SUMMARY OF PRODUCT CHARACTERISTICS

1. **Name of the pharmaceutical product:** Diutor ® 5 (Torsemide Tablets 5mg) Diutor® 10 (Torsemide Tablets 10mg) Diutor® 20 (Torsemide Tablets 20mg)

2. **Qualitative and Quantitative Composition Diutor ® 5**
   Each film coated tablet contains:
   Torsemide USP……..... 5mg
   Excipients… ..... q.s.
   Colour: Approved colour used
   (For the full list of excipients see section 6.1)

   Diutor® 10
   Each film coated tablet contains:
   Torsemide USP……..... 10mg
   Excipients… ..... q.s.
   Colour: Approved colour used
   (For the full list of excipients see section 6.1)

   Diutor® 20
   Each film coated tablet contains:
   Torsemide USP… .....20 mg
   Excipients… ..... q.s.
   Colour: Approved colour used
   (For the full list of excipients see section 6.1)

3. **Pharmaceutical form:**

Diutor® 5
Film coated tablets
White colored, oval shape biconvex, film coated tablets having break line on one side & other side plain.

Diutor® 10
Film coated tablets
Orange coloured, oval shape biconvex, film coated tablets having break line on one side & other side plain.

Diutor® 20
Film coated tablets
Yellow coloured, oval shape biconvex, film coated tablets having break line on one side & other side plain.

4. **Clinical particulars**

4.1 Therapeutic indications

- Edema associated with congestive heart failure, renal disease, or hepatic disease.
- Edema associated with chronic renal failure.
- Pulmonary edema
- Hypertension alone or in combination with other antihypertensive agents.

4.2 Posology and method of administration

Posology

Treatment of Edema (fluid retention)

Edema associated with Congestive Heart Failure

The usual initial dose is 10 mg or 20 mg of once-daily oral or IV torsemide. If the diuretic response is inadequate, titrate upward by approximately doubling until the desired diuretic response is obtained. Doses higher than 200 mg have not been adequately studied.

Edema associated with Chronic Renal Failure

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

Edema associated with Hepatic Cirrhosis

The recommended initial dose is 5 mg or 10 mg of once-daily oral or IV torsemide, administered together with an aldosterone antagonist or a potassium-sparing diuretic. If the diuretic response is inadequate, titrated upward by approximately doubling until the desired diuretic response is obtained. Single doses higher than 40 mg have not been adequately studied.

Treatment of Hypertension

The usual oral 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.

Paediatric dosage

This drug has not been studies in children. It should not be used in children younger than 18 years.

General

DIUTOR tablets may be given at any time in relation to a meal, as convenient. Special dosage adjustment in the elderly is not necessary.

Because of the high bioavailability of torsemide, oral and doses are therapeutically equivalent, so patients may be switched to and from the intravenous form with no change in dose.

Method of

administration:
Diutor® 5, 10, 20
tablets For oral use

4.3 Contraindications
DIUTOR is contraindicated in patients with:
- Hypersensitivity to the active substance or to any other excipients listed in section 6.1
- Renal failure with anuria; hepatic coma and pre-coma; hypotension; pre-exisisting hypovolaemia; cardiac arrhythmias, simultaneous therapy with aminoglycoside, cephalosporins, or renal dysfunction due to drugs which cause renal damage.

4.4 Special warnings and precautions for use
Torsemide may lead to a profound diuresis with water and electrolyte depletion. Therefore, careful medical supervision is required, and dose schedules have to be adjusted to the individual patient's needs. Especially at the start of the treatment and in elderly, patients must be carefully monitored.

Regular blood monitoring of the electrolyte balance, potassium values and the parameters glucose, uric acid, and creatinine should be carried out especially during long-term treatment with torsemide for signs of electrolyte and volume deficiency and haemoconcentration.

