Package leaflet: information for the user

Noradrenaline (Norepinephrine) 1 mg/ml concentrate for solution for infusion

noradrenaline

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, 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 is and what it is used for

Noradrenaline (Norepinephrine) 1 mg/ml concentrate for solution for infusion contains the active substance noradrenaline and act as a vasoconstrictor (causes narrowing of blood vessels). Noradrenaline is used in adults in an emergency to increase blood pressure to normal levels.

2. What you need to know before you are given Noradrenaline

You should not be given Noradrenaline
- if you are allergic to noradrenaline or any of the other ingredients of this medicine (listed in section 6)
- if you have low blood pressure that has been caused by low blood volume
- if you receive some anaesthetics such as halothane or cyclopropane (this may increase the risk of irregular heart beat).

Warnings and precautions
Talk to your doctor or nurse before you are given noradrenaline if you:
- have diabetes
- have liver failure
- have severe kidney disorders
- suffer from high blood pressure
- have an over-active thyroid gland
- have low levels of oxygen in the blood
- have high levels of carbon dioxide in the blood
- have elevated pressure inside the skull (intracranial pressure)
- 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 a type of angina (chest pain) called Prinzmetal’s angina
- have major left ventricular dysfunction (a heart condition)
- have recently had myocardial infarction

- have cardiac rhythm disorders (your heart beats too fast, too slow or irregular), you will need a reduced dose
- are elderly

Children and adolescents
The safety and efficacy of noradrenaline in children less than 18 years of age has not been established. Therefore use in children is not recommended.

Other medicines and Noradrenaline
Tell your doctor or nurse if you are using, have recently used or might use any other medicines. It is particularly important if you use or have recently used any of the following medicines:
- medicines to treat depression called 'monoamine oxidase inhibitors' that are currently being taken or have been taken in the last 14 days
- medicines to treat depression called 'tricyclic antidepressants' e.g. imipramine or desipramine
- adrenergic-serotoninergic medicines, e.g. used in the treatment of asthma and heart conditions
- linezolid (an antibiotic)
- anaesthetics (especially anaesthetic gases such as cyclopropane, halothane, chloroform, enflurane)
- medicines to treat high blood pressure (e.g. guanethidine, reserpine, methyldopa, alpha and beta-blockers)
- medicines to treat heart rhythm disorders
- cardiac glycosides (to treat heart diseases)
- levodopa (to treat Parkinson's disease)
- thyroid hormones
- oxytocin (used to improve uterine contractions)
- antihistamines (for treating allergies)
- amphetamine
- doxapram (for breathing disorders)
- mazindol (to treat obesity)
- medicines to treat migraine (ergot alkaloids)
- lithium (to treat some mental disorders)

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 breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before this medicine is given to you. Noradrenaline may harm the unborn baby. Your doctor will decide if you should be given noradrenaline.
It is not known whether this medicine is excreted in human milk. Because many medicines are excreted in human milk, caution should be exercised when noradrenaline is given to a nursing woman.

Driving and using machines
No information is available. Therefore, driving or operating machinery is not recommended.

Noradrenaline contains sodium
Ampoules containing 1 ml, 2 ml, 4 ml or 5 ml of concentrate for solution for infusion contains less than 1 mmol sodium (23 mg) per ampoule, that is to say essentially 'sodium-free'.

Each ampoule containing 8 ml of concentrate for solution for infusion contains 26.4 mg sodium (main component of cooking/table salt). This is equivalent to 1.32 % of the recommended maximum daily dietary intake of sodium for an adult.

Each ampoule containing 10 ml of concentrate for solution for infusion contains 33 mg sodium (main component of cooking/table salt). This is equivalent to 1.65 % of the recommended maximum daily dietary intake of sodium for an adult.

3. How Noradrenaline will be given

Noradrenaline will be given to you in hospital by a doctor or nurse. It is first diluted and then infused into a vein.

The initial dose of noradrenaline will depend on your medical condition. The usual dose is between 0.4 mg and 0.8 mg noradrenaline 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.

