For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory Only

TIDE

1. **Generic Name:**

Torsemide Tablets I.P. 5 mg, 10 mg, 20 mg and 100 mg

2. **Qualitative and quantitative composition:**

TORSEMIDE-5 mg

Each uncoated tablet contains:
Torsemide I.P……..5 mg
Excipients……...q.s.

TORSEMIDE-10 mg
Each uncoated tablet contains:
Torsemide I.P……..10 mg
Excipients……...q.s.

TORSEMIDE-20 mg
Each uncoated tablet contains:
Torsemide I.P……..20 mg
Excipients……...q.s.

TORSEMIDE-100 mg
Each uncoated tablet contains:

Torsemide I.P……100 mg

Excipients……...q.s.

3. **Dosage form and strength:**

Dosage form: Uncoated tablet

Strength: Torsemide 5 mg, 10 mg, 20 mg, 100 mg

4. **Clinical particulars:**

4.1 Therapeutic indication:

TORSEMIDE is indicated for the treatment of oedema associated with congestive heart failure, renal or hepatic disease and essential hypertension.

4.2 Posology and Method of Administration:

Adults
The usual dose is 5 mg orally once daily. Usually this is the maintenance dose. If necessary, the dose can be increased stepwise up to 20 mg once daily.

Elderly
There is no information on dosage adjustments in elderly patients. Experience is insufficient, however, to establish general recommendations.
Paediatric population
No data are available

Congestive Heart Failure

The usual initial dose is 10 mg or 20 mg of once-daily. If the diuretic response is inadequate, the dose should be titrated upward by approximately doubling until the desired diuretic response is obtained. Single doses higher than 200 mg have not been adequately studied.

Chronic Renal Failure

The usual initial dose of torsemide is 20 mg of once - daily. If the diuretic response is inadequate, the dose should be titrated upward by approximately doubling until the desired diuretic response is obtained. Single doses higher than 200 mg have not been adequately studied.

Hepatic Cirrhosis

The usual initial dose is 5 mg or 10 mg of once-daily, administered together with an aldosterone antagonist or a potassium-sparing diuretic. If the diuretic response is inadequate, the dose should be titrated upward by approximately doubling until the desired diuretic response is obtained. Single doses higher than 40 mg have not been adequately studied. Chronic use of any diuretic in hepatic disease has not been studied in adequate and wellcontrolled trials.

Hypertension

The usual initial dose is 5 mg once daily. If the 5 mg dose does not provide adequate reduction in blood pressure within 4 to 6 weeks, the dose may be increased to 10 mg once daily. If the response to 10 mg is insufficient, an additional antihypertensive agent should be added to the treatment regimen.

4.3 Contraindications:

Torsemide is contraindicated in patients with known hypersensitivity to torsemide or to sulfonylureas. Torsemide is contraindicated in patients who are anuric.

Torsemide is contraindicated in hepatic coma and pre - coma; hypotension; pregnancy and lactation; 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:

WARNINGS

Hepatic Disease with Cirrhosis and Ascites

Torsemide should be used with caution in patients with hepatic disease with cirrhosis and ascites, since sudden alterations of fluid and electrolyte balance may precipitate hepatic coma. In these patients, diuresis with torsemide (or any other diuretic) is best initiated in the hospital.

To prevent hypokalemia and metabolic alkalosis, an aldosterone antagonist or potassium-sparing drug should be used concomitantly with torsemide.

Ototoxicity

Tinnitus and hearing loss (usually reversible) have been reported after rapid intravenous injection of other loop diuretics and have also been reported after oral torsemide. It is not certain that these events were attributable to torsemide. Ototoxicity has also been reported in animal studies when very high plasma levels of torsemide were induced.

Volume and Electrolyte Depletion

Patients receiving diuretics should be observed for clinical evidence of electrolyte imbalance, hypovolemia, or prerenal azotemia. Symptoms of these disturbances may include one or more of the following: dryness of the mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, nausea, and vomiting.

