

Dotarem®

Gadoteric acid

THE 1ST MACROCYCLIC GBCA
ON THE MARKET¹

STABILITY and Experience



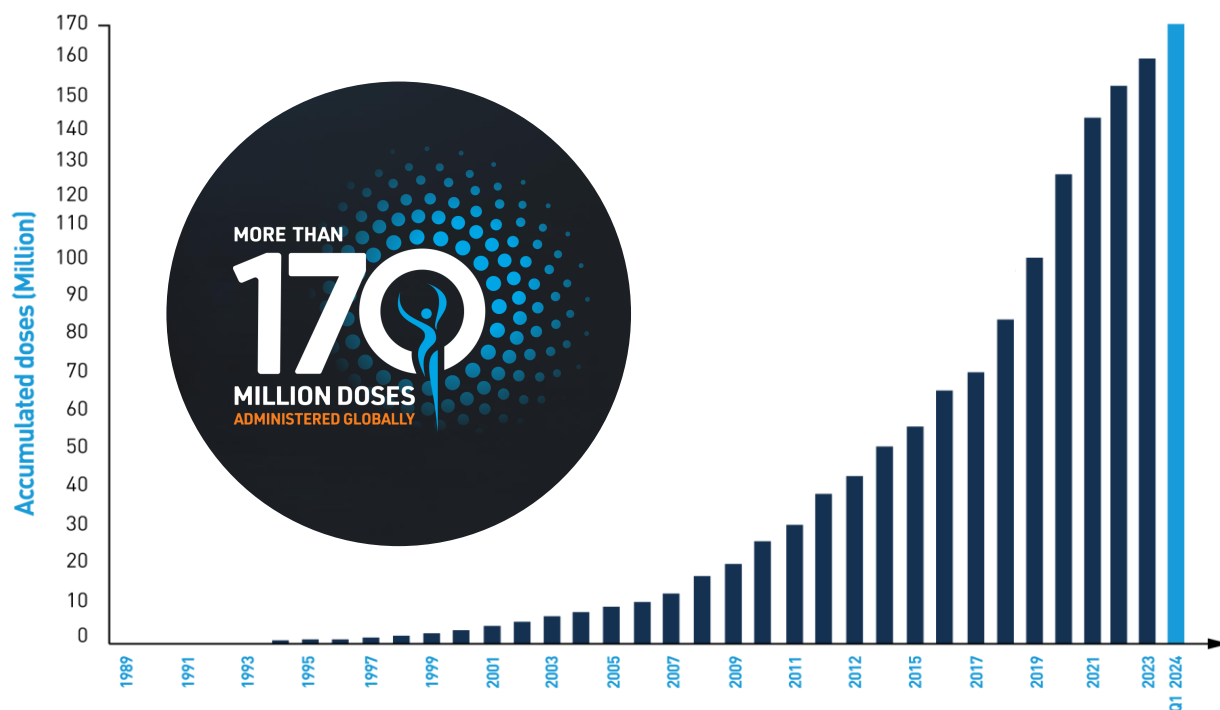
MORE THAN

170

MILLION DOSES
ADMINISTERED GLOBALLY

Dotarem® by Guerbet, the first macrocyclic GBCA in MRI¹

Dotarem® administered doses worldwide²



Dotarem® has been clinically used in **>170 million doses** worldwide²



Zero confirmed unconfounded NSF cases in over 35 years of real-world clinical experience³



Dotarem® is approved in over **80 countries**⁴



To date, Dotarem® is used in an MRI procedure **every 3 seconds** worldwide²

Approve for use from Term Neonates to the Elderly



Recommended dose: 0.1 mmol Gd/kg (0.2 mL/kg)

More than one dose may be considered for specific applications^{5***}:

- ✓ **Angiography**
In exceptional circumstances administration of a second consecutive injection of 0.1 mmol/kg BW (0.2 mL/kg BW) may be justified
- ✓ **Encephalic and spinal MRI**
The dose can vary from 0.1 to 0.3 mmol/kg (0.2–0.6 mL/kg). For brain tumors, an extra 0.2 mmol/kg (0.4 mL/kg) can may be considered after the first injection

Dotarem® is approved for use in **adults, pediatrics, and term neonates*** (<2 years old) for contrast enhancement in⁵:

Adults (≥ 18 years) MRI for:

- ✓ **Cerebral and spinal disease**
- ✓ **Diseases of the vertebral column**
- ✓ **And other whole-body pathologies (including angiography**)**

