This package insert is continually updated: please read carefully before using a new pack!

LASIX®
Active ingredient: Furosemide

[Sanofi logo]

Tablet

Composition

Each tablet contains, as active ingredient, 40 mg furosemide.
Excipients: Maize starch, pregelatinized maize starch, lactose, colloidal anhydrous silica, talc, magnesium stearate.

Properties

Lasix is a medicine which increases urine excretion (loop diuretic) and lowers high blood pressure (antihypertensive).

Indications

Oedema due to cardiac, hepatic, or renal disorders (in the presence of nephrotic syndrome, treatment of the basic disorder is the prime concern). Oedema due to burns. Mild to moderate hypertension.

Contraindications

Lasix must not be used in patients with:
– renal failure accompanied by lack of urine formation (anuria) in patients not responding to furosemide
– hepatic coma and precoma
– severely reduced blood levels of potassium (hypokalaemia – see Adverse Reaction), or of sodium (hyponatraemia)
– decreased volume of blood in the body (hypovolaemia) – with or without reduced blood pressure (hypotension) – or dehydration
– hypersensitivity to furosemide or any of the excipients (see “Composition”). Patients allergic to sulphonamides (e.g. sulphonamide antibiotics or sulphonylureas) may show cross-sensitivity to furosemide.
–- lactation

Pregnancy and lactation

Furosemide crosses the placental barrier. Therefore, Lasix must not be given during pregnancy unless there are compelling medical reasons. If Lasix is given during pregnancy, fetal growth must be monitored.
Furosemide passes into breast milk and inhibits lactation. Therefore, Lasix must not be used during breast-feeding.

Special warnings and precautions

During treatment with Lasix, output of urine must be secured. Patients whose outflow is obstructed (e.g. those with prostatic hypertrophy, ureterostenosis, or hydronephrosis) require careful monitoring, especially at the beginning of treatment.
Treatment with Lasix necessitates regular medical supervision. Particularly careful surveillance is necessary in:
– hypotension
– patients at particular risk from a pronounced fall in blood pressure (e.g. those with significant stenoses of the coronary arteries or of the blood vessels supplying the brain)
– latent or manifest diabetes mellitus (regular blood sugar checks)
– gout (regular uric acid checks)
– renal failure in association with severe liver disease (hepatorenal syndrome)
– reduced protein content in the blood (hypoproteinaemia, e.g. in the nephrotic syndrome) (the effect of Lasix may be weakened and its toxic effect on the ear may be increased; caution is necessary in determining the dose)
– premature infants (possible development of kidney stones containing calcium [nephrolithiasis] and of calcium salt deposition in the renal tissue [nephrocalcinosis]; renal function must be monitored and renal ultrasonography performed)

During treatment with Lasix, serum sodium, potassium, and creatinine should be monitored regularly. Patients at high risk of developing electrolyte imbalances, and those with significant additional fluid loss due to, e.g., vomiting, diarrhoea or intense sweating, must be closely monitored. Hypovolaemia or dehydration, as well as any significant disturbances in electrolyte

content and acid-base balance, must be corrected. A temporary discontinuation of treatment with Lasix may become necessary.

Concomitant use with risperidone

In risperidone placebo-controlled trials in elderly patients with dementia, a higher incidence of mortality was observed in patients treated with furosemide plus risperidone (7.3%; mean age 89 years, range 75-97 years) when compared to patients treated with risperidone alone (3.1%; mean age 84 years, range 70-96 years) or furosemide alone (4.1%; mean age 80 years, range 67-90 years). Concomitant use of risperidone with other diuretics (mainly thiazide diuretics used in low dose) was not associated with similar findings.
No pathophysiological mechanism has been identified to explain this finding, and no consistent pattern for cause of death observed. Nevertheless, caution should be exercised and the risks and benefits of this combination or co-treatment with other potent diuretics should be considered prior to the decision to use. There was no increased incidence of mortality among patients taking other diuretics as concomitant treatment with risperidone. Irrespective of treatment, dehydration was an overall risk factor for mortality and should therefore be avoided in elderly patients with dementia (see Contraindications).

