcutaneous tissue disorders;* oedema face. *Musculoskeletal and connective tissue disorders;* musculoskeletal stiffness. *General disorders and administration site conditions;* chest pain, pyrexia. Not known (cannot be estimated from the available clinical trial data): *Nervous system disorders;* loss of consciousness, coma, vasovagal reactions. *Cardiac disorders;* cardiac arrest. *Renal and urinary system;* acute renal failure. **Additional safety information** Isolated cases of nephrogenic systemic fibrosis (NSF) have been reported with ProHance, most of which were in patients co-administered other gadolinium-containing contrast agents (see below). Impaired renal function Prior to administration of ProHance, it is recommended that all patients are screened for renal dysfunction by obtaining laboratory tests. There have been reports of nephrogenic systemic fibrosis (NSF) associated with use of some gadolinium-containing contrast agents in patients with acute or chronic severe renal impairment (GFR <30 ml/min/1.73m$^2$). Patients undergoing liver transplantation are at particular risk since the incidence of acute renal failure is high in this group. As there is a possibility that NSF may occur with ProHance, it should therefore only be used in patients with severe renal impairment and in patients in the perioperative liver transplantation period after careful risk/benefit assessment and if the diagnostic information is essential and not available with non-contrast enhanced MRI. Haemodialysis shortly after ProHance administration may be useful at removing ProHance from the body. There is no evidence to support the initiation of haemodialysis for prevention or treatment of NSF in patients not already undergoing haemodialysis. Infants from 6 months to 1 year of age Due to immature renal function in infants up to 1 year of age, ProHance should only be used in patients 6 to 12 months of age after careful consideration at a dose not exceeding 0.1 mmol/kg body weight. More than one dose should not be used during a scan. Because of the lack of information on repeated administration, ProHance injections should not be repeated unless the interval between injections is at least 7 days. Use of ProHance is not recommended in children less than 6 months of age. Use for whole body MRI is not recommended in children less than 18 years of age. Elderly (aged 65 years and above) No dosage adjustment is considered necessary. Caution should be exercised in elderly patients (see section Special warnings). Please note: The peel-off tracking label on the vials should be stuck onto the patient records to enable accurate recording of the gadolinium contrast agent used (EU). The dose used should also be recorded (EU). Consult the locally approved package insert. The Marketing Authorisation Holder, the Marketing Authorisation number and the date of approval may be different in different countries. For current prescribing information refer to the package insert and/or contact your local Bracco organisation. **Date of revision of this text** July 2012.

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