PATIENT INFORMATION LEAFLET

SERADRENALİN 4 mg/4 mL IV Ampoule Solution for Infusion

Sterile

Used intravenously.

- ***Active Ingredient:*** Each ampoule (4 ml) contains 8 mg norepinephrine bitartrate equivalent to 4 mg noradrenaline base.
- ***Excipients:*** Sodium chloride, sodium metabisulfite and water for injection.

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 pharmacist.*
- *This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.*
- *Tell your doctor that you are taking this medicine when you go to the doctor or hospital during the use of this medicine.*
- *Follow exactly what is written in this instruction. Do not use high or low doses other than the recommended dosage.*

What is in this leaflet:

1. What SELADRENALİN is and what it is used for?

SELADRENALİN is a medicine that should be used by experienced medical personnel in a hospital.

SELADRENALINE consists of 10 Type I glass ampoules containing 4 ml solution. Every ampoule contains norepinephrine bitartarate as the active ingredient.

SELADRENALİN is presented as a solution and is administered intravenously only after dilution.

SELADRENALİN is used for the following emergencies;

To restore blood pressure to normal in acute hypotension conditions.

2.What you need to know before you use SELADRENALİN

DO NOT USE SELADRENALİN;

- If you are allergic to norepinephrine or other ingredients in SELADRENALİN.
- If you have hypertension (high blood pressure), because hypertensive patients may be more sensitive to the effects of norepinephrine under increased blood pressure.
- If you have hypotension due to lack of blood volume.
- If you have excessive carbon dioxide (hypercapnia), tissue oxygen deficiency (hypoxia) and obstructive vascular disease in the blood.
- If you have heart-related chest pain during rest, called Prinzmetal's Angini, because the coronary (blood veins of the heart) blood flow in these patients may decrease in time and size that can cause myocardial infarction (heart attack).
- If you have hyperthyroidism (overwork of the thyroid gland) such patients are hypersensitive to the effects of norepinephrine, and toxicity may occur at low doses.
- During chloroform, cyclopropane and halothane anesthesia, norepinephrine can increase excitability of the heart muscles and cause rapid and irregular contractions of the heart.

USE SELADRENALİN CAREFULLY if you;

- SELADRENALİN should not be injected into the veins of the lower extremity region.
- Due to the strong effect of SELADRENALİN, there is always a risk of a dangerous rise in blood pressure due to overdose. Treatment should be stopped if blood pressure rises excessively.
- Long-term use of any potent drug that narrows the blood veins can lead to a decrease in plasma volume in the veins. This deficiency should be removed permanently with the help of water and suitable salts.
- Care should be taken in case of diabetes (diabetes), narrow-angle glaucoma or enlarged prostate.
- Norepinephrine is a strong tissue irritant, so only highly diluted solutions should be used. If you feel burning or pain at the injection site, tell your doctor immediately because the solution may be coming into your tissues outside the blood veins.

If any of the above applies to you in the past, please consult to your doctor.

Use of SELADRENALİN with food and drink

Not applicable.

Pregnancy

Consult your doctor or pharmacist before using this medication.

SELADRENALİN can lower the blood circulation of the placenta and cause an acceleration of the fetus's heart rhythm. It can also have a contracting effect on the uterus and cause the fetus to suffocate at the end of pregnancy. Therefore, during returning a pregnant woman to life, it should be used if its clinical benefits are more than possible risks to the baby.

If you notice that you are pregnant during treatment, consult your doctor or pharmacist.

Breast-feeding

Consult your doctor or pharmacist before using this medication.

It is not known whether SELADRENALİN is excreted in human milk. The excretion of SELADRENALİN with milk has not been studied in animals. When deciding whether to stop breastfeeding or whether to stop treatment with SELADRENALİN, your doctor will decide, taking into account the benefits of breastfeeding for the child and the benefit of SELADRENALİN for the nursing mother.

Driving and using machines

SELADRENALİN has no effect on the ability to drive and use machines.

Important information about some of the excipients in SELADRENALİN

SELADRENALİNE contains sodium metabisulfite as an excipient, which can rarely cause severe hypersensitivity reactions and bronchospasm (especially in patients sensitive to sulfides).

SELADRENALİNE contains less than 1 mmol (23 mg) sodium per ampoule; it is not expected to show any side effects at this dose.

