IMPORTANT SAFETY INFORMATION FOR PIXXOSCAN (gadobutrol)

WARNING: RISK ASSSOCAITED WITH INTRATHECAL USE and NEPHROGENIC SYSTEMIC FRIBOSIS

Risk Associated with Intrathecal Use

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

Nephrogenic Systemic Fibrosis (NSF)

GBCAs increase the risk for NSF among patients with impaired elimination of the drugs. Avoid use of Pixxoscan 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 of NSF appears highest among patients with:

- **Chronic, severe kidney disease (GFR <30 mL/min/1.73m^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 Pixxoscan dose and allow a sufficient period of time for elimination of the drug from the body prior to any re-administration.

INDICATIONS AND USAGE

PIXXOSCAN (gadobutrol) injection is a gadolinium-based contrast agent indicated for use with magnetic resonance imaging (MRI):

- To detect and visualize areas with disrupted blood brain barrier and/or abnormal vascularity of the central nervous system in adult and pediatric patients including term neonates
- To assess the presence and extent of malignant breast disease in adult patients
- To evaluate known or suspected supra-aortic or renal artery disease in adult and pediatric patients, including term neonates
- To assess myocardial perfusion (stress, rest) and late gadolinium enhancement in adult patients with known or suspected coronary artery disease (CAD)

CONTRAINDICATION AND IMPORTANT INFORMATION ABOUT HYPERSENSITIVITY REACTIONS:

Pixxoscan is contraindicated in patients with history of severe hypersensitivity reactions to gadobutrol. Anaphylactic and other hypersensitivity reactions with cardiovascular, respiratory, or cutaneous manifestations, ranging from mild to severe, including death, have uncommonly occurred following gadobutrol administration. Before Pixxoscan 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 Pixxoscan.

ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)

ARDS has been reported with gadobutrol administration and may be characterized by severe hypoxemia requiring oxygen support and mechanical ventilation. Onset can occur within <30 minutes to 24 hours

after administration. For patients demonstrating respiratory distress after administration, assess oxygen requirement and monitor for worsening respiratory function.

GADOLINIUM RETENTION

Gadolinium is retained for months or years in several organs. Linear GBCAs cause more retention than macrocyclic GBCAs. At equivalent doses, retention varies among the linear agents. Retention is lowest and similar among the macrocyclic GBCAs. Consequences of gadolinium retention in the brain have not been established, but they have been established in the skin and other organs 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 and minimize repetitive GBCA studies, when possible.

ACUTE KIDNEY INJURY

In patients with chronic renal impairment, acute kidney injury sometimes requiring dialysis has been observed with the use of some GBCAs. Do not exceed the recommended dose; the risk of acute kidney injury may increase with higher than recommended doses.

EXTRAVASATION AND INJECTION SITE REACTIONS

Ensure catheter and venous patency before the injection of Pixxoscan. Extravasation into tissues during Pixxoscan administration may result in moderate irritation.

OVERESTIMATION OF EXTENT OF MALIGNANT DISEASE IN MRI OF THE BREAST

Gadobutrol MRI of the breast overestimated the histologically confirmed extent of malignancy in the diseased breast in up to 50% of the patients.

LOW SENSITIVITY FOR SIGNIFICANT ARTERIAL STENOSIS

The performance of gadobutrol MRA for detecting arterial segments with significant stenosis (>50% renal, >70% supra-aortic) has not been shown to exceed 55%. Therefore, a negative MRA study alone should not be used to rule out significant stenosis.

ADVERSE REACTIONS

The most frequent (≥0.5%) adverse reactions associated with gadobutrol in clinical studies were headache (1.7%), nausea (1.2%) and dizziness (0.5%). 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.

PLEASE SEE FULL PRESCRIBING INFORMATION FOR PIXXOSCAN FOR ADDITIONAL IMPORTANT SAFETY INFORMATION. (*link*)

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