SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

CARDIOLEK-320

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains;

Iodixanol USP----------652 mg equivalent to 320 mg of Iodine

3 PHARMACEUTICAL FORM

Physical description/appearance of the product: Clear, colorless slightly viscousliquid. Free from foreign matter.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

This medicinal product is for diagnostic use only.
X-ray contrast medium for use in adults for cardioangiography, cerebral angiography (conventional and i.a.DSA), peripheral arteriography (conventional and i.a.DSA), abdominal angiography (i.a.DSA), urography, venography, CT-enhancement.

4.2 Posology and method of administration

To be administered Intravenous & Intra-arterial

4.3 Contraindications

Hypersensitivity to Iodixanol or any components of its formulation. Manifested thyrotoxicosis. Decompensated cardiac insufficiency.

4.4 Special warnings and special precautions for useWarnings:

The risk of serious reactions in connection with use of CARDIOLEK is regarded as very minor. However, iodinated contrast media may provoke serious or fatal reactions, anaphylactoid reactions or other manifestations of hypersensitivity. A course of action should therefore be planned in advance with necessary drugs and equipment available for immediate treatment, should a serious reaction occur.
A property of non-ionic contrast media is the low interference with normal physiological functions. As a consequence of this, non-ionic contrast media have less anticoagulant activity in vitro than ionic media. When performing vascular catheterization procedures one should be aware of this and pay meticulous attention to the angiographic technique and flush the catheter frequently with physiological saline (if necessary with the

addition of heparin) so as to minimize the risk of procedure-related thrombosis and embolism.
Iodinated contrast media may give rise to transient renal dysfunction or failure. Patients with preexisting renal dysfunction, diabetic nephropathy in particular and also patients with myelomatosis are at risk. Dehydration prior to contrast medium administration must be avoided.
Contrast medium clearance will be delayed in patients with renal dysfunction. Particular care is required in patients with severe disturbance of both renal and hepatic function as they may have significantly delayed contrast medium clearance.
Care should also be exercised in elderly patients, in hyperthyroidism and inpatients with cardiovascular disease.
A positive history of allergy, asthma or untoward reactions to iodinated contrast media indicates a need for special caution. Premedication with corticosteroids or antihistamines might be considered in these cases.
Cautions:
Preventive measures include-
- Identification of high risk patients
- Ensuring adequate hydration. If necessary by maintaining an i.v. infusion from before the procedure until the contrast medium has been cleared by the kidneys.
- Avoiding additional strain on the kidneys in the form of nephrotoxic drugs, arterial clamping, renal arterial angioplasty, or major surgery, until the contrast medium has been cleared.
- Postponing a repeat contrast medium examination until renal function returns to pre- examination levels.

4.5 Interaction with other medicinal products and other forms of interaction

All iodinated contrast media may interfere with tests on thyroid function. The iodine binding capacity of the thyroid tissue may be reduced for up to two weeks. High concentrations of contrast media in serum and urine may interfere with in-vitro laboratory test results of bilirubin, proteins or inorganic substance (e.g. iron, copper, calcium and phosphate). These substance should therefore not be assayed on the day of examination.

4.6 Pregnancy and lactation

The safety of CARDIOLEK for use in human pregnancy has not been established. An evaluation of experimental animal studies does not indicate direct or indirect harmful effects with respect to reproduction, development ofthe embryo or fetus, the course of gestation and peri- and postnatal development.
Since, wherever possible, radiation exposure should be avoided during pregnancy, the benefits of any X-ray examination, with or without contrast media, should be carefully weighed against the possible risk. The product should not be used in pregnancy unless benefit outweighs risk and it isconsidered essential by the physician.
The degree of excretion into human milk is not known, although

expected to be low. Breast feeding should be discontinued prior to administration and should not be recommended until at least 24 hours after the administration of CARDIOLEK.

4.7 Effects on ability to drive and use machines

No effects are known.

4.8 Undesirable effects

Undesirable effects associated with CARDIOLEK are usually mild to moderate and transient in nature. Serious reactions as well as fatalities are only seen on very rare occasions.