Pediatric population (0–18 years)

- ✓ **MRI for cerebral and spinal disease**
- ✓ **Whole-body MRI**



Dose adjustment⁵

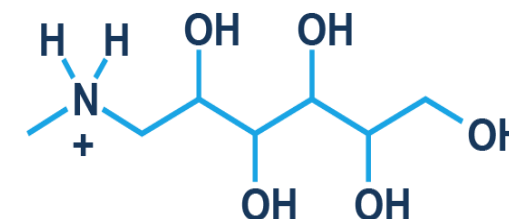
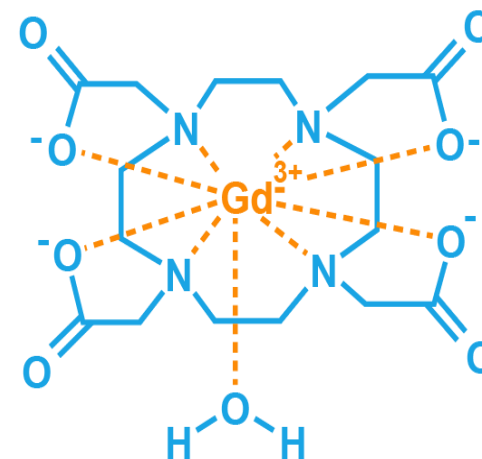
What is Dotarem® (gadoteric acid)?

Dotarem®

is a **gadolinium-based contrast agent**.
It is a paramagnetic, **macrocyclic**, **ionic** compound
used in magnetic resonance imaging (MRI).

Gadolinium (Gd)

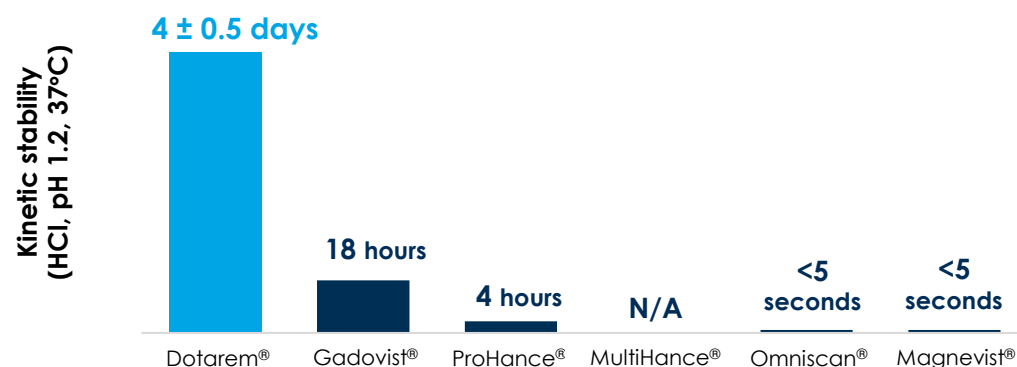
A paramagnetic lanthanide used in GBCAs
to enhance MRI signal by **interacting with water protons**
and **shortening T1-relaxation times**¹



Gd-DOTA (Dotarem®)⁷

Dotarem® offers high kinetic and thermodynamic stabilities compared to other conventional GBCAs – Thanks to its macrocyclic ionic structure

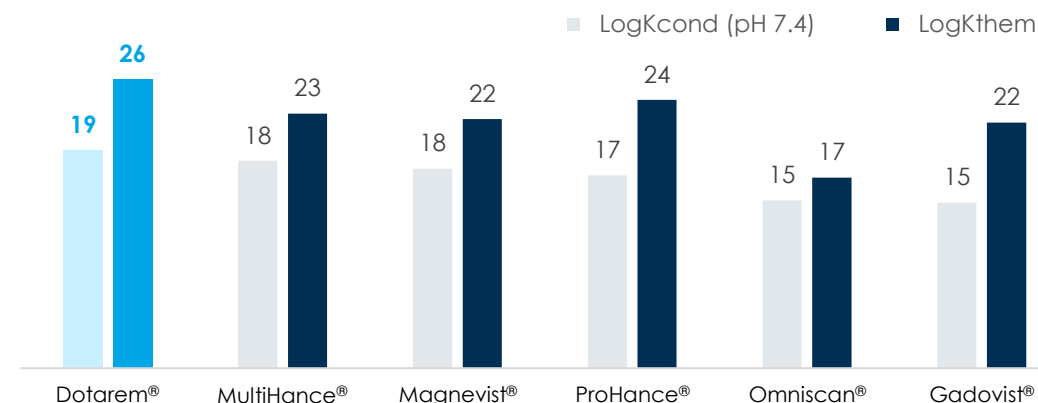
Kinetic stability of conventional GBCAs¹²