Excessive diuresis may cause dehydration, blood-volume reduction, and possibly thrombosis and embolism, especially in elderly patients. In patients who develop fluid and electrolyte imbalances, hypovolemia, or prerenal azotemia, the observed laboratory changes may include hyper - or hyponatremia, hyper - or hypochloremia, hyper - or hypokalemia, acid-base abnormal ities, and increased blood urea nitrogen (BUN). If any of these occur, torsemide should be discontinued until the situation is corrected; torsemide may be restarted at a lower dose. In patients with cardiovascular disease, especially those receiving digitalis glycosides, diuretic-induced hypokalemia may be a risk factor for the development of arrhythmias. The risk of hypokalemia is greatest in patients with cirrhosis of the liver, in patients experiencing a brisk diuresis, in patients who are receiving inadequate oral intake of electrolytes, and in patients receiving concomitant therapy with corticosteroids or ACTH. Periodic monitoring of serum potassium and other electrolytes is advised in patients treated with torsemide. Careful monitoring of patients with a tendency to hyperuricaemia and gout is recommended. Carbohydrate metabolism in latent or manifest diabetes mellitus should be monitored.

PRECAUTIONS

Laboratory Values

Evidences reported that during torsemide treatment, electrolyte levels (calcium, magnesium), blood urea nitrogen, creatinine, uric acid, glucose, serum lipids levels were altered and should be monitored during therapy with torsemide. Clinical trials also reports that torsemide is associated with small mean decrease in hemoglobin, hematocrit, erythrocyte count and small mean increases in white blood cell count, platelet count, and serum alkaline phosphatase. Although statistically significant, all of these changes were medically inconsequential. As for other drugs which produce changes in blood pressure, patients taking Torsemide 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.

4.5 Drug-Interaction:

During clinical trials the torsemide was given with betablockers, ACE inhibitors, calcium-channel blockers in hypertensive individuals, with digitalis glycoside, ACE inhibitors, organic nitrates in patients with congestive heart failure. None of these combined uses was associated with new or unexpected adverse events.

Torsemide does not affect the protein binding of glyburide or of warfarin, the anticoagulant effect of phenprocoumon (a related coumarin derivative), or the pharmacokinetics of digoxin or carvedilol (a vasodilator/ beta-blocker).

In healthy subjects, coadministration of torsemide was associated with significant reduction in the renal clearance of spironolactone, with corresponding increases in the AUC. However, clinical experience indicates that dosage adjustment of either agent is not required. Because torsemide and salicylates compete for secretion by renal tubules, patients receiving high doses of salicylates may experience salicylate toxicity when torsemide is concomitantly administered. Also, although possible interactions between torsemide and NSAIDs (including aspirin) have not been studied clinical trials, but coadministration of these agents with another loop diuretic (furosemide) has occasionally been associated with renal dysfunction. The natriuretic effect of torsemide (like that of many other diuretics) is partially inhibited by the concomitant administration of indomethacin. This effect has been demonstrated for torsemide under conditions of dietary sodium restriction (50 mEq/day) but not in the TORSEMIDE presence of normal sodium intake (150 mEq/day).

The pharma-cokinetic profile and diuretic activity of torsemide are not altered by cimetidine or spironolactone. Coadmini-stration of digoxin is reported to increase the area under the curve for torsemide by 50%, but dose adjustment of torsemide is not necessary.

Concomitant use of torsemide and cholestyramine has not been studied in humans but, in a reported study in animals, coadministration of cholestyramine decreased the absorption of orally administered torsemide. If torsemide and cholestyramine are used concomitantly, simultaneous administration is not recommended. Coadministration of probenecid reduces secretion of torsemide into the proximal tubule and thereby decreases the diuretic activity of torsemide. Other diuretics are known to reduce the renal clearance of lithium, inducing a high risk of lithium toxicity, so coadministration of lithium and diuretics should be undertaken with great caution, if at all. Coadministration of lithium and torsemide has not been studied. Other diuretics have been reported to increase the ototoxic potential of aminoglycoside antibiotics and of ethacrynic acid, especially in the presence of impaired renal function. These potential interactions with torsemide have not been studied. The kaliuretic effect of mineralo-and glucocorticoids and laxatives may be increased. Torsemide potentiates the toxicity of cisplatin preparation, nephrotoxic effects of cephalosporins. The action of curare-containing muscle relaxants and of theophylline can be potentiated. Torsemide may decrease arterial responsiveness to pressor agents e.g. adrenaline, noradrenaline. 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 Torsemide. The action of anti-diabetic drugs may be reduced**.**

Carcinogenesis, Mutagenesis and Impairment of Fertility

No overall increase in tumor incidence was reported when torsemide was given to rats and mice throughout their lives at doses up to 9 mg/kg/day (rats) and 32 mg/kg/day (mice). On a body-weight basis, these doses are 27 to 96 times a human dose of 20 mg; on a body-surface-area basis, they are 5 to 8 times this dose. In the reported rat study, the high-dose female group demonstrated renal tubular injury, interstitial inflammation, and a statistically significant increase in renal adenomas and carcinomas. The tumor incidence in this group was, however, not much higher than the incidence sometimes seen in historical controls. Similar signs of chronic non-neoplastic renal injury have been reported in high-dose animal studies of other diuretics such as furosemide and hydrochlorothiazide.

