AVOZINE 5MG TABLETS

COMPOSITION:

Each tablet contains:
Levocetirizine dihydrochloride 5 mg
equivalent to 4.2mg of Levocetirizine

PRODUCT DESCRIPTION:

Avozine 5mg Tablet is a white to off-white biconvex ellipse film-coated tablet, with '486 imprinted on one side and 'NK' on the other side.

PHARMACOLOGICAL PROPERTIES:

Pharmacodynamic properties

ATC code : R06A E09

Levocetirizine is the active component of cetirizine. It is a selective competitive inhibitor for the H1-histamine receptor, both in vitro and in vivo.

Pharmacokinetic properties

Absorption
Levocetirizine is rapidly and extensively absorbed following oral administration. Steady state is achieved after 2 days. Peak concentrations are typically 270 and 308 ng/mL following a single and repeated 5mg once daily dose, respectively. The extent of absorption is dose-independent and is not altered by food. However, the peak concentration is reduced and delayed. Therefore, levocetirizine can be administered with or without food.

Distribution
No tissue distribution data are available in humans. Levocetirizine is 90% bound to plasma proteins. The distribution of levocetirizine as the volume of distribuition is 0.4 L/kg,

Metabolism
The extent of metabolism of levocetirizine in humans is less than 14% of the dose and therefore differences resulting from genetic polymorphism or concomitant intake of hepatic drug metabolizing enzyme inhibitors are expected to be negligible. Metabolic pathways include aromatic oxidation, N- and O-dealkylation, and taurine conjugation. Dealkylation pathways are primarily mediated by CYP 3A4 while aromatic oxidation involves multiple and/or unidentified CYP isoforms.

Elimination
The plasma half-life in adult healthy subjects is 7.9 +/- 1.9 hours. The mean oral total body clearance for levocetirizine is 0.63 mL/kg/min. The major route of excretion of levocetirizine and its metabolites is via urine.
Excretion via faeces accounts for only 12.9% of the dose. Levocetirizine is excreted both by glomerular filtration and active tubular secretion. In patients with renal impairment the clearance of levocetirizine is reduced.

INDICATIONS:

Levocetirizine is indicated for the symptomatic treatment of allergic rhinitis (including persistent allergic rhinitis) and chronic idiopathic urticaria.

DOSAGE AND ADMINISTRATION:

The tablet must be taken orally, swallowed whole with liquid and may be taken with or without food. It is recommended to take the daily dose in one single intake.

- Adults and Adolescents 12 Years and Above:

The daily recommended dose is 5mg (1 tablet).

- Children Aged 6 to 11 Years:

The daily recommended dose is 5mg (1 tablet). It is not recommended for children aged less than 6 years.

- Elderly:

Adjustment of the dose is recommended in elderly patients with moderate to severe renal impairment (see Patients with Renal Impairment below).

- Patients with Renal Impairment:

The dosing intervals must be individualised according to renal function. Refer to the following table and adjust the dose as indicated. To use this dosing table, an estimate of the patient's creatinine clearance (CLcr) in ml/min is needed. The CLcr (ml/min) may be estimated from serum creatinine (mg/dl) determination using the following formula:

$$CL_{cr} = \frac{[140 - age(years)] * weight(kg)}{72 * serum\ creatinine(mg/dl)} (* 0.85\ for\ women)$$

Dosing Adjustments for Patients with Impaired Renal Function:

Group	Creatinine clearance (ml/min)	Dosage and frequency
Normal	≥ 80	5 mg once daily
Mild	50 – 79	5 mg once daily
Moderate	30 – 49	5 mg once daily once every 2 days
Severe	< 30	5 mg once daily once every 3 days
End-stage renal disease - Patients undergoing dialysis	< 10	Contraindicated

In paediatric patients suffering from renal impairment, the dose will have to be adjusted on an individual basis taking into account the renal clearance of the patient and his body weight. There is no specific data for children with renal impairment.

