PACKAGE LEAFLET: INFORMATION FOR THE USER

Noradrenaline (Norepinephrine) 1mg/ml Concentrate for Solution for Infusion

Noradrenaline (as noradrenaline tartrate)

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

The name of this medicinal product is Noradrenaline (Norepinephrine) 1 mg/ml Concentrate for Solution for Infusion but it will be referred to as Noradrenaline (Norepinephrine) Concentrate throughout this leaflet.

What is in this leaflet:

1. WHAT NORADRENALINE (NOREPINEPHRINE) CONCENTRATE IS AND WHAT IT IS USED FOR

Noradrenaline (Norepinephrine) Concentrate for Solution for Infusion is a drug that belongs to the group of adrenergic and dopaminergic agent. It is used in an emergency to increase blood pressure to normal levels.

2. WHAT YOU NEED TO KNOW BEFORE YOU ARE GIVEN NORADRENALINE (NOREPINEPHRINE) CONCENTRATE

Do not take Noradrenaline (Norepinephrine) Concentrate:
- if you are allergic to noradrenaline preparations or to any of the other ingredients of this medicine (listed in section 6).
- if you are hypotensive (have low blood pressure) that has been caused by hypovolaemia (low blood volume);
- if you are taking some anaesthetics such as halothane or cyclopropane (this may increase the risk of irregular heartbeat)

Tell your doctor if any of the above applies to you before this medicine is used.

Warnings and precautions

Talk to your doctor or pharmacist before taking Noradrenaline (Norepinephrine) Concentrate if you have:
- extravasation risk ;
- major left ventricular dysfunction (a heart condition) ;
- coronary, mesenteric or peripheral vascular thrombosis ;
- hypotension following myocardial infarction ;
- Prinzmetal's variant angina ;
- heart rhythm disorders during your treatment – you will need a reduced dose ;
- hyperthyroidism or diabetes mellitus ;
- or are elderly.

Your blood pressure and heart rate will be checked frequently during your treatment to avoid hypertension.

Other medicines and Noradrenaline

Tell your doctor or pharmacist if you are taking or have recently taken or might take any other medicines.
Noradrenaline (Norepinephrine) Concentrate may affect or be affected by other medicines. In particular, tell your doctor if you are taking any of the following:
- Halothane, cyclopropane: these medicines are anaesthetics, they cause insensibility to pain and are used before some operations. If you are taking these medicines as well as Noradrenaline this may increase the risk of irregular heart-beat.
- Amitriptiline, Imipramine, Trimipramine, Moclobemide, Iproniazide, Phenelzine, Fluoxetine, Sertraline: these medicines are used for treatment of depression. Taking any of these medicines together with Noradrenaline can dangerously increase its concentration in the blood and therefore its pressor action.
- Linezolid, an antibiotic (drug used to treat infections caused by bacteria and other microorganisms), can dangerously increase Noradrenaline concentration in the blood and therefore its pressor action, when taken together.
- Alpha and beta-blockers: if you are taking these medicines as well as Noradrenaline this may increase the risk of severe hypertension.
- Thyroid hormones, Cardiac glycosides, Anti-arrhythmics: if you are taking these medicines as well as Noradrenaline this may cause increased cardiac effects.
- Ergot alkaloids or oxytocin may enhance the vasopressor and vasoconstrictive effects.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

The following information is intended for healthcare professionals only:
Noradrenaline (Norepinephrine) 1 mg/ml Concentrate for Solution for Infusion

Posology and method of administration

For intravenous use.
Dilute before use with Glucose 5% w/v Infusion or Sodium Chloride 0.9% w/v and Glucose 5% w/v Infusion.
Administer as a diluted solution via a central venous catheter. The infusion should be at a controlled rate using either a syringe pump, an infusion pump or a drip counter.

