SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

FUROBE 40 mg TABLET

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each **FUROBE 40 mg TABLET** contains:

Furosemide 40 mg

Sugar Free

For full list if excipients, see section 6.1

3. PHARMACEUTICAL FORM

FUROBE 40 mg TABLET

White to off-white tablet, scored on the one side.

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

Adults:

A dose of 40 mg per day is usually sufficient, but this may be increased to 200 mg per day if necessary. In the event that a dosage of 120 mg per day is exceeded, the treatment should provide for 2 or 3 separate doses. Maintenance therapy varies from 20 mg to 40 mg per day. For the treatment of hypertension of mild or moderate degree, a daily dosage of 40 mg to 80 mg orally. In combination with other hypotensive medicines, lower doses will often suffice.

Children:

Children's dosages are usually in the order of 1 mg per kg body weight, which can be increased to 3 mg per kg bodyweight, if necessary, but a daily dosage of 120 mg should not be exceeded.

Method of administration:

Oral formulations: It is recommended that **FUROBE 40 mg TABLET** be taken on an empty stomach. Tablets are to be swallowed whole without chewing and with sufficient amounts of liquid.

4.3 Contraindications

FUROBE 40 mg TABLET is contraindicated:

- in patients with hypersensitivity to furosemide or any of the excipients of **FUROBE 40 mg TABLET** (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 **FUROBE 40 mg TABLET** 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.

4.5 Interaction with other medicines and other forms of interaction

• **FUROBE 40 mg TABLET** may potentiate the ototoxicity of aminoglycosides and other ototoxic medicines. Since this may lead to irreversible damage these medicines must only be used with **FUROBE 40 mg TABLET** 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 **FUROBE 40 mg TABLET**. **FUROBE 40 mg TABLET** should be given in low doses and with positive fluid balance when used to achieve forced diuresis during cisplatin treatment.

• Oral **FUROBE 40 mg TABLET** and sucralfate must not be taken within 2 hours of each other because sucralfate decreases the absorption of **FUROBE 40 mg TABLET** from the intestine and so reduces its effect.

• **FUROBE 40 mg TABLET** 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 **FUROBE 40 mg TABLET**, 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 **FUROBE 40 mg TABLET** temporarily or at least reducing the dose of **FUROBE 40 mg TABLET** 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 **FUROBE 40 mg TABLET** 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 **FUROBE 40 mg TABLET**. In patients with dehydration or hypovolaemia, NSAIDs may cause acute renal failure. Salicylate toxicity may be increased by **FUROBE 40 mg TABLET**.

• Attenuation of the effect of **FUROBE 40 mg TABLET** may occur following concurrent administration of phenytoin.

• Aliskiren reduces plasma concentration of furosemide given orally. In patients treated with both aliskiren and oral **FUROBE 40 mg TABLET**, 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 **FUROBE 40 mg TABLET**, a more pronounced fall in blood pressure must be anticipated.

• Probenecid, methotrexate and other medicines which, like **FUROBE 40 mg TABLET**, undergo significant renal tubular secretion may reduce the effect of **FUROBE 40 mg TABLET.**

• 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 **FUROBE 40 mg TABLET** and high doses of certain cephalosporins.

• Concomitant use of ciclosporin and **FUROBE 40 mg TABLET** is associated with increased risk of gouty arthritis secondary to **FUROBE 40 mg TABLET** induced hyperuricaemia and ciclosporin impairment of renal urate excretion.

• Patients who were at high risk for radiocontrast nephropathy treated with **FUROBE 40 mg TABLET** 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: **FUROBE 40 mg TABLET** 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

FUROBE 40 mg TABLET 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 **FUROBE 40 mg TABLET**.

4.7 Effects on ability to drive and use machines

The effects on ability to drive or use machines may be impaired, especially at the commencement of treatment or when changing over from other medicines or when alcohol is consumed during **FUROBE 40 mg TABLET** therapy.

