NEFISTOR 10/20
Torsemide Tablets USP 10 mg/20 mg

NEFISTOR 10
COMPOSITION:
Each Uncoated Tablet Contains:
Torsemide USP 10 mg
Excipients q.s.

NEFISTOR 20
COMPOSITION:
Each Uncoated Tablet Contains:
Torsemide USP 20 mg
Excipients q.s.

DESCRIPTION:
NEFISTOR (Torsemide Tablets USP 10 mg/20 mg) contains Torsemide as an active.

PHARMACODYNAMICS:
Pharmacodynamic properties
Pharmacotherapeutic group: High ceiling diuretics, sulphonamide monodrugs,
ATC code: C03CA04

Mechanism of Action:
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 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 An increase in diuresis may also take place if other diuretics are no longer active, e.g. in the presence of impaired renal function.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 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 endstage chronic renal failure there is a reduction of aterial blood pressure in addition to removal of edema and maintenance of residual diuresis.
Pharmacokinetic Properties
Absorption
Torsemide 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 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. Further metabolites (M2 and M4) have been found in animal experiments, but not in humans.
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%.
In patients with congestive heart failure and disorders of liver fnction, 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 the presence of renal failure, elimination half-life of Torsemide is unchanged.

THERAPEUTIC INDICATIONS:
NEFISTOR (Torsemide Tablets USP 10 mg/20 mg) is indicated in treatment of:
Oedema due to congestive heart failure; hepatic, pulmonary or renal oedema.

POSOLOGY AND METHOD OF ADMINISTRATION:
Posology:
Adults
Oedema:
The usual dose is 5 mg. once daily.
If necessary, the dose can be increased stepwise up to 20 mg once daily.
In individual cases, as much as 40 mg Torsemide /day has been administered.
Elderly
No special dosage adjustments are necessary.
Children
There is no experience of Torsemide in children.
Method of Administration:
NEFISTOR (Torsemide Tablets USP 10 mg/20 mg) is given orally.

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

SPECIAL WARNING AND PRECAUTION FOR USE:
Hypokalaemia, hyponatraemia, hypovolaemia and disorders of micturition must be corrected before treatment.
On long-term treatment with Torsemide, 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 Torsemide should be warned not to drive or operate machinery if they experience dizziness or related symptoms.
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.

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

PREGNANCY, BREAST-FEEDING AND FERTILITY
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.

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.

UNDESIRABLE EFFECTS:
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:
Metabolism and nutrition disorders
Common: Metabolic alkalosis, Fluid and electrolyte imbalance (e.g. Hypovolaemia, Hyponatraemia)
Nervous system disorders
Common: Headache, Dizziness
Frequency not known: Cerebral ischaemia, Parenthesia, confusional state
Gastrointestinal disorders
Common: Gastrointestinal disorder (e.g. Loss of appetite, abdominal pain upper, Nausea, Vomiting, Diarrhoea, Constipation)
Frequency not known: Dry mouth, Pancreatitis
Hepatobiliary disorders
Uncommon: Hepatic enzyme increased (e.g. Gamma-glutamyltransferase increased)
Skin and subcutaneous tissue disorders
Very rare: Allergic skin reactions (e.g. Pruritus, Exanthema), Photosensitivity reaction Frequency not known: Serious skin reactions (e.g. Stevens-Johnson syndrome, Toxic epidermal necrolysis
Musculoskeletal and connective tissue disorders
Common: Muscle spasms
Renal and urinary disorders
Uncommon: Urinary retention, Bladder dilatation
Rare: Blood urea increased, Blood creatinine increased
General disorders and administration site conditions
Common: Fatigue, Asthenia
Investigations
Uncommon: Blood uric acid increased, Blood glucose increased, Lipids increased (e.g. Blood triglycerides increased, Blood cholesterol increased)

OVERDOSE
Symptoms and signs
No typical picture of intoxication is known. If over dosage 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.

SHELF LIFE:
36 Months

PACKAGING
10 Tablets are packed in Alu-Alu Blister & such 3 Blisters are packed in printed carton along with pack insert.

STORAGE CONDITION:
Stored at a temperature not exceeding 30°C. Protect from light and moisture.
Keep the medicine out of reach of children.

Imported by:
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MANUFACTURED BY:
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