Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Labrycor 0.2 mg/ml concentrate for solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial of 1 ml contains 0.2 mg of isoprenaline hydrochloride
Each vial of 5 ml contains 1 mg of isoprenaline hydrochloride

Excipient with known effect:
Each ml contains 3.2677 mg (0.14 mmol) of sodium.
Each 5 ml vial contains 16.3385 mg (0.70 mmol) of sodium.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Concentrate for solution for infusion
Clear, colourless to slightly yellow coloured solution
The ph of the solution is 2.5-4.5 and the osmolality is between 240-300 mOsmol/kg

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Short-term treatment of permanent bradycardia due to atrio-ventricular block while pending a pacemaker or when a pacemaker is contraindicated.

Short-term treatment of Adams-Stokes syndrome.

National and international recommendations and guidelines on the appropriate use of isoprenaline should be followed.

4.2 Posology and method of administration

Labrycor must only be administered by physicians trained in anaesthesia, cardiology or intensive care, in an appropriately monitored or critical care setting. Circulatory and respiratory functions should be closely monitored.

Isoprenaline should not be used routinely.

Posology

Labrycor should be carefully titrated under close monitoring to the lowest possible dose that obtains a heart rate of 50-60 beats per minute.

The recommended start dose is 0.01 microgram/kg/minute.
The dose can be increased in increments of 0.01 microgram/kg/minute until a maximal dose of 0.15 microgram/kg/minute.

The rate of infusion should be adjusted based on the heart rate of the patient.

Concomitant use with adrenaline*:*
Do not inject Labrycor at the same time as adrenaline in any circumstances (refer to section 4.3). However, if the administration of the two medicinal products is necessary, they can be given alternately every 4 hours (see sections 4.3 and 4.5).

Method of administration

Intravenous use.
Dilute 10 ml of concentrate for solution for infusion (= 2.0 mg) in 500 ml of sodium chloride 9 mg/ml (0.9 %) solution for injection **or** glucose 50 mg/ml (5 %) solution for injection (see section 6.6). This gives a concentration of 4 microgram/ml isoprenaline solution for infusion.

For instructions on dilution of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Labrycor is contraindicated in the case of:

- hypersensitivity to the active substance or to any of the excipients listed in section 6.1;
- Due to the risk of arrhythmias Labrycor should not be used with other potent beta-1 agonists such as adrenaline (see sections 4.2 and 4.5)
- Pre-existing ventricular arrhythmias
- Cardiac glycoside intoxication
- Myocardial infarction
- Tachyarrhythmias
- Angina pectoris

4.4 Special warnings and precautions for use

The use of Labrycor requires an ECG monitoring and a dose reduction in the case of ventricular myocardial hyperexcitability (polymorphic extrasystoles, repetitive burst pacing or ventricular tachycardia).
Labrycor should be used with caution in hypovolemic patients.
Caution when used in diabetic patients
Caution when used on patients under the effect of digitalis.
In case of hyperthyroidism, caution is recommended. Administration of the medicinal product should be avoided in cases of uncontrolled hyperthyroidism.
Caution in cases of cardiovascular disorders, especially coronary insufficiency, arrhythmias and hypertension.
Caution in cases of convulsive disorders.
Caution when doses are sufficient to reach a heart rate greater than 130 beats per minute.
Caution when using on patients who respond to sympathomimetic amines in an unusual manner.

Excipient:
This medicinal product contains less than 1 mmol sodium (23 mg) per ml, that is to say essentially "sodium-free".

4.5 Interaction with other medicinal products and other forms of interaction

Isoprenaline and epinephrine should not be administered simultaneously because both drugs are direct cardiac stimulants and their combined effects may induce serious arrhythmias, but it may be used simultaneously with dopamine or phenylephrine. If the administration of isoprenaline and adrenaline together is necessary, they can be given alternately every 4 hours (see sections 4.2 and 4.3).

Isoprenaline is contraindicated in cases of intoxication caused by digitalis.

Isoprenaline should not be used during anaesthesia with chloroform, cyclopropane, halothane or other halogenated anaesthetic agents because they may cause or worsen ventricular arrhythmia.

Isoprenaline should not be administered simultaneously with MAOIs.

Isoprenaline toxicity increases when administered at the same time as other cardiotonics or drugs stimulating the central nervous system (such as sympathomimetics, theophylline or thyroid hormone products).

Isoprenaline may worsen cardiovascular side effects of tricyclic antidepressants such as imipramine.

The simultaneous administration of isoprenaline and drugs combined with sulphates, such as salicylamide, may exacerbate the pharmacological effects of isoprenaline.

Administration of entacapone may enhance the effect of isoprenaline.

Doxapram and MAOIs may cause a risk of severe hypertension.

Labrycor may increase the risk of ergotism, if given together with ergotamine.

Hypertension may occur because of the high vasopressor effect of sympathomimetic vasoconstrictors (e.g. oxytocin).

