sodium furosemide

sanofi aventis

Read all of this leaflet carefully before you start using this medicine.

- Keep this leaflet. You may need to read it again. - If you have further questions, please ask your
- doctor or pharmacist. This drug has been prescribed for you personally. Do not pass it on to others. It may harm them. even if their symptoms are the same as yours.
- If any of the side effects mentioned in this leaflet causes considerable discomfort, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

- 1. What Lasix 250 mg solution for infusion is and what it is
- 2. Before you use Lasix 250 mg solution for infusion 3. How to use Lasix 250 mg solution for infusion
- . Possible side effects
- How to store Lasix 250 mg solution for infusion
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1. WHAT Lasix 250 mg solution for infusion IS AND WHAT IT IS USED FOR

Lasix 250 mg solution for infusion is a diuretic (a medicine that promotes urine production).

Lasix 250 mg solution for infusion is a high-dose medicine that is only indicated for patients with severely decreased glomerular filtration (glomerular filtration rate less than 20 ml/min)

Lasix 250 mg solution for infusion is used:

- for imminent and already manifest acute kidney failure (to maintain fluid excretion and to facilitate parenteral nutrition, as long as there is still some filtration)
- chronic kidney failure with fluid retention and high blood pressure, before dialysis is needed,



- end-stage kidney failure, to maintain remaining urine
- nephrotic syndrome (protein loss, lipid metabolism disorders and water retention) in patients not responding to daily oral administration of 120 mg of furosemide (treating the main disease is most important in this case).

2. BEFORE YOU USE Lasix 250 mg solution for infusion Lasix 250 mg solution for infusion must not be used

- if your kidney function is normal or reduced, glomerular filtration more than 20 ml/min, since there may be a risk of excess fluid and salt (electrolyte) loss
- if you are hypersensitive (allergic) to furosemide sulfonamides, or any other ingredient in Lasix 250 mg solution for infusion
- if you have acute kidney failure with no urine production (anuria)
- if you have acute liver failure with consciousness disorders (coma and hepatic precoma),
- if you have a severe potassium deficit, if you have a severe sodium deficit.
- if you have a blood volume deficit (hypovolemia) or body water deficit (dehydration),
- if you are breast-feeding (see also "Pregnancy and breast-feeding").

Lasix 250 mg solution for infusion should not be injected directly from the concentrated amnoules (as a single administration). During administration, the infusion volume and rate must be monitored to reduce the risk of accidental overdose

Take special care with Lasix 250 mg solution for

- if your blood pressure is very low (hypotension), - if you have already existing or underlying diabetes
- mellitus; regular monitoring of blood sugar levels is required.
- if you have gout; regular monitoring of blood uric acid
- if you have impaired urine excretion (e.g. enlarged prostate intrarenal obstruction ureteral stenosis)
- if your blood protein level is decreased (hypoproteinemia), e.g. in nephrotic syndrome (protein loss, lipid metabolism disorders, and water accumulation); dosage must be carefully adjusted.
- if you have liver cirrhosis as well as impaired kidney function.
- if you have blood flow disorders in the brain vessels (cerebrovascular perfusion disorders) or heart vessels (coronary disease), since you would be particularly at risk if you experienced a sharp adverse drop in blood pressure.

In patients with urination disorders (e.g. enlarged prostate). Lasix 250 mg solution for infusion may only be used if normal urine output can be restored, since a sudden onset of urine flow could result in obstructive anuria, which could strain the bladder.

During long-term treatment with Lasix, certain blood tests, particularly potassium, sodium, calcium, bicarbonate, creatinine, urea, and uric acid, as well as blood glucose, should be regularly performed.

Particularly careful monitoring is required if you are at high risk for electrolyte disturbances, or if you have severe fluid loss (e.g. due to vomiting, diarrhea, or excessive sweating). Any deficit in circulating blood volume (hypovolemia), body water deficit (dehydration), nificant electrolyte disturbances, or acid-base balance disturbances must be corrected. This may require temporary adjustment of Lasix treatment

Weight loss due to increased urine excretion should not exceed 1 kg/day regardless of the extent of urine output. If you have nephrotic syndrome (see above), the dose must be carefully adjusted due to the increased risk of adverse effects.