Your doctor will monitor your blood pressure and blood volume.

If you are given more Noradrenaline 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 that may occur if you are given too much noradrenaline are severe high blood pressure, slow heartbeat, violent headache, light sensitivity, pain in the chest, bleeding in the brain, pallor, fever, intense sweating and vomiting, fluid in the lungs causing breathlessness.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor or nurse **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.

Tell your doctor or nurse as soon as possible if you experience:
- anxiety, insomnia, confusion, weakness, psychotic state
- headaches, tremor
- decreased or increased heart rate
- abnormal heart rhythm
- electrocardiogram change
- a potentially life-threatening type of circulatory failure called ‘cardiogenic shock’
- heart muscle weakness due to intense physical or emotional stress, palpitations, increase in the contractility of the heart muscle
- high blood pressure, decrease in oxygen supply to some organ (hypoxia)
- poor blood flow to your hands and feet (may cause coldness, paleness and/or pain in the limbs)
- gangrene (tissue death)
- reduction in blood plasma volume
- breathing difficulties
- paleness, scarification of the skin, bluish skin colour, hot flushes or skin redness, skin rash, hives or itching
- nausea, vomiting
- retention of urine
- irritation or ulceration at the injection site

In case of hypersensitivity or overdose, the following effects may appear more frequently: very high blood pressure, abnormal sensitivity to or intolerance of light, pain behind the breast bone, pharyngeal pain, pallor, intense sweating and vomiting.

Reporting of side effects
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via:
UK: Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
IE: HPRA Pharmacovigilance, Website: www.hpra.ie
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Noradrenaline

Keep this medicine out of the sight and reach of children.

Do not store above 25 °C.
Keep the ampoules in the outer carton in order to protect from light.

Shelf life after opening the ampoule
Once opened, the diluted solution should be prepared immediately.

Shelf life after dilution
Chemical and physical in-use stability has been demonstrated for 48 hours at 25 °C and 2-8 °C when diluted to 4 mg/litre and 40 mg/litre noradrenaline in sodium chloride 9 mg/ml (0.9%) solution or glucose 50 mg/ml (5%) solution, or sodium chloride 9 mg/ml (0.9%) with glucose 50 mg/ml (5%) solution.
From a microbiological point of view, the diluted solution 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.

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

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist 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 contains
– The active substance is noradrenaline.

Each 1 ml of concentrate for solution for infusion contains noradrenaline tartrate equivalent to 1 mg noradrenaline.
Each ampoule containing 2 ml of concentrate for solution for infusion contains noradrenaline tartrate equivalent to 2 mg noradrenaline.
Each ampoule containing 4 ml of concentrate for solution for infusion contains noradrenaline tartrate equivalent to 4 mg noradrenaline.
Each ampoule containing 5 ml of concentrate for solution for infusion contains noradrenaline tartrate equivalent to 5 mg noradrenaline.
Each ampoule containing 8 ml of concentrate for solution for infusion contains noradrenaline tartrate equivalent to 8 mg noradrenaline.

Each ampoule containing 10 ml of concentrate for solution for infusion contains noradrenaline tartrate equivalent to 10 mg noradrenaline.

– The other ingredients are sodium chloride, hydrochloric acid (for pH adjustment), water for injections.

What Noradrenaline looks like and contents of the pack
Clear, colourless or yellowish solution, practically free from visible particles.

1 ml, 2 ml, 4 ml, 5 ml, 8 ml or 10 ml of solution filled in colourless glass ampoules with one point cut. The ampoules are packed in a liner and placed into carton box.

Pack sizes: 5 or 10 ampoules

Not all pack sizes may be marketed.