The possibility exists of exacerbation or activation of systemic lupus erythematosus.

Adverse effects

Furosemide increases excretion of sodium and chloride and, consequently, water, excretion of other electrolytes, in particular, potassium, calcium and magnesium, is increased as well.
Symptomatic electrolyte disturbances and metabolic alkalosis may develop and be manifested as a gradually increasing electrolyte deficit, or – where, e.g., higher doses are used in patients with normal renal function – as acute severe electrolyte losses.
Warning signs of electrolyte disturbances include increased thirst, headache, confusion, muscle cramps, tetany, muscle weakness, disorders of cardiac rhythm and gastrointestinal symptoms. Influencing factors for the development of electrolyte disturbances are, e.g., underlying diseases (such as liver cirrhosis or cardiac failure), concurrent medication (see “Interactions”) and nutrition. Potassium deficiency may occur, particularly as a result of vomiting or diarrhoea. Cases of rhabdomyolysis have been reported, often in the context of severe hypokalaemia.
The diuresis resulting from furosemide may be too strong and may lead or contribute to hypovolaemia and dehydration, especially in elderly patients. Severe fluid depletion may lead to an increase in the concentration of the blood (haemoconcentration) with a tendency for thromboses to develop.
A casual association between furosemide and pseudo-Bartter syndrome has been noted in the context of abuse and long-term use of furosemide.
A reduction in blood pressure may occur and, especially if pronounced, may result in signs and symptoms such as an impairment of concentration and reactions, light-headedness, sensations of pressure in the head, headache, dizziness, drowsiness, weakness, visual impairment, dryness of the mouth, and disturbed circulatory regulation on standing up or standing (fainting/loss of consciousness).
Complaints in patients with an outflow obstruction may be provoked or aggravated by increased urine production. Therefore, in patients with, e.g., bladder-emptying disorders, an enlargement of the prostate gland (prostatic hyperplasia), or a narrowing of the urethra, acute retention of urine with possible secondary complications may occur.
Levels of serum lipids (cholesterol and triglycerides) may rise during furosemide treatment. There may be transient increases in serum levels of creatinine and urea.
The concentration of uric acid in the blood is frequently increased during furosemide treatment. This may lead to gout attacks in predisposed patients.
Glucose tolerance may be reduced during furosemide treatment. In diabetic patients, this may lead to a deterioration of metabolic condition; latent diabetes mellitus may become manifest.
Gastrointestinal disorders such as nausea, vomiting, or diarrhoea may occur in rare cases, as may, in isolated cases, an arrest in bile flow in the liver (intrahepatic cholestasis), an increase in liver transaminases, or an acute inflammation of the pancreas (acute pancreatitis). Usually transient hearing disorders and/or noises in the ears (tinnitus) may occur in rare cases, particularly in patients with renal failure, in those with hypoproteinaemia (e.g. in the nephrotic syndrome), and/or where intravenous administration has taken place too rapidly. Cases of deafness, sometimes irreversible, have also been reported after oral or IV administration of furosemide.
Occasionally, reactions of the skin and mucous membranes may occur. These may take the form of, e.g., itching, urticaria, other rashes or bullous lesions, erythema multiforme, bullous pemphigoid, exfoliative dermatitis or purpura. Very rarely, Stevens-Johnson syndrome and toxic epidermal necrolysis have occurred. Cases of AGEP (acute generalised exanthematous pustulosis) and DRESS (drug rash with eosinophilia and systemic symptoms), lichenoid