The solution for infusion must not be administered in combination with other medicines.

Make sure that the pH of the ready-to-use solution for nfusion is slightly alkaline to neutral (pH not less than 7). Acid solutions must not be used, since the active substance may precipitate.

Co-administration with risperidone

In placebo controlled studies with risperidone in elderly patients with dementia, a higher mortality rate was observed in patients who were treated simultaneously with furosemide and risperidone as compared with those who received risperidone or furosemide alone. Caution is therefore necessary, and the benefits and risks of using this combination or of simultaneous treatment with other potent diuretics should be carefully weighed by your doctor. Loss of water (dehydration) should be avoided.

Children

Particularly careful monitoring is required in premature infants, since they are at risk for renal calcification or kidney stones. Monitoring methods include kidney function tests and ultrasound.

n premature infants with conditions involving difficulty breathing (respiratory distress syndrome) undergoing diuretic treatment with Lasix in the first weeks of life, there may be a higher risk that the vessel that shunts pulmonary circulation before birth will remain open (persistent patent ductus arteriosus).

Effects of improper use for doping purposes

Use of Lasix 250 mg solution for infusion may yield positive results in doping tests. In addition, use of the drug as a doping substance can be hazardous to your health

Taking/using other medicines

Please tell your doctor or pharmacist if you are taking/ using or have recently taken/used any other medicines including those obtained without a prescription.

The effectiveness of Lasix 250 mg solution for infusion may be affected by simultaneous treatment with the following drugs or groups of medicines:

- Glucocorticoids (cortisone) carbenoxolone or laxatives may increase potassium loss, which can result in potassium deficit.
- Medicines with an antiinflammatory effect (nonsteroidal antiinflammatory drugs, such as indomethacin and aspirin) may reduce the effect of Lasix. If Lasix treatment results in a decrease in circulating blood volume (hypovolemia) or body water deficit (dehydration), simultaneous administration of nonsteroidal antiinflammatory drugs may cause acute kidney failure.
- Probenecid (antigout agent), methotrexate (antirheumatic agent and immunosuppressant) and other drugs which, like furosemide, are excreted in the urine, may reduce the effect of Lasix.
- Simultaneous administration of phenytoin (drug used to treat seizures and certain types of pain) has been reported to reduce the effect of Lasix
- Since sucralfate (stomach drug) reduces the intestinal absorption of Lasix and thereby decreases its effect, an interval of at least two hours should be allowed between administration of the two drugs.

The effectiveness of the following drugs or groups of medicines may be affected by simultaneous treatment with Lasix 250 mg solution for infusion.

- During simultaneous treatment with certain cardiac agents (glycosides) it should be noted that the sensitivity of the heart muscle to these drugs may be increased by a potassium or magnesium deficit developing under treatment with Lasix. There is a higher risk of heart rate disturbances (ventricular arrhythmias including torsades de pointes) during simultaneous administration of drugs (e.g. terfenadine, an antiallergic, and certain medicines used in heart rate disturbances [class I and III] antiarrhythmics]) that can cause certain FCG changes (prolongation of QT interval) and in patients with electrolyte disturbances.
- The adverse effects of high-dose salicylates (painkillers) may be enhanced by simultaneous use with Lasix Lasix may enhance the harmful effects of medicines that
- damage the kidneys (nephrotoxic drugs) (e.g. antibiotics such as aminoglycosides, cephalosporins, polymyxins). Kidney function may deteriorate in patients receiving furosemide and high doses of certain cephalosporins.