Urine retention must be corrected before or during treatment with torsemide. Extreme caution is required when torsemide is administered in patients suffering from severe urine retention. Patients with partial occlusion of the urinary tract must be closely monitored. There is an increased risk of gout attacks with patients taking diuretics. Caution is required when torsemide is administered in patients with gout.

Carbohydrate metabolism in latent or manifest diabetes mellitus should be monitored.

In nephrotic syndrome, treatment of the primary disease should take precedence.

In patients with hepatic cirrhosis and ascites, it is recommended that diuresis with any drug be initiated in the hospital. Too rapid diuresis in such patients can precipitate severe electrolyte disturbances and hepatic coma. Extreme caution is required when torsemide is administered in patients with a history of hepatic encephalopathy. The concomitant use of an aldosterone antagonist or a potassium-sparing drug is recommended to prevent hypokalemia and metabolic alkalosis.

Torsemide might cause hypokalaemia that has prominent effects on cardiac, skeletal, and intestinal muscle cells. In particular, it is a major risk factor for both ventricular and atrial arrhythmias. Therefore, the potassium level of patients must be closely monitored during treatment with torsemide. Existing hypokalemia or

hypokalemia developing during torsemide treatment has to be corrected.

Low levels of sodium must be corrected before or during treatment with torsemide.

Hypovolemia must be corrected before or during treatment with torsemide.

Loop diuretics worsen existing hypotension. In case, diuretic treatment is required in hypotensive patients with oedema, hypotension must be corrected before or during treatment with torsemide.

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 potassium-depleting effect of mineralo- and glucocorticoids and laxatives may be increased.

As with other diuretics, the effect of antihypertensive drugs given concomitantly may be potentiated. Combination of loop diuretics with ACE inhibitors or AT2 antagonists may cause severe hypotension.

The risk of ACE-induced renal impairment may be increased.

Torsemide, especially at high doses, may potentiate the phototoxicity and nephrotoxic effects of aminoglycoside antibiotics, cytostatic platinum derivatives the nephrotoxic effects of cephalosporins, and the cardio-and neurotoxic effect of lithium. In patients receiving high doses of salicylates, salicylate toxicity may be increased. The action of anti-diabetic drugs may be reduced. Additionally, the risk of recurrent gout attacks is increased in patients taking salicylates.

Torsemide is a substrate for Cytochrome P450 CYP2C8 and CYP2C9. A mutual interaction between ligands for the same enzyme might occur. Therefore, co-medication that is also affected by these Cytochrome isoforms should be monitored closely to avoid unwanted plasma levels of these drugs. This interaction has been established for coumarin derivates. The possibility of Drug-Drug interaction may be crucial with drugs that have a narrow therapeutic range.

The antihypertensive and diuretic effects of loop diuretics appear to be reduced by NSAIDs. Diuretics may increase the risk of NSAID-induced acute renal failure.

Probenecid may reduce the diuretic effect of torsemide.

The effect of some muscle relaxants and the plasma level of theophylline may be influenced (increase or decrease possible). Monitoring of theophylline plasma levels is recommended.

Concomitant use of torsemide and cholestyramine has not been studied in humans, but in an animal study coadministration of cholestyramine decreased absorption of oral torsemide.

Simultaneous use of alcohol and torsemide may cause dizziness or other related symptoms.

4.5 Fertility, pregnancy and lactation Pregnancy

There is insufficient data from the use of torsemide in pregnant women. Studies in animals have shown reproductive toxicity. Torsemide should not be used during pregnancy, unless the clinical condition of the woman requires treatment with torsemide.

Breastfeeding

There is insufficient information on the excretion of torsemide in human milk. A risk to the suckling child cannot be excluded. Loop diuretics may suppress lactation. A decision should be made whether to discontinue breast-feeding or to discontinue from torsemide therapy taking into account the benefit of breast feeding for the child and the benefit of the
therapy for the woman.

4.6 Effects on ability to drive and use machines

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.

