Lasix®

Furosemide

40 mg

sanofi

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

Pharmaceutical Form
Lasix tablets are almost white and well engraved round tablet with a break line, printed "DLI" on one side.

Properties
Furosemide has a diuretic effect (natrium) depends on the dosis given. Diuretic effect of Furosemide will be affected ½ - 1 hour after oral administration and the maximum effect reached within 1-2 hours. Diuretic effect will last for 4-6 hours.
Different from the thiazid group, Furosemide is still effective in conditions with decreased of glomerulus filtration (renal insufficiency).

Indications
Oedema due to cardiac, hepatic, or renal disorders (in the presence of nephrotic syndrome, treatment of the basic disorder is the prime concern).
Peripheral oedema due to mechanical obstruction or venous insufficiency and hypertension.

Contraindications
Furosemide is contra indicated in patients with:
- Renal failure accompanied by lack of urine formation (anuria)
- Hepatic coma and precoma
- Electrolyte deficiencies, e.g. severely reduced blood levels of potassium (hypokalaemia), 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.

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

Special warnings and precautions
During treatment with Furosemide, 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 Furosemide 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) because latent diabetes may become manifest or the insulin requirement of diabetic patients may increase.
- 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 Furosemide may be weakened and its toxic effect on the ear may be increased; caution is necessary in determined 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 Furosemide 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 Furosemide may become necessary. Where indicated, steps should be taken to correct hypotension or hypovalaemia before commencing therapy.

Concomitant use with risperidone:
In placebo-controlled studies with risperidone 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 low-dose thiazide diuretics) 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 before the decision to treat is made. 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. The possibility exists of exacerbation or activation of systemic lupus erythematosus.

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.

Adverse Effects

The following categories are used to assess the incidence rates of undesirable effects:

Very common (≥ 1/10)
Common (≥ 1/100 to < 1/10)
Uncommon (≥ 1/1,000 to < 1/100)
Rare (≥ 1/10,000 to < 1/1,000)
Very rare (< 1/10,000)
Not known (frequency cannot be evaluated based on available data)

The incidence rates of adverse effects are based on literature data and refer to studies that included a total of 1,387 patients receiving various doses of furosemide in a number of different indications.

Blood and lymphatic system disorders:

Common: hemoconcentration (through excessive diuresis).
Uncommon: thrombocytopenia.
Rare: eosinophilia, leukocytopenia.
Very rare: hemolytic anemia, aplastic anemia, agranulocytosis.
Signs of agranulocytosis may include fever with shivering, mucous membrane changes and sore throat.

Immune system disorders:

Uncommon: allergic skin and mucous membrane reactions (see "Skin and subcutaneous tissue disorders").
Rare: severe anaphylactic and anaphylactoid reactions such as anaphylactic shock
The first signs of shock include skin reactions such as flushing or urticaria, restlessness, headache, sweating, nausea, cyanosis.
Not known: exacerbation or activation of systemic lupus erythematosus.

Metabolism and nutrition disorders

Very common: Electrolyte disorders (including symptomatic manifestations), dehydration and hypovolemia (particularly in elderly patients), elevated triglycerides.
Common: hyponatremia and hypochloremia (particularly in restricted sodium chloride intake), hypokalemia (particularly in concomitant reduction of potassium intake and/or increased

potassium losses, e.g. due to vomiting or chronic diarrhea); elevated blood cholesterol, elevated blood uric acid and episodes of gout.
Uncommon: reduced glucose tolerance and hyperglycemia. In patients with manifest diabetes mellitus, this can lead to deterioration of the metabolic state. Latent diabetes mellitus may become manifest.
Frequency not known: hypocalcemia, hypomagnesemia, metabolic alkalosis, Pseudo-Bartter syndrome in the context of misuse and/or long-term use of furosemide.
Commonly observed symptoms of sodium deficiency include apathy, calf cramps, loss of appetite, weakness, drowsiness, vomiting and confusion.

Hypokalemia may manifest as neuromuscular signs (muscle weakness, paresthesia, paresis), intestinal signs (vomiting, constipation, meteorism), renal signs (polyuria, polydipsia) and cardiac signs (disorders of impulse formation and conduction). Severe potassium depletion can result in paralytic ileus, consciousness disorders or even coma. Hypocalcemia can cause tetany in rare cases. Tetany or the development of cardiac arrhythmias have been observed in rare cases as a result of hypomagnesemia.

