SUMMARY OF PRODUCT CHARACTERISTICS

FUROSEMIDE S.A.L.F 250 MG/25 ML

Composition

Each 25-ml vial contains 250 mg of furosemide solution for infusion at a concentration of 10 mg/ml.

Excipients: sodium hydroxide and water for injections.

Important information about some of the ingredients:

Each vial of Furosemide S.A.L.F. 250 MG/25 ML contains about 0.75 mmol (17.3 mg) of sodium; the maximum daily dose (7 vials) contains approximately 5.25 mmol of sodium (121.1 mg).
Consider this information for administration to patients with impaired renal function or patients on a controlled sodium diet.

Pharmacological classification

Diuretics

Pharmacological action

FUROSEMIDE S.A.L.F 250 MG/25 ML is a high-ceiling diuretic that belongs to the sulfonamide group, acting primarily by inhibiting electrolyte re-absorption in the thick ascending limb of the loop of Henle, as well as in the proximal tubule. It is approximately 98% protein bound, has a half life of about 92 minutes and is short, but rapid acting. It is excreted mainly by the kidneys and, to a much lesser extent, by the liver or in the feces.

Indications

Furosemide is a potent diuretic indicated for use when a prompt and effective diuresis is required. Furosemide is appropriate for use in emergencies or where oral therapy is not feasible. The indications include cardiac, pulmonary, hepatic and renal oedema.

Contraindications

- Hypersensitivity to furosemide or sulphonamides (cross-sensitivity exists between sulphonamides and furosemide).

- Pregnancy and lactation.

- FUROSEMIDE S.A.L.F 250 MG/25 ML should not be given in anuria or in renal failure due to nephrotoxic or hepatotoxic drugs nor in renal failure associated with hepatic coma. FUROSEMIDE S.A.L.F 250 MG/25 ML should not be given to patients with Addison's disease or pre-existing hypercalcaemia.

Warnings and precautions

Fluid balance should be carefully monitored. Furosemide may cause profound diuresis, resulting in fluid and electrolyte depletion. Serum electrolytes (especially sodium, potassium, chloride and bicarbonate) should be determined, and abnormalities corrected or the drug withdrawn. If increasing azotemia and oliguria occur during the treatment of progressive renal disease, the drug should be discontinued.

Except as a single trial dose in acute anuria in the absence of obstruction, FUROSEMIDE S.A.L.F 250 MG/25 ML should be avoided in anuric patients.

Caution should be exercised in patients with impaired hepatic function or renal impairment. Sudden alteration of fluid and electrolyte balance in patients with cirrhosis may precipitate hepatic coma, therefore strict observation is necessary during the period of diuresis.

Patients should be regularly observed for the possible occurrence of blood dyscrasias, liver damage or other idiosyncratic reactions.

Periodic checks on urine and blood glucose should be made in diabetics and those suspected of latent diabetes when receiving furosemide. Increase in blood glucose and alterations in glucose tolerance test, with abnormalities of the fasting and 2-hour post-prandial sugar have been observed and rare cases of precipitation of diabetes mellitus have been reported.

Furosemide may lower serum calcium levels and rare cases of tetany have been reported. Accordingly, calcium should be determined periodically.

Patients with prostatic hypertrophy or impaired micturition have an increased risk of developing acute retention. Care is advised when prescribing Furosemide to patients with either gout or porphyria.

Interaction with other medicinal products and other forms of interaction

Furosemide -induced hypokalaemia may induce potentially fatal cardiac arrhythmias during treatment with cardiac glycosides or drugs that prolong the QT interval. Furosemide may increase the ototoxicity of aminoglycoside antibiotics.
Furosemide may enhance the nephrotoxicity of cephalosporins.
Due to diuretic-induced sodium depletion, renal clearance of lithium is reduced, which may result in increased lithium concentrations leading to lithium toxicity.
Fluid retention caused by steroids may potentially antagonise the diuretic effect but potentiate the potassium loss.
In oedematous hypertensive patients being treated with antihypertensive agents, care should be taken to reduce the dose of these drugs since furosemide potentiates the hypotensive effect.

Severe hypotension and/or renal failure may occur if treatment with angiotensin-converting enzyme-inhibitors is initiated while patients are receiving high doses of loop diuretics. The dose of furosemide should be reduced and severe salt and water depletion corrected before starting the ACE-inhibitor.

Sulphonamide diuretics have been reported to decrease arterial responsiveness to pressor amines and to enhance the effect of tubocurarine. Great caution should be exercised in administering curare or its derivatives to patients undergoing therapy with furosemide and it is advisable to discontinue furosemide two days before elective surgery.

