For Oral Use Only

Indications and Use – Omnipaque™ (iohexol)

Oral or Rectal Administration – Adults: Omnipaque 350 • Oral radiographic examination of the gastrointestinal tract. **Pediatrics: Omnipaque 180, 240, and 300** • Oral and rectal radiographic examination of the gastrointestinal tract. **Oral administration in conjunction with intravenous administration: Diluted Omnipaque Injection – Adults: Omnipaque 240, 300, and 350 diluted and administered orally in conjunction with Omnipaque 300 administered intravenously** • Computed tomography (CT) of the abdomen. **Pediatrics: Omnipaque 240, 300, and 350 diluted and administered orally in conjunction with Omnipaque 240 or Omnipaque 300 administered intravenously** • CT of the abdomen. **Omnipaque Oral Solution – Adults: Omnipaque Oral Solutions 9 and 12 administered orally in conjunction with Omnipaque 300 administered intravenously** • CT of the abdomen. **Pediatrics: Omnipaque Oral Solutions 9 and 12 administered orally in conjunction with Omnipaque 240 or Omnipaque 300 administered intravenously** • CT of the abdomen.

Important Safety Information About Omnipaque™ (iohexol)

WARNING: RISKS WITH INADVERTENT INTRATHECAL ADMINISTRATION OF Omnipaque Injections 140 and 350 mgI/mL

See full Prescribing Information for complete Boxed Warning.

Omnipaque Injections 140 and 350 are contraindicated 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 (4, 5.1).

CONTRAINDICATIONS: Omnipaque 140 and Omnipaque 350 are contraindicated for intrathecal use. Omnipaque Oral Solutions 9 and 12 are contraindicated for parenteral administration. **WARNINGS AND PRECAUTIONS – Risks Associated With Inadvertent Intrathecal Administration:** Omnipaque Injections 140 and 350 are contraindicated for intrathecal use. Inadvertent intrathecal administration can cause death, convulsions/seizures, cerebral hemorrhage, coma, paralysis, arachnoiditis, acute renal failure, cardiac arrest, rhabdomyolysis, hyperthermia, and brain edema. **Risks Associated With Inadvertent Parenteral Administration of Omnipaque Oral Solution:** Omnipaque Oral Solutions 9 and 12 are contraindicated for parenteral administration. Adverse reactions such as hemolysis may occur if administered intravascularly. Do not administer Omnipaque Oral Solutions 9 and 12 parenterally. **Hypersensitivity Reactions:** Omnipaque can cause life-threatening or fatal hypersensitivity reactions, including anaphylaxis. Manifestations include respiratory arrest, laryngospasm, bronchospasm, angioedema, and shock. Most severe

reactions develop shortly after the start of the injection (within three minutes), but reactions can occur up to hours later. There is an increased risk in patients with a history of a previous reaction to contrast agents and known allergies (ie, bronchial asthma, drug, or food allergies) or other hypersensitivities. Premedication with antihistamines or corticosteroids does not prevent serious life-threatening reactions but may reduce both their incidence and severity. Obtain a history of allergy, hypersensitivity, or hypersensitivity reactions to iodinated contrast agents, and always have emergency resuscitation equipment and trained personnel available prior to Omnipaque administration. Monitor all patients for hypersensitivity reactions. **Thromboembolic Events:** Angiocardiography • Serious, rarely fatal, thromboembolic events causing myocardial infarction and stroke can occur during angiocardiography procedures with both ionic and nonionic contrast media. During these procedures, increased thrombosis and activation of the complement system occurs. Risk factors for thromboembolic events include length of procedure, catheter and syringe material, underlying disease state, and concomitant medications. To minimize thromboembolic events, use meticulous angiographic techniques, and minimize the length of the procedure. Avoid blood remaining in contact with syringes containing iodinated contrast agents, which increases the risk of clotting. Avoid angiocardiography in patients with homocystinuria because of the risk of inducing thrombosis and embolism. **Extravasation and Injection-Site Reactions:** Extravasation of Omnipaque during intravascular 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. Monitor patients for extravasation and advise patients to seek medical care for progression of symptoms. **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. Evaluate the risk in such patients before use of Omnipaque. **Hypertensive Crisis in Patients With Pheochromocytoma:** Hypertensive crisis has occurred after the use of iodinated contrast agents in patients with pheochromocytoma. Monitor patients when administering Omnipaque intravascularly if pheochromocytoma or catecholamine-secreting paragangliomas are suspected. 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. Hydrate patients prior to and following Omnipaque administration, and use Omnipaque only if the necessary imaging information cannot be obtained with alternative imaging modalities. **Severe Cutaneous Adverse Reactions (SCARs):** SCARs 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). Reaction severity may increase, and time to onset may decrease, with repeat administration of contrast agents; prophylactic medications may not prevent or mitigate SCARs. Avoid administering Omnipaque to patients with a history of a severe cutaneous adverse reaction to Omnipaque.

