1.5.5 Clean Proposed Professional Prescribing Information

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

Oedema of cardiac, hepatic or renal origin. Refractory oedema (together with diuretics which have a different mode of action, especially potassium sparing medicines).

Symptomatic hypercalcaemia.

Hypertension of mild to moderate degree.

4.2 Posology and method of administration

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'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.

4.3 Contraindications

- Known hypersensitivity to furosemide, sulphonamides or to any of the excipients of **FUROBE 40 mg TABLET.**
- **FUROBE 40 mg TABLET** is contra-indicated if increasing azotaemia and oliguria occur during treatment of severe progressive renal disease, anuria, hypokalaemia, hyponatraemia, hypovolaemia with or without hypotension, dehydration.
- In hepatic coma and in states of electrolyte depletion, therapy with **FUROBE 40 mg TABLET** should not be instituted until the basic condition is corrected.
- **FUROBE 40 mg TABLET** should not be given to women breast-feeding their infants. Furosemide should be administered during pregnancy only if strictly indicated, and then only for short periods of time.

4.4 Special warnings and precautions for use

Caution should be exercised in the simultaneous use of cephalosporins as nephrotoxicity may occur.

Although administration of **FUROBE 40 mg TABLET** only rarely leads to hypokalaemia, a potassium-rich diet (lean meat, potatoes, bananas, tomatoes, cauliflower, spinach, dried fruit, etc.) is always advisable. Treatment with potassium-containing or potassium-sparing preparations may be indicated. As with other diuretics, electrolyte and water balance may be disturbed as a result of diuresis after prolonged therapy.

Mainly at the start of the treatment, excessive diuresis, particularly in elderly patients, may give rise to circulatory disturbances, such as a feeling of pressure in the head, vertigo or visual impairment.

In extreme cases hypovolaemia, dehydration, dryness of mouth, circulatory collapse and blood coagulation disorders may also occur. However, with individualized dosage, acute haemodynamic reactions are generally not to be expected, although diuresis sets in rapidly. **FUROBE 40 mg TABLET** may cause potassium depletion, especially in cases of low potassium diet, vomiting or chronic diarrhoea.

In addition, diseases such as cirrhosis of the liver may cause a predisposition to potassium deficiency states. Appropriate surveillance and replacement therapy are necessary in such cases. If salt intake is restricted too much, sodium deficiency may produce a fall in blood pressure, calf muscle cramps, anorexia, weakness, dizziness, drowsiness, vomiting and confusional states.

The serum calcium level may be reduced under **FUROBE 40 mg TABLET** therapy. In very rare cases tetany has been reported. In premature infants, calcium salts may be deposited in the renal tissue (nephrocalcinosis). When administered to premature infants with respiratory distress syndrome in the first few weeks after birth, diuretic treatment with furosemide may accentuate the risk of a patent ductus arteriosis.

Symptoms of obstructed micturition (e.g. in hydronephrosis, prostatic hypertrophy, uretherostenosis) may become manifest or aggravated under the action of diuretics. In common with other diuretics, treatment with **FUROBE 40 mg TABLET** may induce a transient

rise in serum creatinine and urea levels. It should be remembered that an increase in uric acid concentration in the blood might precipitate attacks of gout in predisposed patients.

Serum cholesterol and triglyceride levels may increase under **FUROBE 40 mg TABLET** treatment but will usually return to normal under long-term treatment, within six months. Diabetes mellitus may be aggravated by furosemide treatment and latent diabetes may become manifest. Reports show that isolated cases of acute pancreatitis in which the treatment with saluretics over several weeks was considered a causal factor, including also a few cases following therapy with furosemide.

Pre-existing metabolic alkalosis may be aggravated by furosemide treatment (e.g. in decompensated cirrhosis of the liver).

4.5 Interaction with other medicines and other forms of interaction

When a cardiac glycoside is administered concurrently it should be remembered that potassium deficiency increases the sensitivity of the myocardium to digitalis. In case of glucocorticoid medication or abuse of laxatives, the risk of increased potassium loss should be borne in mind. **FUROBE 40 mg TABLET** may potentiate the nephrotoxic effects of certain antibiotics (e.g. aminoglycosides). Therefore, **FUROBE 40 mg TABLET** should be used with caution in patients with antibiotic induced renal impairment.

