Professional Information for the LASIX range

SCHEDULING STATUS:

S3

1. NAME OF THE MEDICINE

LASIX 20 mg tablets

LASIX 40 mg tablets

LASIX 80 mg tablets

LASIX 2 mL (10 mg/mL) solution for injection/infusion

LASIX ORAL SOLUTION (10 mg/mL)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

LASIX 20 mg: Each tablet contains 20 mg furosemide.

LASIX 40 mg: Each tablet contains 40 mg furosemide.

LASIX 80 mg: Each tablet contains 80 mg furosemide.

LASIX 2 mL: Each 1 mL contains 10 mg furosemide. Each 2 mL ampoule contains 20 mg furosemide.

LASIX ORAL SOLUTION: Each 1 mL contains 10 mg furosemide.

Excipients with known effect:

LASIX 20 mg contains sugar (lactose monohydrate): 26,50 mg per tablet.

LASIX 40 mg contains sugar (lactose monohydrate): 53,00 mg per tablet.

LASIX 80 mg contains sugar (lactose monohydrate): 106,00 mg per tablet.

LASIX 2 mL ampoule:

Sugar free.

LASIX ORAL SOLUTION:

Alcohol: 9,6 % *m/v*

Preservatives: Methylparaben 0,25 % *m/v and* propylparaben 0,05 % *m/v*

Contains sorbitol (a sugar alcohol): 245 mg per mL.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

LASIX 20 mg tablets: A white round, scored tablet with the company logo on the one side, and coded DLF on the other side.

LASIX 40 mg tablets: Almost white, round, biplanar, scored tablet with a unilateral score line and engraved DLI on each side of the score line. The other face is engraved with the logotype ‘Hoechst’.

LASIX 80 mg tablets: White, round, bevelled-edge tablet, 8-faceted, with a score line and “LASIX 80” imprinted on one side and the company logo on the other side.

LASIX 2 mL solution for injection/infusion: A clear, colourless solution in an amber glass ampoule.

LASIX ORAL SOLUTION: A clear, orange-yellow solution with an orange flavour in an amber glass bottle with a screw cap.

4. Clinical particulars

4.1 Therapeutic indications

- Fluid retention associated with congestive cardiac failure.
- Fluid retention associated with chronic renal failure.
- Maintenance of fluid excretion in acute renal failure.
- Fluid retention associated with nephritic syndrome (if diuretic treatment is required).
- Fluid retention or ascites associated with liver disease.
- Hypertension.
- Hypertensive crisis (as a supportive measure).
- Support of forced diuresis.
- As an adjunct in acute pulmonary oedema.
- Support measures in cerebral oedema.

4.2 Posology and method of administration

The dose used must be the lowest that is sufficient to achieve the desired effect.

LASIX is given intravenously only when oral administration is not feasible or is ineffective or if a rapid effect is required. If intravenous therapy is used, it is recommended that transfer to oral therapy be carried out as soon as possible.

To achieve optimum efficacy and suppress counter-regulation, a continuous furosemide infusion is generally to be preferred to repeated bolus injections. Where continuous furosemide infusion is not feasible for follow-up treatment after one or several acute bolus doses, a follow-up regimen with low doses given at short intervals (approximately 4 hours) is to be preferred to a regimen with higher bolus doses at longer intervals.

In adults, the recommended maximum daily dose of LASIX for both oral and intravenous administration is 1 500 mg.

The duration of treatment depends on the indication and is determined on an individual basis by the doctor or other health care provider.

Adults:

The usual oral dose of LASIX is 20 mg to 80 mg per day given as a single dose, preferably in the morning. This dose may, however, be increased depending on the response of the patient. Six hours after a 40 mg dose, 80 mg may be administered and, if necessary, after another six hours, 120 mg.

After oedema is controlled, maintenance therapy is continued at 20 mg to 40 mg daily.

Daily dose exceeding 120 mg should preferably be distributed over two to three individual doses.

For the treatment of hypertension of mild to moderate degree, a daily dosage of 40 mg to 80 mg is taken orally. In combination with other hypotensive medicines, lower doses will often suffice.

Intravenous and intramuscular administration of LASIX is indicated in all cases where intestinal absorption is impaired or prompt diuresis required.

The rapid and powerful effect produced by intravenous injection may result in a transitory fall in plasma volume.

Pulmonary oedema:

The initial dose is 40 mg intravenously. If necessary, the injection may be repeated after approximately 20 minutes.

Forced diuresis (e.g. management of barbiturate poisoning):

20 mg to 40 mg LASIX is given in addition to infusion of electrolyte solution. Further treatment depends on the elimination of urine and must include substitution of the fluid and electrolyte losses.

