SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Labrycor 1 mg/5 ml concentraat voor oplossing voor infusie

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml vial contains 1mg of Isoprenaline hydrochloride.
Excipient with known effect:

Each 5 ml vial contains 16.3355 mg (0.70 mmol) of sodium.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection/infusion

Clear, colourless to slightly yellow coloured solution

The pH of the solution is 2.5 – 4.5 and the osmolarity is between 240-300 mOsmol/kg

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Emergency drug:

- for Stokes-Adams syndrome by atrioventricular block, while waiting for temporary or permanent equipment;
- for extreme bradycardia by sinoatrial syncopal block, while waiting for temporary or permanent equipment;
- for cardiac arrest when the cardiac activity reappears;
- for low cardiac output, after cardiac surgery;
- for torsades de pointes, in case it is impossible to carry out a stimulation at a fast ventricular rate, associated with the etiological treatment for torsades and the restoration of serum potassium.

4.2. Posology and method of administration

Posology

Following the indications, the effective dose can vary from 0.2 mg to 10 mg/24 hours.

Method of administration

1. For intravenous use only via a central line or large peripheral vein (to avoid potential venous irritation from low pH)

2. Administration should be conducted in an appropriate high care environment, or on transfer to appropriate high care environment.

3. Isoprenaline should be diluted before use (see section 6.3)

4. Administration should be by a clinician with mandatory continuous cardiovascular monitoring. A heart rate of 130 per minute contraindicates the continuation of the treatment.

<Product name> can be used as:

- continuous IV infusion after its dilution in 5% glucose or 0.9% sodium chloride at the following concentrations:

Volume of <Product name>	**Volume of solvent**	**Solvent**	**Final concentration**
1 ml	10 ml	0.9% sodium chloride	0.02 mg/ml
1ml	10 ml	5% glucose	0.02 mg/ml
10 ml	500 ml	5% glucose	0.004 mg/ml
5 ml	500 ml	5% glucose	0.002 mg/ml

- as subcutaneous injection which remains an exceptional route of administration and allows waiting for the setting up of the infusion.

NB: Protect from the perfusion of light.

Monitoring during treatment: The electrocardiogram must be continuously monitored as well as all other cardiocirculatory constants: a heart rate of 130 per minute contraindicates the continuation of the treatment.

Associations: It is possible to associate with <Product name> other therapies in derivation with the perfusion.

4.3. Contraindications

This medicine should never be used in case of:

- hypersensitivity to the active substance or to any of the excipients listed in section 6.1;
- sinus tachycardia greater than 130/minute;
- states of atrial and ventricular hyperexcitability;
- digitalis intoxication;
- acute coronary insufficiency and, in particular, acute myocardial infarction, except in case of complete atrioventricular block with extreme bradycardia.

This medicine is usually not recommended in case of association with volatile halogenated anaesthetics.

4.4. Special warnings and precautions for use

The use of <Product name> requires an ECG monitoring and a dose reduction in case a ventricular myocardial hyperexcitability occurs (polymorphic extrasystoles, repetitive bursts or ventricular tachycardia).

<Product name> should only be used in case of hypovolemic collapse after the restoration of the blood volume.

Caution should be exercised during use in coronary, diabetic patient or in digitalised patient.

In case of hyperthyroidism, caution is recommended. The administration of the speciality will preferably be avoided in case of uncontrolled hyperthyroidism.

This medicine contains less than 1 mmol sodium (23 mg) per vial that is essentially "sodium-free.

4.5. Interaction with other medicinal products and other forms of interaction

Combinations not recommended

+ Volatile halogenated anesthetics :

Serious ventricular rhythm disorders (increasing cardiac excitability).

4.6. Fertility, pregnancy and lactation

Pregnancy

Studies in animals have not highlighted any teratogenic effect. In the absence of teratogenic effects in animals, a malformation effect in the human species is not expected. In fact, to this day, the substances responsible for malformations in the human species proved to be teratogenic in animals during well conducted studies on two species.

There is currently no relevant or sufficient data to evaluate the possible malformation or foetotoxic effect of isoprenaline when it is administered during pregnancy.

Accordingly, as a precautionary measure, it is preferable not to use isoprenaline during pregnancy.

Breastfeeding

During breastfeeding, careful monitoring of the newborn is recommended.

4.7. Effects on ability to drive and use machines

Not applicable.

4.8. Undesirable effects

Cardiac disorders
Tachycardia, ventricular rhythm disorders, anginal pain with possible appearance or increase of a pre-existing ischemia.

Nervous system disorders
Headache, tremor.

Gastrointestinal disorders

Nausea.

Vascular disorders
Hypotension, hot flashes.

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 reporting system listed in Appendix V*.

4.9. Overdose

In case of overdose, the following can be observed:

- nausea,
- headache,
- tachycardia,
- extrasystoles.

One must simply stop the infusion of <Product name> whose therapeutic activity will cease within a few minutes as a result of its speed of inactivation.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Dopaminergic and Adrenergics Agents, ATC code: C01CA02

Mechanism of action

Isoprenaline is a ß stimulant.

At the cardiac level, the ß1 effect causes:

- an increase in heart rate,
- an improvement in the speed of atrioventricular conduction by direct action on the nodal tissue,
- an increase in the contractile force of the myocardium,
- decrease in the threshold of myocardial excitability,
- an increase in systolic flow, cardiac output and myocardial oxygen consumption.

In the periphery, the ß2 effect causes:

- systemic and pulmonary arterial vasodilation leading to a post-load reduction,
- bronchodilation.

5.2. Pharmacokinetic properties

- The half-life is approximately 1 minute via fast IV,
- After a slow IV, the distribution half-life is 2 to 5 minutes and the elimination half-life is 3 to 7 hours,

- Oxidative deamination and O-methylation,
- Elimination by renal route,
- Good reabsorption, subcutaneously. The latency time is of a few minutes.

5.3. Preclinical safety data

Unspecified.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Disodium edetate, Sodium citrate dihydrate, Citric acid anhydrous, Sodium chloride, Hydrochloric acid, Sodium hydroxide, Water for injections.

6.2. Incompatibilities

See section 4.2

6.3. Shelf life

Before opening: 24 months

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 vials in the outer carton in order to protect from light.
Do not refrigerate

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

6.5. Nature and contents of container

<Product name> 1mg/5ml solution for injection/infusion is a clear, colourless to slightly yellow coloured solution, free from visible particles. It is available as 5 ml fill in 5 ml clear type-I glass vial along with 13 mm rubber stopper and 13 mm flip off seal and, is available in pack sizes of 1 vial or 5 vials.

Not all pack sizes may be marketed.

6.6. Special precautions for disposal

No special requirements for disposal.

7. MARKETING AUTHORISATION HOLDER

Macure Healthcare Ltd.
62 Arclight Building
Triq l-Gharbiel
Is-Swieqi, SWQ 3251
Malta

8. MARKETING AUTHORISATION NUMBER(S)

RVG 132439

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Datum van eerste verlening van de vergunning: 5 augustus 2024

10. DATE OF REVISION OF THE TEXT