SUMMARY OF PRODUCT CHARACTERISTICS
TORSEWIN-10 (Torsemide Tablets USP 10 mg)

1. NAME OF THE MEDICINAL PRODUCT

TORSEWIN-10 (Torsemide Tablets USP 10 mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated tablet contains torsemide USP 10 mg.

Excipients with known effect:

Each tablet contains 90.150 mg lactose monohydrate. For warnings, see section 4.4.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet (uncoated).

White, circular, flat, bevel-edged uncoated tablet with a break-line on one surface. The break-line is to facilitate breaking for ease of swallowing only and is not intended for division into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Oedema

TORSEWIN-10 is indicated for the treatment of oedema associated with:

- Heart failure.
- Renal disease.
- Hepatic disease.

Hypertension

TORSEWIN-10 is indicated for the treatment of hypertension to lower blood pressure. Lowering blood pressure reduces the risk of fatal and non-fatal cardiovascular events, primarily strokes and myocardial infarctions. TORSEWIN-10 can be used alone or in combination with other antihypertensive agents.

4.2 Posology and method of administration

Treatment of oedema — heart failure

Recommended initial dose: 10 mg or 20 mg orally once daily. If the diuretic response is inadequate, titrate upward by approximately doubling the dose until the desired response is obtained. Doses higher than 200 mg have not been adequately studied.

Treatment of oedema — chronic renal failure

Recommended initial dose: 20 mg orally once daily. Titrate upward by approximately doubling the dose if the response is inadequate. Doses higher than 200 mg have not been adequately studied.

Treatment of oedema — hepatic cirrhosis

Recommended initial dose: 5 mg or 10 mg orally once daily, administered together with an aldosterone antagonist or a potassium-sparing diuretic. Titrate upward by approximately doubling if the response is inadequate. Doses higher than 40 mg have not been adequately studied in this population.

Treatment of hypertension

Recommended initial dose: 5 mg once daily. If the 5 mg dose does not provide adequate reduction in blood pressure within 4–6 weeks, increase to 10 mg once daily. If the response to 10 mg is insufficient, add another antihypertensive agent to the treatment regimen.

Special populations

Renal impairment: Torsemide undergoes extensive hepatic metabolism (approximately 80% of total clearance); renal clearance is markedly decreased in renal failure but total plasma clearance is not significantly altered. However, a smaller fraction of the administered dose reaches the intraluminal site of action; the natriuretic effect is reduced. Monitor closely. Hepatic impairment: In patients with hepatic cirrhosis, the volume

of distribution, plasma half-life and renal clearance are all increased, but total clearance is unchanged. Patients with hepatic cirrhosis should receive the lowest effective dose with an aldosterone antagonist or potassium-sparing diuretic. Torsemide is contraindicated in hepatic coma. Geriatric patients: Renal clearance of torsemide is lower in elderly patients, consistent with age-related decline in renal function; however, total plasma clearance and elimination half-life remain unchanged.

Method of administration

Oral. May be taken with or without food. Food delays Tmax by approximately 30 minutes but does not alter overall bioavailability or diuretic activity.

4.3 Contraindications

- Known hypersensitivity to torsemide or to any of the excipients listed in section 6.1.
- Anuria.
- Hepatic coma.

4.4 Special warnings and precautions for use

Hypotension and worsening renal function

Excessive diuresis may cause potentially symptomatic dehydration, blood volume reduction and hypotension, and may worsen renal function, including acute renal failure — particularly in salt-depleted patients or those taking RAAS inhibitors. Worsening renal function can also occur with concomitant nephrotoxic drugs (e.g. aminoglycosides, cisplatin, NSAIDs). Volume status and renal function should be monitored periodically.

Electrolyte and metabolic abnormalities

Torsemide can cause hypokalaemia, hyponatraemia, hypomagnesaemia, hypocalcaemia and hypochloraemic alkalosis. Asymptomatic hyperuricaemia can occur; gout may rarely be precipitated. Treatment can increase blood glucose levels and cause hyperglycaemia. Serum electrolytes and blood glucose should be monitored periodically.

Ototoxicity

Tinnitus and hearing loss (usually reversible) have been observed with loop diuretics including torsemide. Higher than recommended doses, severe renal impairment and hypoproteinaemia appear to increase the risk of ototoxicity. Avoid concomitant use with aminoglycoside antibiotics if possible.

Lactose content

This product contains 90.150 mg lactose monohydrate per tablet. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

NSAIDs (including salicylates at high doses):

Torsemide and salicylates compete for renal tubular secretion; patients receiving high doses of salicylates may experience salicylate toxicity when torsemide is co-administered. NSAIDs may reduce the antihypertensive and diuretic effects of torsemide and have been associated with acute renal failure on co-administration.

CYP2C9 inhibitors:

Torsemide is a substrate of CYP2C9. CYP2C9 inhibitors (e.g. amiodarone, fluconazole, miconazole, oxandrolone) can decrease torsemide clearance and increase plasma concentrations. Adjust torsemide dose as necessary.