In poisoning with acid or basic substances the elimination rate can be further increased by alkalisation or acidification of the urine, respectively.

Infants and children under 15 years:

Children generally receive an oral dose of 2 mg/kg body mass per day in divided doses up to a maximum daily dose of 40 mg.
This may be titrated to a maximum of 6 mg/kg/day.

Parenteral administration (if necessary, continuous drip infusion) is indicated only in life-threatening conditions. In this case, infants/children receive parenteral doses of 1 mg/kg body mass per day up to a maximum of 20 mg per day.

Method of administration:

Oral formulations: It is recommended that LASIX be taken on an empty stomach. Tablets are to be swallowed whole without chewing and with sufficient amounts of liquid.

Intravenous injection/infusion: Intravenous LASIX must be injected or infused slowly; a rate of 4 mg per minute must not be exceeded. In patients with severe impairment of renal function (serum creatinine > 5 mg/dL), it is recommended that an infusion rate of 2,5 mg per minute is not exceeded.

Intramuscular injection: Intramuscular administration must be restricted to exceptional cases where either oral or intravenous administration is not feasible. It must be noted that intramuscular injection is not suitable for the treatment of acute conditions such as pulmonary oedema.

During long-term treatment, serum creatinine, urea and also electrolytes, in particular potassium, calcium, chloride and bicarbonate, should be regularly checked.

The medicine may precipitate at pH values below 7.

4.3 Contraindications

LASIX is contraindicated:

- in patients with hypersensitivity to furosemide or any of the excipients of LASIX (see section 6.1). Patients allergic to sulfonamides may show cross-sensitivity to furosemide,
- in patients with hypovolaemia or dehydration,
- in patients with anuric renal failure,
- in patients with severe hypokalaemia,
- in patients with severe hyponatraemia,
- in patients with pre-comatose and comatose states associated with hepatic encephalopathy,
- in breastfeeding women,
- if increasing uraemia and oliguria occur during treatment of severe progressive renal disease.

4.4 Special warnings and precautions for use

Urinary outflow must be secured. In patients with a partial obstruction of urinary outflow, increased production of urine may provoke or aggravate complaints. Thus, these patients require careful monitoring. Treatment with LASIX necessitates regular medical supervision.

Particularly careful monitoring is necessary:

- in patients with hypotension,
- in patients who would be at particular risk from a pronounced fall in blood pressure,
- in patients with latent or manifest diabetes mellitus,
- in patients with gout,
- in patients with hepatorenal syndrome,
- in patients with hypoproteinaemia (cautious dose titration is required),
- in premature infants (renal function must be monitored and renal ultrasonography performed).

Regular monitoring of serum sodium, potassium and creatinine is recommended during furosemide therapy; particularly close monitoring is required in patients at high risk of developing electrolyte imbalances or in case of significant additional fluid loss due to vomiting, diarrhoea or intense sweating. Hypovolaemia or dehydration as well as any significant electrolyte and acid-base disturbances must be corrected.

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 when compared to patients treated with risperidone alone. Caution should be exercised and the risks and benefits of this combination or co-treatment should be considered prior to the decision to use. Dehydration should be avoided.

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

Information on excipients

LASIX tablets:

Lactose monohydrate

LASIX tablets contain lactose monohydrate. Patients with the rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take LASIX tablets.

LASIX 2 mL:

Sodium

LASIX 2 mL contains less than 1 mmol sodium (23 mg) per 2 mL, that is to say essentially ‘sodium free’.

LASIX ORAL SOLUTION:

Alcohol (ethanol)

LASIX ORAL SOLUTION contains 96 mg of alcohol (ethanol) in each 1 mL which is equivalent to 9,6 % *w/v*. The amount in 1 mL of this medicine is equivalent to less than 2,4 mL beer or 0,96 mL wine.

The small amount of alcohol in this medicine will not have any noticeable effects.

Sorbitol

LASIX ORAL SOLUTION contains sorbitol.

The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should
be taken into account. The content of sorbitol in medicines for oral use may affect the bioavailability of other medicines for oral use administered
concomitantly.

Patients with hereditary fructose intolerance (HFI) should not take/be
given LASIX ORAL SOLUTION.

Sorbitol may cause gastrointestinal discomfort and mild laxative effect.

Preservatives and azo colourants

LASIX ORAL SOLUTION contains methylparaben and propylparaben as preservatives, as well as Sunset Yellow FCF as a colourant, which may cause allergic reactions (possibly delayed).

