

Lasix® 20 mg solution for injection

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 20 mg solution for injection is and what it is used for
2. Before you use Lasix 20 mg solution for injection
3. How to use Lasix 20 mg solution for injection
4. Possible side effects
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1. WHAT Lasix 20 mg solution for injection IS AND WHAT IT IS USED FOR

Lasix 20 mg solution for injection is a diuretic (a medicine that promotes urine production).

It is indicated if insufficient diuresis is obtained with oral administration or if oral administration is not possible.

Lasix 20 mg solution for injection is used:

- for fluid accumulation in tissue (edema) and/or “abdominal dropsy” (ascites) due to heart or liver disease,
- for fluid accumulation in tissue (edema) due to renal disease,
- for fluid accumulation in tissue (edema) due to burns,
- for fluid accumulation in lung tissue (pulmonary edema) (e.g. in acute myocardial insufficiency [acute heart failure]),



- as a support measure for fluid accumulation in brain tissue (cerebral edema),
- for decreased urine production (oliguria) due to pregnancy complications (preeclampsia), or after correction of possible blood volume deficit (note: edema and/or hypertension in preeclampsia is not an indication),
- for acute hypertension (hypertensive crisis) in addition to other therapeutic measures.

2. BEFORE YOU USE Lasix 20 mg solution for injection Lasix 20 mg solution for injection must not be used

- if you are hypersensitive (allergic) to furosemide, sulfonamides, or any other ingredient in Lasix 20 mg solution for injection,
- 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 breastfeeding”).

Take special care with Lasix 20 mg solution for injection

- 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 levels is required,
- 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 20 mg solution for injection 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), significant 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 injection must not be administered in combination with other medicines using the same syringe. Make sure that the pH of the ready-to-use solution for injection is slightly alkaline to neutral (pH not less than 7). Acid solutions must not be used, since the active substance may precipitate. Simultaneous 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 recommended, 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.

In premature infants with conditions involving difficulty breathing (respiratory distress syndrome) undergoing diuretic treatment with Lasix 20 mg solution for injection 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 20 mg solution for injection 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 20 mg solution for injection 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 20 mg solution for injection.

- 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 ECG 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 both furosemide and high doses of certain cephalosporins.
- Damage to hearing (ototoxicity) caused by aminoglycosides (e.g. kanamycin, gentamicin, 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 be avoided.
- 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 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 curare-like 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 cyclosporin.
- In 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 20 mg solution for injection with food and drink Eating large quantities of licorice under treatment with Lasix may increase potassium loss.

Pregnancy and breast-feeding

Lasix 20 mg solution for injection 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 production. Consequently, you should not be treated with Lasix 20 mg solution for injection if you are breast-feeding. If necessary, you must stop breast-feeding.

Driving and using machines

Even when this medicine is used as specified, it may affect 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 treatment, when increasing doses, when switching drugs, and in combination with alcohol.

Important information about some of the ingredients of Lasix 20 mg solution for injection

Lasix 20 mg solution for injection contains sodium, but less than 1 mmol (23 mg) per ampoule. It is therefore virtually sodium-free.

3. HOW TO USE Lasix 20 mg solution for injection

Always use Lasix 20 mg solution for injection exactly according to your doctor's instructions. You should check with your doctor or pharmacist if you are unsure of anything.

How much Lasix 20 mg solution for injection should be 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 used. Unless otherwise prescribed, the following **dosages** are recommended for adults:

For fluid accumulation in tissue (edema) and/or “abdominal dropsy” (ascites) due to heart or liver disease:

Initiate treatment with 2 to 4 ml of Lasix 20 mg solution for injection (equivalent to 20 to 40 mg of furosemide) i.v. For edema that is difficult to mobilize, repeat this dose at appropriate intervals or if necessary in repeated doses until the onset of urine excretion.

For fluid accumulation in tissue (edema) due to kidney disease:

Initiate treatment with 2 to 4 ml of Lasix 20 mg solution for injection (equivalent to 20 to 40 mg of furosemide) i.v. For edema that is difficult to mobilize, repeat this dose at appropriate intervals or if necessary in repeated doses until the onset of urine excretion.

In nephrotic syndrome, the dose must be carefully adjusted, due to the increased risk of adverse effects.

For fluid accumulation in tissue (edema) due to burns:

The daily and/or single dose ranges from 4 to 10 ml of Lasix 20 mg solution for injection (equivalent to 40 to 100 mg of furosemide); in exceptional cases, in patients with kidney failure, the dose may be up to 25 ml of Lasix 20 mg solution for injection (equivalent to 250 mg of furosemide).