CYP2C9 inducers:

CYP2C9 inducers (e.g. rifampicin) increase torsemide clearance and decrease plasma concentrations.

CYP2C9 substrates:

Torsemide inhibits CYP2C9 metabolism; it may affect the efficacy and safety of sensitive CYP2C9 substrates such as celecoxib, or substrates with a narrow therapeutic range such as warfarin or phenytoin.

Cholestyramine:

Decreases absorption of orally administered torsemide; administer torsemide at least 1 hour before or 4–6 hours after cholestyramine.

Organic anion drugs (probenecid):

May reduce renal tubular secretion of torsemide, decreasing diuretic activity. Monitor diuretic effect and blood pressure.

Lithium:

Torsemide reduces renal clearance of lithium, inducing a high risk of lithium toxicity. Monitor lithium levels periodically.

Ototoxic drugs (aminoglycosides, ethacrynic acid):

Loop diuretics increase the ototoxic potential of other ototoxic drugs. Avoid concomitant use if possible.

ACE inhibitors / ARBs:

Co-administration increases the risk of hypotension and renal impairment.

Radiocontrast agents:

Torsemide can increase the risk of renal toxicity related to radiocontrast administration.

Corticosteroids and ACTH:

Concomitant use may increase the risk of hypokalaemia.

Digoxin:

Co-administration is reported to increase the AUC for torsemide by 50%, but dose adjustment of torsemide is not necessary. Torsemide does not affect digoxin pharmacokinetics.

Spironolactone:

Co-administration significantly reduces the renal clearance of spironolactone with corresponding increases in spironolactone AUC; the pharmacokinetic profile and diuretic activity of torsemide are not altered.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no available data on the use of torsemide in pregnant women regarding the risk of major birth defects or miscarriage. In pregnant rats and rabbits dosed at 10 and 1.7 times (respectively) the human dose of 20 mg/day (mg/m² basis), there was no foetotoxicity or teratogenicity. At 50 and 6.8 times the human dose, decreases in body weight, decreased foetal resorption and delayed foetal ossification were observed. Torsemide should only be used during pregnancy when clearly necessary and the potential benefits outweigh the risks. Diuretics can suppress lactation.

Breast-feeding

There are no data regarding the presence of torsemide in human milk or its effects on the breast-fed child. Diuretics can suppress lactation. A decision should be made whether to discontinue breast-feeding or to discontinue TORSEWIN-10, taking into account the benefit to the child and the importance of the medicine to the mother.

Fertility

No adverse effect on reproductive performance was observed in rats at doses up to 25 mg/kg/day (approximately 75 times the human dose of 20 mg on a body-weight basis).

4.7 Effects on ability to drive and use machines

Patients taking torsemide should be warned not to drive or operate machinery if they experience dizziness or related symptoms, as torsemide may produce changes in blood pressure.

4.8 Undesirable effects

Summary of the safety profile

In pre-approval studies, torsemide was evaluated for safety in approximately 4,000 subjects. Discontinuation of therapy due to adverse reactions occurred in 3.5% of patients in US studies. The most frequently reported adverse event in placebo-controlled trials was excessive urination (6.7% torsemide vs 2.2% placebo).

System Organ Class	Common/Uncommon	Rare/Not known
Blood/lymphatic		Reduction of corpuscular blood elements (RBCs, WBCs, platelets); leucopenia, thrombocytopenia, anaemia (post-marketing)
Metabolism/nutrition	Water and electrolyte depletion (hypokalaemia, hyponatraemia, hypomagnesaemia, hypocalcaemia); worsening metabolic alkalosis; hyperuricaemia; hyperglycaemia; increased blood lipids	Thiamine (vitamin B1) deficiency (post-marketing)

System Organ Class	Common/Uncommon	Rare/Not known
Nervous system	Headache, dizziness, somnolence	Limb paraesthesia, confusional states, cerebral ischaemia; paresthesia, confusion, visual impairment, loss of appetite (post-marketing)
Eye		Visual disturbances
Ear/labyrinth		Tinnitus, hearing loss (usually reversible; higher risk at doses above recommended, with severe renal impairment or hypoproteinaemia)
Cardiac	Hypotension, thromboembolic complications, cardiac ischaemia	Arrhythmias, angina pectoris, acute MI, syncope
Gastrointestinal	Loss of appetite, gastric pain, nausea, vomiting, diarrhoea, constipation, dry mouth	Pancreatitis, abdominal pain (post-marketing)
Hepatobiliary		Increase in liver enzymes, GGT (post-marketing)
Skin		Pruritus, rash, photosensitisation; SJS, TEN, photosensitivity (post-marketing)
Musculoskeletal	Muscle cramps	
Renal/urinary	Excessive urination (6.7% vs 2.2% placebo)	Urinary retention; acute urinary retention (post-marketing)
General	Asthenia	

Laboratory parameters

Potassium: After 6 weeks at 5–10 mg daily in hypertensive patients, mean decrease in serum potassium was approximately 0.1 mEq/L. Hypokalaemia was observed more frequently at higher doses in patients with heart failure, hepatic cirrhosis or renal disease. BUN, creatinine and uric acid: Small dose-related increases with reversal on discontinuation. Glucose: Mean increase of approximately 5.5 mg/dL after 6 weeks at 10 mg daily in hypertensive patients. Lipids: Small increases in total cholesterol and triglycerides in short-term studies, subsiding with chronic therapy.

