GE Healthcare's Clariscan™ (gadoterate meglumine) Becomes Only FDA-Approved MRI Contrast Agent Available in Polymer Bottle

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- US FDA approves +*PLUS*PAK™ (polymer bottle) Pharmacy Bulk Package for the gadolinium-based contrast agent, Clariscan™ (gadoterate meglumine)
- As the only polymer bottle for an MRI contrast agent, Clariscan in +*PLUS*PAK offers the potential for increased workplace safety, efficiency, convenience and environmental advantages
- Clariscan has been approved in more than 65 countries globally, with more than six million patient doses shipped

Marlborough, US – September 15, 2020 – GE Healthcare's innovative shatterproof polymer + *PLUS*PAK Pharmacy Bulk Package has been approved by the US FDA for use with its macrocyclic gadolinium-based MRI contrast agent, Clariscan (gadoterate meglumine). As the only FDA approved MRI contrast agent in a polymer bottle, Clariscan in +*PLUS*PAK will offer MRI departments a variety of ways in which they can improve safety and workflow efficiency.

With its patented design and pharmaceutical grade polypropylene composition, Clariscan's + *PLUS*PAK Pharmacy Bulk Package reduces risk of breakage and injury from broken glass, while its easy-open cap helps avoid cuts from metal crimps. Injuries associated with glass bottles make up an estimated 16 per cent of sharps injuries in healthcare settings. Avoiding use of glass has the potential to improve productivity by saving time spent treating sharps injuries while also importantly helping to reduce the associated risk of transmission of infectious blood-borne diseases.

The Pharmacy Bulk Package offers improved flexibility, with Clariscan able to be transferred to sterile Syringes (using the appropriate transfer device) for up to 24 hours after initial puncture, for use in multiple patients and across work shifts. Unlike single-use vials, the Pharmacy Bulk Package also enables more efficient application of weight-based dosing, helping minimize contrast waste. In addition to workflow efficiencies, +*PLUS*PAK also offers certain environmental advantages, with the use of polymer resulting in smaller and lighter packaging than glass. The bottle is also fully recyclable.

Clariscan – now approved in over 65 countries globally - is indicated for intravenous use with MRI in brain (intracranial), spine and associated tissues in adult and pediatric patients (two years and older) to detect and visualize areas with disruption of the blood brain barrier (BBB) and/or abnormal vascularity. See Important Safety Information including boxed warning and instructions for use of the Pharmacy Bulk Packaging for Clariscan below.

"Many radiology departments have already experienced the benefits of + *PLUS*PAK with other GE Healthcare contrast media products," said Dr Mark Hibberd, Chief Medical Officer for GE Healthcare's Pharmaceutical Diagnostics unit. "This new addition to the Clariscan portfolio helps improve operational workflow and reduce disposal costs for MR departments, key focus areas particularly in light of COVID-19."

GE Healthcare's Pharmaceutical Diagnostics unit develops and supplies imaging agents used to support around 100 million procedures per year globally, equivalent to three patients every second. Clariscan, approved by U.S. FDA in November 2019, is the latest in a growing range of imaging agents available in the U.S. which are used across MRI, X-ray/CT and ultrasound to enhance the image and support diagnosis.

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. Clariscan is available in single dose vials of 10, 15 and 20 mL and now 100 mL Pharmacy Bulk Package in an innovative +*PLUS*PAK polymer bottle.

ENDS

About GE Healthcare:

GE Healthcare is the $16.7 billion healthcare business of GE (NYSE: GE). As a leading global medical technology and digital solutions innovator, GE Healthcare enables clinicians to make faster, more informed decisions through intelligent devices, data analytics, applications and services, supported by its Edison intelligence platform. With over 100 years of healthcare industry experience and around 50,000 employees globally, the company operates at the center of an ecosystem working toward precision health, digitizing healthcare, helping to drive productivity and improve outcomes for patients, providers, health systems and researchers around the world. Follow us on Facebook, LinkedIn, Twitter and Insights, or visit our website www.gehealthcare.com for more information.

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CLARISCAN™ (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 readministration.

Contraindications
History of clinically important hypersensitivity reactions to Clariscan.

Warnings and precautions

Hypersensitivity reactions:

- Anaphylactic and anaphylactoid reactions have been reported with gadoterate meglumine, involving cardiovascular, respiratory, and/or cutaneous manifestations. Some patients experienced circulatory collapse and died. In most cases, initial symptoms occurred within minutes of gadoterate meglumine 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.

Pharmacy Bulk Package Preparation:

- Do not use the Pharmacy Bulk Package for direct intravenous infusion.
- Do not use if tamper-evident ring is broken or missing.
- Perform the transfer of Clariscan from the Pharmacy Bulk Package in an aseptic work area, such as laminar flow hood and using aseptic technique and suitable transfer device. Penetrate the closure only one time.
- Once the container closure is punctured, do not remove the Pharmacy Bulk Package from the aseptic work area.
- The Pharmacy Bulk Package is used as a multiple dose container with an appropriate transfer device for filling empty sterile syringes.
- Use each individual dose of Clariscan promptly following withdrawal from the Pharmacy Bulk Package.

- Use the contents of the Pharmacy Bulk Package within 24 hours after initial puncture.

Adverse reactions

- The most common adverse reactions (≥ 0.2%) associated with gadoterate meglumine 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 gadoterate meglumine. 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 gadoterate meglumine 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 gadoterate meglumine or any other GBCA have been identified in pediatric patients age 6 years and younger. The safety of gadoterate meglumine has not been established in preterm neonates.

Please see Full Prescribing Information for Clariscan, including Boxed Warning and Medication Guide, for additional important safety information. Click here to access the Full Prescribing information.

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