Ototoxicity, which can be enhanced by amino-glycosides antibiotics (e.g. kanamycin, gentamicin, tobramycin, may occur. The hearing defects that result may be irreversible. Therefore, this drug combination should be restricted to vital indications.

FUROBE 40 mg TABLET may diminish the potency of other medicines (e.g. the effect of antidiabetics and pressor amines) or potentiate their effect (e.g. in the case of salicylates, theophylline, lithium and neuromuscular blocking muscle relaxants).

The action of other hypotensive medicines may be potentiated by **FUROBE 40 mg TABLET**. Especially in combination with ACE-inhibitors a marked fall in blood pressure may be seen. Non-steroidal anti-inflammatory agents (e.g. indomethacin, acetylsalicylic acid) may antagonise the action of **FUROBE 40 mg TABLET** and may cause renal failure in case of pre-existing hypovolaemia.

Concurrent administration of **FUROBE 40 mg TABLET** and sucralfate should be avoided as sucralfate reduces the absorption of furosemide and hence weakens its effect.
Caution should be exercised in the simultaneous use of cephalosporins as nephrotoxicity may occur.

4.6 Fertility, pregnancy and lactation

FUROBE 40 mg TABLET should not be given to lactating women. Furosemide passes into the breast milk and may inhibit Lactation (see section 4.3).
FUROBE 40 mg TABLET crosses the placental barrier. **FUROBE 40 mg TABLET** must not be given during pregnancy. Treatment during pregnancy require monitoring of foetal growth.

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		Anaemia, agranulocytosis, thrombocytopaenia, Eosinophilia, hypocalcaemia, leukopenia, hypokalaemia, haemolytic anaemia, aplastic anaemia, bone marrow depression	Circulatory collapse, blood coagulation disorders
Immune system disorders		Severe anaphylactic reactions with shock, rashes, vasculitis, interstitial nephritis, photosensitivity, vascular cutaneous eruptions, fever	
Metabolism and nutrition disorders		Metabolic alkalosis, potassium depletion, manifest diabetes mellitus may be aggravated and latent diabetes may become manifest. Glucose tolerance may be impaired, tetany and heart rhythm disturbances caused be electrolyte and water	Hypovolaemia, dehydration, electrolyte and water imbalance (sodium and potassium deficiency), dryness of mouth, metabolic acidosis, , Serum cholesterol and triglyceride levels may increase, Transient rise in serum creatinine and urea levels

		imbalance (magnesium and calcium deficiency),	
Nervous System Disorders		Paraesthesia, hyperosmolar coma	Dizziness, fainting, loss of consciousness
Eye disorders		Blurred vision	
Ear and labyrinth disorder			Reversible disorders of hearing and tinnitus may occur particularly in patients with renal insufficiency
Cardiac Disorders	Postural hypotension	Cardiac arrhythmias	
Vascular disorders			Circulatory disturbances
Gastrointestinal disorders		Nausea, vomiting, diarrhea, dry mouth, thirst, bowel motility disturbances, constipation	
Hepato-biliary disorders			Intrahepatic cholestasis, increase liver transaminases, acute pancreatitis, hepatic encephalopathy
Skin and subcutaneous tissue disorders		Several forms of dermatitis	
Renal and Urinary disorders		Increase in uric acid concentration in the blood might precipitate attacks of gout, interstitial nephritis, acute renal failure, urinary	Obstructed micturition

		incontinence and retention	
General disorders and administration site conditions		Fatigue, fever, malaise	

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 asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Fluid, electrolyte depletion and dehydration are the most common symptoms in over dosage. The guiding principal of treatment is water and electrolyte replacement in accordance with urine output. If difficulty in micturition is proved or suspected, as in cases of prostatic hypertrophy or impairment of consciousness, care must be taken to ensure a free outflow of urine from the bladder. Other than the above, treatment is supportive and symptomatic.

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

Furosemide is a diuretic which is incompletely absorbed from the gastro intestinal tract. It is generally bound to plasma protein. It is excreted by glomerular filtration and tubular excretion. With oral administration, the onset of action is rapid usually within half an hour. Peak action is usually achieved after two hours and the duration of action is 4 to 5 hours.

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 ^{o}C 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

14 Lautre Road

Stormill Ext. 1

Roodepoort

1724

South Africa

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

To be allocated