Visipaque Prescribing Information UK
JB8133 – Revised April 2019

PRESCRIBING INFORMATION VISIPAQUE™ Injection (iodixanol)
Please refer to full national Summary of Product Characteristics (SPC) before prescribing. Indications and approvals may vary in different countries. Further information available on request.

PRESENTATION
An isotonic, aqueous solution containing iodixanol, a non-ionic, dimeric contrast medium, available in two strengths containing either 270 mg or 320 mg iodine per ml.

INDICATIONS
For diagnostic use only X-ray contrast medium for use in adults in cardioangiography, cerebral angiography (conventional), peripheral arteriography (conventional), abdominal angiography (i.a. DSA), urography, venography, CT enhancement, studies of the upper gastrointestinal tract, arthrography and hysterosalpingography (HSG) Lumbar, thoracic and cervical myelography in adults.
In children for cardioangiography, urography, CT enhancement and studies of the upper gastrointestinal tract.

DOSAGE AND ADMINISTRATION
Adults and children: Dosage varies depending on the type of examination, age, weight, cardiac output, general condition of patient and the technique used (see SPC and package leaflet). For correct use of 500 mL multi-dose bottles, refer to full SPC. Multi-dose bottles must be used within 24 hours of opening.

CONTRAINDICATIONS
Manifest thyrotoxicosis. Hypersensitivity to the active substance or to any of the excipients.

WARNINGS AND PRECAUTIONS
A positive history of allergy, asthma, or reaction to iodinated contrast media indicates need for special caution. Premedication with corticosteroids or H1 and H2 antagonists might be considered in these cases. Although the risk of serious reactions with VISIPAQUE is regarded as remote, iodinated contrast media may provoke serious life-threatening hypersensitivity reactions, including fatal anaphylactic reactions. Therefore the necessary drugs and equipment must be available for immediate treatment. Patients should be observed closely for at least 30 minutes following administration of contrast medium, however delayed reactions may occur. Use of beta blockers may be a risk factor for anaphylactoid reactions and patients may present with atypical symptoms of hypersensitivity which may be misinterpreted as a vagal response.
Non-ionic iodinated contrast media inhibit blood coagulation in vitro, less than ionic contrast media. When performing vascular catheterisation procedures one should pay meticulous attention to the angiographic technique and flush the catheter frequently (e.g. with heparinised saline) so as to minimize the risk of procedure-related thrombosis and embolism. Serious, rarely fatal, thromboembolic events causing, myocardial infarction and stroke have been reported during angio-cardiographic procedures with both ionic and non-ionic contrast media. Advanced life support facilities should be readily available. There is a risk of thromboembolism in patients with homocystinuria. Ensure adequate hydration before and after examination especially in patients with multiple myeloma, renal dysfunction, diabetes mellitus, paraproteinemias, the elderly, children and infants. Care should be taken in patients with serious cardiac disease and pulmonary hypertension as they may develop hemodynamic changes or arrhythmias. In intravascular application, care should be taken in patients with acute stroke, or acute intracranial bleeding, in patients with altered blood brain barrier, cerebral oedema or acute demyelinisation. Particular care is required in patients with severe disturbance of both renal and hepatic function as they may have significantly delayed contrast medium clearance. For haemodialysis patients, correlation of time of contrast media injection with the haemodialysis session is unnecessary. To prevent lactic acidosis in diabetic patients treated with metformin, administration of metformin should be discontinued at the time of administration of contrast medium and withheld for 48 hours and reinstituted only after renal function has been re-evaluated and found to be normal. (Refer to SPC). Special care should also be taken in patients with hyperthyroidism, serious cardiac disease, pulmonary hypertension, arteriosclerosis, patients predisposed to seizures (acute cerebral pathology, tumours, epilepsy, alcoholics and drug addicts), and patients with myasthenia gravis or phaeochromocytoma. One should also be aware of the possibility of inducing transient hypothyroidism in premature infants receiving contrast media. After intrathecal use the patient should rest with head and thorax elevated for one hour and outpatients should not be alone for 24 hours.
All iodinated contrast media may interfere with laboratory tests for thyroid function, bilirubin, proteins, or inorganic substances (e.g. iron, copper, calcium, and phosphate). An increased risk of delayed reactions (flu-like or skin reactions) has been associated with patients treated with interleukin-2 up to two weeks previously.

PREGNANCY AND LACTATION
The safety of VISIPAQUE in pregnancy has not been established. Contrast media are poorly excreted in breast milk and minimal amounts are absorbed by the intestine. Breast feeding may be continued normally. Thyroid function should be checked in neonates during the first week of life, following administration of iodinated contrast agents to the mother during pregnancy and repeat testing of thyroid function is recommended at 2 to 6 weeks of age, particularly in low birth weight newborn or premature newborn.

ABILITY TO DRIVE AND USE MACHINES
It is not advisable to drive or use machines for one hour after injection or for 24 hours after intrathecal procedure.