- Damage to hearing (ototoxicity) caused by aminoglycosides kanamyciń, gentamicin (e.g. tobramycin) and other ototoxic drugs may be increased by simultaneous administration of Lasix. Hearing impairment may not be reversible Consequently simultaneous use of the drugs mentioned above should
- Simultaneous use of cisplatin (treatment for malignant diseases) and Lasix may result in hearing impairment. In addition. Lasix must be used with special care since it. may enhance the harmful effect of cisplatin on the kidneys (nephrotoxicity).
- Simultaneous use of Lasix and lithium (used in certain forms of depression) may enhance the harmful effects of lithium on the heart (cardiotoxicity) and nerves (neurotoxicity). The blood lithium level should therefore be closely monitored in natients receiving this closely monitored in patients receiving this combination
- If other medicines used to reduce high blood pressure (antihypertensives) or diuretic drugs or products that may have a hypotensive effect are used at the same time as Lasix, a substantial decrease in blood pressure can be expected. Major drops in blood pressure, even leading to shock, and a deterioration of kidney function (with isolated cases of acute kidney failure) have been observed, particularly during initial administration of ACE inhibitors or angiotensin II receptor antagonists or during initial administration of higher doses. If possible. Lasix treatment should therefore be stopped temporarily. or at least the dose should be reduced for three days. before treatment with an ACE inhibitor or angiotensin II receptor antagonist is started or the dose increased.
- Lasix may reduce the elimination of probenecid. methotrexate, and other drugs which, like furosemide. are excreted via the kidneys. High-dose treatment may result in high levels of active substances in the blood and increase the risk of adverse effects.
- The effect of theophyllin (antiasthmatic drug) or curarelike agents that cause muscle relaxation (muscle relaxants) may be enhanced by Lasix.
- The effect of drugs that lower blood sugar levels (antidiabetics) or increase blood pressure (pressor amines e g adrenalin noradrenalin) may be reduced by simultaneous use of Lasix.
- Caution is necessary in patients treated with risperidone, and the benefits and risks of using this combination or of simultaneous treatment with other potent diuretics should be carefully weighed by your doctor

Other interactions:

- Simultaneous use of cyclosporin A and Lasix is linked to a higher risk of arthritis due to gout, as a result of increased blood uric acid levels caused by furosemide and impaired urine excretion of uric acid caused by cvclosporin.
- n patients treated with furosemide who are at high risk for renal impairment during x-rays with contrast agents. renal function deteriorated more frequently after the examination in patients who received contrast materials than in those who only received intravenous fluids before the contrast-enhanced examination
- In isolated cases, intravenous use of Lasix within 24 hours of administration of chloral hydrate resulted in sensations of warmth, sweating, agitation, nausea, and increased blood pressure and heart rate (tachycardia). Consequently, simultaneous use of Lasix and chloral hydrate should be avoided.

Using Lasix 250 mg solution for infusion with food and drink

Eating large quantities of licorice under treatment with Lasix may increase potassium loss.

Pregnancy and breast-feeding

Lasix 250 mg solution for infusion must not be used during pregnancy unless the attending physician considers it absolutely necessary, since the active substance furosemide crosses the placenta

Furosemide is excreted in breast milk and inhibits its

. Consequently, you should not be treated with Lasix 250 mg solution for infusion if you are breast-feeding. If necessary, you must stop breast-feeding.

anything.

Even when this medicine is used as specified, it may anect your capacity to react to such extent that your ability to drive, use machines, or work without a safe footing is impaired. This applies even more at the beginning of includes when switching drugs, and in combination with alcohol.