Non-steroidal anti-inflammatory drugs may partially antagonise the action of furosemide. Because of competition for renal excretion, patients receiving high doses of salicylates together with furosemide may experience salicylate toxicity.

The following drugs have been reported to result in a disturbance in the electrolyte balance if given concurrently with furosemide: hormone antagonists, sympathetomimetics, carbamazepine, ulcer healing drugs
e.g. carbenoxolone and metalozone.

Estrogens, antiepileptics, probenicid and lipid lowering resins may result in reduction in the diuretic effects of furosemide if administered concurrently.

Flushing, tachycardia, elevated blood pressure and severe diaphoresis have been seen in patients receiving intravenous furosemide having taken oral chloral hydrate in the preceding 24 hours.

Concurrent administration of furosemide and clofibrate may result in marked diuresis and muscle symptoms in patients with marked nephrotic syndrome.

The muscle relaxants baclofen and tizanidine may increase the hypotensive effect of furosemide. Furosemide may enhance the hyperglycaemic action of diazoxide.

Pregnancy and lactation

Animal teratology studies indicate that furosemide may cause fetal abnormalities. Therefore, furosemide should only be used in women of child-bearing age when appropriate contraceptive measures are taken or if the potential benefits justify the potential risks to the fetus.

Furosemide is excreted in breast milk and breast-feeding should be discontinued if treatment is essential.

Effects on ability to drive and use machines

Furosemide may reduce mental alertness. Patients should be warned not to drive or operate machinery if affected.

Dosage and directions for use

Duration of the treatment will depend on usage and is determined by the doctor for each individual.

For adults, the maximum recommended dose is 1,500 mg daily, although it may reach 2,000 mg in exceptional cases.

For children, the maximum recommended daily dose of FUROSEMIDE S.A.L.F 250 MG/25 ML for parenteral administration is 1 mg of furosemide per each kilogram of body weight, up to a maximum of 20 mg.

Treatment is to be switched to the oral route as soon as possible. FUROSEMIDE S.A.L.F 250 MG/25 ML should be injected or infused slowly by intravenous route, at a rate not exceeding 4 mg per minute. In patients with severe kidney problems (serum creatinine >5 mg/dl), it is recommended that the rate of infusion does not exceed 2.5 mg per minute.It should not be administered in the form of intravenous bolus. It should be infused using only infusion pumps that control volume or speed in order to avoid a possible risk of accidental overdose.

Furosemide, as an anthranilic acid derivative, dissolves in an alkaline environment with salt formation. The solution has a pH of about 9 and does not have a buffering effect; below pH 7 the active ingredient precipitates. Therefore, you should consider that Furosemide S.A.L.F. 250MG/25ML can be mixed with alkaline, neutral or weakly acidic solutions with a modest buffering capacity (Ringer lactate, glucose solution).
The diluted solutions should be used immediately after preparation.
Acidic solutions, especially those with a high buffering capacity, can not be mixed with Furosemide S.A.L.F. 250MG/25ML. However, Furosemide S.A.L.F. 250MG/25ML should not be combined with other drugs in the same syringe.

It is recommended that the ready-to-use solution be administered as soon as possible.

Use in children:

Parenteral administration is contraindicated for infants and children under the age of 15; this may be carried out only in cases involving a threat to life.

Possible Adverse Effects

As with all medicines, FUROSEMIDE S.A.L.F 250 MG/25 may have adverse effects. Like other diuretics, the prolonged administration of this medicament may increase the elimination of sodium (hyponatremia), chloride (hypochloremic alkalosis) and of water as a result of this. It may also increase the loss of potassium (hypopotassemia), calcium and magnesium. Such alterations present themselves with intense thirst, headaches, confusion, muscle cramps, painful muscular contractions especially in the limbs (tetany), muscle weakness, alterations in the cardiac rhythm, and gastrointestinal symptoms.

In older patients in particular,FUROSEMIDE S.A.L.F 250 MG/25 may result or contribute to the occurrence of a reduction in total blood volume, dehydration, and coagulation alterations (thrombosis). FUROSEMIDE S.A.L.F 250 MG/25 may cause or aggravate discomfort in patients with difficulties to urinate; In addition, acute urinary retention may occur and cause possible secondary complications.

On rare occasions, cases of kidney problems that might result from an allergy-type renal reaction (interstitial nephritis) have been reported.

Treatment with FUROSEMIDE S.A.L.F 250 MG/25 may allow for a temporary rise in the levels of urea and creatinine in the blood, and to an increase in the serum levels of cholesterol, triglycerides and uric acid, and it may result in gout attacks.

