Applied Radiology and Guerbet Launch 'Elucirem (Gadopiclenol) injection | The Reveal Image Challenge'

Partnership Features New Imaging Contest for MR Imaging Professionals using Elucirem™ (Gadopiclenol) Injection, a Novel New Macrocyclic GBCA for Use in Contrast-Enhanced Magnetic Resonance Imaging (MRI)

Winning Images to Be Featured on Applied Radiology Website and First Place "Image of the Year" Winner to be Announced at Annual RSNA Conference in November

Princeton, NJ, May 23, 2023 – Guerbet, a global leader in medical imaging with more than 30 years of experience in MRI, announced today a partnership with Applied Radiology, the leading peer reviewed radiology publication in the United States, where they will introduce "Elucirem | The Reveal Image Challenge." The program provides MR imaging professionals with an opportunity to reveal their MR imaging potential and to share their MRI images using Elucirem™ (gadopiclenol) injection. MRI imaging using Elucirem™ and supporting case information can be submitted on a secure image portal at appliedradiology.com/reveal and will be accepted starting in May-Dec 2023.

A winning image will be selected each month by a review committee, including MRI thought leaders and educators, Applied Radiology board members and Guerbet associates. Throughout the challenge, winning images will be featured on the Applied Radiology website and social media platforms. The program will culminate at the Guerbet booth at the annual RSNA (Radiology Society of North America) Annual Conference from November 26-30, 2023, where the Image of the Year will be revealed. In order to participate in the Elucirem | The Reveal Image Challenge, MRI professionals are encouraged to consider the following criteria when submitting their images: the MRI images should be taken only for the FDA-approved indications for Elucirem and using approved dosing for Elucirem™ as well as Image Assessment (Contrast Resolution, Contrast to Noise Ratio, Spatial Resolution, Artifacts, MR Contrast Protocol, etc.)

"This partnership with Applied Radiology was conceived as we began to see some extraordinary images coming from the radiology community with the use of Elucirem™," said David Hale, Chief Executive Officer at Guerbet. "We are excited to share the Elucirem™ difference by showcasing these images which tell the story about the future of the industry."

About Elucirem™

This next generation GBCA from Guerbet, highly stable macrocyclic gadolinium-based contrast agent (GBCA), gadopiclenol has the highest relaxivity in its class for magnetic resonance imaging (MRI) and is indicated for use in adults and children aged 2 years and older.[1,2] Elucirem™ requires only half the gadolinium dose of conventional non-specific GBCAs, addressing practitioners' concerns about gadolinium exposure.[3,4] Elucirem™ (Gadopiclenol) injection is used to detect and visualize lesions with abnormal vascularity in the central nervous system (brain, spine, and associated tissues) and the body (head and neck, thorax, abdomen, pelvis, and musculoskeletal system).[1] Guerbet received FDA approval of Elucirem™ (NDA 216986) on September 21, 2022 after priority review, a designation assigned to applications for drugs that provide significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions compared to available therapies.[5]

GBCAs improve the contrast between lesions and surrounding tissues by accelerating the relaxation of protons thanks to interaction with gadolinium atoms. Gadopiclenol, the active drug substance of Elucirem™, has been designed to enable twice as much interaction, resulting in the highest relaxivity among all non-specific GBCAs.[2] This allows use at half the conventional gadolinium dose to reveal high quality images.

https://www.appliedradiology.org/userfiles/2/files/GU04230046%20AR_PR_5-4-2023.pdf

Elucirem is manufactured by Liebel-Flarsheim™ Company LLC, a Guerbet Group company, in Raleigh, North Carolina.

About Guerbet

At Guerbet, we build lasting relationships so that we enable people to live better. That is our purpose. We are a global leader in medical imaging, offering a comprehensive range of pharmaceutical products, medical devices, and digital and AI solutions for diagnostic and interventional imaging. As pioneers in contrast products for over 95 years, with more than 2,600 employees worldwide, we continuously innovate and devote 8%-10% of our revenue to research and development in five centers in France, Israel, and the United States. Guerbet (GBT) is listed on Euronext Paris (segment B – mid caps) and generated €732 million in revenue in 2021. For more information, please visit www.guerbet.com.

About Gadopiclenol

Gadopiclenol, initially invented by Guerbet with subsequent contribution of Bracco intellectual property, is a new macrocyclic gadolinium-based contrast agent (GBCA) with high relaxivity. The efficacy and safety of Gadopiclenol have been evaluated in MRI of the central nervous system (brain, spine, and associated tissues) and the body (head and neck, thorax, abdomen, pelvis, and musculoskeletal system) in adult and pediatric patients aged 2 years and older. (refer to the approved USPI for full information). Details on Phase III clinical trials are available on www.ClinicalTrials.gov:

- *Efficacy and Safety of Gadopiclenol for Central Nervous System (CNS) Magnetic Resonance Imaging (MRI) Full Text View - ClinicalTrials.gov*
- Efficacy and Safety of Gadopiclenol for Body Magnetic Resonance Imaging (MRI) - *Full Text View - ClinicalTrials.gov*

Gadopiclenol is currently in the process of examination by the European Medicines Agency.

Forward-looking statements

This press release may contain statements of a forward-looking nature, based on assumptions and predictions made by the management of Guerbet group. Various known and unknown risks, uncertainties and other factors could lead to marked differences between the future results, financial situation, development and performances of the company, and the estimates made here. These factors include those mentioned in the public reports of Guerbet, available on its website www.guerbet.com. The company assumes no responsibility whatsoever in relation to the updating of these forward-looking statements, or how they correspond to future events or developments.