Important information about some of the ingredients of Lasix 250 mg solution for infusion Lasix 250 mg solution for infusion contains sodium, but

less than 1 mmol (23 mg) per ampoule. It is therefore virtually sodium-free. 3. HOW TO USE Lasix 250 mg solution for infusion Always use Lasix 250 mg solution for infusion exactly according to your doctor's instructions. You should check

with your doctor or pharmacist if you are unsure of

How much Lasix 250 mg solution for infusion should he used

Dosage should be determined on a case-by-case basis and above all depending on treatment response. The lowest dose that achieves the desired effect should always be

Unless otherwise prescribed, the following dosages are recommended for adults: Acute kidney failure:

In patients suffering from circulatory shock, appropriate measures should be taken to correct low blood volume and low blood pressure before starting treatment. Marked serum electrolyte abnormalities and acid-base imbalances should also be corrected. If a test dose of 40 mg of furosemide, administered as a slow intravenous injection. does not increase fluid excretion, treatment with Lasix 250 mg solution for infusion may begin. 50 mg to 100 mg of furosemide per hour may be administered over one day using an infusion nump. The daily dose is determined based on sufficient urine excretion and should not exceed 1,500 mg of furosemide daily.

Chronic kidney failure with fluid retention and high blood pressure before dialysis; nephrotic syndrome:

ince the drug's effect on sodium elimination via the urine depends on a number of factors, such as severity of kidney failure and sodium balance, etc. and cannot therefore in principle be predicted in individual cases, the correct dose is best obtained by gradually increasing the dose. Because the drug starts to work quickly, the dose may be increased at intervals of half an hour to an hour. The recommended initial dose is an infusion of 0.1 mg/min. Since fluids retained in body tissue should be flushed out slowly in patients with chronic renal failure, the dose should be chosen so that the patient loses about 1 kg of body weight (140 mmol Na⁺) per day. In nephrotic syndrome, the dose must be carefully

adjusted, due to the increased risk of adverse effects. Unless otherwise prescribed, Lasix should be administered

narenterally to infants and children under 15 years of age only in exceptional circumstances, i.e. life-threatening conditions. The mean daily dose is 0.5 mg of furosemide/kg body weight. In exceptional cases, up to 1 mg of furosemide/kg body weight can be administered i.v.

How and how long Lasix 250 mg solution for infusion should be used for

Lasix 250 mg solution for infusion is usually administered using an infusion pump. The infusion rate must not exceed 0.4 ml of Lasix 250 mg solution for infusion per minute (equivalent to 4 mg of furosemide per minute). In patients with advanced kidney failure (serum creatinine more than 5 mg/dl), the infusion rate should not exceed 0.25 ml of Lasix 250 mg solution for infusion per minute (equivalent to 2.5 mg of furosemide per minute). If necessary, the solution for infusion can be diluted with normal saline. The solution for infusion must not be administered with other medicines.

Make sure that the nH of the ready-to-use solution for infusion is slightly alkaline to neutral (pH not less than 7) Acid solutions must not be used, since the active substance may precipitate.

DM The chemical and physical stability of the ready-to-use medicine has been demonstrated for 24 hours at 25 °C. For sterility reasons, it should be used immediately.

Reflex

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If it is not used immediately, the user is responsible for storage duration and conditions.

To achieve optimal efficacy and prevent counterregulation. continuous furosemide infusion is preferable to repeated infusions. Furosemide should be administered intravenously only if

oral administration is not possible or is ineffective (e.g. in nationts with intestinal absorption) or if rapid action is required. Parenteral use of Lasix should be replaced by oral administration as soon as treatment conditions allow. The attending physician should decide on the duration of treatment. This is based on the type and severity of the disease

If you feel that the effect of Lasix is too strong or too weak. talk to your doctor.

If you use more Lasix 250 mg solution for infusion than you should If you suspect a significant overdose of Lasix 250 mg solution

for infusion, you should inform a doctor immediately. The doctor can decide on the measures that may be necessary, depending on the extent of overdose. The signs of acute or chronic overdose depend on the

severity of the salt and fluid loss.

Overdose may result in low blood pressure (hypotension) and circulatory disorders when changing from a lying to a standing position (orthostatic regulation disorders), electrolyte disturbances (decreased potassium, sodium, and chloride levels) and increased blood pH (alkalosis). Severe fluid loss may result in dehydration and, due to blood volume losses (hypovolemia), in circulatory shock and thickening of the blood (hemoconcentration) with a tendency for thrombosis (blood clots)

Sudden water and electrolyte losses can result in a confusional state (delusional states).