ADVERSE REACTIONS – Oral Administration of Undiluted Omnipaque 350 for Radiographic Examination of the Gastrointestinal Tract • Adults: Diarrhea, nausea, vomiting, abdominal pain, flatulence, and headache. **Pediatric Patients:** Adverse reactions were found to mostly affect the gastrointestinal system with diarrhea, vomiting, nausea, and abdominal pain. Fever, hypotension, and urticaria were also reported. **Oral Administration for Computed Tomography (CT) of the Abdomen in Conjunction With Intravenous Administration • Adults:** In a controlled clinical study

involving 44 adult patients receiving oral administration of diluted Omnipaque (4-9 mgI/mL), in conjunction with intravenously injected Omnipaque 300, for CT examination of the abdomen, adverse reactions were limited to a single report of vomiting. **Pediatric Patients:** In clinical studies involving 69 pediatric patients receiving oral administration of diluted Omnipaque (9-29 mgI/mL), in conjunction with intravenously administered Omnipaque 240 and Omnipaque 300, for CT examination of the abdomen, adverse reactions were limited to a single report of vomiting (1.4%). **Body Cavity Use • Adults:** In controlled clinical studies involving 285 adult patients for various body cavity examinations using Omnipaque 240, 300, and 350, the most frequent adverse reactions were administration-site reactions: Pain (26%) and swelling (22%), were exclusively reported for arthrography and were generally related to the procedure rather than the contrast medium. Patients also experienced heat (7%). All other adverse reaction occurred at a rate less than or equal to 1%. **Pediatric Patients:** No adverse reactions associated with the use of Omnipaque for voiding cystourethrogram (VCU) procedures were reported in 51 pediatric patients studied.

Postmarketing Experience – General Immune System Disorders: Hypersensitivity reactions, anaphylactic or anaphylactoid reactions, anaphylactic or anaphylactoid shock, including life-threatening or fatal anaphylaxis. **General Disorders and Administration-Site Conditions:** Pyrexia, chills, pain and discomfort, asthenia, administration-site conditions, including extravasation. **Musculoskeletal and Connective Tissue Disorders:** Pain, muscle spasms, or spasticity. **Psychiatric Disorders**: Confusional state, agitation, anxiety. **Eye Disorders:** Transient visual impairment, including cortical blindness. **Renal Reactions:** Acute kidney injury. **Intravascular Administration – Cardiovascular Disorders:** Severe cardiac complications (including cardiac arrest, cardiopulmonary arrest), shock, peripheral vasodilatation, palpitations, vasospasm, including spasm of coronary arteries, myocardial infarction, syncope, cyanosis, pallor, flushing, chest pain. **Hemodynamic Reactions:** Vasospasm and thrombophlebitis following intravenous injection. **Blood and Lymphatic System Disorders**: Neutropenia. **Nervous System Disorders:** Disorientation, coma, depressed or loss of consciousness, transient contrast-induced toxic encephalopathy (including amnesia, hallucination, paralysis, paresis, speech disorder, aphasia, dysarthria), restlessness, tremors, hypoesthesia. **Psychiatric Disorders:** Confusional state, agitation. **Eye Disorders:** Eye irritation or itchiness, periorbital edema, ocular or conjunctival hyperemia, lacrimation. **Renal Reactions:** Acute kidney injury, toxic nephropathy (cervical intraepithelial neoplasia), transient proteinuria, oliguria or anuria, increased serum creatinine. **Gastrointestinal Disorders:** Abdominal pain, pancreatitis aggravated, salivary gland enlargement. **Endocrine Reactions:** Hyperthyroidism. Thyroid function tests indicative of hypothyroidism or transient thyroid suppression have been uncommonly reported following iodinated contrast media administration to adult and pediatric patients, including infants. Some patients were treated for hypothyroidism. **Respiratory, Thoracic, and Mediastinal Disorders:** Respiratory distress, respiratory failure, pulmonary edema, bronchospasm, laryngospasm, throat irritation, throat tightness, laryngeal edema, wheezing, chest discomfort, asthmatic attack. **Skin and Subcutaneous Tissue Disorders**: Contrast media reactions range from mild (eg, pleomorphic rashes, drug eruption, erythema and skin discoloration, blisters, hyperhidrosis, angioedema, localized areas of edema) to severe: (eg, Stevens-Johnson syndrome and toxic epidermal necrolysis [SJS/TEN], bullous or exfoliative dermatitis, acute generalized exanthematous pustulosis [AGEP], and drug reaction with eosinophilia and systemic symptoms [DRESS]). **Oral administration – Gastrointestinal Disorders:** Dysphagia, abdominal pain. **Body Cavity Administration – Gastrointestinal disorders:** Pancreatitis. **Musculoskeletal and Connective Tissue Disorders**: Arthritis (arthrography).