Kinetic stability

Rate of free Gd release (transmetalation),
i.e. the **speed that Gd³⁺ ions dissociate**
from the chelate¹³

Thermodynamic stability of conventional GBCAs¹²



Thermodynamic stability

Affinity of free Gd to the chelate,
i.e. the **quantity of Gd³⁺ ions**
released from the chelate¹³

Why stability is important?

A high stability GBCA reduces both the quantity and rate of Gd^{3+} being dissociated from the chelated complexes.⁶

Free Gd^{3+} ions in the body

may compete with and disrupt calcium-dependent processes, potentially causing **enzyme dysfunction, cellular imbalance and injury**¹¹

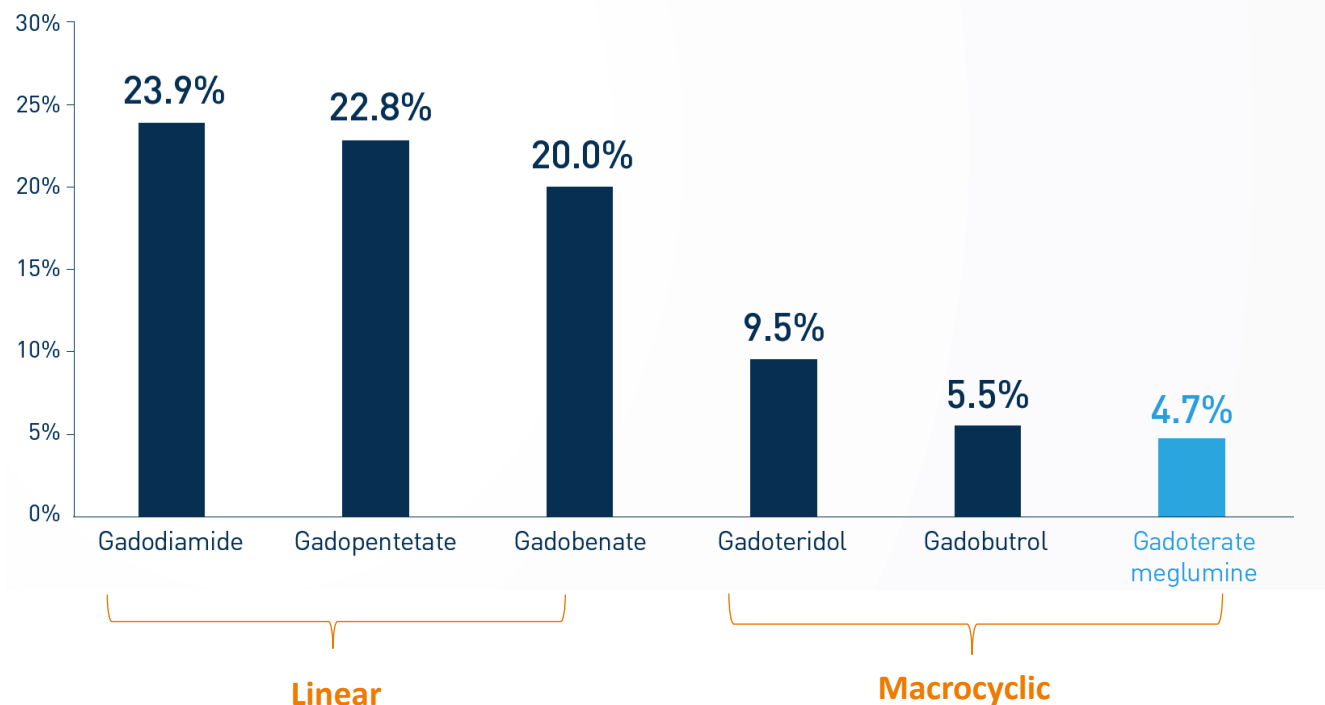
Nephrogenic systemic fibrosis (NSF)

is a rare, serious condition linked to **gadolinium exposure**, especially in patients with **renal impairment**, and is more associated with **linear GBCAs** due to their lower chelate stabilities⁸⁻¹⁰