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 the National Regulatory Authority.

4.9 Overdose

Symptoms

Signs and symptoms include dehydration, hypovolaemia, hypotension, hyponatraemia, hypokalaemia, hypochloraemic alkalosis and haemoconcentration.

Treatment

Fluid and electrolyte replacement. No data suggest that manoeuvres to change urine pH would accelerate elimination. Torsemide is not dialyzable; haemodialysis will not accelerate elimination.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: High-ceiling diuretics, sulphonamide monodrugs. ATC code: C03CA04.

Micropuncture studies in animals have shown that 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. Diuretic activity correlates better with the rate of drug excretion in the urine than with blood concentration. Torsemide increases urinary excretion of sodium, chloride and water but does not significantly alter GFR, renal plasma flow or acid-base balance.

With oral dosing, onset of diuresis occurs within 1 hour; peak effect occurs during the first or second hour; diuresis lasts about 6–8 hours. In patients with essential hypertension, torsemide has been shown in controlled

studies to lower blood pressure when administered once daily at 5–10 mg; the antihypertensive effect is near maximal after 4–6 weeks of treatment. The antihypertensive effects of torsemide are, like those of other diuretics, on average greater in Black patients than in non-Black patients.

5.2 Pharmacokinetic properties

Absorption

Oral bioavailability of torsemide tablets is approximately 80% (90% CI: 75–89%). Peak serum concentration (Cmax) is reached within 1 hour after oral administration. Cmax and AUC are proportional to dose over the range of 2.5–200 mg. Food delays Tmax by approximately 30 minutes but does not alter overall bioavailability or diuretic activity.

Distribution

Volume of distribution is 12–15 L in normal adults or in patients with mild to moderate renal failure or congestive heart failure; approximately doubled in patients with hepatic cirrhosis. Torsemide is extensively bound to plasma protein (>99%).

Metabolism

Torsemide is metabolised by hepatic CYP2C9 (and, to a minor extent, CYP2C8 and CYP2C18). Three main metabolites have been identified in humans: metabolite M1 (methyl-hydroxylation of torsemide), M3 (ring hydroxylation) and M5 (oxidation of M1; carboxylic acid derivative — the major metabolite in humans, biologically inactive). M1 and M3 possess some pharmacological activity but have much lower systemic exposure than torsemide.

Elimination

The elimination half-life of torsemide is approximately 3.5 hours in normal subjects. Torsemide is cleared by hepatic metabolism (approximately 80% of total clearance) and excretion into urine (approximately 20% in patients with normal renal function). After a single oral dose, the following were recovered in urine: torsemide 21%, M1 12%, M3 2% and M5 34%.

Renal impairment

Renal clearance of torsemide is markedly decreased in renal failure but total plasma clearance is not significantly altered; a smaller fraction of administered dose reaches the intraluminal site of action, reducing natriuretic effect.

Hepatic impairment

In hepatic cirrhosis, volume of distribution, plasma half-life and renal clearance are all increased, but total clearance is unchanged.

5.3 Preclinical safety data

No overall increase in tumour incidence was found when torsemide was given to rats (up to 9 mg/kg/day) and mice (up to 32 mg/kg/day) throughout their lives. In the rat study, the high-dose female group demonstrated renal tubular injury, interstitial inflammation and a statistically significant increase in renal adenomas and carcinomas; however, the tumour incidence was not much higher than in historical controls. Similar non-neoplastic renal injury has been reported with other diuretics. No mutagenic activity was detected in a variety of in vivo and in vitro tests including the Ames test, chromosome aberration and sister-chromatid exchange tests in human lymphocytes, nuclear anomaly tests in bone marrow, and unscheduled DNA synthesis tests. Torsemide had no adverse effect on reproductive performance in rats at doses up to 25 mg/kg/day.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate (excipient with known effect — 90.150 mg per tablet), microcrystalline cellulose, maize starch, povidone, purified talc, magnesium stearate, croscarmellose sodium, isopropyl alcohol.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months from the date of manufacture.

6.4 Special precautions for storage

Store below 30°C. Keep out of the reach and sight of children.

6.5 Nature and contents of container

ALU-ALU blister pack of 10 tablets. Pack size: 10 tablets.

6.6 Special precautions for disposal and other handling

No special requirements. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

WIN PHARMA LTD.

P.O. Box 2482-00200, Nairobi, Kenya.

8. MARKETING AUTHORISATION NUMBER (PPB REGISTRATION NUMBER)

H2019/5258/1163ER

9. DATE OF FIRST AUTHORISATION / RENEWAL OF AUTHORISATION

08.02.2026

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