ELUCIREM™ (gadopiclenol) injection Important Safety Information

WARNING: NEPHROGENIC SYSTEMIC FIBROSIS (NSF)
See full prescribing information for complete boxed warning

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.

- **The risk for NSF appears highest among patients with:**
  - **Chronic, severe kidney disease (GFR <30 mL/min/1.73 m²), 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 (for example, age >60 years, hypertension or diabetes), estimate the glomerular filtration rate (GFR) through laboratory testing.**

Indications and Usage

ELUCIREM™ (gadopiclenol) injection is indicated in adult and pediatric patients aged 2 years and older for use with magnetic resonance imaging (MRI) to detect and visualize lesions with abnormal vascularity in the central nervous system (brain, spine, and associated tissues), and the body (head and neck, thorax, abdomen, pelvis, and musculoskeletal system).

Contraindications

History of hypersensitivity reactions to ELUCIREM

Warnings and Precautions

- **Nephrogenic Systemic Fibrosis:** GBCAs increase the risk for NSF among patients with impaired elimination of the drugs. Avoid use of GBCAs among these patients unless the diagnostic information is essential and not available with non-contrast MRI or other modalities. The GBCA-associated NSF risk appears highest for patients with chronic, severe kidney disease as well as patients with acute kidney injury.
- **Hypersensitivity Reactions:** With GBCAs, serious hypersensitivity reactions have occurred. In most cases, initial symptoms occurred within minutes of GBCA administration and resolved with prompt emergency treatment. Before ELUCIREM 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 ELUCIREM.
- **Gadolinium Retention:** Gadolinium is retained for months or years in several organs. Linear GBCAs cause more retention than macrocyclic GBCAs. Consequences of gadolinium retention in the brain have not been established. Pathologic and clinical consequences of GBCA administration and retention in skin and other organs have been established in patients with impaired renal function. While clinical consequences of gadolinium retention have not been established in patients with normal renal function, certain patients might be at higher risk. These include patients requiring multiple lifetime doses, pregnant and pediatric patients, and patients with inflammatory conditions. Consider the retention characteristics of the agent when choosing a GBCA for these patients. Minimize repetitive GBCA imaging studies, particularly closely spaced studies when possible
- **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. Do not exceed the recommended dose.
- **Extravasation and Injection Site Reactions:** Injection site reactions such as injection site pain have been reported in the clinical studies with ELUCIREM. Extravasation during ELUCIREM administration may result in tissue irritation. Ensure catheter and venous patency before the injection of ELUCIREM.

- **Interference with Visualization of Lesions Visible with Non-Contrast MRI**: As with any GBCA, ELUCIREM may impair the visualization of lesions seen on non-contrast MRI. Therefore, caution should be exercised when Gadopiclenol MRI scans are interpreted without a companion non-contrast MRI scan.

Adverse Reactions:

In clinical trials, the most frequent adverse reactions that occurred in > 0.2% of patients who received ELUCIREM included: injection site pain, headache, nausea, injection site warmth, injection site coldness, dizziness, and localized swelling. Adverse reactions that occurred with a frequency ≤ 0.2% in patients who received 0.05 mmol/kg BW.

ELUCIREM included: maculopapular rash, vomiting, worsened renal impairment, feeling hot, pyrexia, oral paresthesia, dysgeusia, diarrhea, pruritus, allergic dermatitis, erythema, injection site paresthesia, Cystatin C increase, and blood creatinine increase.

Use in Specific Populations

- **Pregnancy:** GBCAs cross the human placenta and result in fetal exposure and gadolinium retention. There are no available data on ELUCIREM use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes.
- **Lactation:** There are no data on the presence of ELUCIREM 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 excreted in breast milk.
- **Pediatric Use:** The safety and effectiveness of ELUCIREM have not been established in pediatric patients younger than 2 years of age.
- **Geriatric Use:** This drug is known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with impaired renal function.
- **Renal Impairment:** In patients with renal impairment, the exposure of gadopiclenol is increased compared to patients with normal renal function. This may increase the risk of adverse reactions such as nephrogenic systemic fibrosis (NSF). Avoid use of GBCAs among these patients unless the diagnostic information is essential and not available with non-contrast MRI or other modalities. No dose adjustment of ELUCIREM is recommended for patients with renal impairment. ELUCIREM can be removed from the body by hemodialysis

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 Medication Guide, for additional important safety information.

[1]*Elucirem [package insert]. Princeton, NJ: Guerbet LLC; 2022*
[2] *Robic, C., Port, M., Rousseaux, O., Louguet, S., Fretellier, N., Catoen, S., Factor, C., Le Greneur, S., Medina, C., Bourrinet, P., Raynal, I., Idée, J. M., & Corot, C. (2019). Physicochemical and Pharmacokinetic Profiles of Gadopiclenol: A New Macrocyclic Gadolinium Chelate With High T1 Relaxivity. Investigative radiology, 54(8), 475–484. https://doi.org/10.1097/RLI.0000000000000563*
[3]*Loevner LA, Kolumban B, Hutóczki G, et al. Efficacy and Safety of Gadopiclenol for Contrast-Enhanced MRI of the Central Nervous System: The PICTURE Randomized Clinical Trial. Investigative Radiology ():10.1097/RLI.0000000000000944, December 19, 2022. | DOI: 10.1097/RLI.0000000000000944*
[4] *Data on file (PROMISE trial. GDX-44-011)*
[5] *US FDA. Priority Review. Available at: https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/priority-review. Accessed August 22, 2022*

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