SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Isoprenaline Macure 0.2 mg/ml concentrate for solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains 0.2 mg isoprenaline hydrochloride equivalent to 0.17 mg isoprenaline.

Each ampoule of 5 ml contains 1.0 mg isoprenaline hydrochloride.

Excipients(s) with known effect:

Each ampoule contains 16 mg sodium.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Concentrate for solution for infusion (sterile concentrate).

The concentrate for solution for infusion is clear and colourless or pale yellow.

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

Isoprenaline Macure 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

Isoprenaline Macure 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 Isoprenaline Macure at the same time as adrenaline in any circumstances. 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 (2 ampoules à 5 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 of infusion.

4.3 Contraindications

Isoprenaline Macure is contraindicated in the case of:

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Concomitant use with adrenaline (see sections 4.2 and 4.5)
- Pre-existing ventricular arrythmias
- Tachyarrythmias
- Cardiac glycoside intoxication
- Myocardial infarction
- Angina pectoris

4.4 Special warnings and precautions for use

- The use of Isoprenaline Macure requires ECG monitoring and reduction of doses in the case of ventricular myocardial hyperexcitability (polymorphic extrasystoles, repetitive burst pacing or ventricular tachycardia).
- Isoprenaline Macure 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 cases 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.

Isoprenaline Macure contains 16 mg sodium per ampoule. This is equivalent to 0.8 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

4.5 Interaction with other medicinal products and other forms of interaction

Isoprenaline must not be administered at the same time as adrenaline 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.

Isoprenaline Macure 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

Isoprenaline has often been administered during pregnancy.
Animal tests have not shown any teratogenic effect. Over 30 years of clinical experience failed to reveal any teratogenic effects attributable to isoprenaline.

In any event, as with any medication administered to a pregnant woman, you need to carefully weigh the clinical benefits against the possible risks to the mother and child.

Breast-feeding

Administration of Isoprenaline Macure during breast-feeding is not recommended.

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	fast heartbeat arrhythmia precordial pain
Vascular disorders	low blood pressure high blood pressure
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 the Yellow card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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

Isoprenaline Macure is a □̃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 □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 □ 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
Data not provided.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride

EDTA

Sodium citrate

Citric acid monohydrate

Water for injections

Sodium hydroxide (for pH adjustment)

Hydrochloric acid (for pH adjustment)

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

18 months.

After dilution with sodium chloride 9 mg/ml (0.9 %) solution for injection or glucose 50 mg/ml (5 %) solution for injection, the chemical and physical in-use stability has been demonstrated for 48 h at 25 °C and 2 °C – 8 °C.

From a microbiological point of view, diluted solutions should be used immediately. If not used immediately, in-use storage times and conditions prior to use of the diluted solution are the responsibility of the user and would normally not be longer than 24 hours at 2 °C to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions. If not used immediately, protect the diluted solution from light.

6.4 Special precautions for storage

Do not store above 25°C. Do not freeze.

6.5 Nature and contents of container

Amber type I glass ampoules containing 5 ml solution, in a carton.
Pack size: 5 ampoules.

6.6 Special precautions for disposal

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

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.

7 MARKETING AUTHORISATION HOLDER

Macure Pharma ApS
Hejrevej 39
2400 Copenhagen NV
Denmark

8 MARKETING AUTHORISATION NUMBER(S)

PL 53749/0001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

02/02/2026

10 DATE OF REVISION OF THE TEXT

02/02/2026