reactions have also been reported with furosemide use. Severe anaphylactic and anaphylactoid reactions with e.g., circulatory collapse (shock) are rare. Exacerbation or activation of systemic lupus erythematosus has been reported. In rare cases, fever, inflammation of the blood vessels or kidneys (vasculitis or interstitial nephritis), eosinophilia, or disturbances of sensation (paraesthesiae) may occur, as may, occasionally, photosenstitivity.
Hepatic encephalopathy in patients with hepatocellular insufficiency
Occasionally, a decrease in the number of platelets (thrombopenia), or, rarely in the number of white blood cells (leucopenia) may develop, as may, in isolated cases, a decrease in the numbers of red blood cells (haemolytic or aplastic anaemia) or the absence of certain white blood cells (agranulocytosis).
In premature infants, kidney stones containing calcium (nephrolithiasis) may develop and calcium salts may be deposited in the renal tissue (nephrocalcinosis).
Furosemide administered in premature infants during the first weeks of life may increase the risk of persistence of Botallo's duct.
Please speak with your doctor if you notice any of the adverse effects listed in this package insert or any other undesired effects or unexpected changes.
Since some adverse effects (e.g., changes in blood picture, severe anaphylactic or anaphylactoid reactions, severe bullous skin reactions) may under certain circumstances become life-threatening, it is essential that, if sudden or severe reactions do occur, you inform a doctor at once.

Driving
Some adverse effects, such as a pronounced fall in blood pressure, may impair this ability to concentrate and react, and, therefore, constitute a risk in situations where these abilities are of particular importance (e.g. operating a vehicle or machinery).

Interactions
Certain electrolyte disturbances, e.g. hypokalaemia or hypomagnesaemia, may develop during treatment, and increase the toxicity of certain other drugs (e.g. digitalis preparations and drugs inducing QT interval prolongation syndrome).
Corticosteroids, carbenoxolone, large amounts of liquorice, and prolonged use of laxatives may increase the risk of hypokalaemia.
The toxic effects of aminoglycosides on the ear and of other drugs having the same potential may be increased by concomitant administration of furosemide. Since damage may be irreversible, concurrent use of these drugs is restricted to compelling medical reasons.
Toxic effects on the ear are possible if cisplatin and furosemide are used concurrently. In addition, when furosemide is used to increase urine excretion (forced diuresis) during cisplatin treatment, it must only be given in low doses (e.g. 40 mg in patients with normal kidney function) and in conjunction with a positive fluid balance, since otherwise the toxic effects of cisplatin on the kidneys (nephrotoxicity) may increase.
Furosemide may potentiate the harmful effects of nephrotoxic drugs on the kidney.
Concurrent administration of non-steroidal anti-inflammatory medicines may reduce the effect of furosemide. Concurrent administration of such medicines in patients with dehydration or hypovolaemia may cause acute renal failure. The toxicity of salicylates may be increase.
Attenuation of the effect of furosemide may also occur following concurrent administration of phenytoin.
Concurrent use of antihypertensive agents, diuretics, or other medicines with blood-pressure-lowering potential may lead to a more pronounced fall in blood pressure.
When an ACE inhibitor or angiotensin II receptor antagonist is given for the first time or when a first dose increase is given, severe hypotension and a deterioration in renal function may result. Therefore, consideration must be given to interrupting the administration of furosemide temporarily or, as a minimum, to reducing the dose of furosemide three days before starting treatment with, or increasing the dose of, an ACE inhibitor or angiotensin II receptor antagonist.
Medicines such as probenecid or methotrexate which, like furosemide, are secreted significantly via the renal tubuli, may reduce the effect of furosemide. On the other hand, furosemide may decrease renal elimination of such medicines. Particularly where both furosemide and the other medicines are administered in high doses concurrently, serum levels of the medicines, as well as the risk of adverse effects resulting from them, may increase.
The effects of antidiabetics and blood-pressure increasing sympathomimetics (e.g. epinephrine, norepinephrine) may be reduced, and those of theophylline or curare-type muscle relaxants may be increased.