No mutagenic activity was detected in any of a variety of in vivo and in vitro tests of torsemide and its major human metabolite. The tests included the Ames test in bacteria (with and without metabolic activation), tests for chromosome aberrations and sister-chromatid exchanges in human lymphocytes, tests for various nuclear anomalies in cells found in hamster and murine bone marrow, tests for unscheduled DNA synthesis in mice and rats, and others. In doses up to 25 mg/kg/day (75 times a human dose of 20 mg on a body-weight basis; 13 times this dose on a bodysurface-area basis), torsemide had no adverse effect on the reproductive performance of male or female rats.

Pregnancy and Lactation Pregnancy Category B.

There are no data from experience in humans of the effect of torsemide 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, torsemide is contra-indicated in pregnancy and lactation.

4.6 Use in special populations

Labor and Delivery

The effect of torsemide on labor and delivery is unknown.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

No specific age-related differences in effectiveness or safety were reported between younger patients and elderly patients.

4.7 Effects on ability to drive and use machines:

As for other medicinal products that produce changes in blood pressure, patients taking Torsemide should be warned not to drive or operate machinery if they experience dizziness or related symptoms. This applies in particular at the beginning of the therapy, when increasing the dosage, changing the preparation or when concomitantly ingesting alcohol.

4.8 Undesirable effects:

Blood chemistry/volume:
As with other diuretics, depending on the dosage and duration of treatment, there may be disturbances of water and electrolyte balance, especially with markedly limited salt intake. Hypokalaemia may occur (especially if a low potassium diet is being taken, or if vomiting, diarrhoea, or excessive use of laxatives takes place, or in cases of hepatic failure). Symptoms and signs of electrolyte and volume depletion, such as headache, dizziness, hypotension, weakness, drowsiness, confusional states, loss of appetite and cramps, can occur if diuresis is marked, especially at the start of treatment and in elderly patients. Dose adjustment may be necessary. Raised serum uric acid, glucose and lipids can occur. There may be aggravation of metabolic alkalosis.

Cardiovascular system:
In isolated cases, thromboembolic complications and circulatory disturbances due to haemoconcentration may occur. Other adverse events for which causal relationship can not be established were atrial fibrillation, ventricular tachycardia, shunt thrombosis, rectal bleeding, digitalis intoxication.

Gastro-intestinal system:
Patients may experience gastro-intestinal symptoms (vomiting, esophageal haemorrhage, dyspepsia, constipation etc.), Pancreatitis

Renal and Urinary system:
In patients with urinary outflow obstruction, retention of urine may be precipitated. Raised serum urea and creatinine may occur, excessive urination

Liver:
Increases in certain liver enzymes, eg. gamma-GT

Haematology:
Isolated cases of decreases in red and white blood cells and platelets have been reported.

Skin/allergy:
In isolated cases, there may be allergic reactions, such as pruritis, rash, angioedema, photosensitivity.

Nervous system:

Isolated reports of visual disturbance, tinnitus and hearing loss have occurred in isolated cases. Rarely, limb paraesthesia has been reported.

Others:
Dry mouth, excessive thirst, hypovolaemia, impotence, rhinitis, asthenia, ECG abnormality, cough increased, arthralgia, sore throat, myalgia, chest pain, insomnia, nervousness, edema

Reporting of side effects:

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at:

http://www.torrentpharma.com/index.php/site/info/adverse_event_reporting.

4.9 Overdose:

There is no human experience with overdoses of torsemide, but the signs and symptoms of overdosage can be anticipated to be those of excessive pharma-cologic effect: dehydration, hypovolemia, hypotension, hyponatremia, hypokalemia, hypochloremic alkalosis, and hemoconcentration. Treatment of overdosage should consist of fluid and electrolyte replacement. Laboratory determinations of serum levels of torsemide and its metabolites are not widely available. No data are available to suggest physiological maneuvers (eg, maneuvers to change the pH of the urine) that might accelerate elimination of torsemide and its metabolites. Torsemide is not dialyzable, so hemodialysis will not accelerate elimination.

