LASIX® 20 mg

Furosemide, Solution for injection
Administration in ampoules
sanofi aventis

COMPOSITION

Active substance: furosemide
Each ampoule of 2ml contains 21.3mg furosemide sodium, equivalent to 20mg furosemide.
Excipients: Sodium hydroxide, sodium chloride, water for injections.

PROPERTIES

Furosemide is a loop diuretic which increases urine excretion.

THERAPEUTIC INDICATIONS

- Oedema due to cardiac and hepatic diseases (ascites).
- Oedema due to renal disease (in the nephrotic syndrome, therapy of the underlying diseases has precedence).
- Acute cardiac insufficiency, especially in pulmonary oedema (administration in conjunction with other therapeutic measures).
- Reduced urinary output due to gestoses (pregnancy-related nephrosis), after restoring the fluid volume to normal.
- Supportive measures in brain oedema.
- Oedema due to burns.
- Hypertensive crisis (in addition to other antihypertensive measures).
- To support forced diuresis in poisoning.

DOSAGE AND ADMINISTRATION

Strictly follow the recommended dosage unless directed otherwise by the physician.

DOSAGE

The duration of treatment is determined by the physician and will depend on the nature and severity of illness. A change from parenteral to oral administration should be carried out as soon as possible.
In general, the dose used must be the lowest which is sufficient to achieve the desired effect.

- Unless otherwise prescribed, the initial dose for adults and adolescents of 15 years or over is 20 to 40mg LASIX (1-2 ampoules) intravenously or, in exceptional cases, intramuscularly (see "ADMINISTRATION").
  If after a single dose of 20 to 40mg LASIX (1-2 ampoules) the diuretic effect is not satisfactory, the dose may be increased stepwise by 20 mg (1 ampoule), at two-hourly intervals, until a satisfactory effect is obtained. The individual dose thus established should then be given once or twice daily.
- Acute pulmonary oedema
  An initial dose of 40mg LASIX (2 ampoules) is administered intravenously. If the patient's condition requires it, a further dose of 20-40mg LASIX (1-2 ampoules) is injected after 20 minutes.
- Forced dieresis
  20-40mg LASIX (1-2 ampoules) 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 alkalization or acidification, respectively, of the urine.
- Infants and children under 15 years
  In principle, LASIX should be administered orally.
  Parenteral administration (if necessary, continuous drip infusion) is indicated only in life-threatening conditions. The dosage schedule is 1mg furosemide per kg body weight up to a daily maximum of 20mg LASIX (1 ampoule).

ADMINISTRATION

Intravenous administration of LASIX 20mg is indicated in all cases where oral administration is either not feasible or is ineffective (e.g., in impaired intestinal absorption), or where a rapid effect is necessary. Intravenous injection of LASIX 20mg should be given slowly, not exceeding an injection rate of 4mg per minute. In patients with severe impairment of renal function (serum creatinine > 5mg/dl), the infusion rate should not exceed 2.5mg/min.
Intramuscular administration must be restricted to exceptional cases where neither oral nor intravenous administration is feasible. Intramuscular injection is not suitable for the treatment of acute conditions such as pulmonary oedema.
LASIX 20mg injection solution has a pH of about 9; it has no buffering capacity. For this reason, the active ingredient may precipitate at pH values below 7. Therefore, if LASIX 20mg is diluted, care must be taken to ensure that the pH of the solution is within the slightly alkaline to neutral range. Normal saline is suitable as diluents. Diluted solutions should be used as soon as possible. LASIX 20mg must not be mixed with other drugs in the same syringe.

CONTRAINDICATIONS

LASIX 20mg must not be used in case of:

- renal failure accompanied by lack of urine formation (anuria),
- hepatic coma and precoma,
- 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 (allergy) 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,
- breast feeding (see " PREGNANCY AND LACTATION").

WARNINGS AND PRECAUTIONS

- Urinary outflow must be secured.
  In patients with a partial obstruction of urinary outflow (e.g. in patients with bladder-emptying disorders, prostatic hyperplasia, narrowing of the urethra or hydronephrosis), increased product of urine may provoke or aggravate complaints.
  Thus, these patients require careful monitoring – especially during the initial stages of treatment.
- 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, e.g. patients with significant stenoses of the coronary arteries or of the blood vessels supplying the brain.
  - in patients with latent or manifest diabetes mellitus. (regular blood sugar checks)
  - in patients with gout. (regular uric acid checks)
  - in patients with hepatorenal syndrome, i.e. functional renal failure associated with severe liver disease.
  - in patients with hypoproteinaemia, e.g. associated with nephrotic syndrome (the effect of furosemide may be weakened and its ototoxicity potentiated). Cautious dose titration is required.
  - in premature infants (possible development nephrocalcinosis/nephrolithiasis; renal function must be monitored and renal ultrasonography performed).
- Regular monitoring of serum sodium, potassium, and creatinine is generally recommended during furosemide therapy; particularly closed monitoring is required in patients at high risk of developing electrolyte imbalances or in case of significant additional fluid loss (e.g. due to vomiting, diarrhoea or intense sweating). Hypovolaemia or dehydration as well as any significant electrolyte and acid-base disturbances must be corrected. This may require temporary discontinuation of furosemide.
- Although administration of Lasix 20mg 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.
- 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.
- Emergency measures to be taken in the event of anaphylactic shock :
  Generally, the following emergency procedure is recommended:
  - At the first signs (sweating, nausea, cyanosis), interrupt the infusion immediately, but leave the venous cannula in place, or perform venous cannulation. In addition to the usual emergency measures,