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, Omnipaque administration in patients with an estimated glomerular filtration rate (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. Reevaluate 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 for six to eight weeks. **Beta-Adrenergic Blocking Agents:** The use of beta-adrenergic blocking agents lowers the threshold for, and increases the severity of, contrast reactions and reduces the responsiveness of treatment of hypersensitivity reactions with epinephrine. Because of the risk of hypersensitivity reactions, use caution when administering Omnipaque to patients taking beta-blockers. **Drugs That Lower Seizure Threshold:** Drugs that lower seizure threshold, especially phenothiazine derivatives, including those used for their antihistaminic or antinauseant properties, are not recommended for use with intrathecal administration of Omnipaque. **Central Nervous System (CNS) Active Drugs:** Drugs such as monoamine oxidase (MAO) inhibitors, tricyclic antidepressants, CNS stimulants, psychoactive drugs described as analeptics, major tranquilizers, or antipsychotic drugs. Such medications should be discontinued at least 48 hours before myelography, should not be used for the control of nausea or vomiting during or after myelography, and should not be resumed for at least 24 hours post-procedure. In nonelective procedures in patients on these drugs, consider prophylactic use of anticonvulsants.

USE IN SPECIFIC POPULATIONS – Pregnancy: There are no data with iohexol use in pregnant women to inform any drug-associated risks. Iohexol crosses the placenta and reaches fetal tissues in small amounts. **Lactation**: Interruption of breastfeeding after exposure to iodinated contrast agents is not necessary because the potential exposure of the breastfed infant to iodine is small. However, a lactating woman may consider interrupting breastfeeding, and pumping and discarding breast milk, for 10 hours (approximately 5 elimination half-lives) after Omnipaque administration to minimize drug exposure to a breastfed infant. **Pediatric Patients**: In general, the frequency of adverse reactions in pediatric patients was similar to that seen in adults. Pediatric patients at higher risk of experiencing adverse events during contrast-medium administration may include those having asthma, a sensitivity to medication and/or allergens, congestive heart failure, a serum creatinine greater than 1.5 mg/dL, or those less than 12 months of age. Thyroid function tests indicative of hypothyroidism or transient thyroid suppression have been uncommonly reported following iodinated contrast media administration to pediatric patients, including infants. Some patients were treated for hypothyroidism. **Geriatric Use:** In clinical studies of Omnipaque for computed tomography (CT), 52/299 (17%) of patients were 70 and older. No overall differences in safety were observed between these patients and younger patients. Other reported clinical experience has not identified differences in response between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Prior to Omnipaque administration, please read the full Prescribing 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.