

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Noradrenalin Abcur 1 mg/ml concentrate for solution for infusion.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml concentrate for solution for infusion contains 2 mg noradrenaline tartrate corresponding to 1 mg noradrenaline.

Excipients with known effect

0.14 mmol (3.2 mg) sodium per ml.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Concentrate for solution for infusion.

Appearance: Clear colourless solution.

pH 3-4.5

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Short-term treatment of acute hypotension, such as in septic shock.

4.2 Posology and method of administration

The patient should be closely monitored during the entire treatment. The blood pressure should be monitored during the entire treatment and the infusion rate should be adjusted to the desired blood pressure.

Posology:

Adults

Initially, usually between 0.05-0.15 microgram/kg/min.

Titration of dose: The dose is titrated in steps of 0.05-0.1 microgram/kg/min until adequate blood pressure is achieved (usually mean arterial blood pressure >75-80 mmHg). The dose should be adjusted according to the pressor effect observed. There is great individual variation in the dose required to attain and maintain the desired blood pressure.

Maximum recommended dose is 2.5 microgram/kg/min.

Dosage table: Reconstituted solution of Noradrenalin Abcur 40 microgram/ml

	Infusion rate ml/hour								
Body weight	40 kg	50 kg	60 kg	70 kg	80 kg	90 kg	100 kg	110 kg	120 kg
Dose									
0.05 µg/kg/min	3.0	3.8	4.5	5.3	6.0	6.8	7.5	8.3	9.0
0.10 µg/kg/min	6.0	7.5	9.0	10.5	12.0	13.5	15.0	16.5	18.0

0.15 µg/kg/min	9.0	11.3	13.5	15.8	18.0	20.3	22.5	24.8	27.0
0.20 µg/kg/min	12.0	15.0	18.0	21.0	24.0	27.0	30.0	33.0	36.0
0.25 µg/kg/min	15.0	18.8	22.5	26.3	30.0	33.8	37.5	41.3	45.0
0.30 µg/kg/min	18.0	22.5	27.0	31.5	36.0	40.5	45.0	49.5	54.0
0.35 µg/kg/min	21.0	26.3	31.5	36.8	42.0	47.3	52.5	57.8	63.0
0.40 µg/kg/min	24.0	30.0	36.0	42.0	48.0	54.0	60.0	66.0	72.0
0.45 µg/kg/min	27.0	33.8	40.5	47.3	54.0	60.8	67.5	74.3	81.0
0.50 µg/kg/min	30.0	37.5	45.0	52.5	60.0	67.5	75.0	82.5	90.0

Discontinuation of treatment

Infusion of noradrenaline should be reduced gradually since abrupt withdrawal may cause acute hypotension.

Elderly patients

See section 4.4.

Paediatric population

The safety and efficacy of Noradrenalin Abcur 1 mg/ml in children and adolescents have not been established.

Patients with renal and hepatic impairment

There is no experience of treatment with Noradrenalin Abcur 1 mg/ml in patients with renal and hepatic impairment.

Method of administration

Noradrenalin Abcur 1 mg/ml should be diluted before use and administered as an intravenous infusion via a central venous catheter. The infusion should be at a controlled rate using either a syringe pump or an infusion pump.

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

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Noradrenaline should only be used in conjunction with appropriate blood volume replacement.

Noradrenaline should be administered with caution to patients being treated with MAO inhibitors or within 14 days after treatment with MAO inhibitors and in patients treated with tricyclic antidepressants since prolonged hypertension can occur.

Elderly patients may be especially sensitive to the effects of noradrenaline.

Caution should also be exercised in patients with coronary, mesenteric or peripheral vascular thrombosis because noradrenaline may exacerbate the ischemia and enlarge the infarct region. Caution should also be taken in hypotensive patients after myocardial infarction and in patients with angina, especially Prinzmetal's angina and in patients with diabetes, hypertension or hyperthyroidism.

Noradrenaline should only be administered by healthcare professionals who are well familiar with the use of the product.

Paravenous infusion should be avoided and may cause local tissue necrosis. The infusion site should therefore be monitored frequently and regularly.

This medicine 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

Noradrenaline should be administered with caution to patients being treated with MAO inhibitors or within 14 days after treatment with MAO inhibitors and in patients treated with tricyclic antidepressants due to the risk of serious, prolonged hypertension.

The use of noradrenaline with cyclopropane, halothane, chloroform, enflurane or other inhalation anesthetics may cause serious cardiac arrhythmias. Due to the increased risk of ventricular fibrillation noradrenaline should be used with caution in patients receiving these agents or other cardiac sensitizing agents or in patients showing hypoxia or hypercapnia.