4.8 Undesirable effects

Allergic skin reactions
Metabolic alkalosis, fluid and electrolyte imbalance e.g. hypovolaemia and hyponatremia
Headache, dizziness
Loss of appetite, abdominal pain upper, nausea, vomiting, diarrhea, constipation
Muscle spasms
Fatigue, asthenia

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org.

4.9 Overdose.

Signs and symptoms of overdosage are those of excessive pharmacologic effects. 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. No data are available to suggest physiological manoeuvres (e.g., manoeuvers to change the pH of the urine) that might accelerate elimination of torsemide and its metabolites. torsemide is not dialyzable, so haemodialysis will not accelerate elimination. Symptoms and signs of overdosage require the reduction of the dose or withdrawal of torsemide, and simultaneous replacement of fluid and electrolytes.

5. Pharmacological properties

5.1 Pharmacodyna

5.2 mic properties Mechanism of Action

Pharmacotherapeutic group: High ceiling diuretics, sulphonamide monodrugs,

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 dependent manner with a high ceiling of effect.

Torsemide 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 torsemide dose has to be adequately increased in order to achieve effective amounts of drug at the site of action.

Torsemide leads to a gentle removal of oedema 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 oedema and maintenance of residual diuresis.

5.3 Pharmacokinetic properties

Absorption

Torsemide is absorbed rapidly and almost completely after oral administration, and peak serum levels are reached after one to two hours. More than 99% of torsemide is bound to plasma proteins.

Distribution

The apparent distribution volume is 16 litres

Metabolism

Torsemide is metabolised to three metabolites, M1, M3 and M5 by stepwise oxidation, hydroxylation or ring hydroxylation.

Elimination

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

Torsemide is eliminated by hepatic metabolism and renal excretion of the unchanged drug and its metabolites.

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

In spite of decreased renal elimination, the total clearance and elimination half-life of torsemide is unaffected in renal failure; the half-lives of M3 and M5 are prolonged, while the half-life of M1 is unchanged. The duration of action is not influenced by the severity of renal failure. Torsemide and its metabolites are not eliminated by hemodialysis or
hemofiltration.

5.4 Preclinical safety data

None available

6. Pharmaceutical particulars

6.1 List of Excipients:

Diutor® 5;

- Base granules
- Magnesium stearate
- Talc
- Croscarmellose sodium
- Colloidal silicon dioxide
- Film coating white color
- Isopropyl alcohol
- Methylene chloride

Diutor® 10;

- Base granules
- Magnesium stearate
- Talc
- Croscarmellose sodium
- Colloidal silicon dioxide
- Film coating (Sunset yellow)
- Isopropyl alcohol
- Methylene chloride

Diutor® 20;

- Base granules
- Magnesium stearate
- Talc
- Croscarmellose sodium
- Colloidal silicon dioxide
- Film coating (Tartrazine Lake)
- Isopropyl alcohol
- Methylene chloride

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
Diutor® 5, Diutor® 10 and Diutor® 20
36 months.

6.4 Special precautions for storage
Store below 30°C, Protect from direct sunlight, heat & moisture.

6.5 Nature and contents of container
Diutor® 5, Diutor® 10 and Diutor® 20 are available in the Pack of 3 x 10 Tablets.

6.6 Special precautions for disposal and other handling
Any unused medicine product or waste material should be disposed of in accordance with the local requirements.

7. Marketing authorization holder and manufacturing site addresses

Diutor® 5, Diutor® 10 and Diutor® 20 Manufactured in India by:
DAGON PHARMACEUTICALS PVT. LTD.
Located at Baddi-Nalagarh Road,
Village & Post: Manpura, Dist:
Solan, Himachal Pradesh – 174
101 – India.

Manufactured For & Marketed by:
KRISHNA CHEMISTS LTD.
P.O. BOX 3328-00506
NAIROBI, KENYA.

8. Marketing authorisation number(s)
H2009/24133/575

9. Date of first Registration/renewal of the Registration

03/06/2026

10. Date of revision of text

03/06/2026