Using other medicines

SELADRENALİN should not be used with certain medications such as chloroform, cyclopropane or halothane (substances that increase the excitability of the heart muscles and cause rapid and irregular contractions of the heart) used during general anesthesia. It should be used with caution in slow heartbeat, hypotension and heart rhythm disorder and Atropine sulfate, antihistamines (diphenhydramine, tripelennamine, dexchlorpheniramine) used in allergies.

Some ergotamine-derived alkaloids (guanethidine or methyldopa) can potentiate the vasopressor effect of norepinephrine and cause severe and persistent hypertension.

Patients who take large amounts of digitalin and quinidine may experience cardiac rhythm disturbances.

Reserpine, guanethidine, and cocaine may increase the effects of SELADRENALİN.
It should not be used with tricyclic antidepressants (e.g. imipramine) and monoamine oxidase inhibitors used to treat depression.
It should be used with caution with furosemide and other diuretics (drugs used to increase urine production).
Norepinephrine has been shown to increase circulating levels of glycerol, acetoacetate, β-hydroxybutyrate and glucose. Plasma insulin, lactate, pyruvate and alanine levels decrease with norepinephrine.
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

3.How to use SELADRENALİN

Instructions for use and dose/administration frequency:
SELADRENALİN will be diluted in 5% glucose solution and applied to you.
Your doctor will determine the dose of your medicine depending on your illness.
Information for health personnel is included at the end of this leaflet.

Method of administration
SELADRENALİN will preferably be administered by infusion into a wide vein in your arm.
Talk to your doctor or pharmacist if you have the impression that the effect of SELADRENALİN is too strong or weak.

If you use more SELADRENALİN than you should

SELADRENALİN will be applied by your doctor in a hospital. Therefore, it is not possible to give more medication than necessary. However, if you have any concerns, talk to your doctor or nurse.

In cases of overdose or usual doses in hypersensitive people, the following effects may be more common. Hypertension, fear of light, pain behind the breastbone, paleness, excessive sweating and vomiting.

Treatment:

The administration should be stopped until the patient's condition stabilizes.

Antidote: Intravenous administration of an alpha-blocker (5-10 mg), such as phentolamine mesylate. If necessary, this dose may be repeated.
Talk to a physician or pharmacist if you have used more SELADRENALİN than you should use.

If you forget to use SELADRENALİN

Not applicable.

Do not take double doses to make up for forgotten doses.

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

4. Possible side effects

Like all medicines, people who are sensitive to ingredients of SELADRENALİN may have side effects.

Side effects are listed as follows.

Very common	: It can be seen in at least one of 10 patients.
Common	: Less than one in 10 patients, but more than one in 100 patients.
Uncommon	: less than one in 100 patients, but more than one in 1000 patients.
Infrequent	: Less than one in 1000 patients, but more than one in 10,000 patients
Very rare	: Less than one in 10000 patients may be seen.

Very common:

- High blood pressure and oxygen deficiency in tissue: Ischemic damage due to strong vasodilating effect.

Common:

- Palpitations, low pulse, impaired heart rhythm, irregular heartbeat, increased heart muscle contraction from β1 adrenergic effect in the heart, acute heart failure.

Uncommon:

- Anxiety, insomnia, lightheadedness, headache, psychotic state, weakness, palpitations, increased attention, loss of appetite, nausea and vomiting.
- Sudden rise of intraocular pressure: It is very common in those who have anatomically predisposed closure of the iridocorneal angle.
- Respiratory failure and difficulty, shortness of breath.
- Irritation and tissue death at the injection site, limb and shrinkage of blood veins that may result in cold and pallor face.

Continuous administration of norepinephrine to maintain blood pressure without replacing blood volume can cause the following symptoms:

- Serious peripheral and internal splanchnic narrowing

- Decreased renal blood output
- Decrease in urine production
- Insufficient oxygen level in tissues
- An increase in the level of lactic acid in the blood.

The potential life-threatening effects of norepinephrine are due to its dose-related hypertensive effect. Acute hypertension may occur with pulmonary edema and cerebral hemorrhage.

Leaking of norepinephrine during intravenous infusion can cause drowsiness and tissue death around the infusion site. Prolonged infusions can follow gangrene of the extremities.

