Clariscan Important Safety Information

WARNING: RISK ASSOCIATED WITH INTRATHECAL USE and NEPHROGENIC SYSTEMIC FIBROSIS

Risk Associated with Intrathecal Use

Intrathecal administration of gadolinium-based contrast agents (GBCAs) can cause serious adverse reactions including death, coma, encephalopathy, and seizures. Clariscan is not approved for intrathecal use.

Nephrogenic Systemic Fibrosis

GBACs increase the risk for nephrogenic systemic fibrosis (NSF) among patients with impaired elimination of the drugs. Avoid use of Clariscan 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 m^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 (for example, age > 60 years, hypertension or 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.

INDICATIONS

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.

CONTRAINDICATIONS

History of clinically important hypersensitivity reactions to Clariscan.

WARNINGS AND PRECAUTIONS

Risk Associated with Intrathecal Use: Intrathecal administration of GBCAs can cause serious adverse reactions including death, coma, encephalopathy, and seizures. The safety and effectiveness of Clariscan have not been established with intrathecal use

Nephrogenic Systemic Fibrosis: GBCAs increase the risk for NSF among patients with impaired elimination of the drugs. Avoid use of Clariscan among these patients unless the diagnostic information is essential and not available with non-contrast MRI or other modalities.

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.

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. Observe for signs and symptoms of hypersensitivity reactions during and following administration.

Gadolinium Retention: Gadolinium is retained for months or years in several organs. The highest concentrations have been identified in the bone, followed by other organs (e.g. brain, skin, kidney, liver and spleen). 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. 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; 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

In clinical trials, the most frequent adverse reactions that occurred in > 0.2% of patients who received Clariscan included: nausea, headache, injection site pain, injection site coldness and rash. Postmarketing experience reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure: acute pancreatitis with onset within 48 hours after GCBA administration. Please see full prescribing information for a complete list of adverse reactions including postmarketing events.

USE IN SPECIFIC POPULATIONS

Pregnancy and Lactation: 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. 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.

Prior to Clariscan administration, please read the full Prescribing Information for additional Important Safety Information.

To report SUSPECTED ADVERSE REACTIONS, contact GE HealthCare at 800 654 0118 (option 2 then option 1) or by email at GPV.drugsafety@gehealthcare.com or FDA at 800 FDA 1088 or www.fda.gov/medwatch