Press release

Medical Imaging Leader Reports Record-Breaking Demand for DOTAREM® (Gadoterate Meglumine) Injection

Princeton, NJ – November 29, 2021– Guerbet LLC, the US affiliate of Guerbet, a global leader in medical imaging, announces a recent boom for DOTAREM®, (gadoterate meglumine) injection. DOTAREM's significant increases come in the face of the continued presence of a pandemic and supply chain disruptions. The company shipped more doses of its flagship MRI contrast agent in October than in any other monthly period since its US release in 2013.

"We are making great strides in the U.S. with our flagship product," says Thomas McLaughlin, Vice President of North America. "DOTAREM is a trusted solution that supports our commitment to radiologists in the MR suite. There's no doubt that our macrocyclic and ionic molecule has the highest kinetic and thermodynamic stability among currently approved GBCAs."

Since its release in 1989, DOTAREM (gadoterate meglumine) Injection has been a leading MR contrast agent in Europe, Asia, Africa, the Middle East, and South America. DOTAREM received U.S. Food and Drug Administration (FDA) approval in 2013, becoming the first macrocyclic, ionic gadolinium-based contrast agent (GBCA) in the United States. It has become the No. 2 MR contrast agent in the US and is currently No. 1 in the world, with more than 120 million doses delivered in 70 countries.

The news of DOTAREM's success follows a long legacy of Guerbet committing itself to the radiology community. In the midst of the COVID-19 crisis in 2020, the company mobilized partners and colleagues across the industry to continue making treatment-critical products available to healthcare professionals. In addition, the organization continually supports the industry with research, education, and development, as is the case in their participation in the annual Radiological Society of North America (RSNA) Conference.

For information regarding DOTAREM, visit https://www.guerbet.com/en-us/products-solutions/contrast-agents/dotarem-gadoterate-meglumine-injection/.

Media relations

Kelly Starkey + 435.901.3278 **+** kelly@starkeyconsulting.com

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About Guerbet

At Guerbet, we build lasting relationships so that we enable people to live better. This is our purpose. We are a leader in medical imaging worldwide, offering a wide range of pharmaceutical products, medical devices, digital and AI solutions for diagnostic and interventional imaging. A pioneer since 95 years in the field of contrast media with over 2,600 people globally, we are continuously innovating with 10% of revenue dedicated to Research & Development and four centers in France, Israel, and the United States. Guerbet (GBT) is listed on Euronext Paris (segment B – mid-caps) and generated €712 million in revenue in 2020. For more information, please visit www.guerbet-us.com.

DOTAREM® (gadoterate meglumine) injection Important Safety Information

WARNING: NEPHROGENIC SYSTEMIC FIBROSIS (NSF)

Gadolinium-based contrast agents (GBCAs) increase the risk for NSF among patients with impaired elimination of the drugs. Avoid use of GBCAs in these patients unless the diagnostic information is essential and not available with non-contrasted MRI or other modalities. NSF may result in fatal or debilitating fibrosis affecting the skin, muscle and internal organs.

- The risk for NSF appears highest among patients with:
  - Chronic, severe kidney disease (GFR < 30 mL/min/1.73m^2), or
  - Acute kidney injury.
- Screen patients for acute kidney injury and other conditions that may reduce renal function. For patients at risk for chronically reduced renal function (e.g. age > 60 years, hypertension, diabetes), estimate the glomerular filtration rate (GFR) through laboratory testing.
- For patients at highest risk for NSF, do not exceed the recommended DOTAREM dose and allow a sufficient period of time for elimination of the drug from the body prior to any re-administration.

Indications and Usage

DOTAREM® (gadoterate meglumine) injection is a prescription gadolinium-based contrast agent indicated for intravenous use with magnetic resonance imaging (MRI) in brain (intracranial), spine and associated tissues in adult and pediatric patients (including term neonates) to detect and visualize areas with disruption of the blood brain barrier (BBB) and/or abnormal vascularity.

Contraindications

History of clinically important hypersensitivity reactions to DOTAREM.

Warnings and Precautions

- Hypersensitivity Reactions: Anaphylactic and anaphylactoid reactions have been reported with DOTAREM, involving cardiovascular, respiratory, and/or cutaneous manifestations. Some patients experienced circulatory collapse and died. In most cases, initial symptoms occurred within minutes of DOTAREM administration and resolved with prompt emergency treatment.
- Before DOTAREM administration, assess all patients for any history of a reaction to contrast media, bronchial asthma and/or allergic disorders. These patients may have an increased risk for a hypersensitivity reaction to DOTAREM.

- Administer DOTAREM only in situations where trained personnel and therapies are promptly available for the treatment of hypersensitivity reactions, including personnel trained in resuscitation.
- Gadolinium Retention: Gadolinium is retained for months or years in several organs. The highest concentrations have been identified in the bone, followed by brain, skin, kidney, liver and spleen. The duration of retention also varies by tissue, and is longest in bone. Linear GBCAs cause more retention than macrocyclic GBCAs.
- Consequences of gadolinium retention in the brain have not been established. Adverse events involving multiple organ systems have been reported in patients with normal renal function without an established causal link to gadolinium retention.
- Acute Kidney Injury: In patients with chronically reduced renal function, acute kidney injury requiring dialysis has occurred with the use of GBCAs. The risk of acute kidney injury may increase with increasing dose of the contrast agent; administer the lowest dose necessary for adequate imaging.
- Extravasation and Injection Site Reactions: Ensure catheter and venous patency before the injection of DOTAREM. Extravasation into tissues during DOTAREM administration may result in tissue irritation.

Adverse Reactions

- The most common adverse reactions associated with DOTAREM in clinical trials were nausea, headache, injection site pain, injection site coldness and rash.
- Serious adverse reactions in the Postmarketing experience have been reported with DOTAREM. These serious adverse reactions include but are not limited to: arrhythmia, cardiac arrest, respiratory arrest, pharyngeal edema, laryngospasm, bronchospasm, coma and convulsion.

Use in Specific Populations

- **Pregnancy:** GBCAs cross the human placenta and result in fetal exposure and gadolinium retention. Use only if imaging is essential during pregnancy and cannot be delayed.
- **Lactation:** There are no data on the presence of gadoterate in human milk, the effects on the breastfed infant, or the effects on milk production. However, published lactation data on other GBCAs indicate that 0.01 to 0.04% of the maternal gadolinium dose is present in breast milk.
- **Pediatric Use:** The safety and efficacy of DOTAREM at a single dose of 0.1 mmol/kg has been established in pediatric patients from birth (term neonates ≥ 37 weeks gestational age) to 17 years of age based on clinical data. The safety of DOTAREM has not been established in preterm neonates. No cases of NSF associated with DOTAREM or any other GBCA have been identified in pediatric patients age 6 years and younger.

You are encouraged to report negative side effects of prescription drugs to the FDA.
Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see the full Prescribing Information, including the patient Medication Guide, for additional important safety information.

Reference: Dotarem [package insert]. Princeton, NJ: Guerbet LLC; Oct 2019.