UNDESIRABLE EFFECTS
Undesirable effects are usually mild to moderate, and transient in nature. Serious reactions and fatalities are only seen on very rare occasions. Serious reactions as well as fatalities are only seen on very rare occasions, these may include acute or chronic renal failure,

anaphylactic or anaphylactoid shock, hypersensitivity reaction followed by cardiac reactions (Kounis' syndrome), cardiac or cardio-respiratory arrest and myocardial infarction.
Hypersensitivity may present as respiratory or cutaneous symptoms like dyspnoea, rash, erythema, urticaria, pruritus, skin reactions, angioneurotic oedema, hypotension, fever, laryngeal oedema, bronchospasm or pulmonary oedema. In patients with autoimmune diseases cases of vasculitis and SJS-like syndrome were observed. They may occur immediately after injection or up to a few days later, irrespective of dose, and mild symptoms may be the first signs of serious anaphylactoid reaction/shock.
Intravascular use: Uncommon: hypersensitivity, headache, flushing, nausea, vomiting, rash, pruritus, urticaria, feeling hot, chest pain. Rare: dizziness, arrhythmia (including bradycardia, tachycardia), myocardial infarction, hypotension, cough, pain, discomfort, shivering (chills), pyrexia, administration site reactions including extravasation. Very rare: agitation, anxiety, cerebrovascular accident, sensory abnormalities including taste, amnesia, paraesthesia, syncope, cardiac arrest, transient cortical blindness, visual impairment, hypertension, ischaemia, dyspnoea, abdominal pain/discomfort, angioedema, erythema, back pain, muscle spasm, impairment of renal function including acute renal failure, feeling cold, asthenic conditions (e.g. malaise, fatigue). Frequency unknown: thrombocytopenia, anaphylactoid reaction, anaphylactoid shock, confusional state, coma, motor dysfunction, disturbances in consciousness, convulsion, transient contrast-induced encephalopathy (including hallucination), tremor, cardiac failure, ventricular hypokinesia, myocardial ischaemia, cardio-respiratory arrest, conduction abnormalities, coronary artery thrombosis, angina pectoris, arterial spasm, thrombosis, thrombophlebitis, shock, pulmonary oedema, respiratory arrest, respiratory failure, acute or aggravated pancreatitis, salivary gland enlargement, bullous dermatitis, Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis, acute generalised exanthematous pustulosis, drug rash with eosinophilia and systemic symptoms, drug eruption, dermatitis allergic, skin exfoliation, arthralgia, iodism.
Intrathecal use: Uncommon: headache (may be severe and lasting), vomiting. Frequency unknown: hypersensitivity including anaphylactic/anaphylactoid reactions, dizziness, transient contrast-induced encephalopathy including amnesia, hallucination, confusion, nausea, muscle spasm, shivering, pain at injection site.
Hysterosalpingography: Very common: abdominal pain, vaginal haemorrhage. Common: headache, nausea, pyrexia. Frequency unknown: hypersensitivity, vomiting, shivering, injection site reaction.
Arthrography: Common: injection site pain. Frequency unknown: hypersensitivity including anaphylactic/anaphylactoid reactions, shivering.
GI tract: Common: diarrhoea, abdominal pain, nausea. Uncommon: vomiting. Frequency unknown: hypersensitivity including anaphylactic/anaphylactoid reactions, shivering.

OVERDOSE
In the event of accidental overdosing, the water and electrolyte losses must be compensated by infusion. Renal function should be monitored for at least the next 3 days. If needed, haemodialysis may be used to remove iodixanol from the patient's system. Treatment of overdose is symptomatic.

PHARMACODYNAMIC PROPERTIES
ATC code: V08A B09.
In 64 diabetic patients with serum creatinine levels of 115 - 308 µmol/L, VISIPAQUE use resulted in 3% of patients experiencing a rise in creatinine of ≥ 44.2 µmol/L and 0% of the patients with a rise of ≥ 88.4 µmol/L. The release of enzymes (alkaline phosphatase and N-acetyl-β-glucosaminidase) from the proximal tubular cells is less than after injections of non-ionic monomeric contrast media and the same trend is seen compared to ionic dimeric contrast media. VISIPAQUE is also well tolerated by the kidney.

INSTRUCTIONS FOR USE AND HANDLING
Do not mix with other medicinal products. Like all parenteral products, VISIPAQUE should be inspected visually for particulate matter, discolouration and the integrity of the container prior to use. The product should be drawn into the syringe immediately before use. Containers are intended for single use only; any unused portions must be discarded. VISIPAQUE may be warmed to body temperature (37°C) before administration.

MARKETING AUTHORISATION HOLDER
GE Healthcare AS, Nycoveien 1-2, Postboks 4220 Nydalen, N-0401 Oslo, Norway.

CLASSIFICATION FOR SUPPLY
Subject to medical prescription (POM).

MARKETING AUTHORISATION NUMBERS
PL 0637/0018-19 (Glass vials/bottles and polypropylene bottles with stopper and screw cap).

DATE OF REVISION OF TEXT
April 2019

PRICE
(to be added by Marketing at time of going to press)

Adverse events should be reported.
Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/
Adverse events should also be reported to GE Healthcare at Gpv.drugsafety@ge.com