Furosemide reduces the excretion of lithium salts, which may lead to an increase in serum lithium levels, and, consequently, in lithium toxicity. For this reason, lithium levels should be carefully monitored in patients receiving this combination.
Intravenous administration of furosemide within 24 hours after the ingestion of chloral hydrate may, in isolated cases, lead to reddening of the skin with a sensation of heat (flushing), sweating, restlessness, nausea, increase in blood pressure, and rapid heart beat (tachycardia). Therefore, concurrent use of chloral hydrate and furosemide should be avoided.
Furosemide and sucralfate must not be taken within two hours of each other, since sucralfate reduces the absorption of furosemide and hence, weakens its effect.
Impairment of renal function may develop in patients receiving concurrent treatment with furosemide and high doses of certain cephalosporins.
Concomitant use of cyclosporine A and furosemide is associated with increased risk of gouty arthritis secondary to furosemide-induced hyperurecemia and cyclosporine impairment of renal urate excretion.
Patients who were at high risk for radiocontrast nephropathy treated with furosemide experienced a higher incidence of deterioration in renal function after receiving radiocontrast compared to high-risk patients who received only intravenous hydration prior to receiving radiocontrast.

In patients treated with risperidone, caution should be exercised and the risks and benefits of the combination or co-treatment with furosemide or with other potent diuretics should be considered prior to the decision to use. (See Special warnings and precautions,regarding increased mortality in elderly patients with dementia concomitantly receiving risperidone.)

Levothyroxine: High doses of furosemide may inhibit binding of thyroid hormones to carrier proteins and thereby lead to an initial transient increase in free thyroid hormones, followed by an overall decrease in total thyroid hormone levels. Thyroid hormone levels should be monitored.

Dosage
In general, the dose used must be the lowest which is sufficient to achieve the desired effect. Unless otherwise prescribed, the following dosage guidelines apply:
In adults, treatment is usually started with 1/2–1–2 tablets daily; the maintenance dose is 1/2–1 tablet daily.
In infants and children, Lasix should in principle be administered orally. The dosage recommendation is 2 mg furosemide per kg body weight up to a daily maximum of 40 mg. Parenteral administration (if necessary, continuous drip infusion) is indicated only in life-threatening conditions.

Administration
The tablets should be swallowed without chewing and with sufficient amounts of liquid on an empty stomach.
The duration of treatment is determined by the doctor and will depend on the nature and severity of illness.

Overdose
Medical treatment may be required in the event of an overdose. Therefore, please inform your doctor if you suspect an overdose.
The clinical picture of an acute or chronic overdose depends primarily on the extent and consequences of electrolyte and fluid loss, e.g. hypovolaemia, dehydration, haemoconcentration, cardiac arrhythmias (including A-V block and ventricular fibrillation). Symptoms of these disturbances include severe hypotension (progressing to shock), acute renal failure, thrombosis, delirious states, flaccid paralysis, apathy and confusion.
No specific antidote to furosemide is known. If ingestion has only just taken place, attempts may be made to limit further systemic absorption of the active ingredient by measures such as gastric lavage or those designed to reduce absorption (e.g. activated charcoal).
Clinically relevant disturbances in electrolyte and fluid balance must be corrected. Together with the prevention and treatment of serious complications resulting from such disturbances and of other effects on the body, this corrective action may necessitate general and specific intensive medical monitoring and therapeutic measures.

Special notes
Although administration of Lasix 40 mg only rarely leads to hypokalaemia, a potassium-rich diet (lean meat, potatoes, bananas, tomatoes, cauliflower, spinach, dried fruit, etc.) is always advisable. Occasionally, treatment with potassium-containing or potassium-sparing preparations may be indicated.

Storage
Protect from light.

Expiry date
Do no use later than the date of expiry.

Keep medicines out of the reach of children.

Presentation
Blister of 100 tablets / bottle of 250 tablets.
Not all presentations may be available locally.

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Last revision : 18 October 2018
Reference : CCDS v12