Nervous system disorders:
Common: hepatic encephalopathy in patients with hepatic insufficiency
Rare: paresthesia.
Not known: dizziness, fainting or loss of consciousness, headache

Ear and labyrinth disorders:
Uncommon: hearing disorders, mostly reversible, particularly in patients with renal insufficiency or hypoproteinemia (e.g. in nephrotic syndrome) and/or on excessively rapid intravenous injection. Cases of deafness, sometimes irreversible have been reported after oral or IV administration of furosemide.
Very rare: tinnitus.

Vascular disorders:
Very common (on intravenous infusion): hypotension including orthostatic dysregulation
Rare: vasculitis.
Frequency not known: thrombosis (particularly in elderly patients).

In excessive diuresis, circulatory disorders (even circulatory collapse) may occur, especially in children and elderly patients, and mainly manifest as headaches, dizziness, visual disorders, dry mouth and thirst, hypotension and orthostatic dysregulation.

Gastrointestinal disorders:
Uncommon: nausea.
Rare: vomiting, diarrhea.
Very rare: acute pancreatitis.

Hepatobiliary disorders:
Very rare: intrahepatic cholestasis, elevated transaminases.

Skin and subcutaneous tissue disorders:
Uncommon: pruritus, urticaria, rash, bullous dermatitis, erythema multiforme, pemphigoid, exfoliative dermatitis, purpura, photosensitivity.
Frequency not known:
Stevens-Johnson syndrome, toxic epidermal necrolysis, acute generalized exanthematic pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS).

Renal and urinary disorders:
Very common: elevated blood creatinine.
Common: increased urine volume.
Rare: tubulointerstitial nephritis.
Frequency not known: elevated urine sodium, elevated urine chloride, elevated blood urea, symptoms of impaired micturition (e.g. in patients with prostatic hypertrophy, hydronephrosis, ureteral stenosis) to urinary retention with secondary complications (see Section 4.4), nephrocalcinosis and/or nephrolithiasis in premature infants, renal failure.

Congenital, familial and genetic disorders:
Frequency not known: increased risk of a persistent ductus arteriosus if premature infants are treated with furosemide in the first weeks of life.

General disorders:
Rare: fever.

Musculoskeletal and connective tissue disorders:
Not known: cases of rhabdomyolysis have been reported, often in the context of severe hypokalaemia

Interaction with other medicinal products and other forms of interaction
The simultaneous use of furosemide and glucocorticoids, carbenoxolone or laxatives can lead to increased potassium depletion with the risk of hypokalemia. In this respect, large amounts of licorice act like carbenoxolone.

Non-steroidal anti-inflammatory drugs (e.g. indomethacin and acetylsalicylic acid) can reduce the effect of furosemide. In patients who develop hypovolemia during furosemide therapy, or in those who are dehydrated, the simultaneous administration of non-steroidal anti-inflammatory agents can trigger acute renal failure.

Probenecid, methotrexate and other medicinal products which, like furosemide, are extensively secreted in the renal tubules, can reduce the effect of furosemide.

On concomitant administration with phenytoin, a reduced effect of furosemide has been described. As sucralfate reduces the uptake of furosemide from the intestine and therefore reduces its effect, an interval of at least 2 hours should be allowed between administration of the two medicinal products.

On concomitant administration with cardiac glycosides, furosemide-related hypokalemia and/or hypomagnesemia increase the sensitivity of the myocardium to cardiac glycosides. There is a greater risk of ventricular arrhythmias (including torsades de pointes) if furosemide is used

concomitantly with medicinal products that can cause a prolonged QT interval (e.g. terfenadine, some class I and class III antiarrhythmic agents), and in patients with electrolyte disturbances.
The toxicity of high-dose salicylates can be potentiated when they are administered concomitantly with furosemide.

Furosemide can potentiate the harmful effects of nephrotoxic medicinal products (e.g. antibiotics such as aminoglycosides, cephalosporins, polymyxins). Deterioration in renal function may be observed in patients who are treated concomitantly with furosemide and high doses of certain cephalosporins.

The ototoxicity of aminoglycosides (e.g. kanamycin, gentamicin, tobramycin) and other ototoxic medicinal products can be increased by the simultaneous administration of furosemide. Any hearing disorders that occur may be irreversible. The simultaneous use of the above mentioned medicinal products should therefore be avoided.

If cisplatin and furosemide are administered concomitantly, hearing damage may occur. If forced diuresis with furosemide is attempted during cisplatin treatment, furosemide should only be used at low doses (e.g. 40 mg in patients with normal renal function) and when there is a positive fluid balance. Otherwise, cisplatin nephrotoxicity may be enhanced.

