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

(Levocetirizine Dihydrochloride Tablets USP 5 mg / Levocetirizine Dihydrochloride Syrup)

LEVOZIN Tablets 5 mg
LEVOZIN Syrup 2.5 mg/5ml

(Levocetirizine Dihydrochloride Syrup 2.5mg/5ml):

Description and composition: Orange coloured syrup pleasantly flavoured having a sweet taste and no sediment filled in amber colour bottle, sealed with ROPP cap labeled and placed in a printed carton. Each 5ml contains: Levocetirizine Dihydrochloride 2.5mg and sunset yellow as permitted colour.

Levocetirizine Tablets 5mg (Levocetirizine Dihydrochloride Tablet 5mg):

Description and composition: Yellow coloured circular, biconvex film coated tablets plain on both sides.

Each film coated tablet contains: Levocetirizine Dihydrochloride 5mg, Titanium dioxide and Quinoline yellow as colouring agents.

Pharmacodynamics

Levocetirizine is the active component of Cetirizine. It is a selective competitive inhibitor for the H1- histamine receptor, both in vitro and in vivo. There is no evidence of any binding with other receptors at concentrations 500 fold higher than those displacing a H1- ligand. It is effective in antagonizing histamine effects in both cutaneous and pulmonary models after IV and PO administration of 0.1-0.2 mg/kg. As with cetirzine safety pharmacology studies indicate a high margin of safety for adverse effects on the CNS, GI, immune and cardiovascular systems. Levocetirizine is unlikely to be involved in torsades de pointes or other arrhythmias. In addition, as levocetirizine is mainly excreted unchanged in man and does not inhibit the major CYP isoforms in human liver microsomes, cardiac and other adverse effects due to pharmacokinetic interactions are also unlikely.

Pharmacokinetics

The pharmacokinetic profile of levocetirizine is linear and time-independent with low inter-subject variability. The clearance of levocetirizine differs slightly in men and women. This difference is clearance, however, does not necessitate the use of a different dose or different dosage intervals in men and women. The pharmacokinetic profiles is the same when given as the single enantiomer or when given as Cetirizine. No chiral inversion occurs during the process of absorption and elimination.

Absorption

Levocetirizine is rapidly and extensively absorbed following oral administration. Peak plasma concentrations are achieved 0.9 h after dosing. Steady state is achieved after two days. Peak concentrations are typically 270ng/ml and 308ng/ml following a single and repeated 5 mg o.d. dose, respectively. The extent of absorption is dose-independent and is not altered by food, but the peak concentration is reduced and delayed.

Distribution

No tissue distribution data are available in humans. Levocetirizine is 90% bound to plasma proteins. The distribution of Levocetirizine is restrictive, as the volume of distribution is 0.41 /kg.

Elimination

The plasma half-life in adults is 7.9 ± 1.9 hours. The mean apparent total body clearance is 0.63 ml/min/kg. The major route of excretion is via urine, accounting for a mean of 85.4% of the dose. Excretion via faeces accounts for only 12.9% of the dose. The renal clearance of levocetirizine is close to 30 ml /min/ 1.73m^2. When corrected for protein binding the value is about 260ml /min/1.73 m^2. Therefore, levocetirizine is excreted both by glomerularfiltration and active tubular secretion.

Renal Impairment

The apparent body clearance of levocetirizine is correlated to the creatnine clearance. It is therefore recommended to adjust the dosing intervals of levocetirizine, based on creatinine clearance in patients with moderate and severe renal impairment. In anuric end stage renal disease subjects, the total body clearance is decreased by approximately 80% when compared to normal subjects. The amount of levocetirizine removed during a standard 4- hour hemodialysis procedure was <10%.

Indication

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

Recommended dosage

Tablet: The film-coated 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 5 mg (1 film-coated tablet).

Elderly:

Adjustment of the dose in recommended in elderly patients with compromised renal function (see patients with renal impairment below).

Children aged 6 to 12 years: The daily recommended dose is 5 mg (1 film-coated tablet). For children aged less than 6years no adjusted dosage is yet possible.
Solution:
Instruction for use
Appropriate volume of oral solution should be measured with the oral syringe, and poured in a spoon or in a glass of water. The oral solution must be taken orally immediately after dilution, and may be taken with or without food.

