# Tibina® (Tablets)

Torasemide

High ceiling diuretic

TIBINA® 10MG TABLETS

TIBINA® 20MG TABLETS

20700

Ref. No.: B2120700/21.05

## PRESENTATION

**Tibina® Tablets 10mg:** White to off white, round flat bevelled edge tablets plain on one side and breakline on the other side. Each tablet contains: Torasemide 10mg, Lactose and other excipients.

**Tibina® Tablets 20mg:** White to off white, round, standard convex shaped tablets embossed 'C' on one side and breakline on the other side. Each tablet contains: Torasemide 20mg, Lactose and other excipients.

## CLINICAL PHARMACOLOGY

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 dependent 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 An increase in diuresis may also take place if other diuretics are no longer active, e.g. in the presence of impaired renal function.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.

## PHARMACOKINETICS

***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 function, 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.

## USES

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

## DOSAGE AND ADMINISTRATION

***Adults***

*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.

## CONTRA-INDICATIONS

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.

## ADVERSE EFFECTS

**Blood and lymphatic system disorders**

Frequency not known: Thrombocytopenia, Leukopenia, Anaemia

**Immune system disorders**

Very rare: Allergic skin reactions (eg Pruritus, Exanthema), Photosensitivity reaction

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Frequency not known: Serious skin reactions (eg Stevens-Johnson syndrome, Toxic epidermal necrolysis

**Metabolism and nutrition disorders**

Common: Metabolic alkalosis, Fluid and electrolyte imbalance (eg Hypovolaemia, Hyponatraemia)

**Nervous system disorders**

Common: Headache, Dizziness
Frequency not known: Cerebral ischaemia, Parenthesia, confusional state

**Eye disorders**

Frequency not known: Visual impairment

**Ear and labyrinth disorders**

Frequency not known: Tinnitus, Deafness

## OVERDOSAGE

***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.

## DRUG INTERACTIONS

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 (e.g. 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.

## SPECIAL WARNINGS AND PRECAUTIONS

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.

**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.

## PHARMACEUTICAL PRECAUTIONS

Store in a dry place below 30°C. Protect from light. Keep all medicines out of the reach of children.

## LEGAL CATEGORY

Prescription Only Medicine (POM)

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