Decreased blood volume must be corrected before using Lasix 20 mg solution for injection.

For fluid accumulation in lung tissue (pulmonary edema) (e.g. in acute myocardial insufficiency [acute heart failure]):

Use in combination with other treatments.

Initiate treatment with 2 to 4 ml of Lasix 20 mg solution for injection (equivalent to 20 to 40 mg of furosemide) i.v. If urine excretion does not increase, repeat the dose after 30 to -60 minutes, if necessary by doubling the dose.

As a support measure for fluid accumulation in brain tissue (cerebral edema):

The daily and/or single dose ranges from 4 to 10 ml of Lasix 20 mg solution for injection (equivalent to 40 to 100 mg of furosemide); in exceptional cases, in patients with kidney failure, the dose may be up to 25 ml of Lasix 20 mg solution for injection (equivalent to 250 mg of furosemide).

For decreased urine production (oliguria) due to pregnancy complications (preeclampsia):

Strict assessment of the indication is essential.

Decreased blood volume must be corrected before using Lasix 20 mg solution for injection.

The daily dosage ranges from 1 to 10 ml of Lasix 20 mg solution for injection (equivalent to 10 to 100 mg of furosemide).

Edema and/or hypertension in preeclampsia is not an indication for Lasix 20 mg solution for injection.

For acute hypertension (hypertensive crisis):

Use 2 to 4 ml of Lasix 20 mg solution for injection (equivalent to 20 to 40 mg of furosemide) along with other treatment.

Children:

Unless otherwise prescribed, Lasix 20 mg solution for injection should be administered parenterally 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 injected i.v.

How and how long Lasix 20 mg solution for injection should be used for

Lasix 20 mg solution for injection is usually injected intravenously (i.v.). This must be done slowly. The injection rate must not exceed 0.4 ml of Lasix 20 mg solution for injection (equivalent to 4 mg of furosemide) per minute. In patients with advanced kidney failure (serum creatinine more than 5 mg/dl), the injection rate should not exceed 0.25 ml of Lasix 20 mg solution for injection per minute (equivalent to 2.5 mg of furosemide per minute). If the dose is increased to 25 ml (equivalent to 250 mg of furosemide) an infusion pump (dosing apparatus) should be used. If necessary, the solution for injection can be diluted with normal saline. Intramuscular (i.m.) administration, i.e. injection into a muscle, should only be used in exceptional cases, if neither oral nor i.v. administration is possible. However, it is not suitable for acute conditions (e.g. pulmonary edema).

The solution for injection must not be administered in combination with other medicines using the same syringe.

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

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 injections.

Furosemide should be administered intravenously only if oral administration is not possible or is ineffective (e.g. in patients 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 20 mg solution for injection than you should

If you suspect a significant overdose of Lasix 20 mg solution for injection, 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 20 mg solution for injection can cause side effects, although not everybody has them.

In assessing the frequency of side effects, the following categories are used:

Very common:	more than 1 treated patient in 10
Common:	1 to 10 treated patients in 100
Uncommon:	1 to 10 treated patients in 1 000
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 blood 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).

Hormone system

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, potassium intake is reduced or potassium 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, constipation, build-up of gas in the digestive tract (tympantics), 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. Increased 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 attacks. Blood lipids (cholesterol, triglycerides) may increase during Lasix therapy.

Nervous system

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

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

Sense organs

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.

Digestive tract

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

Liver / pancreas

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

Skin

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).

Kidneys

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).

Overall state / local reactions

Rare: feverish state.

Local reactions such as pain may occur after intramuscular injections.

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 measures.

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 20 mg solution for injection 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 tell your doctor or pharmacist.

5. HOW TO STORE Lasix 20 mg solution for injection

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:

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 20 mg solution for injection contains:

The active substance is sodium furosemide.

One ampoule containing 2 ml of solution for injection has 21.3 mg of sodium furosemide (equivalent to 20 mg of furosemide).

The other ingredients are:

sodium chloride, sodium hydroxide, water for injection.

What Lasix 20 mg solution for injection looks like and contents of the pack:

Lasix 20 mg solution for injection is a clear, colorless solution. Lasix 20 mg solution for injection is available in boxes of 1 or 5 x 2 ml ampoules (some presentations of the drug may not be marketed).

Marketing Authorization Holder / Operating Company and Manufacturer

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