ensure that the patient remains lying down, with the legs raised and airways patent.
- Emergency drug therapy: Immediately epinephrine (adrenaline) intravenously : In the first instance, slowly inject 1 ml of as solution containing 0.1mg epinephrine per ml while monitoring pulse and blood pressure (watch for disturbances in cardiac rhythm). Repeat as required.
- Then volume substitution intravenously, e.g. plasma expanders, human albumin, balanced electrolyte solution.
- Subsequently glucocorticoids intravenously, e.g. 250-1000mg methyl- prednisolone. Repeat as required. The dosage recommendations refer to adults of normal weight. In children, the reduction of dose should be in relation to body weight.
- Other therapeutic measures, e.g. artificial respiration, oxygen inhalation, antihistaminics.

INTERACTIONS

FOOD

Whether and to what extent the absorption of furosemide is affected by taking it with food seems to depend on the pharmaceutical formulation. It is recommended that oral formulations of LASIX be taken on an empty stomach.

DRUG INTERACTIONS

In order to avoid possible interactions with other medicines, inform your physician or pharmacist about any other current treatment.

Not recommended associations

In isolated cases intravenous administration of furosemide within 24 hours of taking chloral hydrate may lead to flushing, sweating attacks, restlessness, nausea, increase in blood pressure and tachycardia. Use of furosemide concomitantly with chloral hydrate is, therefore, not recommended.

Furosemide may potentiate the ototoxicity of aminoglycosides and other ototoxic drugs. Since this may lead to irreversible damage, these drugs must only be used with furosemide if there are compelling medical reasons.

Precautions for use

- There is a risk of ototoxic effects if cisplatin and furosemide are given concomitantly. In addition, nephrotoxicity of cisplatin may be enhanced if furosemide is not given in low doses (e.g. 40 mg in patients with normal renal function) and with positive fluid balance when used to achieve forced diuresis during cisplatin treatment.
- Furosemide decreases the excretion of lithium salts and may cause increased serum lithium levels, resulting in increased risk of lithium toxicity, including increased risk of cardiotoxic and neurotoxic effects of lithium. Therefore, it is recommended that lithium levels are carefully monitored in patients receiving this combination.
- If antihypertensive agents, diuretics or other drugs with blood-pressure-lowering potential are given concomitantly with furosemide, a more pronounced fall in blood pressure must be anticipated.
- Patients who are receiving diuretics may suffer severe hypotension and deterioration in renal function, including cases of renal failure, especially when an angiotensin converting enzyme inhibitor (ACE inhibitor) 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 furosemide temporarily or at least reducing the dose of furosemide 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 furosemide or with other potent diuretics should be considered prior to the decision to use. (See "WARNINGS AND PRECAUTIONS")
- 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.

Take into account

- Concomitant administration of non-steroidal anti-inflammatory drugs including acetylsalicylic acid may reduce the effect of furosemide. In patients with dehydration or hypovolaemia, non-steroidal anti-inflammatory drugs may cause acute renal failure. Salicylate toxicity may be increased by furosemide.
- Attenuation of the effect of furosemide may occur following concurrent administration of phenytoin.
- 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 drugs (e.g. digitalis preparations and drugs inducing QT interval prolongation syndrome).
- Probenecid, methotrexate and other drugs which, like furosemide, undergo significant renal tubular secretion may reduce the effect of furosemide. Conversely, furosemide may decrease renal elimination of these drugs. In case of high-dose treatment (in particular, of both furosemide and the other drugs), this may lead to increased serum levels and an increased risk of adverse effects due to furosemide or the concomitant medication.
- The effects of antidiabetic drugs and blood-pressure-increasing sympathomimetics (e.g. epinephrine, norepinephrine) may be reduced. The effects of curare-type muscle relaxants or of theophylline may be increased.
- The harmful effects of nephrotoxic drugs on the kidney may be increased.
- 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 hyperuricaemia 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.

PREGNANCY AND LACTATION

PREGNANCY: Furosemide crosses the placental barrier. It must not be given during pregnancy unless there are compelling medical reasons. Treatment during pregnancy requires monitoring of foetal growth.