It is a rare **systemic disease marked by fibrosis** that hardens skin and tissues, limits mobility, and in severe cases, affects internal organs such as the lungs, liver, or heart⁸⁻¹⁰

Symptoms associated with Gd exposure (SAGE) in real-life

Global SAGE weights per GBCA from FAERS database (2014 – 2019)
A total of 35,314 adverse events were analyzed¹⁵



✓ SAGE events were more frequent with **linear GBCAs**¹⁴⁻¹⁵

Gadoterate meglumine (Gadoteric acid) demonstrated the lowest percentage of global SAGE weights of all studied GBCAs¹⁵

Dotarem® is registered in the USA with gadoterate meglumine as the active substance



Study information¹⁵

SAGE weights = number of SAGE events / total number of adverse events

Diagnostic efficacy: REMIND study

Patient Distribution by Lesion Visualization and Characterization Score (Excellent, Good, Fair, Poor)¹⁶



In the REMIND Study, Dotarem® was found to be non-inferior to Gadovist® in the overall visualization and characterization of primary brain tumors¹⁶

✓ **>90% of images presented with good or excellent overall lesion visualization and characterization with both agents**

✓ **Diagnostic confidence was high/excellent in >81% of the patients with both contrast agents for all readers**



Study information¹⁶

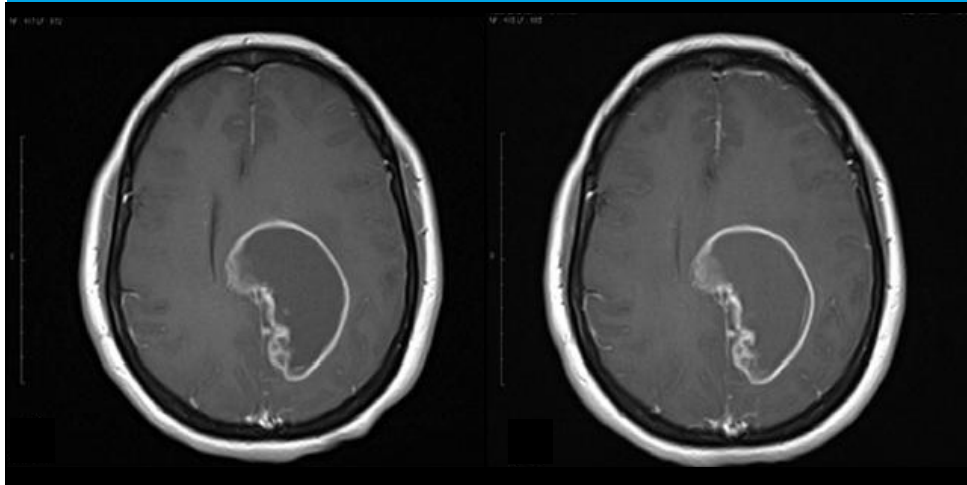
REMIND Study demonstrated that Dotarem® was non-inferior to Gadovist® for overall visualization and characterization of primary brain tumors¹⁶

Case Study A

A 46-year-old woman with glioblastoma

Post administration of
Dotarem® 0.1 mmol Gd/kg

Post administration of
Gadovist® 0.1 mmol Gd/kg



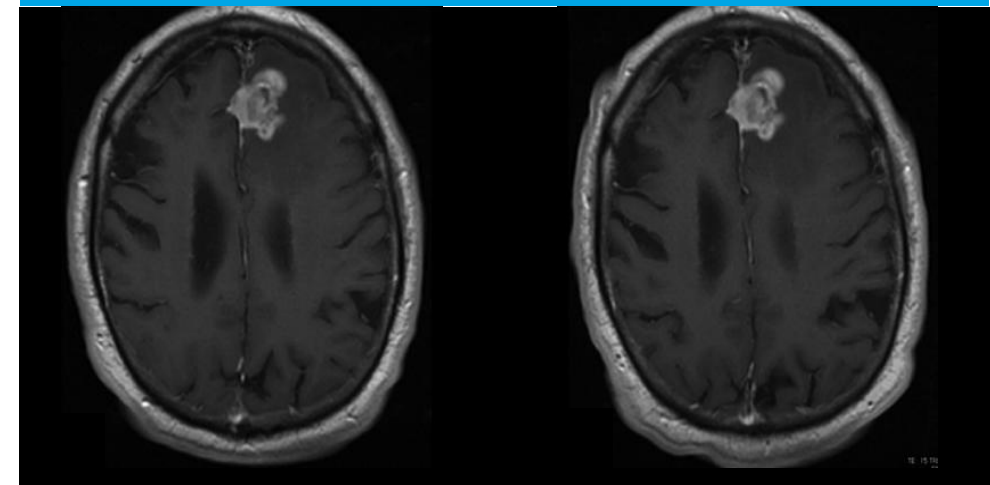
T1 spin-echo images (1.5T) show an approximate 65-mm lesion
Time interval between the two MRI examinations was 7 days