Occasionally, the number of platelets may be excessively reduced (thrombocytopenia). In rare cases, leukopenia (reduction of white blood cells), eosinophilia (increase of one type of white blood cells, the eosinophils), or fever may occur; in isolated cases, agranulocytosis (diminution of one type of white blood cells, the granulocytes) and reduction in the number of red or white cells (aplastic anemia or hemolytic anemia) may appear.

FUROSEMIDE S.A.L.F 250 MG/25ML may reduce tolerance to glucose. In patients with diabetes mellitus a deterioration of metabolic control can be observed and latent diabetes mellitus may become manifest. A decrease in arterial pressure can occur. If severe, it can cause deterioration in the capacity to concentrate and react, slight clouding, a sense of pressure on the head, headaches, dizziness, drowsiness, weakness, vision disorders, dryness of the mouth and inability to keep a straight posture (orthostatic intolerance). Cases of allergic inflammation of blood vessels (vasculitis) have been described on rare occasions.

Skin and mucous reactions, for example, itches, rashes, blisters, as well as other, more serious reactions, such as erythema multiforme, exfoliative dermatitis, purpura, and allergic reaction to the sun (photosensitivity), can occur occasionally. On rare occasions, serious allergy-type (anaphylactic or anaphylactoid) reactions can occur.

A sensation of tingling in the limbs (paresthesia) can occur rarely. On rare occasions, hearing problems and a reversible, subjective tinkling sensation (tinnitus) can occur in patients with severe kidney problems, reduced levels of protein in the blood (hypoproteinemia), and/or after a too-quick intravenous administration of furosemide.

Acute diuresis in male patients with prostatic obstruction may cause acute retention of urine.

Digestive disorders, such as nausea, vomiting, or diarrhea, can occur rarely. Liver problems, such as intrahepatic cholestasis, increase in hepatic enzymes, or inflammation of the pancreas (acute pancreatitis) can occur in isolated cases. In premature infants, furosemide can result in the formation of kidney stones (nephrocalcinosis/nephrolithiasis) that can increase the risks in a serious clinical picture (patent ductus arteriosus).

In children, complaints of mild to moderate abdominal pain and cramping have been reported after intravenous furosemide. Nephrocalcaemia has been reported in premature infants.

Asymptomatic hyperuricaemia can occur and rarely gout may be precipitated. These are associated with dehydration which should be avoided particularly in patients with renal insufficiency.

Known symptoms of overdose and particulars of its treatment

Symptoms: Overdose with furosemide may lead to excessive loss of water and electrolytes. Severe potassium loss may cause serious cardiac arrhythmias.

Treatment: Restoration of fluid and electrolytes balance by administration of sodium chloride and water, intravenously if necessary.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il.

Pharmacological Properties

Pharmacodynamic properties:

Furosemide is a short-acting sulphonamide diuretic, chemically similar to the thiazides. With parenteral administration, the diuretic effect is immediate and lasts approximately two hours. Furosemide primarily inhibits the reabsorption of sodium in the proximal and distal tubules as well as in the Loop of Henle, thus increasing the urinary excretion of sodium, chloride and water. Urinary excretion of potassium, calcium and magnesium are also increased, together with bicarbonate; urinary pH rises.

Pharmacokinetic properties:

Furosemide is 91% to 99% bound to serum albumin but protein binding is reduced in patients with uraemia and nephrosis. The plasma half life ranges from 45 to 60 minutes. Furosemide crosses the placenta and enters breast milk. It is eliminated by renal excretion of unchanged drug, metabolism to a glucuronide conjugate and faecal excretion.

Preclinical safety data:

Toxicity studies in animals have not demonstrated toxic effects relevant to clinical use. There is no evidence of mutagenic or carcinogenic potential.

Incompatibilities:

Furosemide, as an anthranilic acid derivative, dissolves in an alkaline environment with salt formation. The solution has a pH of about 9 and does not have a buffering effect; below pH 7 the active ingredient precipitates. Therefore, you should consider that Furosemide S.A.L.F. 250MG/25ML can be mixed with alkaline, neutral or weakly acidic solutions with a modest buffering capacity (Ringer lactate, glucose solution).

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Presentation

Clear and colorless or slightly colorless solution for infusion in 25 ml glass vial.

Pack

Boxes containing 5 vials of 25 ml.

Storage Instructions

Store below 25°C. Store in its original package tightly closed, In order to protect it from light.

Shelf life

The expiry date of the product is indicated on the packaging materials.

Registration Number

166-77-35843-00

Manufacturer

S.A.L.F. S.p.A. Laboratorio Farmacologico - Cenate Sotto (Bergamo), Italy.

Marketing Authorization Holder

RAZ PHARMACEUTICS LTD.,
6 Hamatechet st., Kadima, Israel.

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