Hypersensitivity reactions may present as respiratory or cutaneous symptoms like dyspnoea, rash, erythema, urticaria, pruritus, skin reactions including severe bullous or pustular reactions, angioneurotic oedema, hypotension, fever, laryngeal oedema, bronchospasm or pulmonary
oedema.
They may appear either immediately after the injection or up to a few dayslater.Hypersensitivity reactions may occur irrespectively of the dose and mode of administration and mild symptoms may represent the first signs of a serious anaphylactoid reaction/shock.

Administration of the contrast medium must be discontinued immediately and, if necessary, specific therapy instituted via the vascular access. Patients using beta blockers may present with atypical symptoms of hypersensitivity which may be misinterpreted as a vagal reaction. A minor transient increase in serum creatinine is common after iodinated contrast media, but is usually of no clinical relevance.

4.9 Overdose

Overdosage is unlikely in patients with a normal renal function. Animal data indicate a very high safety margin for non-ionic contrast media, and no fixed upper dosage limit has been established.
In the event of accidental overdosing, the water and electrolyte losses must becompensated 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 patients system.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

The organically bound iodine absorbs radiation in the blood vessels / tissues when it is injected.
For most of the haemodynamic, clinical-chemical and coagulation parameters examined following intravenous injection of iodixanol in healthy volunteers, no significant deviation from preinjection values

has been found. The few changes observed in the laboratory parameters were minor and considered to be no clinical importance.
CARDIOLEK induces only minor effects on renal function in patients. The release of enzymes (alkaline phosphates and N-acetyl-ß-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. CARDIOLEK is also well tolerated by theglomerulus.
Cardiovascular parameters such as LVEDP, LVSP, heart rate and QT-time as well aas femoral blood flow were less influenced after CARDIOLEK than after other contrast media, where measured.

5.2 Pharmacokinetic properties

Iodixanol is rapidly disturbed in the body with a mean distribution half-life ofapproximately 21 minutes. The apparent volume of distribution is of the same magnitude as the extracellular fluid (0.26 l/kg b.w), indicating that iodixanol is distributed in the extra-cellular volume only.

No metabolites have been detected. The protein binding is less than 2%. The mean elimination half-life is approximately 2 hours. Iodixanol is excreted mainly through the kidneys by glomerular filtration. Approximately 80% of the administered dose is recovered un-metabolized in the urine within
4 hours and 97% within 24 hours after intravenous injection in healthy volunteers. Only about 1.2% of the injected dose is excreted in faeces within 72 hours.
The maximum urinary concentration appears within approximately 1 hour after injection.
No dose dependent kinetics has been observed in the recommended dose range.

5.3 Pre-clinical Safety Data

Reproduction studies in rats and rabbits have revealed no evidence if impaired fertility or teratogenicity due to iodixanol.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sr. no.	Name of excipient	Specification
1	Trometamol	BP
2	Edetate Calcium Disodium	US P
3	Sodium Chloride	BP
4	Calcium Chloride Dihydrate	BP
5	Hydrochloric Acid	BP

6	Water for Injection	BP

6.2 Incompatibilities

No incompatibility has been found. However, CARDIOLKE should not be directly mixed with other drugs. A separate syringe should be used.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Do not store above 30°C. Keep the glass container in the outer carton in orderto protect from light and secondary X-rays. Do not freeze.

6.5 Nature and contents of container

50 mL a clear USP Type I glass vial.

6.6 Instructions for use and handling

Refer pack insert.

7 MARKETING AUTHORISATION HOLDER

UNIQUE PHARMACEUTICAL LABORATORIES
(A Div. of J. B. Chemicals and Pharmaceuticals Ltd.)
Neelam Centre, B-wing, 4th floor, Hind Cycle Road,
Worli,Mumbai - 400 030. India.

8 MARKETING AUTHORISATION NUMBER

TAN 21 HM 0213

9 DATE OF FIRST AUTHORISATION

03 June, 2021

10 DATE OF REVISION OF THE TEXT

April, 202