Impaired circulation in the infusion site (with or without leakage) can be mitigated by hot wrap and infiltration of the area with phentolamine (diluted with 5 mg / 10 ml of saline).
Plasma insulin, lactate, pyruvate and alanine levels decrease with norepinephrine. Prolonged administration of any potent vasopressor can cause plasma volume depletion; this can be corrected by appropriate fluid and electrolyte replacement therapy. If plasma volumes do not improve, hypotension may recur when norepinephrine treatment is discontinued or blood pressure may continue with a reduced risk of peripheral and visceral vasoconstriction with a decrease in blood flow.

If you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Reporting of suspected adverse reactions
If you get any side effects not listed in this leaflet, talk to your doctor or pharmacist. You can also report side effects directly to your doctor or pharmacist. You can also report side effects directly to your country's related health authority. By reporting side effects, you can help provide more information on the safety of this medicine.

5.How to store SELADRENALİN

Keep TRANEXEL 5% out of the reach and sight of children and within its packaging.
Store the SELADRENALİN ampoules at a temperature between 2-8 °C (in the refrigerator) and in its original packaging, protecting it from light.
Use in compliance with the expiry date.
Do not use SELADRENALİN after the expiry date which is stated on the packaging.
Do not use SELADRENALİN if you notice any damage in the product and/or its package.

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This patient information leaflet approved in 15/04/2020.

THE FOLLOWING INFORMATION IS FOR HEALTHCARE PERSONNEL WHO WILL ADMINISTER THIS MEDICINE

Usage, packaging and disposal information

1) Concentrated solution for infusion should be diluted with the dilution solution mentioned below.

Use aseptic technique during norepinephrine dilution for intravenous infusion.

2) Products applied by injection should always be visually inspected and should not be used in case of particle presence or color change.

3) Norepinephrine is used only as an intravenous infusion. Norepinephrine infusions should be made into a wide vein. Antecubital veins are especially preferred because in this case, the risk of necrosis of the tissue covering it due to prolonged vasoconstriction appears to be weak. It is necessary to avoid lower extremity veins.

4) In the case of injection outside the vein, the affected areas should be washed with phentolamine mesylate.

5) Insert the intravenous catheter through a syringe needle into a suitable central vein and fix it with adhesive tape.

6) Infusion site should be checked frequently for free flow.

7) Regular monitoring of blood pressure is required. It should be done every two minutes from the beginning of the infusion until the desired blood pressure is achieved, if administration should continue, every five minutes after reaching the desired blood pressure.

8) Infusion flow rate should be constantly monitored with an infusion system and the patient should be observed throughout the infusion.

9) Unused product should be discarded in accordance with local regulations.

Correction of blood pressure

In acute hypotensive conditions: Blood volume depletion should be corrected as precisely as possible before using any vasopressor. Norepinephrine can be administered before or during blood volume replacement.

The usual dose:

Infusion is usually given at the beginning of 2-3 ml / minute (8-12 µg per minute) or 0.11-0.17 µg / kg / minute) and the amount is adjusted according to the state of blood pressure. The blood pressure value is recorded every two minutes initially and the infusion rate is constantly observed. After observing the patient's response to the initial dose, the flow rate is adjusted to

create and maintain sufficient normal blood pressure (usually 80-100 mm Hg systolic) to maintain circulation in vital organs. It is recommended that blood pressure should not be increased to more than 400 mm Hg of pre-existing systolic pressure in patients who were previously hypertensive.

The average flow of the diluted solution 0.5-1 ml / min (or 0.03-0.06 μg / kg / min) is usually sufficient to achieve satisfactory blood pressure values.

The posology mentioned above is not certain. The dose is determined depending on the condition of the patient's heart and blood vessels. Sensitivity to the product may differ significantly from person to person.

If the patient remains hypotensive, it may be necessary to administer up to 17 ampoules of 4 ml in 24 hours (the amount corresponding to 0.67 micrograms / kg / min), but hidden blood volume depletion should always be suspected and corrected if necessary. Central venous pressure monitoring usually helps in the detection and treatment of this condition.

Treatment period:

The treatment period is different for each clinical case and can vary from 1-2 hours to 6 days.

Infusion should be continued until sufficient tissue infusion and sufficient blood pressure.

The infusion should be gradually reduced and stopped to prevent a serious drop in blood pressure.

- Dilution:

SELADRENALİN is administered as iv infusion by diluting in 1 liter of 5% glucose or 0.9% sodium chloride and 5% glucose mixture (50/50). It is diluted only in 5% glucose solution in patients without a salt-free diet. The glucose solution is used to prevent oxidation of norepinephrine to L-norepinephrine.