Case Study B

A 74-year-old man with a high-grade glioma

Post administration of
Dotarem® 0.1 mmol Gd/kg

Post administration of
Gadovist® 0.1 mmol Gd/kg



T1 spin-echo images (1.5T) show an approximate 30-mm mass
Time interval between the two MRI examinations was 8 days

In the REMIND study, off-site readers showed no preference between Dotarem® and Gadovist® across three quantitative secondary criteria¹⁶



Internal morphology

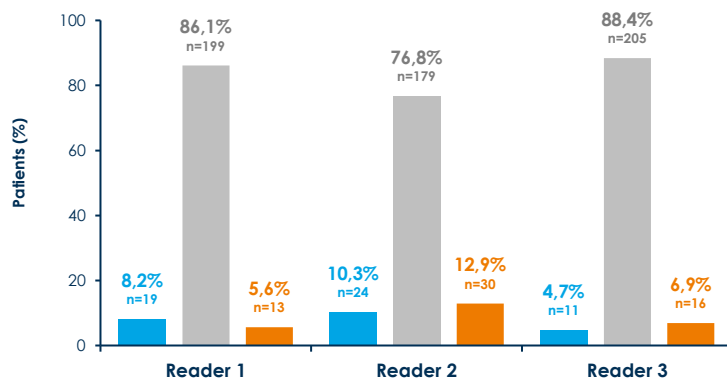


Degree of contrast enhancement

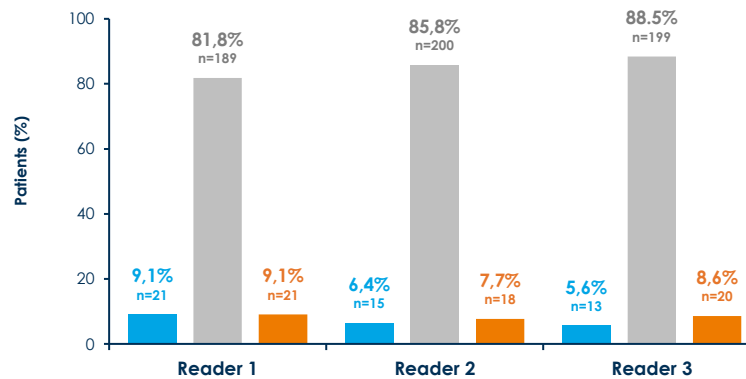


Border delineation

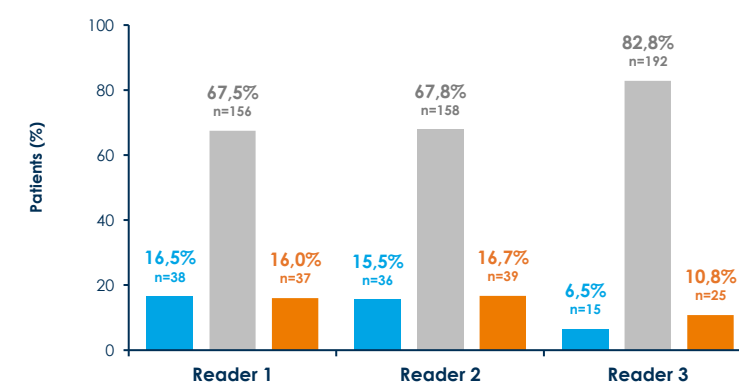
Internal morphology



Degree of contrast enhancement



Border delineation



Dotarem® preferred

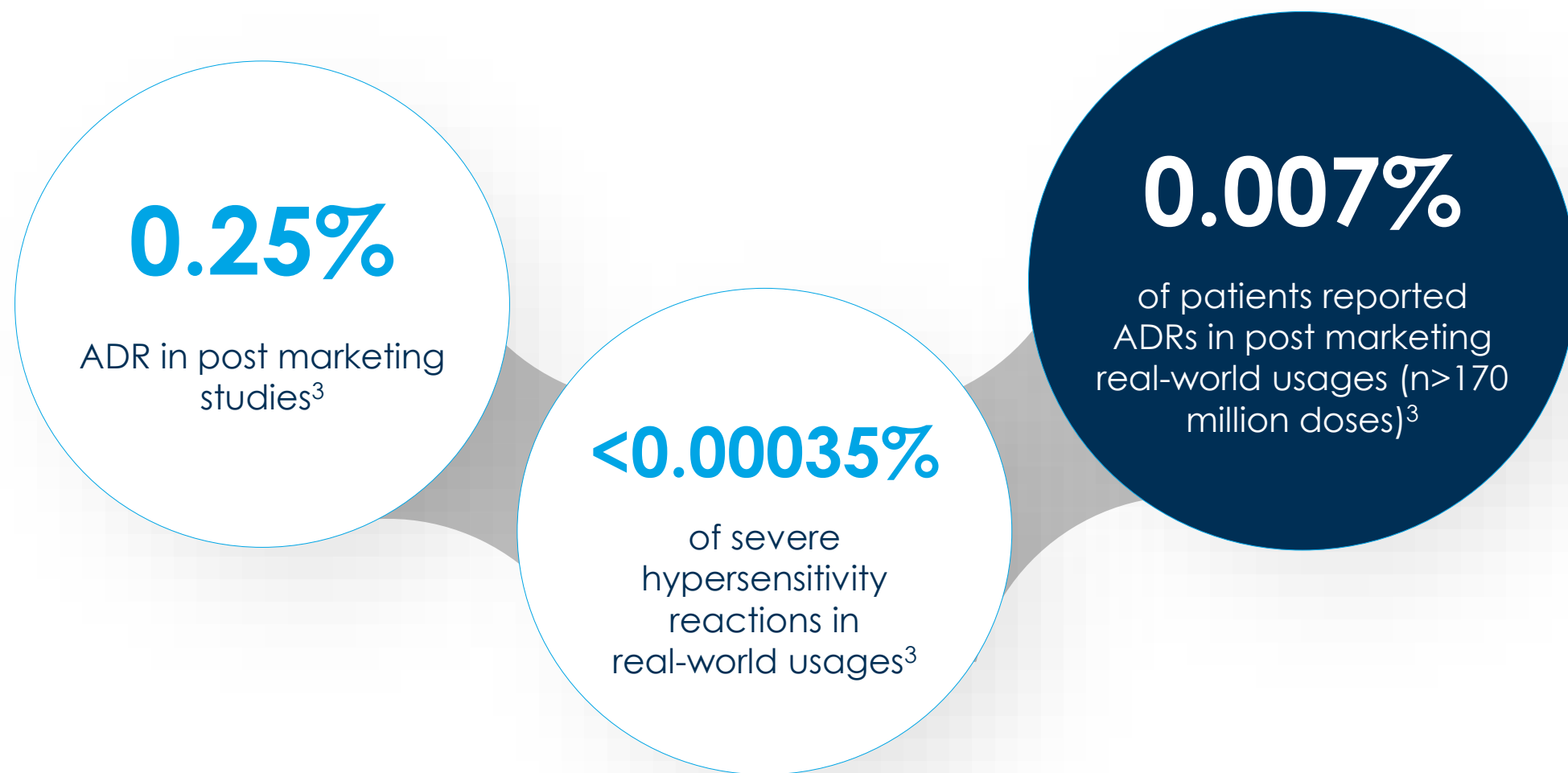


No preference



Gadovist® preferred

Low rates of adverse events (AEs) and adverse drug reactions (ADRs) in clinical and real-world use



To date, Zero confirmed unconfounded NSF cases have been reported in patients with a clear history of exposure to Dotarem® alone¹⁷

Confirmed unconfounded cases of NSF

For Dotarem the data cut was 2024, while the data cut was up to September 2019 for the other GBCAs

	Macrocytic GBCAs	Linear GBCAs
Ionic	Dotarem®: 0 ¹⁷	Magnevist®: 74 ²⁰ MultiHance®: 1 ²¹
Non-ionic	Gadovist®: 3 ¹⁸ ProHance®: 1 ¹⁹	Omniscan®: 197 ²⁰

 **Gadovist®¹⁸**

All three cases involve the use of Gadovist® alone (unconfounded cases). Patients were multimorbid and renal dysfunction (two patients with dialysis and one patient with CKD stage 3). The largest single dose administered to any patient with reported NSF was 0.49 mmol/kg body weight. Onset latency ranged from 14 days to 18 months.