The concomitant administration of furosemide and lithium leads to an increase in the cardiac and neurotoxic effects of lithium via reduced lithium excretion. It is therefore recommended that plasma lithium levels be carefully monitored in patients receiving this combination.

If other antihypertensive agents, diuretics or medicinal products with blood-pressure-lowering potential are used at the same time as furosemide, a greater drop in blood pressure is to be expected. A severe drop in blood pressure or even shock, and a deterioration in renal function (in isolated cases acute renal failure), have been observed, particularly when an ACE inhibitor or angiotensin-II-receptor antagonist were administered for the first time or for the first time in higher doses. If possible, the furosemide therapy should therefore be temporarily discontinued, or the dose at least reduced for three days before treatment with an ACE inhibitor or angiotensin-II-receptor antagonist is started or doses are increased.

Furosemide can reduce the renal elimination of probenecid, methotrexate and other medicinal products which, like furosemide, are extensively secreted in renal tubules. In high-dose treatment (especially with both furosemide and the other medicinal product), this can lead to elevated serum levels and a greater risk of undesirable effects due to furosemide or the concomitant medication.

The effect of theophylline or curare-type muscle relaxants may be increased by furosemide.
The effect of antidiabetic agents or hypertensive sympathomimetics (e.g. epinephrine, norepinephrine) may be reduced if furosemide is coadministered.
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 before a decision to treat is made.

Other interactions

The concomitant administration of cyclosporin A and furosemide is associated with an increased risk of gouty arthritis as a result of furosemide-induced hyperuricemia and impairment of renal uric acid excretion by cyclosporin.

In patients who were at high risk of renal damage due to X-ray contrast media and who were treated with furosemide, a deterioration in renal function occurred more frequently after a contrast examination than in at-risk patients who received only an intravenous supply of fluid (hydration) before the contrast-enhanced examination.

After intravenous administration of furosemide within 24 hours of treatment with chloral hydrate, a feeling of heat, outbreaks of sweating, restlessness, nausea, a rise in blood pressure, and tachycardia may be experienced in isolated cases. The simultaneous use of furosemide and chloral hydrate should therefore be avoided.

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:

- Oral Eedema *:* Therapy should be individualized according to patient's response. This therapy should be titrated to gain maximal therapeutic response with the minimum dose possible to maintain that diuretic response.

Adults : The usual initial daily dose is 20-80 mg given as single dose. If it is not satisfactory, increase this dose by increments of 20-40 mg not sooner than 6-8 hours after the previous dose until the desired diuretic effect is obtained. This individually determined dose should be given once or twice (e.g. at 8 am and 2 pm) daily. The dose may be carefully titrated up to 600 mg/day (except in advanced renal failure) in those patients with severe clinical oedematous states.

This mobilization of oedema may be most efficiently and safely accomplished by giving it on 2-4 concecutive days each week.

Children : Dose is based on body weight: 1-2 mg/kg of body weight for a single dose. If the diuretic response to a single dose is not satisfactory, increase this dose by increments 1-2 mg/kg not sooner than 6-8 hours after the previous dose until the desired diuretic effect is obtained. Maximum dose is 6 mg/kg of body weight.

Maintenance dose should be titrated to gain maximal therapeutic response with minimum dose.

- *Hypertension :* Therapy should be individualized according to the patient's response. This Therapy should be titrated to gain maximal therapeutic response

Adults : The usual initial daily dose for hypertension is 80 mg, usually divided into 40 mg twice a day. Dosage should then be adjusted according to response. If response is not satisfactory, add other antihypertensive agents. Changes in blood pressure must be carefully monitored when furosemide is used with other antihypertensive drugs, especially during initial therapy.

To prevent an excessive drop in blood pressure, the dosage of other agents should be reduced by at least 50% when Furosemide is added to the regimen. As the blood pressure falls under the potentiating effect of Furosemide, a further reduction in dosage or even discontinuation of other antihypertensive drugs may be necessary.

In the elderly, Furosemide is generally eliminated more slowly. Dosage should be titrated until the required response is achieved.

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.
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 ofFurosemide 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
Store at temperature 25°C - 30°C
Protect from light

Expiry date
Do not use later than the date of expiry

Keep medicines out of the reach of children

Presentation
Boxes of 10 blisters x 10 tablets of
40 mg
Reg.No.DKL0121203710A1

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ON MEDICAL PRESCRIPTION ONLY

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