Product Indications and Important Safety Information – VISIPAQUE – 04/2023

INDICATIONS AND USE – VISIPAQUE™ (IODIXANOL) INJECTION

Intra-Arterial Procedures
Adult and pediatric patients 12 years of age and older: Intra-arterial digital subtraction angiography (270 and 320 mg iodine/mL); angiocardiography (left ventriculography and selective coronary arteriography), peripheral arteriography, visceral arteriography, and cerebral arteriography (320 mg iodine/mL). **Pediatric patients less than 12 years of age:** Angiocardiography, cerebral arteriography, and visceral arteriography (320 mg iodine/mL)

Intravenous Procedures
Adult and pediatric patients 12 years of age and older: Computed tomography (CT) imaging of the head and body (270 and 320 mg iodine/mL); excretory urography (270 and 320 mg iodine/mL); peripheral venography (270 mg iodine/mL); coronary computed tomography angiography (CCTA) to assist in the diagnostic evaluation of patients with suspected coronary artery disease (320 mg iodine/mL). **Pediatric patients less than 12 years of age:** CT imaging of the head and body (270 mg iodine/mL); excretory urography (270 mg iodine/mL)

IMPORTANT SAFETY INFORMATION FOR VISIPAQUE (iodixanol) INJECTION

WARNING: NOT FOR INTRATHECAL USE

Inadvertent intrathecal administration may cause death, convulsions/seizures, cerebral hemorrhage, coma, paralysis, arachnoiditis, acute renal failure, cardiac arrest, rhabdomyolysis, hyperthermia, and brain edema.

CONTRAINDICATION:
Visipaque injection is contraindicated for intrathecal use.

WARNINGS AND PRECAUTIONS:
• **Hypersensitivity Reactions:** Life-threatening or fatal reactions can occur. Most severe reactions develop shortly after the start of the injection, but reactions can occur up to hours later. Always have emergency equipment and trained personnel available.
• **Contrast-Induced Acute Kidney Injury:** Acute injury including renal failure can occur. Minimize dose and maintain adequate hydration to minimize risk.
• **Cardiovascular Adverse Reactions:** Life-threatening or fatal cardiovascular reactions, including hypotension, shock, and cardiac arrest have occurred with the use of Visipaque. Most deaths occur during injection or five to ten minutes later, with cardiovascular disease as the main aggravating factor. Use the lowest necessary dose of Visipaque in patients with congestive heart failure.
• **Thromboembolic Events:** Serious, rarely fatal, thromboembolic events causing myocardial infarction and stroke can occur during angiocardiography procedures with both ionic and nonionic contrast agents.

• **Extravasation and Injection Site Reactions:** Extravasation of Visipaque injection may cause tissue necrosis and/or compartment syndrome, particularly in patients with severe arterial or venous disease. Ensure intravascular placement of catheters prior to injection.
• **Thyroid Storm in Patients with Hyperthyroidism:** Thyroid storm has occurred after the intravascular use of iodinated contrast agents in patients with hyperthyroidism, or with an autonomously functioning thyroid nodule.
• **Thyroid Dysfunction in Pediatric Patients 0 to 3 Years of Age:** Thyroid dysfunction characterized by hypothyroidism or transient thyroid suppression has been reported after both single exposure and multiple exposures to iodinated contrast media (ICM) in patients 0 to 3 years of age.
• **Hypertensive Crisis in Patients with Pheochromocytoma:** Hypertensive crisis has occurred after the use of iodinated contrast agents in patients with pheochromocytoma. Inject the minimum amount of contrast necessary, assess the blood pressure throughout the procedure, and have measures for treatment of a hypertensive crisis readily available.
• **Sickle Cell Crisis in Patients with Sickle Cell Disease:** Iodinated contrast agents when administered intravascularly may promote sickling in individuals who are homozygous for sickle cell disease.
• **Severe Cutaneous Adverse Reactions (SCAR):** SCAR may develop from one hour to several weeks after intravascular contrast agent administration. These reactions include Stevens-Johnson syndrome and toxic epidermal necrolysis (SJS/TEN), acute generalized exanthematous pustulosis (AGEP), and drug reaction with eosinophilia and systemic symptoms (DRESS). Avoid administering Visipaque to patients with a history of a SCAR to Visipaque.

USE IN SPECIFIC POPULATIONS:
• **Pediatric Use:** Pediatric patients at high risk of adverse reactions during and after administration of contrast agents include those with asthma, hypersensitivity to other medication and/or allergens, cyanotic and acyanotic heart disease, chronic heart failure, or a serum creatinine >1.5 mg/dL. Patients with immature renal function or dehydration may be at increased risk due to prolonged elimination of iodinated contrast agents.
• **Geriatric Use:** While no overall differences in safety or effectiveness were observed in patients >65 years, greater sensitivity regarding some older individuals cannot be ruled out.

ADVERSE REACTIONS:
• Serious, life-threatening, and fatal reactions, mostly of cardiovascular origin, have been associated with the administration of iodine-containing contrast agents, including Visipaque Injection.
• Most common adverse reactions (incidence greater than 0.5%) in adult patients after Visipaque injection: Discomfort, warmth, pain; Cardiovascular: angina. Gastrointestinal: diarrhea, nausea, vomiting. Nervous System: agitation, anxiety, insomnia, nervousness, dizziness, headache, migraine, unusual skin sensations, sensory disturbance, fainting, sensation of spinning. Skin: itchy rash, severe itching, hives. Special Senses: Smell, taste, and vision alteration. Pediatric patients experienced similar adverse reactions.

DRUG-DRUG INTERACTIONS:

• **Metformin**: In patients with renal impairment, metformin can cause lactic acidosis. Iodinated contrast agents appear to increase the risk of metformin-induced lactic acidosis, possibly as a result of worsening renal function. Stop metformin at the time of, or prior to, Visipaque administration in patients with an eGFR between 30 and 60 mL/min/1.73 m2; in patients with a history of hepatic impairment, alcoholism or heart failure; or in patients who will be administered intra-arterial iodinated contrast. Re-evaluate eGFR 48 hours after the imaging procedure and reinstitute metformin only after renal function is stable.

• **Radioactive Iodine:** Administration of iodinated contrast agents may interfere with thyroid uptake of radioactive iodine (I-131 and I-123) and decrease therapeutic and diagnostic efficacy in patients with carcinoma of the thyroid. The decrease in efficacy lasts 6 to 8 weeks.

• **Beta-adrenergic Blocking Agents:** The use of beta-adrenergic blocking agents lowers the threshold for and increases the severity of contrast reactions and the responsiveness of treatment of hypersensitivity reactions with epinephrine. Because of the risk of hypersensitivity reactions, use caution when administering Visipaque to patients taking beta-blockers.

• **Oral Cholecystographic Contrast Agents:** Renal toxicity has been reported in patients with liver dysfunction who were given an oral cholecystographic agent followed by intravascular iodinated contrast agents. Postpone the administration of Visipaque in patients who have recently received an oral cholecystographic agent.

Please see the full Prescribing Information, including Boxed Warning for additional important safety information.

To report SUSPECTED ADVERSE REACTIONS, contact GE HealthCare at 800 654 0118 (option 2, then option 1), or the FDA at 800 FDA 1088 or www.fda.gov/medwatch