 **ProHance®¹⁹**

One case of NSF with unconfounded usage of ProHance® was reported to the European Medicines Agency based on 12.3 million administrations. The estimated relative risk for NSF with ProHance® is <1% ('low risk').

ADR rates with Dotarem® remain consistent over time, despite more than 3 times the number of doses administered³

De Kerviler et al. 2016

50M doses

>3 X

0.017%
ADR
incidence

0.007%
Patients
with ADRs

Shahid I et al. 2025³

> 170M doses



0.015%

ADR
incidence



0.007%

Patients with
ADRs

- The **most frequently reported ADRs** were urticaria, nausea, and vomiting (0.001% of each)³
- Most reported ADRs were **mild** in intensity³

Dotarem® - high quality GBCA with the least amount of non-Gd rare earth elements vs other conventional macrocyclic GBCA^{24,28,29}

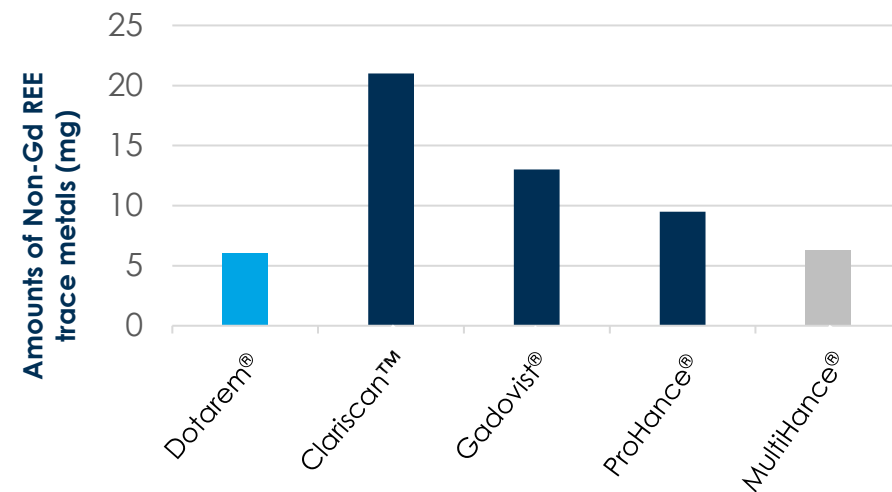
✓ Data showed that GBCA solutions contained trace amounts of non-gadolinium rare earth elements (REEs), with levels varying by brand²⁴

Dotarem® showed the low levels of non Gd REE-impurity contaminants, including barium, lead and yttrium.^{24, 28-29}



Study information²⁴

Amounts of Non-Gd Trace Metals Injected into a 70 kg Patient per MRI examination



- Non-Gd Trace metals, including Non-Gd REE, Yttrium, Lead, and Barium.
- Adapted from Ben Salem D, Barrat JA. Talanta. 2021 1:221:121589

A well-established efficacy and safety profile supported by:

