GE Healthcare Announces U.S. FDA approval of macrocyclic MRI Contrast Agent Clariscan™ (gadoterate meglumine) in Pre-Filled Syringes

November 24, 2020

- *U.S. FDA approves pre-filled syringe packaging for the macrocyclic gadolinium-based contrast agent, Clariscan™ (gadoterate meglumine).*
- *Clariscan has been approved in more than 70 countries globally, with more than seven million patient doses shipped, and now offers a wider range of packaging solutions.*
- *Clariscan in pre-filled syringes offers potential advantages for workflow safety and efficiency.*
- *GE Healthcare will focus on the theme of efficiency during its presence at RSNA.*

Marlborough, US – November 24, 2020 – GE Healthcare has received U.S. FDA approval of its macrocyclic gadolinium-based MRI contrast agent, Clariscan (gadoterate meglumine), in pre-filled syringes. Pre-filled with 10, 15 and 20mL of contrast agent, Clariscan's ready-assembled, clear plastic syringes save time and reduce the risk of injury from broken glass, while the color-coded volume labels allow for easy identification of the required patient-specific volume. Its 2D data matrix contains scannable key information to be uploaded onto electronic medical systems, reducing the risk of manual data entry errors and helping to further increase workflow efficiency at medical centers.

Already available in glass vials and plastic polymer bottles, the approval of Clariscan in crystal clear polymer pre-filled syringes adds to the range of packaging solutions available to meet departmental needs and follows the recent FDA approval of Clariscan's + *PLUS*PAK Pharmacy Bulk Package. This patented, pharmaceutical grade polypropylene bottle is the only FDA-approved polymer bottle for an MRI contrast agent.

With injuries from glass bottles making up an estimated 16 percent of sharps injuries in healthcare settings, Clariscan's + *PLUS*PAK - and now plastic pre-filled syringes – both have the potential to improve workflow efficiencies while helping to reduce the associated risk of sharps injuries. With the approach of the Radiological Society of North America (RSNA) 2020 Annual Meeting from November 29-December 5, GE Healthcare will focus on the theme of driving greater efficiency, an imperative to addressing the challenges of many health systems around the globe, especially in the context of the global COVID-19 pandemic.

Clariscan – now approved in over 70 countries globally – is 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. **Please see Clariscan Important Safety Information, including Boxed Warning, below.**

"The addition of pre-filled syringes expands the Clariscan portfolio to address a wider range of departmental requirements" said Dr Mark Hibberd, Chief Medical Officer for GE Healthcare's Pharmaceutical Diagnostics unit. "The potential timesaving and efficiency advantages further enhance operational workflow improvements for radiology departments".

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; 100 mL Pharmacy Bulk Package in +*PLUS*PAK polymer bottles; and now 10, 15 and 20mL clear plastic pre-filled syringes.

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 (including term neonates) to detect and visualize areas with disruption of the blood brain barrier (BBB) and/or abnormal vascularity.

IMPORTANT SAFETY INFORMATION ABOUT CLARISCAN™

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/1.73 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

- **Nephrogenic Systemic Fibrosis (NSF):**
  - NSF has occurred in patients with impaired elimination of GBCAs. Higher than recommended dosing or repeat dosing appear to increase the risk.
- **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.
- **Pre-filled syringes must not be frozen. Frozen syringes should be discarded.**

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:** 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:** While no data is available for gadoterate meglumine, 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 have been established in pediatric patients from birth (term neonates ≥ 37 weeks gestational age) to 17 years of age based on clinical data in 133 pediatric patients 2 years of age and older, and clinical data in 52 pediatric patients birth to less than 2 years of age that supported extrapolation from adult data. 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, contact GE Healthcare at 800-654-0118 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.