4.8 Undesirable effects

System Organ Class	Frequent	Less frequent	Frequency Unknown
Blood and lymphatic system disorders	Haemocon-centration	thrombocytopenia, leukopenia, agranulocytosis, aplastic or haemolytic anaemia, eosinophilia	blood coagulation disorders
Immune system disorders		severe anaphylactic or anaphylactoid reactions (e.g. shock)	exacerbation or activation of systemic lupus erythematosus

Metabolism and nutrition disorders	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	impaired glucose tolerance, dryness of mouth, diabetes mellitus (latent becoming manifest; and aggravation of manifest)	hypocalcaemia, hypomagnesaemia, increased blood urea, metabolic alkalosis, pseudo-Bartter's syndrome
Nervous System Disorders	hepatic encephalopathy in patients with hepatocellular insufficiency	paraesthesia	dizziness, fainting or loss of consciousness, headache
Ear and labyrinth disorder	dizziness, fainting or loss of consciousness, headache		
Vascular disorders	hypotension including orthostatic hypotension	vasculitis	tendency for thromboses, circulatory collapse, circulatory disorders (vertigo, feeling pressure in head, visual impairment), embolism

Gastrointestinal disorders	nausea, vomiting, diarrhoea, acute pancreatitis		
Hepato-biliary disorders	intrahepatic cholestasis, increase in liver transaminases		
Skin and subcutaneous tissue disorders	pruritus, urticaria, other rashes or bullous lesions; erythema multiforme, bullous pemphigoid, photosensitivity, purpura		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			tetany, cases of rhabdomyolysis often in the context of hypokalaemia
Renal and Urinary disorders	Musculoskeletal, connective tissue and bone disorders	tubulointerstitial nephritis	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			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		fever	following intramuscular infection, local reactions such as pain

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Suspected adverse reactions can also be reported directly to the HCR via email:

pharmacovigilance.africasme@sunpharma.com or

tel: +27(0) 12 643 2000.

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

A.18.1 Diuretics

Pharmacotherapeutic Group: High-ceiling diuretic sulfonamides, loop diuretics;

ATC code: C03CA01

The primary action is to inhibit sodium and chloride absorption in the ascending part of the Henle loop. Inhibition of electrolyte reabsorption in the proximal tube has been observed. The increase in potassium excretion occurs as a result of the distal secretion and is more or less proportional to the flow speed in this segment. It is often possible, in situations where other methods of treatment fail to induce diuresis, to increase the excretion of sodium and water with **FUROBE 40 mg TABLET**, even when glomerular filtration rate is markedly impaired. Phosphaturic response varies. **FUROBE 40 mg TABLET** lowers pathologically raised blood pressure, but does not affect normal levels.

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

Ac-Di-Sol

Magnesium stearate

Microcrystalline cellulose

Purified talc

Purified Water

Sodium bicarbonate

Starch maize

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Containers of 30, 84, 250 and 5000 tablets: 24 Months

Patient ready packs: 15 Months

6.4 Special precautions for storage

Store in a cool place at or below 25 ºC and protect against light.

6.5 Nature and contents of container

FUROBE 40 mg TABLET

Containers of 30, 84, 250 and 5000 tablets. Patient ready packs of different pack sizes.

6.6 Special precautions for disposal and other handling

Return all unused or expired medicines to your pharmacist for safe disposal. Do not dispose of unused medicines in drains or sewage systems (e.g. toilets).

7. HOLDER OF CERTIFICATE OF REGISTRATION

Ranbaxy Pharmaceuticals (Pty) Ltd

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Roodepoort

1724

South Africa

Telephone: +27(0) 12 643 2000

8. REGISTRATION NUMBERS

FUROBE 40 mg TABLET - S/18.1/31

Namibia 30's, 250's:	NS2	90/18.1/00371

9. DATE OF FIRST AUTHORISATION

30 AUGUST1989

10. DATE OF REVISION OF THE TEXT

02 February 2026