Sodium

LASIX ORAL SOLUTION contains less than 1 mmol sodium (23 mg) per mL, that is to say essentially ‘sodium free’.

4.5 Interaction with other medicines and other forms of interaction

- Intravenous administration of LASIX within 24 hours of taking chloral hydrate may lead to flushing, sweating attacks, restlessness, nausea, increase in blood pressure and tachycardia. Use of LASIX concomitantly with chloral hydrate is, therefore, not recommended.
- LASIX may potentiate the ototoxicity of aminoglycosides and other ototoxic medicines. Since this may lead to irreversible damage these medicines must only be used with LASIX if there are compelling medical reasons.
- There is a risk of ototoxic effects if cisplatin and furosemide are given concomitantly. In addition, nephrotoxicity of cisplatin may be enhanced by a high dose of LASIX. LASIX should be given in low doses and with positive fluid balance when used to achieve forced diuresis during cisplatin treatment.
- Oral LASIX and sucralfate must not be taken within 2 hours of each other because sucralfate decreases the absorption of LASIX from the intestine and so reduces its effect.
- LASIX decreases the excretion of lithium salts and may cause increased risk of lithium toxicity, including increased risk of cardiotoxic and neurotoxic effects of lithium. It is recommended that lithium levels are carefully monitored in patients receiving this combination.
- Patients who are receiving diuretics, such as LASIX, may suffer severe hypotension and deterioration in renal function, including renal failure, especially when an angiotensin-converting enzyme inhibitor (ACE) or angiotensin II receptor antagonist is given for the first time or for the first time in an increased dose. Consideration must be given to interrupting the administration of LASIX temporarily or at least reducing the dose of LASIX for three days before starting treatment with, or increasing the dose of, an ACE inhibitor or angiotensin II receptor antagonist.

- Risperidone: Caution should be exercised and the risks and benefits of the combination or co-treatment with LASIX should be considered prior to the decision to use (see section 4.4).
- Concomitant administration of nonsteroidal anti-inflammatory drugs (NSAIDs) including aspirin (acetylsalicylic acid) may reduce the effect of LASIX. In patients with dehydration or hypovolaemia, NSAIDs may cause acute renal failure. Salicylate toxicity may be increased by LASIX.
- Attenuation of the effect of LASIX may occur following concurrent administration of phenytoin.
- Aliskiren reduces plasma concentration of furosemide given orally. In patients treated with both aliskiren and oral LASIX, it is recommended to monitor for reduced diuretic effect and adjust the dose accordingly.
- Corticosteroids, carbenoxolone, liquorice in large amounts, and prolonged use of laxatives may increase the risk of developing hypokalaemia.
- Some electrolyte disturbances (e.g. hypokalaemia, hypomagnesaemia) may increase the toxicity of certain other medicines (e.g. digoxin and medicines inducing QT interval prolongation syndrome).
- If antihypertensive medicines, diuretics or other medicines with blood pressure-lowering potential are given concomitantly with LASIX, a more pronounced fall in blood pressure must be anticipated.
- Probenecid, methotrexate and other medicines which, like LASIX, undergo significant renal tubular secretion may reduce the effect of LASIX.
- The effects of antidiabetic medicines and blood pressure-increasing sympathomimetics may be reduced. The effects of curare-type muscle relaxants or of theophylline may be increased.
- Impairment of renal function may develop in patients receiving concurrent treatment with LASIX and high doses of certain cephalosporins.
- Concomitant use of ciclosporin and LASIX is associated with increased risk of gouty arthritis secondary to LASIX-induced hyperuricaemia and ciclosporin impairment of renal urate excretion.
- Patients who were at high risk for radiocontrast nephropathy treated with LASIX 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.

- The harmful effects of nephrotoxic medicines on the kidney may be increased.
- When digoxin is administered concurrently it should be remembered that potassium deficiency increases the sensitivity of the myocardium to digoxin.
- Levothyroxine: LASIX 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 hormone levels. Thyroid levels should be monitored.

4.6 Fertility, pregnancy and lactation

Furosemide crosses the placental barrier.

Pregnancy

LASIX must not be given during pregnancy. Treatment during pregnancy requires monitoring of foetal growth.

Breastfeeding

Furosemide passes into breast milk and may inhibit lactation. Women must not breastfeed their infant while they are treated with LASIX.

4.7 Effects on ability to drive and use machines

Taking LASIX may inhibit the patient's ability to concentrate, drive or operate machinery (see section 4.8). Caution is advised before driving a vehicle or operating machinery until the effects of LASIX are known.