Adults

Initial rate of infusion:
When diluted as recommended below, (the concentration of the prepared infusion is 40 mg/litre noradrenaline base (80 mg/litre noradrenaline tartrate)) the initial rate of infusion, at a body weight of 70 kg, should be between 10 ml/hour and 20 ml/hour (0.16 to 0.33 ml/min). This is equivalent to 0.4 mg/hour to 0.8 mg/hour noradrenaline base (0.8 mg/hour to 1.6 mg/hour noradrenaline tartrate). Some clinicians may wish to start at a lower initial infusion rate of 5 ml/hour (0.08 ml/min), equivalent to 0.2 mg/hour noradrenaline base (0.4 mg/hour noradrenaline tartrate).

Titration of dose:
Once an infusion of noradrenaline has been established the dose should be titrated in steps of 0.05 -0.1 µg/kg/min of noradrenaline base according to the pressor effect observed. There is great individual variation in the dose required to attain and maintain normotension. The aim should be to establish a low normal systolic blood pressure (100 - 120 mm Hg) or to achieve an adequate mean arterial blood pressure (greater than 65 - 80 mm Hg – depending on the patient's condition).

Noradrenaline Infusion Solution 40 mg/litre (40 micrograms /ml) noradrenaline base			
Patient's Weight	Posology (µg/kg/min) noradrenaline base	Posology (mg/hour) noradrenaline base	Infusion Rate (ml/hour)
50 kg	0.05	0.15	3.75
	0.1	0.3	7.5
	0.25	0.75	18.75
	0.5	1.5	37.5
	1	3	75
60 kg	0.05	0.18	4.5
	0.1	0.36	9
	0.25	0.9	22.5
	0.5	1.8	45
	1	3.6	90
70 kg	0.05	0.21	5.25
	0.1	0.42	10.5
	0.25	1.05	26.25
	0.5	2.1	52.5
	1	4.2	105

Noradrenaline (Norepinephrine) Concentrate may harm the unborn baby. Your doctor will decide if you should be given Noradrenaline (Norepinephrine) Concentrate.

Information on the ingredients of Noradrenaline (Norepinephrine) Concentrate
This medicine contains less than 1 mmol sodium (23 mg) per 4ml vial, that is to say essentially 'sodium-free'.

3. HOW TO USE NORADRENALINE (NOREPINEPHRINE) CONCENTRATE

Noradrenaline (Norepinephrine) Concentrate will be given to you in hospital by a doctor or nurse. It is first diluted and then infused into a vein.
The recommended dose of Noradrenaline (Norepinephrine) Concentrate will depend on your medical condition. The usual dose is between 0.4 and 0.8 mg per hour. Your doctor will determine the correct dose for you. After the initial dose your doctor will assess your response and adjust the dose accordingly.
If you are given more or forget to take Noradrenaline (Norepinephrine) Concentrate:
It is unlikely that you will receive too much or too little of this medicine, as this medicine will be given to you in hospital. However, talk to your doctor or nurse if you have any concerns.
Symptoms of overdose are severe high blood pressure, slow heartbeat, violent headache, light sensitivity, pain in the chest, pale colour, intense sweating and vomiting.

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them. Tell your doctor immediately if you experience:
- sudden itchy rash (hives), swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing), feeling that you are going to faint.
- pain and/or swelling at the injection site.

The following side effects have been reported:
- skin necrosis (death) if the infusion is not given directly into the vein,
- anxiety, insomnia, confusion, headaches, psychotic state, weakness, tremor, lower vigilance, anorexia, nauseas, vomiting,
- difficulty in breathing, fast or slow heart rate, pain in the chest or throat,
- retention of urine, pallor (loss of skin colour), sweating, sensitivity to light.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly 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. By reporting side effects, you can help provide more information on the safety of this medicine.

5. HOW TO STORE NORADRENALINE (NOREPINEPHRINE) CONCENTRATE

Keep this medicine out of the sight and reach of children.
Store below 25° C.
Keep ampoules in outer carton in order to protect from light.