LACTATION: Furosemide passes into breast milk and may inhibit lactation. Women must not breast-feed if they are treated with furosemide.

DRIVING A VEHICLE OR PERFORMING OTHER HAZARDOUS TASKS

Some adverse effects (e.g. an undesirably pronounced fall in blood pressure) may impair the patient's ability to concentrate and react, and, therefore, constitute a risk in situations where these abilities are of special importance (e.g. operating a vehicle or machinery).

ADVERSE REACTIONS

The frequencies are derived from literature data referring to studies where furosemide is used in a total of 1387 patients,at any dose and in any indication.When the frequency category for the same ADR was different,the highest frequency category was selected.

The following CIOMS frequency rating is used,when applicable:Very common ≧10%; Common ≧1 and ＜10%; Uncommon≧0.1and ＜1%;rare ≧0.01 and ＜ 0.1%; very rare ＜ 0.01%,Unknown(cannot be estimated from available data).

- Metabolism and nutrition disorders(see section " WARNINGS AND PRECAUTIONS")

Very common:
- electrolyte disturbances (including symptomatic)
- dehydration and hypovolaemia especially in elderly patients
- blood creatinine increased, blood triglyceride increased

Common:
- hyponanatremia, hypochloremia, hypokalaemia, blood cholesterol increased blood uric acid increased and attacks of gout,urine volume increased.

Uncommon:
- glucose tolerance imparied. Latent diabetes mellitus may become manifest (see "WARNINGS AND PRECAUTIONS")

Not known:
- hypocalcemia, hypomagnesemia, blood urea increased, metabolic alkalosis.
- Pseudo-Bartter syndrome in the context of misuse and/or long-term use of furosemide.

- Vascular disorders

Very common (for intravenous infusion):
- hypotension including orthostatic hypotension(see section " WARNINGS AND PRECAUTIONS")

Rare:
- vasculitis

Not known:
- thrombosis

- Renal and urinary disorders

Common:
- urine volume increased.

Rare:
- tubulointerstitial nephritis

Not known:

- urine sodium increased,urine chloride increase,urine retention(in patients with a partial obstruction of urinary outflow)(see section " WARNINGS AND PRECAUTIONS")
- nephrocalcinosis/nephrolithiasis in premature infants(see section " WARNINGS AND PRECAUTIONS")
- renal failure(see section "INTERACTIONS")

♦ Gastrointestinal disorders

Uncommon:
- nausea

Rare:
- vomiting, diarrhoea

Very rare:
- pancreatitis acute

♦ Hepato-biliary disorders

Very rare:
- cholestasis, transaminases increased.

♦ Ear and labyrinth disorders

Uncommon:
- hearing disorders , although usually transitory, particularly in patients with renal failure, hypoproteinaemia (e.g. in nephrotic syndrome) and/or when intravenous furosemide has been given too rapidly.
- Cases of deafness, sometimes irreversible have been reported after oral or IV administration of furosemide.

Very rare: tinnitus.

♦ Skin and subcutaneous tissue disorders

Uncommon:
- pruritus urticaria, rashes dermatitis bullous, erythema multiforme, pemphigoid, dermatitis exfoliative, purpura, photosensitivity reaction.

Not known:
- Stevens-Johnson syndrome, toxic epidermal necrolysis, AGEP (acute generalized exanthematous pustulosis)and DRESS (Drug Rash with Eosinophilia and Systemic Symptoms), lichenoid reactions

♦ Immune system disorders

Rare:
- severe anaphylactic or anaphylactoid reactions (e.g. with shock)

Unknown:
- exacerbation or activation of systemic lupus erythematosus

♦ Nervous system disorders

Rare:
- paraesthesia

Common:
- hepatic encephathy in patients with hepatocellular insufficiency(see section " CONTRAINDICATIONS")

Not known:
- dizziness, fainting or loss of consciousness, headache

♦ Blood and the lymphatic system disorders

Common:
- haemoconcentration

Uncommon:
- thrombocytopenia,

Rare:
- leucopenia, eosinophilia

Very rare:
- agranulocytosis, aplastic anaemia or haemolytic anaemia

♦ Musculoskeletal and connective tissue disorders

Not known:
- Cases of rhabdomyolysis have been reported, often in the context of severe hypokalaemia

♦ Congential and familial/genetic disorders

Not known:
- 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

Not known:
- following intramuscular injection,local reactions such as pain.

Rare:
- fever

OVERDOSE

SIGNS AND SYMPTOMS

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 arrhythmias (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.

MANAGEMENT

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.

Storage

Protect from light. Do not store above 30℃.
Keep out of the reach of children.

Expiry date

Do not use later than the date of expiry stated on the outer packaging.

Presentation

Box of 5 ampoules of 2ml. Hospital pack of 20 x 5 ampoules of 2ml.

Manufacturer

Sanofi Winthrop Industrie
6 Boulevard de l'Europe, 21800 Quetigny, France

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