5. Pharmacological properties:

5.1 Mechanism of Action:

Torsemide is a loop diuretic. However, at low doses its pharmaco-dynamic profile resembles that of the thiazide class regarding the level and duration of diuresis. At higher doses, Torsemide induces a brisk diuresis in a dose dependant manner with a high ceiling of effect. Torsemide acts from within the lumen of the thick ascending portion of the loop of Henle, where it inhibits the Na+/K+/2Cl- carrier system. Clinical pharmacology studies have confirmed this site of action in humans, and effects in other segments of the nephron have not been demonstrated. Diuretic activity thus correlates better with the rate of drug excretion in the urine than with the concentration in the blood. Torsemide increases the urinary excretion of sodium, chloride, and water, but it does not significantly alter glomerular filtration rate, renal plasma flow, or acid-base balance.

5.2 Pharmacodynamic properties:

Pharmacotherapeutic group: Sulfonamides, plain, ATC Code: C03CA04
Torsemide 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, Torsemide induces a brisk diuresis in a dose dependant manner with a high ceiling of effect. Torsemide has maximal diuretic activity 2-3 hours after oral administration. In healthy subjects given doses between 5 and 100mg it has a logproportional increase in diuretic activity.

5.3 Pharmacokinetic properties:

Torsemide is well absorbed from the gastrointestinal tract. Peak serum concentrations are achieved within 1 hour of oral doses. Cmax and area under the serum concentrationtime curve (AUC) after oral administration are proportional to dose over the range of 2.5 mg to 200 mg. Simultaneous food intake delays the time to Cmax by about 30 minutes, but overall bioavailability (AUC) and diuretic

activity are unchanged. Torsemide is metabolised by the cytochrome

P450 isoenzyme CYP2C9, which shows genetic poly-morphism. Metabolism takes place in the liver and inactive metabolites are excreted in the urine. The elimination half-life of torsemide is about 3.5 hours. Torsemide is extensively > 99 % bound to plasma proteins. The apparent distribution volume is 12 liters to 15 liters in normal adults or in patients with mild to moderate renal failure or congestive heart failure. In patients with hepatic cirrhosis, the volume of distribution is approximately doubled. In patients with heart failure both hepatic and renal clearance are reduced. In patients with renal impairment, the renal clearance is reduced but total plasma clearance is not significantly altered. In patients with hepatic cirrhosis, the volume of distribution, plasma half-life, and renal clearance are all increased, but total clearance is unchanged. The pharmacokinetic profile of torsemide in healthy elderly subjects is similar to that in young subjects except for a decrease in renal clearance related to the decline in renal function that commonly occurs with aging. However, total plasma clearance and elimination half-life remain unchanged.

6. Nonclinical properties:

Non-clinical data reveal no special hazard for humans based on single dose toxicity, genotoxicity and carcinogenicity studies.

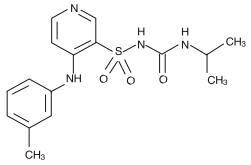
The changes observed in toxicity studies in dogs and rats at high doses are considered attributable to an excess pharmacodynamic action (diuresis). Changes observed were weight reduction, increases in creatinine and urea and renal alterations such as tubular dilatation and interstitial nephritis. All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

Reproduction toxicology: Studies in the rat have shown no teratogenic effects, but foetal and maternal toxicity have been observed after high doses in pregnant rabbits and rats. No effects on fertility have been seen. Torsemide passes into the foetus and causes electrolyte disturbances.

In mice Torsemide showed no evidence of tumorigenic potential. In rats a statistically significant increase in renal adenomas and carcinomas was observed in the high-dose female group. This seems to have no relevance for therapeutic doses in humans.

7. Description:

Torsemide is a diuretic of the pyridine-sulfonylurea class. Its chemical name is 3-Pyridinesulfonamide, N-[[(1-methylethyl) amino]carbonyl]-4-[(3-methylphenyl) amino]-1-Isopropyl-3[(4-m-toluidino-3-pyridyl) sulfonyl] urea and its structural



Its empirical formula is C16H20N4O3S, its pKa is 7.1, and its molecular weight is 348.42.
Torsemide is a white to off-white, crystalline powder. Slightly soluble in 0.1 N sodium hydroxide, in 0.1 N hydrochloric acid, in alcohol, and in methanol; very slightly soluble in acetone and in chloroform; practically insoluble in water and in ether.