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

4. POSSIBLE SIDE EFFECTS

Like all medicines, Lasix 250 mg solution for infusion can cause side effects, although not everybody has them. In assessing the frequency of side effects, the following categories are used:

more than 1 treated patient in 10 Very common: Common 1 to 10 treated patients in 100 Uncommon 1 to 10 treated patients in 1000 Rare: 1 to 10 treated patients in 10 000 Very rare: fewer than 1 treated patient in 10 000 Unknown: cannot be estimated based on available data

Possible side effects

Blood

Uncommon: platelet depletion (thrombocytopenia) Rare: Increase in certain white blood cells (eosinophilia) decrease in white blood cells (leukopenia)

Very rare: anemia due to increased decomposition of red plood cells (hemolytic anemia), anemia due to blood cell formation disorders in the bone marrow (aplastic anemia), severe decrease in certain white blood cells with increased susceptibility to infections and poor general health (agranulocytosis).

Immune system/hypersensitivity reactions

Uncommon: itching, skin and mucosal reactions (see side effects on skin)

Rare: feverish state, inflammation of blood vessels (vasculitis), kidney inflammation (interstitial nephritis), serious hypersensitivity reactions such as circulatory shock (anaphylactic shock). The first signs of shock include skin reactions such as severe flushing or hives, agitation, headache, bout of sweating, nausea, and bluish discoloration of the skin (cyanosis).

The blood sugar level may increase under furosemide treatment. In patients with existing diabetes (manifest diabetes mellitus) this may lead to deterioration of the patient's metabolism. Underlying diabetes mellitus may become manifest

Metabolism/electrolytes

Fluid and electrolyte disturbances are often observed during treatment with Lasix, due to increased elimination. of fluids and electrolytes. For this reason, certain blood parameters should be tested regularly (especially potassium, sodium, and calcium)

Underlying diseases (e.g. liver cirrhosis, heart failure), simultaneous medication (see Section 2) and food are factors that may lead to electrolyte disturbances. Due to increased sodium loss in the urine, a sodium deficit

(hyponatremia) may occur, with corresponding symptoms particularly if salt (sodium chloride) intake is reduced Symptoms that are often reported with sodium deficit. include apathy, calf cramps, loss of appetite, weakness, drowsiness, vomiting, and confusional state

A potassium deficit may occur as a result of increased potassium excretion in the urine, especially if, during treatment notassium intake is reduced or notassium loss increased (e.g. due to vomiting or chronic diarrhea). This condition may lead to symptoms such as muscle weakness, abnormal touch sensations in the hands and feet (paresthesia), minor paralysis (paresis), vomiting constination, build-up of gas in the digestive tract (tympanites), excessive urine output (polyuria), abnormal feeling of thirst with excessive fluid intake (polydipsia) and irregular pulse (e.g. excitation-conduction disorders). Severe potassium loss may result in bowel paralysis (paralytic ileus) or consciousness disorders and even coma. ncreased calcium excretion in the urine may cause a calcium deficit. In rare cases, this may result in neuromuscular hyperexcitability (tetany).

Increased magnesium loss in the urine may result in a magnesium deficit, and in rare cases, tetany and heart rate disorders have been reported.

Electrolyte and fluid loss during Lasix treatment may cause or exacerbate metabolic alkalosis (increased blood pH) Blood uric acid levels are often increased during Lasix treatment. Predisposed patients are likely to suffer gout

Blood lipids (cholesterol, triglycerides) may increase during Lasix therapy.

Rare: A sensation of prickling or numbness in the hands and feet (paresthesia).

In patients with advanced liver failure, hepatic encephalopathy (a disease affecting the brain) may occur.