Do not use this medicine if the solution is brown in colour.

Do not use this medicine after the expiry date which is stated on the carton after EXP. The expiry date refers to the last day of that month.

Chemical and physical in-use stability has been demonstrated for 48 h at 22 ± 2° C exposed to daily light cycles and 30° C for diluted concentrate in glucose 5% (w/v), sodium chloride 0.9% (w/v) and sodium chloride 0.45% (w/v) with glucose 5% (w/v). From a microbiological point of view, the diluted 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 h at 2 to 8° C, unless dilution has taken place in controlled and validated aseptic conditions.
Do not throw away any medicines via wastewater. Ask your pharmacists how to throw away medicines you no longer use. These measures will help protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Noradrenaline (Norepinephrine) Concentrate contains
The active substance is noradrenaline (as noradrenaline tartrate).
1 ml of concentrate for solution for infusion contains 2mg noradrenaline tartrate equivalent to 1 mg noradrenaline base.
Each 4ml ampoule of concentrate for infusion contains 8mg noradrenaline tartrate equivalent to 4 mg noradrenaline base.
The other ingredients are:
- Sodium chloride
- Disodium edetate
- Sodium hydroxide (for pH adjustment)
- Hydrochloric acid (for pH adjustment)
- Water for injections.

What Noradrenaline (Norepinephrine) Concentrate looks like and contents of the pack:
This medicinal product is presented as a concentrate for solution for infusion in a clear glass ampoule. The contents is a clear and colourless to yellowish solution, free of any visible particulate matter.
It is supplied in packs of 5 x 4 ml ampoules and 10 x 4 ml ampoules.
Not all pack sizes may be marketed.

Marketing Authorisation Holder is: Zentiva Pharma UK Limited, 12 New Fetter Lane, London, EC4A 1JP, United Kingdom

Manufacturer is: Zentiva, k. s.,
U kabelovny 130, Prague 10, Czech Republic

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80 kg	0.05	0.24	6
	0.1	0.48	12
	0.25	1.2	30
	0.5	2.4	60
	1	4.8	120
90 kg	0.05	0.27	6.75
	0.1	0.54	13.5
	0.25	1.35	33.75
	0.5	2.7	67.5
	1	5.4	135

Instructions for dilution
The following dilution instructions provide a 40 mg/litre solution of noradrenaline (40 micrograms/ml) equivalent to 80 mg/litre noradrenaline tartrate:
Administration by syringe pump:
Add 2 ml of concentrate to 48 ml glucose 5% solution (or Sodium Chloride 0.9% w/v and Glucose 5% w/v Infusion) for, or
Administration by drip counter:
Add 20 ml of concentrate to 480 ml glucose 5% solution (or Sodium Chloride 0.9% w/v and Glucose 5% w/v Infusion).
Dilutions other than 40 mg/litre noradrenaline base may also be used. If dilutions other than 40 mg/litre noradrenaline base are used, check the infusion rate calculation carefully before starting treatment.
Any unused product or waste material should be disposed of in accordance with local requirements.

Incompatibilities:
Infusion solutions containing noradrenaline tartrate have been reported to be incompatible with the following substances: alkalis and oxidising agents, barbiturates, chlorpheniramine, chlorothiazide, nitrofurantoin, novobiocin, phenytoin, sodium bicarbonate, sodium iodide, streptomycin.

Do not use this medicine if the solution is brown in colour.

Shelf life after dilution: Chemical and physical in-use stability has been demonstrated for 48 h at 22 ± 2° C exposed to daily light cycles and 30° C for diluted concentrate in glucose 5% (w/v), sodium chloride 0.9% (w/v) and sodium chloride 0.45% (w/v) with glucose 5% (w/v) exposed to daily light cycles. Appearance of diluted solution has to be clear, colourless and free of visible particles.

From a microbiological point of view, the diluted 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 to 8° C, unless dilution has taken place in controlled and validated aseptic conditions.

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