8. Pharmaceutical particulars:

8.1 Incompatibilities:

Not applicable.

8.2 Shelf-life:

Do not use later than the date of expiry.

8.3 Packaging information:

TORSEMIDE 5/10/20/100 are available in strip of 10 tablets.

8.4 Storage and handing instructions:

Store at a temperature not exceeding 30º C, in dry place.

9. Patient Counselling Information

Package leaflet: Information for the user

TORSEMIDE

Torsemide Tablets I.P. 5 mg, 10 mg, 20 mg and 100 mg

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet?

9.1 What Torsemide is and what it is used for

Torsemide contains a medicine called Torsemide. This belongs to a group of medicines called 'diuretics' or 'water tablets'.

TORSEMIDE is indicated for the treatment of oedema associated with congestive heart failure, renal or hepatic disease and essential hypertension.

9.2 Before you take Torsemide

Do not take Torsemide if you are allergic (hypersensitive) to:

- Torsemide or any of the other ingredients of Torsemide
- Similar medicines called 'sulphonylureas'. These are used to treat diabetes (high blood sugar). These medicines include chlorpropamide, glibenclamide, glipizide and tolbutamide.
- Do not take Torsemide if any of these apply to you. If you are not sure, talk to your doctor or pharmacist before taking Torsemide.

Do not take Torsemide if:

- You have kidney problems (renal failure).
- You have kidney problems that have been caused by medicines.

- You have liver problems.
- You have a low volume of blood (hypovolaemia)
- You have low blood pressure (hypotension).
- You have heart beat problems (cardiac arrhythmia).
- You are taking an antibiotic called an 'aminoglycoside' or 'cephalosporin' (for an infection). These medicines include streptomycin, gentamycin, cephalexin and ceftriaxone. See the section on 'Taking other medicines'.
- You are pregnant or breast-feeding a baby. See the section on 'Pregnancy and breast-feeding'.

Do not take Torsemide if any of these apply to you. If you are not sure, talk to your doctor or pharmacist before taking Torsemide.

Take special care with Torsemide

Check with your doctor or pharmacist before taking Torsemide if:

- You have low levels of potassium or sodium in your blood (shown in blood tests).
- You have difficulty with micturition (passing urine) including prostatic hypertrophy
- You have diabetes (diabetes mellitus)

If any of these apply to you, or if you are not sure, talk to your doctor or pharmacist before you take Torsemide.

Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines. This includes medicines that you buy without a prescription and herbal medicines.
This is because Torsemide can affect the way some other medicines work.
Also some other medicines can affect the way Torsemide works.

Do not take Torsemide if you are already taking an antibiotic called an 'aminoglycoside' or 'cephalosporin' (for an infection). These medicines include streptomycin, gentamycin, cephalexin and ceftriaxone. If this applies to you, ask your doctor or pharmacist for advice.
It is particularly important to **tell your doctor or pharmacist** if you are taking any of the following medicines:

- Other medicines to treat high blood pressure.
- Medicines called 'ACE inhibitors' (used to treat heart disease).
- Medicines like digoxin or digitoxin (used to treat heart disease).
- Adrenaline (also called epinephrine) or noradrenaline (also called norepinephrine). These are used to treat low blood pressure.
- Cholestyramine, or other 'ionexchange resins' (used to treat high levels of cholesterol in your blood).
- High doses of medicines called 'salicylates', such as aspirin.
- Medicines called 'non-steroidal antiinflammatory drugs' (NSAIDs).
- These include indomethacin and ibuprofen.
- Laxatives.
- Steroid medicines, such as hydrocortisone, prednisolone and dexamethasone.
- Medicines to relax your muscles (muscle relaxants).
- Cisplatin (used to treat cancer).
- Lithium (used to treat mental health problems).
- Probenecid (used to treat gout).
- Theophylline (used to treat asthma).

Pregnancy and breast-feeding

Do not take Torsemide if you are pregnant, might become pregnant or are breast-feeding. This is because it is not known if Torsemide will affect your baby.

Driving and using machines
As for other medicinal products that produce changes in blood pressure, patients taking Torsemide should be warned not to drive or operate machinery if they experience dizziness or related symptoms. This applies in particular at the beginning of the therapy, when increasing the dosage, changing the preparation or when concomitantly ingesting alcohol.