The effect of noradrenaline may be enhanced by guanethidine, reserpine, methyldopa or tricyclic antidepressants.

Concomitant treatment with maprotiline and digoxin may require dose adjustment.

4.6 Fertility, pregnancy and lactation

Pregnancy

Noradrenaline may impair placental perfusion and induce fetal bradycardia. It may also exert a contractile effect on the pregnant uterus and lead to fetal asphyxia in late pregnancy. These possible risks to the fetus should therefore be considered against the potential benefit to the mother.

Breastfeeding

There is insufficient information on the effects of noradrenaline during lactation.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

A tabulated list of undesirable effects is outlined below:

The undesirable effects are listed according to organ systems and following frequency:

Not known (cannot be estimated from the available data)

System Organ Class	Frequency	Adverse Reaction
Psychiatric disorders	Not known	Anxiety
Nervous system disorders	Not known	Headache
Cardiac disorders	Not known	Hypertension, reflex bradycardia, ventricular arrhythmia Stress cardiomyopathy
Vascular disorders	Not known	Peripheral ischemia with sequential gangrene Decreased blood volume at prolonged administration
Respiratory, thoracic and mediastinal disorders	Not known	Dyspnea

Noradrenaline is a tissue irritant and must be diluted before use. Extravasation may cause necrosis of the skin and the surrounding tissue. Development of tolerance to the effects of noradrenaline may occur after prolonged use.

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

[To be completed nationally]

4.9 Overdose

Overdosage may result in severe hypertension, reflex bradycardia, marked increase in peripheral resistance and decreased cardiac output. This may be accompanied by violent and sudden headache, photophobia, retrosternal pain, pallor, intense sweating and vomiting.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Adrenergic and dopaminergic agents, ATC code: C01CA03

Pharmacodynamic effects

Noradrenaline provides a strong stimulation of alpha receptors in blood vessels at which these are counter-extracted. Noradrenaline also has effect on beta-1 receptors in the heart leading to a positive inotropic and initially positive chronotropic effect. The increase in blood pressure may cause a reflex reduction in heart rate. Vasoconstriction may lead to decreased blood flow in the kidneys, liver, skin and smooth muscle. Local constriction of the vessels may cause hemostasis and/or necrosis.

The pressor effect disappears 1-2 min after terminated infusion.

Development of tolerance to the effects of noradrenaline may occur.

5.2 Pharmacokinetic properties

Elimination

Up to 16% of an intravenous dose is excreted unchanged in the urine as methylated and deaminated metabolites in free and conjugated forms.

5.3 Preclinical safety data

Most of the undesirable effects can be derived to sympathomimetic results from excessive stimulation of the sympathetic nervous system through the various adrenergic receptors.

Noradrenaline may impair placental perfusion and induce fatal fetal bradycardia. It may also exert a contractile effect on the pregnant uterus and lead to fatal fetal asphyxia in late pregnancy.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride

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

2 years

The chemical and physical stability of the solution after dilution is 24 hours when stored at 25°C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use 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.

6.4 Special precautions for storage

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

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

6.5 Nature and contents of container

1 ml in clear glass ampoules (type I): pack sizes of 10, 20, 50 or 100 ampoules.

2 ml in clear glass ampoules (type I): pack sizes of 10, 20, 50 or 100 ampoules.

4 ml in clear glass ampoules (type I): pack sizes of 10, 20, 50 or 100 ampoules.

5 ml in clear glass ampoules (type I): pack sizes of 10, 20, 50 or 100 ampoules.

8 ml in clear glass ampoules (type I): pack sizes of 10, 20, 50 or 100 ampoules.

10 ml in clear glass ampoules (type I): pack sizes of 10, 20, 50 or 100 ampoules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

SHOULD BE DILUTED

Dilution with 50 mg/ml (5%) glucose solution, 9 mg/ml (0.9%) sodium chloride, 9 mg/ml (0.9%) sodium chloride with 50 mg/ml (5%) glucose solution, 50 mg/ml (5%) glucose solution and 9 mg/ml (0.9%) sodium chloride (50:50): 4 ml concentrate for infusion (1 mg/ml) is diluted with 96 ml of the dilution solution to a concentration of 40 microgram/ml. The solution for infusion should be used immediately after dilution.

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

7. MARKETING AUTHORISATION HOLDER

Abcur AB
P.O. Box 1452
251 14 Helsingborg
Sweden

8. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

To be completed nationally

10. DATE OF REVISION OF THE TEXT

2019-09-26