Marketing authorisation holder and Manufacturer
AS KALCEKS
Krustpils iela 71E, Rīga, LV-1057, Latvia
Tel.: +371 67083320
E-mail: kalceks@kalceks.lv

This medicine is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names:

Denmark	Noradrenalin Kalceks
Austria	Norepinephrin Kalceks 1 mg/ml Konzentrat zur Herstellung einer Infusionslösung
Belgium	Noradrenaline (Norepinephrine) Kalceks 1 mg/ml concentraat voor oplossing voor infusie / solution à diluer pour perfusion / Konzentrat zur Herstellung einer Infusionslösung
Czech Republic	Norepinephrine Kalceks
Estonia	Norepinephrine Kalceks
Finland	Noradrenalin Kalceks
France	NORADRENALINE TARTRATE KALCEKS 1 mg/mL, solution à diluer pour perfusion
Germany	Norepinephrin Kalceks 1 mg/ml Konzentrat zur Herstellung einer Infusionslösung
Hungary	Norepinephrine Kalceks 1 mg/ml koncentrátum oldatos infúzióhoz
Ireland	Noradrenaline (Norepinephrine) 1 mg/ml concentrate for solution for infusion
Italy	Norepinefrina Kalceks
Latvia	Norepinephrine Kalceks 1 mg/ml koncentrāts infūziju šķīduma pagatavošanai
Lithuania	Norepinephrine Kalceks 1 mg/ml koncentratas infuziniam tirpalui
Norway	Noradrenalin Kalceks
Poland	Noradrenalin Kalceks
Portugal	Noradrenalina Kalceks
Romania	Noradrenalină Kalceks 1 mg/ml concentrat pentru soluţie perfuzabilă
Slovakia	Norepinephrine Kalceks 1 mg/ml infúzny koncentrát
Spain	Noradrenalina Kalceks 1 mg/ml concentrado para solución para perfusión EFG
Sweden	Noradrenalin Kalceks
The Netherlands	Noradrenaline Kalceks 1 mg/ml concentraat voor oplossing voor infusie
United Kingdom (Northern Ireland)	Noradrenaline (Norepinephrine) 1 mg/ml concentrate for solution for infusion

This leaflet was last revised in 02/2022

The following information is intended for healthcare professionals only:

Method of administration
Intravenous use after dilution.
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.
Do not use undiluted.

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.
This medicinal product must not be mixed with other medicinal products except those mentioned below.

Dilution instructions

For single use only. Discard any unused contents.

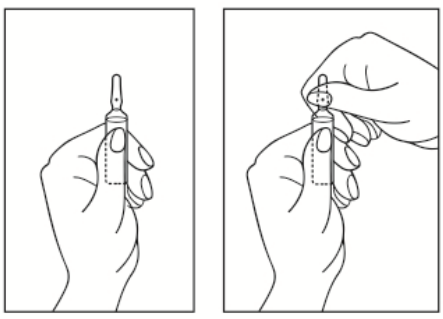
The solution should be visually inspected prior to use. The medicine should not be used if the solution contains visible particles/solids. Do not use the solution for infusion if it has a brown colour.

Dilute before use with:
– glucose 50 mg/ml (5%) solution or
– sodium chloride 9 mg/ml (0.9%) solution or
– sodium chloride 9 mg/ml (0.9%) with glucose 50 mg/ml (5%) solution.

Either add 2 ml concentrate to 48 ml glucose 50 mg/ml (5%) solution (or any of the other above mentioned solutions for dilution) for administration by syringe pump, or add 20 ml of concentrate to 480 ml glucose 50 mg/ml (5%) solution (or any of the other above mentioned solutions for dilution) for administration by drip counter. In both cases the final concentration of the infusion solution is 40 mg/litre noradrenaline (which is equivalent to 80 mg/litre noradrenaline tartrate). Dilutions other than 40 mg/litre noradrenaline may also be used. If dilutions other than 40 mg/litre noradrenaline are used, check the infusion rate calculation carefully before starting treatment.

The product is compatible with polyvinyl chloride (PVC), ethyl vinyl acetate (EVA) or polyethylene (PE) infusion bags.

Instruction of ampoule opening
1) Turn the ampoule with coloured point up. If there is any solution in the upper part of the ampoule, gently tap with your finger to get all the solution to the lower part of the ampoule.
2) Use both hands to open; while holding the lower part of the ampoule in one hand, use the other hand to break off the upper part of the ampoule in the direction away from the coloured point (see the pictures below).



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