In calculating dilutions of bulb contents to achieve the desired concentrations of norepinephrine, the following table can be used as a reference:

Norepinephrine base content desired to be obtained	Number of ampoules to be used	Dilution solution volume to be used
4 micrograms/ml	1	1 liter
8 micrograms /ml	2	1 liter
12 micrograms /ml	3	1 liter
16 micrograms /ml	4	1 liter
20 micrograms /ml	5	1 liter

SERADRENALİN is not mixed with plasma or whole blood, the administration should be done separately (for example, if it is given at the same time, Y-tube or separate containers should be used).

- Fluid intake:

The degree of dilution depends on clinical volume requirements.
If a large volume of fluid (dextrose) is required for a flow rate containing an overdose of pressurizing agent per unit time, a solution less than 4 micrograms / ml should be used. On the other hand, when high volumes of fluid are undesirable, a concentration higher than 4 micrograms / ml may be required.

- Injection site:

Norepinephrine is administered only as an intravenous infusion. Norepinephrine infusions should be administered into large veins. Antecubital veins are especially preferred because in this case, the risk of necrosis of the tissue covering it due to prolonged vasoconstriction appears to be weak. Injection into the veins in the lower limb area should be avoided.

- Blood pressure control:

Blood pressure should be controlled every two minutes until the desired blood pressure is obtained from the beginning of the infusion. If administration is to be continued, it should be controlled every five minutes after reaching the desired blood pressure.

Infusion flow rate should be checked frequently and the patient should never be left alone during the infusion.

- Extravasation risk:

Infusion flow freeness should be checked frequently.

Due to the increased permeability and vasoconstriction of the vein wall, drug leakage may occur in the tissues around the vein. This condition is not due to certain extravasation and causes the tissues to fade. Therefore, if fading occurs, the infusion site should be changed to reduce the effects of local vasoconstriction.

- Treatment of ischemia due to extravasation:

Tissue damage due to the vasoconstrictive effect of the drug may occur in the blood vessels during leakage of the drug out of the vein or injecting outside the vein.

The injection site should be washed as quickly as possible with a physiological salt solution containing 5-10 mg of phentolamine mesylate.

For this purpose, a fine syringe needle syringe should be used and injected locally.
Ampoules should be visually inspected before use, and should not be used if particle presence and color change are observed.

Additional information on special populations:

Renal / Hepatic failure:

The pharmacokinetics of norepinephrine is not significantly affected by renal or hepatic diseases.

Care should be taken when using sympathomimetics in liver and kidney patients, as blood flow may decrease in organs such as liver and kidney.

Pediatric population:

Studies on norepinephrine effects in newborns are not sufficient. When giving norepinephrine to children, care should be taken similarly to that of adults. As an initial dose, norepinephrine can usually be infused to 0.05 µg / kg / minute norepinephrine base and increased to 0.5 µg / kg / minute base by blood pressure control.

Geriatric population:

It should be used with caution in the elderly, especially those who are sensitive to sympathomimetic agents and norepinephrine.

Warnings for use:

Norepinephrine; It is incompatible with alkaline solutions or oxidative substances, barbiturates, chlorpheniramine, chlorothiazide, nitrofurantoin, novobiosin, phenytoin, sodium bicarbonate, sodium iodide, streptomycin, insulin (reported incompatibility), plasma or whole blood.

SERADRENALİN should not be mixed with plasma or whole blood. If there is indication to increase blood volume, SELADRENALİN should be administered separately from plasma or whole blood, for example, using the Y system.

The infusion site should be checked frequently. Care should be taken to avoid extravasation, which causes necrosis of tissues around the vein used for infusion.

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For this purpose, a fine syringe needle syringe should be used and injected locally.

Treatment of other problems of circulation:

Impaired circulation in the infusion site (with or without extravasation) can be alleviated by infusion of the area with 10 ml of sodium chloride solution injection containing 5 mg of phentolamine mesylate.

If you have applied more SELADRENALİN than you should:

The administration should be stopped urgently until the patient's condition stabilizes.

An alpha-blocker such as phentolamine mesylate (5-10 mg) may be administered intravenously as an antidote. If necessary, this dose can be repeated.

Interaction with laboratory tests:

Norepinephrine has been shown to increase circulating levels of glycerol, acetoacetate, β-hydroxybutyrate and glucose. Plasma insulin, lactate, pyruvate and alanine levels decrease with the effect of norepinephrine.