Package leaflet: Information for the user

Noradrenaline (norepinephrine) 1:1000 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 nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Noradrenaline (norepinephrine) 1:1000 concentrate for solution for infusion is and what it is used for

Noradrenaline (norepinephrine) 1:1000 concentrate for solution for infusion is used in an emergency to increase blood pressure to normal levels.

2. What you need to know before you are given Noradrenaline (norepinephrine) 1:1000 concentrate for solution for infusion

Do not use Noradrenaline (norepinephrine) 1:1000 concentrate for solution for infusion:
- If you are allergic (hypersensitive) to noradrenaline preparations or to any of the other ingredients of this medicine (listed section 6).

Warnings and precautions

- You will not be given Noradrenaline (norepinephrine) 1:1000 concentrate for solution for infusion if you have been given the anaesthetic gases cyclopropane or halothane

Talk to your doctor or nurse before using Noradrenaline (norepinephrine) 1:1000 concentrate for solution for infusion if you:

- have diabetes
- suffer from high blood pressure
- have an over-active thyroid
- have low levels of oxygen in the blood
- have high levels of carbon dioxide in the blood
- have clots or obstructions in the blood vessels supplying the heart, intestines, or other parts of the body
- have low blood pressure following a heart attack
- have angina (chest pain), in particular Prinzmetal's angina

- are elderly
- have liver or kidney impairment

The safety and efficacy of Noradrenaline (norepinephrine) 1:1000 concentrate for solution for infusion in children aged less than 18 years old has not been established. Therefore use in children is not recommended.

Other medicines and Noradrenaline (norepinephrine) 1:1000 concentrate for solution for infusion
Tell your doctor or nurse if you are taking, have recently taken, or might have taken any other medicines.

A number of medicines are known to increase the toxic effects of noradrenaline, such as:
- antidepressants, including monoamine oxidase inhibitors that are currently being taken or have been taken in the last 14 days and tricyclic antidepressants
- anaesthetics (especially anaesthetic gases such as cyclopropane, halothane, chloroform, enflurane)
- medicines used to treat high blood pressure, (e.g. guanethidine, reserpine, methyldopa)
- linezolid (an antibiotic)
- adrenergic-serotoninergic medicines (e.g. used in the treatment of asthma and heart conditions)

Using noradrenaline with propofol (an anaesthetic) may lead to propofol infusion syndrome (PRIS), which is a serious condition that affects patients who are being sedated with propofol in intensive care units. Your doctor would notice disorders in your body's metabolism from blood tests and this could lead to kidney failure, heart failure and death.

Pregnancy and breast-feeding

If you are pregnant or breastfeeding, think you might be pregnant or are planning to have a baby, ask your doctor or nurse for advice before taking this medicine. Noradrenaline may harm the unborn baby. Your doctor will decide if you should be given Noradrenaline (norepinephrine) 1:1000 concentrate for solution for infusion.

Ask your doctor or nurse for advice before taking any medicine.

Driving and using machines

You should not drive or use machinery if you are affected by the administration of Noradrenaline (norepinephrine) 1:1000 concentrate for solution for infusion.

Noradrenaline (norepinephrine) 1:1000 concentrate for solution for infusion contains sodium.

Noradrenaline (Norepinephrine) 1 mg/ml Concentrate for Solution for Infusion contains 6.7 mg of sodium (main component of cooking/table salt) in each 2 ml ampoule. This is equivalent to 0.3% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use Noradrenaline (norepinephrine) 1:1000 concentrate for solution for infusion

Noradrenaline (norepinephrine) 1:1000 concentrate for solution for infusion will be given to you in hospital by a doctor or nurse. Blood volume replacement fluids will also be given to you, both before and during noradrenaline treatment. It is first diluted and then infused into a vein.

The initial dose of Noradrenaline (norepinephrine) 1:1000 concentrate for solution for infusion will depend on your medical condition. The usual dose is between 0.4 and 0.8 mg per hour (noradrenaline base). Your doctor will determine the correct dose for you. After the initial dose your doctor will assess your response and adjust the dose accordingly.

Your doctor will frequently check the vein where the Noradrenaline is being administered to make sure none of the drug is leaking into the surrounding tissues as this could cause a severe skin reaction, especially if a vein in your leg is being used. Sometimes the drug can make the vein appear whiter than usual and this may be associated with leakage of Noradrenaline into the tissues so your doctor may decide to change the

site of administration. If leakage into the tissues does occur, your doctor will treat this with an injection into the site as soon as possible.

