SUMMARY OF PRODUCT CHARACTERISTICS
CONTRAPAQUE 300 (Iohexol Injection USP 300 mg I/mL)

1. NAME OF THE MEDICINAL PRODUCT

CONTRAPAQUE 300 (Iohexol Injection USP 300 mg Iodine/mL)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL contains iohexol 647 mg (equivalent to 300 mg organically bound iodine/mL).

Concentration	Osmolality (mOsm/kg H_2O) 37°C	Viscosity (mPa·s) 37°C
300 mg I/mL	640	6.1

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection/infusion.

A clear, colourless to pale yellow solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

CONTRAPAQUE 300 is indicated for diagnostic use only as an X-ray contrast medium for use in adults and children for: urography, phlebography, i.v. DSA (digital subtraction angiography), CT enhancement, arteriography (including cardioangiography, coronary arteriography, aortography, selective cerebral arteriography, femoral arteriography), i.a. DSA, and myelography. Also for use in body cavities: arthrography, ERP/ERCP, herniography, hysterosalpingography, sialography and use in the gastrointestinal tract.

4.2 Posology and method of administration

The dosage depends on the type of investigation and the technique used. The same iodine concentration and volume as for other iodinated X-ray contrast media currently in use should typically be employed. Adequate hydration should be assured before and after administration.

CONTRAPAQUE 300 (300 mg I/mL) is used for: urography (adults 40–80 mL; children >7 kg 2 ml/kg), phlebography (20–100 mL/leg), CT enhancement (100–200 mL), selective cerebral arteriography (5–10 mL/injection), coronary arteriography (4–8 mL/injection), left ventricle/aortic root (30–60 mL/injection), aortography/femoral (30–50 mL/injection). For intrathecal/myelographic use, CONTRAPAQUE 300 should be used at the minimum effective concentration compatible with satisfactory imaging.

Method of administration

For intravenous, intra-arterial and intrathecal use, and use in body cavities. Must be warmed to body temperature (37°C) before use. Inspect visually before use.

4.3 Contraindications

- Hypersensitivity to iohexol or to any of the excipients listed in section 6.1.
- Manifest thyrotoxicosis.
- Concomitant use with biguanides: metformin should be withheld before or at the time of administration and not restarted for at least 48 hours (until renal function has been confirmed normal).

4.4 Special warnings and precautions for use

Hypersensitivity reactions

Anaphylactoid/anaphylactic reactions may occur. Resuscitative equipment and trained personnel must be available. Patients should be observed for at least 30 minutes after administration. Extreme caution is required in patients with a history of iodine contrast media sensitivity, bronchial asthma, hay fever or other allergic disorders.

Renal impairment

Adequate hydration should be ensured before and after administration. Avoid nephrotoxic concomitant medications. The age-dependent reduced GFR in infants can result in delayed excretion. Symptomatic overdosage is unlikely unless >2,000 mg I/kg is given over a limited period.

Thyroid function

Iodine-containing contrast media can interfere with thyroid function tests. Avoid in patients with manifest thyrotoxicosis. In premature infants, neonates and other children, transient hypothyroidism has been reported.

Thromboembolic events

Serious, rarely fatal, thromboembolic events have been reported during angiographic procedures. Flush the catheter frequently with heparinised saline. The examination should be kept as short as possible. Special care is required in patients with homocystinuria.

Extravasation

Extravasation can cause local pain, oedema and, rarely, tissue necrosis and compartment syndrome. If extravasation occurs, the injection should be stopped immediately.

Metformin

Metformin must be withheld before administration and not restarted until at least 48 hours after, provided renal function has been re-evaluated and found stable.

4.5 Interaction with other medicinal products and other forms of interaction

Metformin: see section 4.4. Thyroid function tests may be unreliable for up to two weeks after iodinated contrast media. Beta-blockers, calcium channel blockers, other antihypertensives and angiotensin-converting enzyme (ACE) inhibitors may increase the risk of cardiovascular reactions in association with contrast media administration.

4.6 Fertility, pregnancy and lactation

Pregnancy

The risk of radiation to the mother and the foetus must be considered. Iohexol should be used during pregnancy only if clearly necessary.

Breast-feeding

Iohexol is excreted in breast milk in very small amounts. Breast-feeding may be continued after administration.

Fertility

No effects on fertility have been reported with iohexol.

4.7 Effects on ability to drive and use machines

CONTRAPAQUE 300 is for diagnostic use only; it is generally administered in clinical settings. Any neurological adverse reactions may impair the ability to drive or use machines.

4.8 Undesirable effects

Adverse reactions to iohexol are generally mild and transient. The most common are injection site pain, warmth or burning sensation, nausea, vomiting and headache. Rare but serious reactions include anaphylaxis/anaphylactoid shock, cardiovascular collapse, hypoxic encephalopathy, renal failure and hepatic failure. Thromboembolic events (myocardial infarction, stroke) have been reported. In children: transient hypothyroidism (particularly in premature infants and neonates), bradycardia.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the National Regulatory Authority.

4.9 Overdose

Preclinical data indicate a high safety margin; no fixed upper dose level has been established for routine intravascular use. Symptomatic overdosage is unlikely with normal renal function unless >2,000 mg I/kg is given over a limited period. In overdose, correct any water or electrolyte imbalance. Monitor renal function for the next 3 days. Haemodialysis may be used for clearance of excess contrast medium. No specific antidote.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: X-ray contrast media, iodinated. ATC code: V08AB02.

Iohexol is a non-ionic, monomeric, tri-iodinated, water-soluble X-ray contrast medium. Its X-ray attenuation properties are due to the organically bound iodine. At the 300 mg I/mL concentration, CONTRAPAQUE is essentially isotonic with blood and tissue fluid. In healthy volunteers, no significant changes in haemodynamic, clinical-chemical or coagulation parameters were found following intravenous injection of iohexol.

5.2 Pharmacokinetic properties

Close to 100% of intravenously injected iohexol is excreted unchanged through the kidneys within 24 hours in patients with normal renal function. Maximum urinary concentration appears within approximately 1 hour after injection. No metabolites have been detected. Protein binding is very low (<2%).

5.3 Preclinical safety data

Iohexol has a very low acute intravenous toxicity in mice and rats. It has very low protein binding and is well tolerated by the kidneys. No genotoxicity or carcinogenicity concerns have been identified.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Trometamol (tromethamine) USP, edetate calcium disodium USP, hydrochloric acid BP (for pH adjustment), water for injections BP.

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products. A separate syringe should always be used.

6.3 Shelf life

4 years.

6.4 Special precautions for storage

Store below 30°C. Protect from light and secondary X-rays. Do not freeze. Keep out of the reach and sight of children.

6.5 Nature and contents of container

Clear, colourless Type I glass bottles. Available pack sizes: 50 mL and 100 mL. Each bottle packed in a carton with package insert.

6.6 Special precautions for disposal and other handling

Warm to body temperature (37°C) before use. Inspect visually before use; do not use if particulate matter or discolouration is present. Not for multi-dose use. Any unused product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

UNIQUE PHARMACEUTICAL LABORATORIES

(A Division of J.B. Chemicals & Pharmaceuticals Ltd.)

Neelam Centre, B Wing, 4th Floor, Hind Cycle Road, Worli, Mumbai 400030, India.

8. MARKETING AUTHORISATION NUMBER (PPB REGISTRATION NUMBER)

H2016/CTD3660/435

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16.08.2016

10. DATE OF REVISION OF THE TEXT

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