Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Tibina (Torasemide 10mg) tablets
Tibina (Torasemide 20mg) tablets

2. Qualitative and quantitative composition

Each uncoated tablet contains: Torasemide 10mg.
Torasemide 20mg.
For a full list of excipients, see section 6.1.

3. Pharmaceutical form

Uncoated tablet

4. Clinical particulars

4.1 Therapeutic indications

Oedema due to congestive heart failure; hepatic, pulmonary or renal oedema.

4.2 Posology and method of administration

Oedema: The usual dose is 5mg. once daily. If necessary, the dose can be increased stepwise up to 20mg once daily. In individual cases, as much as 40mg Torasemide/day has been administered.

Elderly

No special dosage adjustments are necessary.

Children

There is no experience of Torasemide in children
Method of administration
Tibina tablets should be swallowed whole.

4.3 Contraindications

Renal failure with anuria; hepatic coma and pre-coma; hypotension; pre-existing hypovolaemia; pregnancy and lactation; hypersensitivity to Torasemide and sulphonylureas; cardiac arrhythmias, simultaneous therapy with aminoglycosides or cephalosporins, or renal dysfunction due to drugs which cause renal damage.

4.4 Special warnings and precautions for use

Special warnings and precautions for use
Hypokalaemia, hyponatraemia, hypovolaemia and disorders of micturition must be corrected before treatment.

On long-term treatment with Torasemide, regular monitoring of the electrolyte balance, glucose, uric acid, creatinine and lipids in the blood, is recommended.

Careful monitoring of patients with a tendency to hyperuricaemia and gout is recommended. Carbohydrate metabolism in latent or manifest diabetes mellitus should be monitored.

As for other drugs which produce changes in blood pressure, patients taking Torasemide should be warned not to drive or operate machinery if they experience dizziness or related symptoms.

Patients with rare hereditary problems of glucose intolerance, the Lapp lactase deficiency of glucose-galactose malabsorption should not take this medication

Difficulty with micturition

Particular caution is required in patients with difficulty with micturition including prostatic hypertrophy because they have an increased risk of developing acute urinary retention and require careful close monitoring.

4.5 Interaction with other medicinal products and other forms of interaction

When used simultaneously with cardiac glycosides, a potassium and/or magnesium deficiency may increase sensitivity of the cardiac muscle to such drugs. The kaliuretic effect of mineralo-and glucocorticoids and laxatives may be increased.As with other diuretics, the effect of antihypertensive drugs given concomitantly may be potentiated.

Torasemide, especially at high doses, may potentiate the toxicity of aminoglycoside antibiotics, cisplatin preparations, the nephrotoxic effects of cephalosporins, and the cardio-and neurotoxic effect of lithium. The action of curare-containing muscle relaxants and of theophylline can be potentiated. In patients receiving high doses of salicylates, salicylate toxicity may be increased. The action of anti-diabetic drugs may be reduced.

Sequential or combined treatment, or starting a new co-medication with an ACE inhibitor may result in transient hypotension. This may be minimised by lowering the starting dose of the ACE inhibitor and/or reducing or stopping temporarily the dose of Torasemide. Torasemide may decrease arterial responsiveness to pressor agents e.g. adrenaline, noradrenaline.

Non-steroidal anti-inflammatory drugs (eg. Indometacin) and probenecid may reduce the diuretic and hypotensive effect of Torasemide.

Concomitant use of Torasemide and colestyramine has not been studied in humans, but in an animal study co-administration of cholestyramine decreased absorption of oral Torasemide.

4.6 Fertility, pregnancy, and lactation

There are no data from experience in humans of the effect of Torasemide on the embryo and foetus. Whilst studies in the rat have shown no teratogenic effect, malformed foetuses have been observed after high doses in pregnant rabbits. No studies have been conducted on excretion in breast milk. Consequently, Torasemide is contra-indicated in pregnancy and lactation.

4.7 Effects on ability to drive and use machines.

As for other drugs which produce changes in blood pressure, patients taking Torasemide should be warned not to drive or operate machinery if they experience dizziness or related symptoms.

4.8 Undesirable effects

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

Tabulated list of adverse reactions of Torasemide 20mg and 10mg

Within the system organ classes, adverse reactions are listed under headings of frequency (number of patients expected to experience the reaction), using the following categories:

Very common (≥1/10),Common (≥1/100 to <1/10),Uncommon (≥1/1,000 <1/100)

Rare (≥1/10,000 to <1/1,000),Very rare (<1/10,000)

Not known (cannot be estimated from available data)

The following undesirable effects were observed whereas the frequency of undesirable effect is not known:

System Organ Class	Common	Uncommon	Rare	Very Rare	Not Known
Blood and lymphatic system disorders					Thrombocytopenia, Leukopenia, Anaemia
Immune system disorders				Allergic skin reactions (eg Pruritus, Exanthema), Photosens	Serious skin reactions (e.g Stevens-Johnson syndrome, Toxic epidermal necrolysis

				itivity reaction	
Metabolism and nutrition disorders	Metabolic alkalosis, Fluid and electrolyte imbalance (eg Hypovolaemia, Hyponatraemia)				
Nervous system disorders	Headache, Dizziness				Cerebral ischaemia, Parenthesia, confusional state
Eye disorders					Visual impairment
Ear and labyrinth disorders					tinnitus, Deafness
Cardiac disorders					Acute myocardial infarction, Myocardial ischaemia, Angina pertoris, Syncope, Hypotension
Vascular disorders					Embolism
Gastrointestinal disorders	Gastrointestinal disorder (e.g. Loss of appetite, abdominal pain upper, Nausea, Vomiting, Diarrhoea, Constipation)				Dry mouth, Pancreatitis
Hepatobiliary disorders		Hepatic enzyme increased (e.g. Gamma-glutamyltransferase increased)			
Skin and subcutaneous tissue disorders				Allergic skin reactions (e.g. Pruritus, Exanthema), Photosensitivity reaction	Serious skin reactions (e.g. Stevens-Johnson syndrome, Toxic epidermal necrolysis