4.6 Fertility, pregnancy and lactation

Pregnancy
There are limited data from the use of isoprenaline in pregnant women. Over 30 years of clinical experience failed to reveal malformative or feto/neonatal toxicity attributable to isoprenaline.

Studies in animals have shown reproductive toxicity (see section 5.3).

As a precautionary measure, it is preferable to avoid the use of isoprenaline during pregnancy. The clinical benefits should be weighed against the possible risks to the mother and child.

Breastfeeding
It is unknown whether isoprenaline/metabolites are excreted in human milk. A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from isoprenaline therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

Fertility
There is no effect on fertility from the animal data available.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Serious adverse reactions to isoprenaline occur infrequently. Most adverse reactions subside rapidly when isoprenaline is discontinued or may abate while the drug is still in use. Isoprenaline has almost exclusively beta-agonist properties but also stimulates the CNS.

MedDRA frequency / MedDRA-system organ class	Not known (cannot be estimated from the available data)
Cardiac disorders	tachycardia arrhythmia precordial pain
Vascular disorders	hypotension hypertension
Nervous system disorders	nervousness shakiness dizziness headache
Gastrointestinal disorders	nausea
General disorders and administration site conditions	asthenia

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 HPRA Pharmacovigilance Website: www.hpra.ie.

4.9 Overdose

Symptoms

- nausea,
- headache,
- sinus tachycardia,
- polymorphic extrasystoles,
- ventricular tachycardia

Treatment
Simply discontinue isoprenaline hydrochloride infusion. The therapeutic activity will disappear after a few minutes given the speed of inactivation.

If necessary, plasma or whole blood will then be administered.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Cardiac therapy, adrenergic and dopaminergic agents, ATC code: C01CA02

Labrycor is a *b*-sympathomimetic drug affecting intra-cardiac flow, without affecting blood pressure at low dose.

Heart
Isoprenaline hydrochloride has a pronounced inotropic and chronotropic effect (effect of *ß* 1 receptors) which results in a significant increase in cardiac output.

Isoprenaline hydrochloride acts immediately at the nodal tissue level, by lowering the myocardium's excitability threshold and by increasing heart contraction and systolic flow.

Blood vessels
Isoprenaline hydrochloride causes peripheral vasodilation (effect of *ß* 2 receptors) associated with decreased resistance, increased blood volume and regulation of the central venous pressure.

5.2 Pharmacokinetic properties

Absorption
After intravenous injection, isoprenaline has a plasma half-life of about one to several minutes according to whether the rate of injection is rapid or slow.

Distribution
Isoprenaline is rapidly inactivated in the liver and other tissues by metabolism. It does hardly cross the blood-brain barrier. It is not known if isoprenaline is distributed into milk in humans.

Biotransformation
Isoprenaline is metabolised by catechol-O-methyltransferase in the liver, lungs, and other tissues. The major metabolite after intravenous administration is 3-O-methylisoproterenol (which has been reported to have weak β-adrenergic blocking activity) and its conjugates.

Elimination
About 40–50% of the dose is excreted in the urine unchanged and the remainder as 3-O-methylisoproterenol within 24 hours.

5.3 Preclinical safety data

Isoprenaline, administered subcutaneously in a single dose on the eighth day of gestation to pregnant hamsters produced a variety of gross malformations of the brain, eyes, spinal cord, heart, liver and skeleton. Isoprenaline injection into either the unanaesthetized ovine foetus or the pregnant ewe produced a transient tachycardia and hypotension in either the ewe or the foetus. No evidence was obtained for placental transfer, in either direction, of pharmacologically active isoprenaline.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium edetate
Sodium citrate dihydrate
Citric acid
Sodium chloride
Hydrochloric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

Before opening: 3 years
After opening: The product must be used immediately.
After dilution:

Chemical and physical in-use stability of the solution diluted in 5% glucose or 0.9% sodium chloride has been demonstrated for 24 hours at 25°C.

From a microbiological point of view, unless the method of opening precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

Before opening: Keep the vial in the outer carton in order to protect from light.
Do not refrigerate.

For storage conditions after dilution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

1 ml in a glass vial with bromobutyl rubber stopper and aluminium seal with plastic flip-off cap. Each pack contains 1 or 5 vials.

5 ml in a glass vial with bromobutyl rubber stopper and aluminium seal with plastic flip-off cap. Each pack contains 1 or 5 vials.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

This medicinal product may be diluted in 500 ml of the following solutions: sodium chloride 9 mg/ml (0.9 %) solution for injection or glucose 50 mg/ml (5 %) solution for injection.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Macure Healthcare Limited
62 Archlight Building
Triq L-Gharbiel
Is-Swieqi
SWQ 3251
Malta

8 MARKETING AUTHORISATION NUMBER

PA23314/002/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 18th July 2025

Date of Last Renewal: 18th August 2026

10 DATE OF REVISION OF THE TEXT

April 2026