4.8 Undesirable effects

Blood and lymphatic system disorders:

Frequent: haemoconcentration

Less frequent: thrombocytopenia, leukopenia, agranulocytosis, aplastic or haemolytic anaemia, eosinophilia

Frequency unknown: blood coagulation disorders

Immune system disorders:

Less frequent: severe anaphylactic or anaphylactoid reactions (e.g. shock)

Frequency unknown: exacerbation or activation of systemic lupus erythematosus

Metabolism and nutrition disorders:

Frequent: symptomatic electrolyte disturbances, dehydration, hypovolaemia, blood creatinine increased, increase in cholesterol and triglyceride serum levels, increase in uric acid serum levels and attacks of gout. Hyponatraemia, hypochloraemia, hypokalaemia

Less frequent: impaired glucose tolerance, dryness of mouth, diabetes mellitus (latent becoming manifest; and aggravation of manifest)

Frequency unknown: hypocalcaemia, hypomagnesaemia, increased blood urea, metabolic alkalosis, pseudo-Bartter's syndrome

Nervous system disorders:

Frequent: hepatic encephalopathy in patients with hepatocellular insufficiency

Less frequent: paraesthesia

Frequency unknown: dizziness, fainting or loss of consciousness, headache

Ear and labyrinth disorders:

Less frequent: hearing disorders, tinnitus, deafness, sometimes irreversible

Vascular disorders:

Frequent: hypotension including orthostatic hypotension

Less frequent: vasculitis

Frequency unknown: tendency for thromboses, circulatory collapse, circulatory disorders (vertigo, feeling pressure in head, visual impairment), embolism

Gastrointestinal disorders:

Less frequent: nausea, vomiting, diarrhoea, acute pancreatitis

Hepatobiliary disorders:

Less frequent: intrahepatic cholestasis, increase in liver transaminases

Skin and subcutaneous tissue disorders:

Less frequent: pruritus, urticaria, other rashes or bullous lesions; erythema multiforme, bullous pemphigoid, photosensitivity, purpura

Frequency unknown: Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis, vesicular cutaneous eruptions, AGEP (acute generalised exanthematous pustulosis) and DRESS (drug rash with eosinophilia and systemic symptoms), lichenoid reactions

Musculoskeletal, connective tissue and bone disorders:

Frequency unknown: tetany, cases of rhabdomyolysis often in the context of hypokalaemia

Renal and urinary disorders:

Frequent: increased urine volume

Less frequent: tubulointerstitial nephritis

Frequency unknown: acute retention of urine in patients with a partial obstruction of urinary outflow, nephrocalcinosis/nephrolithiasis in premature infants, renal failure, increased urine sodium, increased urine chloride

Congenital familial and genetic disorders:

Frequency unknown: increased risk of persistence of patent ductus arteriosus when furosemide is administered to premature infants during the first weeks of life

General disorders and administration site conditions:

Less frequent: fever

Frequency unknown: following intramuscular infection, local reactions such as pain.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of LASIX is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse reactions to:

- The Pharmacovigilance Unit at Sanofi: za.drugsafety@sanofi.com (email), https://ae.reporting.sanofi/ (web portal) or +27 11 256 3700 (tel), or
- SAHPRA via the Med Safety App (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA's website.

4.9 Overdose

The clinical picture in acute or chronic overdose depends primarily on the extent and consequences of electrolyte and fluid loss, e.g. hypovolaemia, dehydration, haemoconcentration, cardiac dysrhythmias (including AV-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 oral ingestion has taken place, attempts may be made to limit further systemic absorption of furosemide by measures such as 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 may necessitate general and specific intensive medical monitoring and therapeutic measures.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 18.1 Diuretics

Pharmacotherapeutic group: High-ceiling diuretics, sulfonamides, plain

ATC code: C03CA01

Furosemide inhibits reabsorption of sodium and water predominantly in the ascending loop of Henle but also in the proximal tubule. Diuretic activity following a single oral dose usually commences after half an hour, gradually increases and reaches a peak in 2 hours and tapers off during the next four to five hours. With parenteral administration, the onset is more rapid.

LASIX lowers pathologically raised blood pressure.

5.2 Pharmacokinetic properties

Absorption

Furosemide is rapidly absorbed from the gastrointestinal tract; bioavailability has been reported to be about 60 to 70 % but absorption is variable and erratic.

