GE Healthcare announces U.S. FDA approval of macrocyclic MRI contrast agent Clariscan™ (gadoterate meglumine) injection for intravenous use

November 4, 2019

- Clariscan, approved in more than 55 countries globally with over four million patient doses shipped, is now FDA-approved in the U.S.
- Expands the GE Healthcare portfolio of contrast media products

Chalfont St Giles, UK – November 4 2019 – The U.S. Food and Drug Administration (FDA) has approved Clariscan™, a macrocyclic, ionic, gadolinium-based, MRI contrast agent, expanding the GE Healthcare portfolio for U.S. patients and radiologists. Clariscan is a 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 to detect and visualize areas with disruption of the blood brain barrier (BBB) and/or abnormal vascularity.

Clariscan has been approved in more than 55 countries globally and has had more than four million patient doses shipped in those countries. It is the latest in a growing range of imaging agents available in the U.S. from GE Healthcare. For more than 40 years, GE agents have been routinely used across MRI, X-ray/CT and ultrasound to enhance the image and support diagnosis.

“Demand for contrast media has significantly increased over the past decade. The introduction of Clariscan increases our clinical offering for U.S. radiologists, enhancing visualization to provide better patient care. Our customers rely on our high-quality products, first-rate supply network, and surrounding services to support their day-to-day work,” explained Kevin O’Neill, President & CEO Pharmaceutical Diagnostics at GE Healthcare.

“The FDA’s approval of this macrocyclic MR agent adds to the range of contrast media options available here in the U.S. and as radiologists we welcome this broader choice,” said Dr. Lawrence N Tanenbaum, M.D., FACR.

GE Healthcare offers diagnostic imaging agents used in approximately 90 million procedures per year globally, equivalent to three patients every second. In the U.S., GE Healthcare has a strong record of innovation in new contrast media products and indications, with recent FDA approvals for Omnipaque™ (iohexol) in CT of the abdomen and for Visipaque™ (iodixanol) in coronary CT angiography. GE Healthcare has invested $240 million ir its global manufacturing and supply network over the past five years to deliver imaging agents to hospitals and pharmacies globally.

Clariscan is manufactured in Norway using a proprietary manufacturing process. As with all GE Healthcare contrast media products, all stages of manufacturing, from development of the active pharmaceutical ingredient (API) to finished product, are managed entirely by GE Healthcare. Clariscan is available in single dose vials of 10, 15 and 20 mL. The packaging contains a 2D data matrix (barcode) on every Clariscan pack, which conveys key information, including national drug code number, individual lot number, and expiration date. This information can be easily scanned and uploaded onto electronic medical systems, helping to reduce the risk of manual data entry errors and helping workflow efficiencies at medical centers.

ENDS

About GE Healthcare:
GE Healthcare is the $19.8 billion healthcare business of GE (NYSE: GE). As a leading provider of medical imaging, monitoring, biomanufacturing, and cell and gene therapy technologies, GE Healthcare enables precision health in diagnostics, therapeutics and monitoring through intelligent devices, data analytics, applications and services. With over 100 years of experience in the healthcare industry and more than 50,000 employees globally, the company helps improve outcomes more efficiently for patients, healthcare providers, researchers and life sciences companies around the world. Follow us on Facebook, LinkedIn, Twitter and The Pulse for latest news, or visit our website https://corporate.gehealthcare.com/ for more information.

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CLARISCANTM (gadoterate meglumine) injection for intravenous use

PRODUCT INDICATIONS AND USE:
CLARISCAN™ (gadoterate meglumine) is a 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 to detect and visualize areas with disruption of the blood brain barrier (BBB) and/or abnormal vascularity.

Additional pediatric use information is approved for Guerbet LLC’s Dotarem (gadoterate meglumine injection). However, due to Guerbet LLC’s marketing exclusivity, this drug product is not labeled with that pediatric information.

IMPORTANT SAFETY INFORMATION ABOUT CLARISCAN™

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. 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/1.73 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 (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 Clariscan dose and allow a sufficient period of time for elimination of the drug from the body prior to any re-administration.**

Contraindications
History of clinically important hypersensitivity reactions to Clariscan.

Warnings and precautions

- **Hypersensitivity reactions:** Anaphylactic and anaphylactoid reactions have been reported with Clariscan, involving cardiovascular, respiratory, and/or cutaneous manifestations. Some patients experienced circulatory collapse and died. In most cases, initial symptoms occurred within minutes of Clariscan administration and resolved with prompt emergency treatment.
  - Before Clariscan 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 Clariscan.
  - Administer Clariscan 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 Clariscan. Extravasation into tissues during Clariscan administration may result in tissue irritation.

Adverse reactions
- The most common adverse reactions (≥ 0.2%) associated with Clariscan 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 Clariscan. 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. The human data on the association between GBCAs and adverse fetal outcomes are limited and inconclusive. Because of the potential risks of gadolinium to the fetus, use Clariscan only if imaging is essential during pregnancy and cannot be delayed. Advise pregnant women of the potential risk of fetal exposure to GBCAs.
- **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 Clariscan at a single dose of 0.1 mmol/kg has been established in pediatric patients from 2 to 17 years of age based on clinical data in 133 pediatric patients 2 years of age and older. Adverse reactions in pediatric patients were similar to those reported in adults. No dosage adjustment according to age is necessary in pediatric patients. No cases of NSF associated with Clariscan or any other GBCA have been identified in pediatric patients age 6 years and younger. The safety of Clariscan has not been established in preterm neonates.

Additional pediatric use information is approved for Guerbet, LLC's Dotarem (gadoterate meglumine injection). However, due to Guerbet LLC's marketing exclusivity, this drug product is not labeled with that pediatric information.

Prior to Clariscan administration please read the full Prescribing Information, including the Boxed Warning and patient Medication Guide, for additional important safety information at:
https://www.gehealthcare.com/-/media/A4F1C1C8F50D489387BF91292DBA5629.pdf

To report SUSPECTED ADVERSE REACTIONS, contact GE Healthcare at 800-654-0118 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

For additional safety information for Omnipaque™, please see full Prescribing Information at https://www.gehealthcare.com/-/jssmedia/c66966a70fe946afa829483a1d6c848c.pdf?la=en-us

For additional safety information for Visipaque™, please see full Prescribing Information at https://www.gehealthcare.com/-/jssmedia/1f0478f5573f47538b0e4bdcc619ac3c.pdf?la=en-us

November 2019 JB72654US