Musculoskeletal and connective tissue disorders	Muscle spasms				
Renal and urinary disorders		Urinary retention, Bladder dilatation	Blood urea increased, Blood creatinine increased		
General disorders and administration site conditions	Fatigue, Asthenia				
Investigations		Blood uric acid increased, Blood glucose increased, Lipids increased (e.g. Blood triglycerides increased, Blood cholesterol increased			

4.9 Overdose

Symptoms and signs

No typical picture of intoxication is known. If overdosage occurs, then there may be marked diuresis with the danger of loss of fluid and electrolytes which may lead to somnolence, confusion, hypotension, hyponatremia, hypokalemia, hypochloremic alkalosis, hemoconcentration dehydration and circulatory collapse. Gastrointestinal disturbances may occur.

Treatment

No specific antidote is known. Symptoms and signs of overdosage require the reduction of the dose or withdrawal of Torasemide, and simultaneous replacement of fluid and electrolytes.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Torasemide is a loop diuretic. However, at low doses its Pharmacodynamic profile resembles that of the thiazide class regarding the level and duration of diuresis. At higher doses, Torasemide induces a brisk diuresis in a dose dependant manner with a high ceiling of effect. Torasemide acts as a salidiuretic by inhibition of renal sodium and chloride reabsorption in the ascending limb of the loop of Henle. After oral administration the onset of diuresis is within the 1st hour with a peak action within 2 to 3h. The action may last up to 12h.

In healthy subjects an increase in dose results in a linear increase in urine excretion corresponding to the logarithm of the dose (high-ceiling activity) within the 5 to 100 mg dose range. An increase in diuresis may also take place if other diuretics are no longer active, e.g. in the presence of impaired renal function.
In renal failure endogenous organic acids compete with loop diuretics for the acid secretion mechanism in the proximal tubule. Therefore, the Torasemide dose has to be adequately increased in order to achieve effective amounts of drug at the site of action.
Torasemide leads to a gentle removal of edema and especially to an improvement of the working condition of the heart failure by reducing the preload and afterload. In patients with severe to end stage chronic renal failure there is a reduction of arterial blood pressure in addition to removal of edema and maintenance of residual diuresis.

5.2 Pharmacokinetic properties

Absorption

Torasemide is absorbed rapidly and almost completely after oral administration, and peak serum levels are reached after one to two hours.

Serum protein binding

More than 99% of Torasemide is bound to plasma proteins.

Distribution

The apparent distribution volume is 16 litres.

Metabolism

Torasemide is metabolised to three metabolites, M1, M3 and M5 by stepwise oxidation, hydroxylation or ring hydroxylation. Further metabolites (M2 and M4) have been found in animal experiments, but not in humans.

Elimination

The terminal half-life of Torasemide and its metabolites is three to four hours in healthy subjects. Total clearance of Torasemide is 40ml/min and renal clearance about 10ml/min. About 80% of the dose administered is excreted as Torasemide and metabolites into the renal tubule - Torasemide 24%, M1 12%, M3 3%, M5 41%.

In patients with congestive heart failure and disorders of liver fnction, the elimination half-lives of Torasemide and metabolite M5 are only slightly increased compared with those in healthy volunteers. The amounts of Torasemide and metabolites excreted in the urine are similar to those in healthy subjects; therefore no accumulation is to be expected.

In the presence of renal failure, elimination half-life of Torasemide is unchanged.

5.3 Preclinical safety data

Acute toxicity

Very low toxicity.

Chronic toxicity

The changes observed in toxicity studies in dogs and rats at high doses are attributable to an excess Pharmacodynamic action (diuresis). Changes observed were weight reduction, increases in creatinine and urea and renal alterations such as tubular dilatation and interstitial nephritis. All drug induced changes were shown to be reversible.

Teratogenicity

Reproduction toxicology studies in the rat have shown no teratogenic effect, but malformed foetuses have been observed after high doses in pregnant rabbits. No effects on fertility have been seen.

Torasemide showed no mutagenic potential. Carcinogenicity studies in rats and mice showed no tumorigenic potential

6. Pharmaceutical particulars

6.1 List of excipients

Lactose monohydrate,

Maize starch,

Colloidal silicon dioxide,

Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage:

Store in a dry place below 30°C. Protect from light

Keep all medicines out of the reach of children

6.5 Nature and contents of container

Alu – Alu blister pack containing 10 x 10 Tablets, packed in an outer carton.

6.6 Special precautions for disposal and other handling:

No special requirements.

7. Marketing authorization holder and manufacturing site addresses

Marketing authorization holder:

Cosmos Limited
Rangwe Road; Off Lunga Lunga, Industrial Area
P.O Box 41433, GPO 00100-Nairobi, Kenya
Telephone: + (254-20) 2519603/4/5, 020 8042200/2/3/4/5
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E-mail: admin@cosmos-pharm.com

Manufacturing site address:

Cosmos Limited
Rangwe Road; Off Lunga Lunga, Industrial Area
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E-mail: admin@cosmos-pharm.com

8. **Marketing authorization number**
   CTD9349
9. **Date of first registration**
   29/11/2022

10. **Date of revision of the text:**
    September 2023

11. **Dosimetry:**
    Not Applicable

12. **Instructions for Preparation of Radiopharmaceuticals:**
    Not Applicable