If you use more Noradrenaline (norepinephrine) 1:1000 concentrate for solution for infusion than you should:

It is unlikely that you will receive too much 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, bleeding in the brain, slow heartbeat, violent headache, light sensitivity, pain in the chest, pale colour, high fever, intense sweating, vomiting and fluid in the lungs causing breathlessness.

If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

Like all medicines, noradrenaline 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

Other possible side effects include:

- anxiety
- high blood pressure
- slow heart rate
- fast heart rate
- abnormal heart rhythm
- abnormal ECG heart tracing
- breathing difficulties
- headaches
- poor blood flow to your hands and feet
- a potentially life-threatening type of circulatory failure called 'cardiogenic shock'
- gangrene
- becoming tolerant to your treatment so it becomes less effective
- reduction in blood plasma volume
- pain, swelling, irritation or ulceration at the injection site
- propofol Infusion syndrome (PRIS)

Your doctor will monitor your blood pressure and blood volume.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or nurse.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in the leaflet. You can also report side effects directly via:

Ireland
HPRA Pharmacovigilance
Website: www.hpra.ie

Malta
ADR Reporting
Website: www.medicinesauthority.gov.mt/adrportal

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Noradrenaline (norepinephrine) 1:1000 concentrate for solution for infusion

Keep this medicine out of sight and reach of children. Do not store above 25°C.

Keep the ampoules in the outer carton in order to protect from light.

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

From a microbiological point of view, the product should be used immediately after dilution.

Do not use this medicine if the solution is slightly pink, yellow or brown in colour or if it is cloudy or contains visible particles/solids.

6. Contents of the pack and other information

What Noradrenaline (norepinephrine) 1:1000 concentrate for solution for infusion contains:

The active substance is noradrenaline (as noradrenaline tartrate).

Each millilitre (ml) of concentrate for solution for infusion contains 2 milligrams (mg) of noradrenaline (norepinephrine) as the acid tartrate, equivalent to 1 mg noradrenaline base. Each 2 ml ampoule contains 4 mg of noradrenaline (norepinephrine) as the acid tartrate equivalent to 2 mg noradrenaline base. When diluted as recommended, each ml contains 80 micrograms noradrenaline tartrate, equivalent to 40 micrograms noradrenaline base.
The other ingredients are:

- sodium chloride
- sodium hydroxide (for pH adjustment)
- hydrochloric acid (for pH adjustment)
- water for injections

What Noradrenaline (norepinephrine) 1:1000 concentrate for solution for infusion looks like and contents of the pack:

This medicinal product is presented as a concentrate for solution for infusion. The solution is a clear, colourless solution.

The product is supplied in a pack containing 5 x 2ml glass ampoules. Each ampoule contains 2 ml of concentrate for solution for infusion.

Marketing Authorisation Holder

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Noradrenaline (norepinephrine) 1:1000 concentrate for solution for infusion
The following information is intended for healthcare professionals only:

For intravenous use.

Route and method of infusion:
Administer as a diluted solution via a central venous catheter.

The infusion should be at a controlled rate using either a syringe pump or an infusion pump or a drip counter.

Incompatibilities:

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

Use and handling:

Dilution instructions:

For single use only. Discard any unused contents.

This medicine should not be used if the solution is slightly pink, yellow or brown in colour or if it is cloudy or contains visible particles/solids.

Dilute before use with glucose 5% solution or sodium chloride 9 mg/ml (0.9%) with glucose 5 % solution. These dextrose containing fluids are protection against significant loss of potency due to oxidation. Administration in saline solution alone is not recommended as deterioration occurs more rapidly in normal saline than in dextrose solution. Either add 2 ml concentrate to 48 ml glucose 5% solution (or sodium chloride 9 mg/ml (0.9%) with glucose 5% solution) for administration by syringe pump, or add 20 ml of concentrate to 480 ml glucose 5 % solution (or sodium chloride 9 mg/ml (0.9%) with glucose 5% solution) for administration by drip counter. In both cases the final concentration of the infusion solution is 40 mg/litre noradrenaline base (which is equivalent to 80 mg/litre noradrenaline tartrate). 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.

The diluted solution should be used immediately after preparation.

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