

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Fruside 40 mg Tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 40 mg of furosemide.

Excipients: also contains 63.0mg of lactose monohydrate.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.
White, flat, bevel-edged tablets, engraved with 2B2 on one tablet side and a single breakline on the reverse. The breakline is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Fruside 40 mg Tablets are indicated for the management of fluid retention, oedema of cardiac, hepatic or renal origin, pulmonary oedema and mild or moderate hypertension.

4.2 Posology and method of administration

For oral administration.

Adults

The usual initial dosage is one tablet daily, thereafter adjusted to the minimum effective dose which may range from 1/2 tablet (20 mg) on alternate days to 3 tablets (120 mg) daily.

Children

From 1 to 3 mg/kg body weight daily.

Elderly

In the elderly, elimination of Furosemide is generally slower. Therefore, dosage should be titrated until the required response is achieved.

4.3 Contraindications

Fruside 40mg Tablets are contra-indicated in patients with hypovolaemia or dehydration, anuria or renal failure with anuria not responding to furosemide, renal failure as a result of poisoning by nephrotoxic or hepatotoxic agents or renal failure associated with hepatic coma, severe hypokalaemia, or other electrolyte imbalance (hyponatraemia), pre-comatose and comatose states associated with liver cirrhosis (hepatic encephalopathy), and breast feeding women. Fruside tablets are also contra-indicated in patients with hypersensitivity to Furosemide or sulphonamides or to any of the excipients of Fruside 40 mg tablets.

4.4 Special warnings and precautions for use

Too vigorous diuresis may cause orthostatic hypotension or acute hypotensive episodes. Hence, where indicated, steps should be taken to correct hypotensive or hypovolaemia before commencing therapy.

Patients being treated with Furosemide require regular supervision with monitoring, of serum sodium, potassium and creatinine. Particularly close monitoring is required in patients at high risk of developing electrolyte imbalances or in case of significant additional fluid loss. Hypovolaemia or dehydration as well as any significant electrolyte and acid-base disturbances must be corrected. This may require temporary discontinuation of furosemide.

Urinary output must be secured in patients receiving furosemide treatment. In patients with a partial obstruction of urinary outflow, increased production of urine may provoke or aggravate complaints. These patients require careful monitoring. Patients with partial obstruction of urinary outflow, for example patients with prostatic hypertrophy or impairment of micturition have an increased risk of developing acute retention and require careful monitoring.

Particular caution and/or dose reduction required in:

- Patients with hypotension
- Patients who are at risk from a pronounced fall in blood pressure; symptomatic hypotension leading to dizziness, fainting or loss of consciousness can occur in patients treated with furosemide, particularly in the elderly, patients on other medications which can cause hypotension and patients with other medical conditions that are risks for hypotension.
- Patients with latent or manifest diabetes. Furosemide 40 mg tablets may necessitate adjustment of control by hypoglycaemic agents in cases of diabetes mellitus
- Patients with gout
- Patients with hepatorenal syndrome
- Patients with hypoproteinaemia, e.g. associated with nephritic syndrome (the effect of furosemide may be weakened and its ototoxicity potentiated). Cautious dose titration is required.
- Premature infants (possible development nephrocalcinosis nephrolithiasis; renal function must be monitored and renal ultrasonography performed).

The use of diuretics is considered to be unsafe in acute porphyria therefore caution should be exercised.

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 or furosemide alone. Cautions 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.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose – galactose malabsorption, should not take this medicinal product.

Caution is advised in patients who have undergone coronary bypass surgery.

4.5 Interaction with other medicinal products and other forms of interaction

The concomitant administration of Furosemide with cardiac glycosides or hypotensive agents may necessitate adjustment of the dosage of those drugs.

Furosemide may increase the harmful effects of nephrotoxic antibiotics on the kidney.

Impairment of renal function may develop in patients receiving treatment with furosemide and high doses of certain cephalosporins.

Oral furosemide and sucralfate must not be taken within 2 hours of each other because sucralfate decreases the absorption of furosemide from the intestine and so reduces its effect.

Corticosteroids, corticotrophin and amphotericin B, also cause potassium loss and severe potassium depletion may occur when administered concurrently with furosemide. Also, corticosteroids administered concurrently may cause sodium retention.

A more pronounced fall in blood pressure may be seen if antihypertensive drugs, diuretics or other drugs with blood-pressure-lowering potential are given concomitantly with furosemide.

Concomitant administration of carbamazepine or aminoglutethimide may increase the risk of hyponatraemia.

Carbenoxolone, liquorice, B2 sympathomimetics in large amounts, prolonged use of laxatives, reboxetine and amphotericin may increase the risk of developing hypokalaemia.

As with other diuretics, concomitant administration of lithium may decrease the excretion of lithium salts and may cause increased serum lithium levels, resulting in increased 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.

Concomitant use of ciclosporin and furosemide is associated with increased risk of gouty arthritis secondary to furosemide induced hyperuricemia and cyclosporine impairment of renal urate excretion.