57

clinical studies (Phase I-IV)³

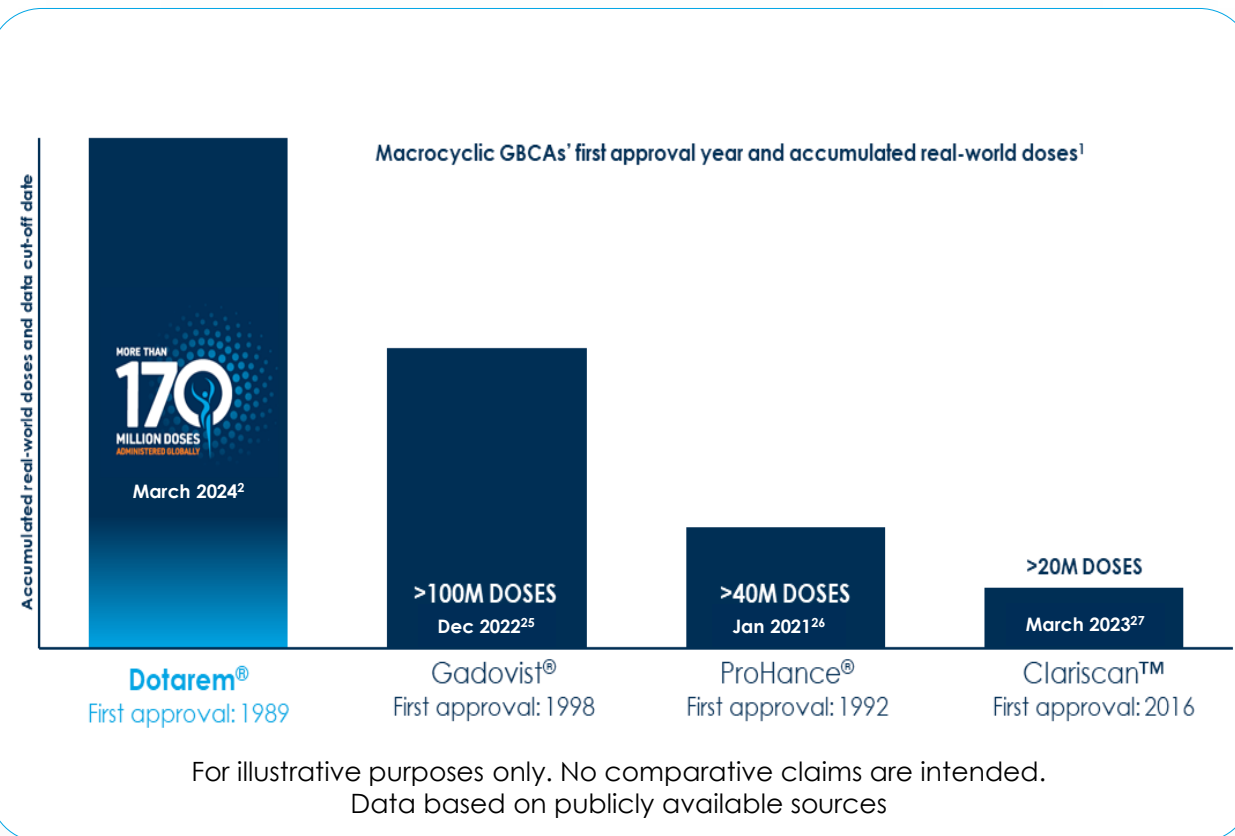
10

post-marketing studies across
300+ centers³

>170_M

doses in over 35 years of
clinical use³

Proven efficacy with consistently low rate of ADRs and HSRs in a broad range of patients and indications³



Multiple options to meet various clinical needs

Vials

5, 10, 15, 20 mL
glass vials

Pre-filled syringe

10, 15, and 20 mL
plastic pre-filled syringes

Vials for Multiple Use

60 and 100 mL
glass vials



Choose Dotarem® for your patients



Extensive real-world experience
with **OVER 170 MILLION DOSES**
administered worldwide across MRI
procedures³

Slides



Zero confirmed unconfounded NSF
cases in over 35 years of real-world
clinical experience³

Slides



Low levels of non Gd REE-impurity
contaminants in the solution^{24, 28, 29}

Slides



Non-inferior to Gadovist®
for overall visualization and
characterization of primary
brain tumors¹⁶

Slides



Low rates of ADRs and HSRs
in a broad range of patients and
indications from real world
experience³

Slides



Approved in all age groups⁵

Slides

Guerbet offers a comprehensive diagnostic imaging portfolio, built on a century of passion and dedication to patient care

The Home of MRI Innovations

**Elucirem™ (Gadopiclenol),
Dotarem® (Gadoteric acid)**

Designed to personalize the MRI diagnostic approach with confidence 'Registered' symbols after each of the three trade names (Elucirem™, Dotarem®)



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Dotarem®
Summary of Product
Characteristics (SmPC)



Elucirem™
Summary of Product
Characteristics (SmPC)



OptiStar Elite™
Legal mentions

- Reporting of suspected adverse reactions is important. Guerbet encourages you to report any adverse reactions to your health authorities or to local Guerbet representatives or through email: Pharmacovigilance.Headquarters@Guerbet.com
- Dotarem® (gadoteric acid) and the–Elucirem™ (gadopiclenol) and OptiStar Elite™ are not registered in all countries. In countries where Guerbet products are registered, indications and dosage may vary from country to country.
- For full information, please refer to the country's local Summary of Product Characteristics (SmPC).
- All trademarks and registered trademarks are the property of their respective owners.