9.3 How to take Torsemide

Always take Torsemide exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

High blood pressure

- The usual dose for adults and elderly people is between 2.5 mg and 5 mg once a day. **Water retention (oedema)**
- The usual dose for adults and elderly people is 5 mg once a day.
- Your doctor may increase the dose to 20 mg a day if needed.
- If you take more Torsemide than you should, talk to a doctor or go to a hospital straight away. Take the medicine pack with you.
- If you take too many tablets, you may pass a lot of urine, become sleepy, or feel confused, faint or dizzy. You may also have stomach upset.
- **If you forget to take Torsemide**
- If you forget to take a dose, take it as soon as you remember it.
- However, if it is nearly time for the next dose, skip the missed dose. ***** Do not take a double dose to make up for a forgotten dose.

If someone else takes your Torsemide tablets by mistake, they should talk to a doctor or go to a hospital straight away.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

9.4 Possible side effects

Like all medicines, Torsemide can cause side effects, although not everyone will get them.
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 effects is not known:

See your doctor as soon as possible if you get the following side effects:

- Thrombocytopenia, Leukopenia, Anaemia
- Allergic skin reactions (e.g. Pruritus, Exanthema), Photosensitivity reaction
- Serious skin reactions (e.g. Stevens-Johnson syndrome, Toxic epidermal necrolysis)
- Metabolic alkalosis, Fluid and electrolyte imbalance (e.g. Hypovolaemia, Hyponatraemia)
- Headache, Dizziness
- Cerebral ischaemia, Parenthesia, Confusional state
- Visual impairment
- Tinnitus, Deafness
- Acute myocardial infarction, Myocardial ischaemia,
- Angina pertoris, Syncope, Hypotension
- Embolism

- Gastrointestinal disorder (e.g. Loss of appetite, Abdominal pain
- upper, Nausea, Vomiting, Diarrhoea, Constipation) Frequency not known: Dry mouth, Pancreatitis
- Muscle spasms
- Urinary retention, Bladder dilatation
- Blood urea increased, Blood creatinine increased
- Fatigue, Asthenia
- Blood uric acid increased, Blood glucose increased, Lipids increased (e.g. Blood triglycerides increased, Blood cholesterol increased)

Other possible side effects:

Blood

- An increase in the levels of certain substances in your blood, including sugar, uric acid and fats (lipids). Your doctor may do blood tests from time to time to make sure that Torsemide is working safely.

Stomach and gut

- Stomach upset.
- Inflammation of the pancreas causing pain in the stomach (pancreatitis).
- Changes in how your liver is working (shown by blood tests).

Skin

- Skin rashes and itchy skin.
- Skin being more sensitive to the sun (photo-sensitivity).

Eyes and ears

- Blurred eyesight.
- Ringing in the ears (tinnitus) and loss of hearing.

Other

- Feeling numb or tingling in the legs or arms.
- Dry mouth.
- Some people may have difficulty passing water (urinating).

If any of the side effects become serious or troublesome, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Reporting of side effects:

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at:

http://www.torrentpharma.com/index.php/site/info/adverse_event_reporting.

9.5 How to store Torsemide

- **Keep out of the sight and reach of children.**
- This medicinal product does not require any special storage conditions.
- Do not use after the expiry date which is stated on the blister label and carton. If your doctor tells you to stop using this medicine, take any remaining medicine back to the pharmacist for safe disposal. Only keep this medicine if your doctor tells you to.
- If your medicine becomes discoloured or shows any signs of deterioration, ask your pharmacist who will advise you what to do.
- Medicines should not be disposed of via wastewater or household waste.
- Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

9.6 Further information

What Torsemide contains

- The active substance in Torsemide is Torsemide.
- Each tablet contains 5/10/20/100 mg of Torsemide.

What Torsemide contents of the pack

- TORSEMIDE 5/10/20/100 are available in strip of 10 tablets.

10 Details of manufacturer

M/s Swiss Garnier Genexiaa Sciences Pvt. Ltd.,
Plot no.54 & 78,
Mamring Basthi, Rangpo Post,
South Sikkin – 737132.

11 Details of permission or licence number with date

Mfg Lic. No. M/605/2012 issued on 05 Dec. 2018

12 Date of revision

APR 2021

MARKETED BY

torrent PHARMA

TORRENT PHARMACEUTICALS LTD.

IN/TORSEMIDE 5,10,20/100 mg/APR-21/02/PI