Due to the possible damage to hearing (ototoxicity) caused

by Lasix, hearing disorders and/or noises in the ears (tinnitus) may occur in rare cases, which are usually curable (reversible). This can especially occur if the intravenous injection of Lasix is too rapid, particularly in patients who also have kidney failure or decreased blood protein levels (hypoproteinemia, e.g. in nephrotic syndrome).

Cardiovascular system Excessive urine output may be accompanied by circulation

disorders, especially in elderly patients and children, which are manifested in particular by headache, dizziness, sight disorders, dry mouth and thirst, low blood pressure (hypotension) and circulation disorders with a drop in blood pressure when changing from a lying to a standing position (orthostatic regulation disorders). Considerable



(excessive) urine output may result in dehydration leading to decreased blood volume (hypovolemia), circulatory shock, and thickening of the blood (hemoconcentration Hemoconcentration can increase patients' tendency for thrombosis (blood clots), particularly in the elderly.

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Rare: stomach and bowel disorders (e.g. nausea, vomiting,

diarrhea)

Very rare: acute inflammation of the pancreas, obstruction of bile flow (intrahenatic cholestasis), and increase in certain liver values (elevated transaminases).

Uncommon: itching, skin and mucosal reactions with redness, formation of blisters or scales (e.g. bullous exanthema, hives, purpura, erythema multiforme, bullous pemphigoid, exfoliative dermatitis) and increased sensitivity to light (photosensitivity). Rare: blood vessel inflammation (vasculitis)

Lasix treatment may cause a temporary increase in blood levels of substances that are eliminated by the kidneys (creatinine, urea). Signs of impaired urine excretion (e.g. enlarged prostate,

build-up of urine in the kidneys, narrowed ureter) may appear or worsen with Lasix. Urinary obstruction (urine retention) with complications may occur. Rare: kidney inflammation (interstitial nephritis)

Newborns In premature children treated with Lasix, kidney stones and/or calcification of kidney tissue may develop. In premature infants with respiratory distress syndrome

(major difficulty breathing) undergoing diuretic treatment with Lasix in the first weeks of life, there may be a higher risk that the vessel that shunts pulmonary circulation before birth will remain open (persistent patent ductus arteriosus).

General status Rare: feverish state.

Should any of the side effects described above occur, inform your doctor as soon as possible, so that he/she can determine the severity and, if necessary, decide on further

If a side effect occurs suddenly or becomes more severe inform your doctor immediately, since some drug reactions may become life-threatening in certain circumstances. The doctor will decide what measures must be taken and whether the therapy can be continued.

At the first signs of a hypersensitivity reaction, Lasix 250 mg solution for infusion should not be used again. If any of the above side effects worsen considerably, or if you notice any side effects not listed in this leaflet, please

5. HOW TO STORE Lasix 250 mg solution for infusion Keep out of the reach and sight of children

Do not use after the expiry date given on the ampoule and the box. The expiry date is the last day of the month stated.

Special precautions for storage:

tell your doctor or pharmacist.

This medicine must always be stored in its original packaging away from light. Store below 30 °C.

Shelf-life after preparation:

The chemical and physical stability of the ready-to-use medicine has been demonstrated for 24 hours at 25 °C.

6. FURTHER INFORMATION

What Lasix 250 mg solution for infusion contains:

The active substance is sodium furosemide One ampoule containing 25 ml of solution for infusion has 266.6 mg of sodium furosemide (equivalent to 250 mg of

furosemide). The other ingredients are:

sodium hydroxide, mannitol (European Pharmacopoeia), water for injection.

What Lasix 250 mg solution for infusion looks like and contents of the pack:

Lasix 250 mg solution for infusion is a clear, colorless

Lasix 250 mg solution for infusion is available in boxes of 5 x 25 ml break-open ampoules. How to open the ampoules: hold the ampoule with the

blue dot facing upwards, and break off the tip by pushing

Marketing Authorization Holder / Operating Company and Manufacturer sanofi-aventis Deutschland GmbH - 65926 Frankfurt am

Main. Germany

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