Distribution and elimination

The half-life of furosemide is up to about 2 hours although it is prolonged in neonates and in patients with renal and hepatic impairment. Furosemide is up to 99 % bound to plasma albumin, and is mainly excreted in the urine, largely unchanged. There is also some excretion via the bile and non-renal elimination is considerably increased in renal impairment. The clearance of furosemide is not increased by haemodialysis.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

LASIX 20 mg, 40 mg and 80 mg tablets:

Colloidal silicon dioxide

Lactose monohydrate

Magnesium stearate

Maize starch

Talc (E 553b).

LASIX 2 mL ampoule:

Sodium chloride

Sodium hydroxide (for pH adjustment)

Water for injection.

LASIX ORAL SOLUTION:

Alcohol 9,6 % *m/v*

Glycerol

Methylparaben 0,25 % *m/v* (preservative) (E 218)

Natural orange flavour

Propylparaben 0,05 % *m/v* (preservative) (E 216)

Quinoline Yellow (colourant) (E 104)

Sodium hydroxide

Sorbitol solution

Sunset Yellow (colourant) (E 110).

6.2 Incompatibilities

LASIX 2 mL, being an anthranilic acid derivative, dissolves in alkaline media with salt formation. The solution for parenteral application contains the sodium salt of the carboxylic acid without a solubiliser. The solution has a pH of about 9 but no buffer capacity, which means that the medicine may precipitate at pH values below 7.

LASIX 2 mL must not be mixed with other medicines in the same injection syringe.

6.3 Shelf life

LASIX 20 mg, 40 mg and 80 mg tablets in amber glass bottles: 24 months.

LASIX 40 mg blister pack: 36 months.

LASIX 2 mL: 36 months.

If the ready-to-use solution has a pH ranging from weakly alkaline to neutral, the mixture may be used for up to 24 hours (see section 6.6).

LASIX ORAL SOLUTION: 24 months.

Once opened, the contents of the bottle remain stable for a period of 60 days under refrigerated conditions.

6.4 Special precautions for storage

LASIX 20 mg, 40 mg and 80 mg tablets in amber glass bottles:

Store at or below 25 °C and protect from light.

Exposure to light may produce a yellowish discolouration.

LASIX 40 mg tablets in blister strips: Store at or below 30 °C and protect from light.

LASIX 2 mL:

Store at or below 25 °C and protect from light.

For storage conditions after dilution, see section 6.3.

LASIX ORAL SOLUTION:

Store between 2 °C and 8 °C in a refrigerator.

Do not freeze.

Protect from light.

6.5 Nature and contents of container

LASIX 20 mg: Amber glass bottle with a white screw cap, containing 30 tablets.

LASIX 40 mg: Amber glass bottle with a white screw cap, containing 30 tablets or 250 tablets.

Bottle-green PVC/aluminium blisters strips containing 15 tablets each and packed in an outer carton.

Pack size of 30 tablets.

LASIX 80 mg: Amber glass bottle with a white screw cap, containing 30 tablets or 100 tablets.

LASIX 2 mL: 2 mL amber glass ampoules with a one-point cut (OPC) break system, placed in an outer carton.

Pack size of 5 ampoules.

LASIX ORAL SOLUTION: 100 mL amber glass bottles with a screw cap.

6.6 Special precautions for disposal and other handling

LASIX ORAL SOLUTION: Dispense in light-resistant containers.

7. HOLDER OF CERTIFICATE OF REGISTRATION

sanofi-aventis south africa (pty) ltd

Hertford Office Park, Building I, 5th Floor

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8. REGISTRATION NUMBERS

LASIX 20 mg: E/18.1/201

LASIX 40 mg: E/18.1/202

LASIX 80 mg: V/18.1/9

LASIX 2 mL: H 1777 (Act 101/1965)

LASIX ORAL SOLUTION: N/18.1/6

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

LASIX 20 mg: 18/06/1973

LASIX 40 mg: 18/06/1973

LASIX 80 mg: 21/11/1988

LASIX 2 mL: Act 101/1965

LASIX ORAL SOLUTION: 24/10/1980

10. DATE OF REVISION OF THE TEXT

18 March 2025

Namibia:

Scheduling status: NS2

Reg. no.:

Lasix 20 mg: 90/18.1/00315

Lasix 40 mg: 90/18.1/00316

Lasix 80 mg: 90/18.1/00318

Lasix ORAL SOLUTION: 90/18.1/00319

Lasix ampoules 10 mg/mL: 14/18.1/0352

Botswana:

Scheduling status: S2

Reg. no.:

Lasix 20 mg: B9315570

Lasix 40 mg: B9315575

Lasix 80 mg: B9315580

Lasix ORAL SOLUTION: B9315595

Lasix ampoules 10 mg/mL: B9315600