Patients who are at high risk of 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.

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, and ACE inhibitor or angiotensin II receptor antagonist.

Concomitant administration of certain of the non-steroidal anti-inflammatory drugs such as acetylsalicylic acid or indomethacin may reduce the effect of furosemide. In patients with dehydration or hypovolaemia, non-steroidal antiinflammatory drugs may cause acute renal failure. Salicylate toxicity may be increased by furosemide.

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.

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.

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).

Attenuation of the effect of furosemide may occur following concurrent administration of phenytoin.

Severe diuresis may occur if metolazone is administered concomitantly.

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.

Risperidone: Caution should be exercised and the risks and benefits of the combination or co-treatment with furosemide should be considered prior to the decision to use.

4.6 Fertility, pregnancy and lactation

Furosemide crosses the placental barrier. Furosemide should only be used in pregnancy only if there are compelling medical reasons. Treatment during pregnancy requires monitoring of foetal growth. Furosemide passes into breast milk and may inhibit lactation. Women must not breast-feed if they are treated with furosemide.

4.7 Effects on ability to drive and use machines

Reduced mental alertness may impair the ability to drive or operate machinery.

4.8 Undesirable effects

Metabolism and nutrition disorders

- Increased excretion of sodium and chloride and consequently water.
- Increased excretion of other electrolytes (in particular potassium, calcium and magnesium).
- Symptomatic electrolyte disturbances and metabolic alkalosis.
- Hypovolaemia and dehydration, especially in elderly patients. Severe fluid depletion may lead to haemoconcentration with a tendency for thromboses to develop.
- Transitory increases in blood creatinine and urea levels.
- Increase in cholesterol and triglyceride serum levels.
- Increase in uric acid serum levels and attacks of gout.
- Decrease of glucose tolerance.

Vascular disorders

- Hypotension including orthostatic hypotension.
- Tendency for thromboses.
- Vasculitis.

Renal and urinary disorders

- Acute retention of urine in patients with a partial obstruction of urinary outflow.
- Interstitial nephritis.
- Nephrocalcinosis/nephrolithiasis in premature infants.

Gastrointestinal disorders

- Nausea, vomiting, diarrhoea.
- Acute pancreatitis.

Hepatobiliary disorders

- Intrahepatic cholestasis, increase in liver transaminases.

Ear and labyrinth disorders

- Hearing disorders, tinnitus.
- Deafness (sometimes irreversible)

Skin and subcutaneous tissue disorders

- Itching, urticaria, other rashes or bullous lesions, erythema multiforme, bullous pemphigoid, exfoliative dermatitis, purpura, photosensitivity.
- Acute generalised exanthematous pustulosis (AGEP)

Immune system disorders

- Severe anaphylactic or anaphylactoid reactions.

Nervous system disorders

- Paraesthesia.
- Hepatic encephalopathy in patients with hepatocellular insufficiency.
- Dizziness, fainting and loss of consciousness (caused by symptomatic hypotension’.

Blood and lymphatic system disorders

- Thrombocytopenia, leucopenia, agranulocytosis, aplastic anaemia, haemolytic anaemia.
- Eosinophilia.
- Haemoconcentration.

Congenital, familial and genetic disorders

- 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

- Following intramuscular injection, local reactions such as pain.
- Fever.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail: medsafety@hpra.ie.

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 arrhythmias due to excessive diuresis. Symptoms of these disturbances include severe hypotension (progressing to shock), acute renal failure, thrombosis, delirious states, flaccid paralysis, apathy and confusion.

Treatment should therefore be aimed at fluid replacement and correction of the electrolyte imbalance. 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.

No specific antidote of 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 designated to reduce absorption (e.g. activated charcoal).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Diuretics

ATC code: C03CA01

Furosemide is a potent diuretic. Its principle site of action is the ascending limb of the loop of Henle. It has a steep dose-response curve.

5.2 Pharmacokinetic properties

Furosemide is rapidly absorbed after oral administration with peak plasma levels and activity within 1 hour of a dose, lasting about 2 hours. It is strongly bound to plasma protein and is excreted mostly unchanged through the kidney.

5.3 Preclinical safety data

Preclinical information has not been included because the safety profile of Furosemide has been established after many years of clinical use. Please refer to section 4.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Maize starch
Microcrystalline cellulose (E460)
Sodium starch glycolate (Type A)
Talc (E553b)
Silica, colloidal anhydrous
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

HDPE or polypropylene containers with caps or child resistant closures in packs of 30, 50, 100, 500, 1000 and 5000 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Pinewood Laboratories Limited
Ballymacarbry
Clonmel
Co. Tipperary
Ireland

8 MARKETING AUTHORISATION NUMBER

PA 0281/087/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 16th August 1993

Date of last renewal: 16th August 2008

10 DATE OF REVISION OF THE TEXT

April 2016