No dose adjustment is needed in patients with solely hepatic impairment. In patients with both hepatic impairment and renal impairment, adjustment of the dose is recommended.

Duration of Use:
Intermittent allergic rhinitis (symptoms < 4 days/week or during less than 4 weeks) has to be treated according to the disease and its history; it can be stopped once the symptoms have disappeared and can be restarted again when symptoms reappear. In case of persistent allergic rhinitis (symptoms > 4 days/week and during more than 4 weeks), continuous therapy can be proposed to the patient during the period of exposure to allergens. Clinical experience with 5 mg levocetirizine as a film-coated tablet formulation is currently available for a 6-month treatment period. For chronic urticaria and chronic allergic rhinitis, up to one year's clinical experience is available for the racemate cetirizine.

CONTRAINDICATIONS:

Contraindicated in the followings:

- History of hypersensitivity to levocetirizine or any of the other constituents of the formulation or to any piperazine derivatives.
- Patients with severe renal impairment at less 10ml/min creatinine clearance.

PRECAUTIONS AND WARNINGS

- The use of levocetirizine 5mg is not recommended in children aged less than 6 years since the currently available film-coated tablets do not yet allow dose adaptation.
- Precaution is recommended with intake of alcohol
- Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Effects on ability to drive and use machines

There is no evidence that levocetirizine at the recommended dose impairs mental alertness, reactivity or the ability to drive. Nevertheless, some patients could experience somnolence, fatigue and asthenia under therapy with levocetirizine 5mg. Therefore, patients intending to drive, engage in potentially hazardous activities or operate machinery should take their response to the medicinal product into account.

Risk of urinary retention

Urinary retention has been reported with use of levocetirizine. Hence, it should be given with cautions in patients with predisposing factors of urinary retention (eg. spinal cord lesion, prostatic hyperplasia) as levocetirizine may increase the risk of urinary retentions. Discontinue levocetirizine if urinary retention occurs.

PREGNANCY:

Pregnancy and Lactation

For levocetirizine no clinical data on exposed pregnancies are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/fetal development, parturition or postnatal development. Caution should be exercised when prescribing to pregnant or lactating women.

DRUG INTERACTIONS:

- No interaction studies have been performed with levocetirizine (including no studies with CYP3A4 inducers); studies with the racemate compound cetirizine demonstrated that there were no clinically relevant adverse interactions (with pseudoephedrine, cimetidine, ketoconazole, erythromycin, azithromycin, glipizide and diazepam). A small decrease in the clearance of cetirizine (16%) was observed in a multiple dose study with theophylline (400mg once a day); while the disposition of theophylline was not altered by concomitant cetirizine administration.
- The extent of absorption of levocetirizine is not reduced with food, although the rate of absorption is decreased.
- In sensitive patients the simultaneous administration of cetirizine or levocetirizine and alcohol or other CNS depressants may have effects on the central nervous system, although it has been shown that the racemate cetirizine does not potentiate the effect of alcohol.

SIDE EFFECT

- Immune system disorders: hypersensitivity.
- Common: somnolence, dizziness, headache, fatigue and gastrointestinal disorders, such as abdominal pain, dry mouth and nausea
- Asthenia and malaise has been observed.
- Respiratory, thoracic, and mediastinal disorders: dyspnea
- Skin and subcutaneous tissue disorders: angioneurotic oedema, pruritus, rash, urticaria
- Increase in body weight

OVERDOSAGE:

Symptoms: symptoms of overdose may include drowsiness in adults and initially agitation and restlessness, followed by drowsiness in children. Management of overdoses: There is no known specific antidote to levocetirizine. Should overdose occur, symptomatic or supportive treatment is recommended. Gastric lavage should be considered following short-term ingestion. Levocetirizine is not effectively removed by haemodialysis.

STORAGE:

Store below 30°C. Protect from light and moisture.
Keep out of reach of children.

PACKING:

10 tablets in an alu-alu blister, 1, 3 and 10 blisters is packed in a printed box.

Manufactured Under License from

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