Adults and adolescents 12 years and above:
The daily recommended dose is 5 mg (10 ml of solution).

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

Children aged 6 to 12 years:
The daily recommended dose is 5 mg (10 ml of solution).

Children aged 2 to 6 years:

The daily recommended dose is 2.5 mg to be administered in 2 intakes of 1.25 mg (2.5 ml of solution twice daily).
Due to the lack of data in this population, the administration of the product to infants and toddlers aged less than 2 years is not recommended.

Patients with renal impairment:

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

$$CLcr = \frac{[140 - \text{Age (years)} \times \text{weight (kg)}]}{72 \times \text{serum creatinine}} \times (0{,}85 \text{ for women})$$

Dosing adjustments for patients with impaired renal function:

Group	Creatinine clearance (ml/min)	Dosage and frequency
Normal	≥ 80	1 tablet once daily
Mild	50- 79	1 tablet once daily
Moderate	30- 49	1 tablet once every 2 days
Severe	<30	1 tablet once every 3 days
End-stage renal disease	< 10	Contra-indicated
Patients undergoing dialysis		

Patients with hepatic impairment:
No dose adjustment is needed in patients with solely hepatic impairment. In patients with hepatic impairment and renal impairment, adjustment of the dose is recommended (see patients with renal impairment above).

Duration of use:
Intermittent allergic rhinitis (symptoms <4days/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 >4days/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, clinical experience is available for the racemate.

Mode of administration

Oral

Contraindication

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

Warning and precautions:

The use of Levocetirizine Dihydrochloride Tablets 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 (see interactions). Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-glactose malabsorption should nottake this medicine.

Effects on ability to drive and use machines:

Comparative clinical trials have revealed no evidence that cetirizine, the racemate of levocetirizine, impairs mental alertness, reactivity or the ability to drive. This also applies to the use of this drug in the recommended dosage. Neverthless, patients intending to drive, engage in potentially hazardous activities or operate machinery should not exceed the recommended dose and should take their response to the medicinal product into account. In those sensitive patients, concurrent use with alcohol or other CNS depressants may cause additional reductions in alertness and impairment of performance.

Interactions with other medicinal products and other forms of interaction:

No interactions studies have been performed with levocetirizine (including no studies with CYP3A4 inducer); studies with the racemate compound cetirizine demonstrated that there were no clinically relevant adverse interactions (with pseudoephdrine, cimetidine, ketoconazole, erythromycin, azithromycin, glipzide and diazepam). A small decrease in the clearance of cetirizine (16%) was observed in a multiple dose study with theophylline (400 mg once a day); while the disposition of theophylline was not altered by concomitant cetirizine administration. The extent absorption of levocetirizine is not reduced with food, although the rate of absorption is decreased. In sensitive patients the simultaneous administration of cetrizine 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.

Pregnancy and Lactation

For Levocetirizine no clinical data an 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.

Side effects:

From clinical studies, mainly mild to moderate side effects such as dry mouth, headache, fatigue and somnolence have been reported commonly (above 1%). Further uncommon incidences of adverse reactions like asthenia or abdominal pain were observed. In addition to the adverse reported during clinical studies and listed above, very rare cases of the following adverse drug reactions have been reported in post-marketing experience: hypersensitivity including anaphylaxis, dyspnoea, nausea, angioneurotic oedema, pruritus, rash, urticaria and weight increased also periorbital swelling and swelling of face reported.

Symptoms and Treatment of Overdose

Symptoms
Symptoms of overdose may include drowsiness in adults and initially agitation and restlessness, followed by drowsiness in children.

Management of overdose
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. Levocetrizine is not effectively removed by haemodialysis.

Storage condition

Store in a dry place below 30°C and protect from light.

Shelf life

2 years from the date of manufacture.

Presentation

LEVOZIN Syrup 2.5 mg/5ml (Levocetirizine Dihydrochloride Syrup):
60 and 30 ml type III amber colored round bottles with 25 mm ROPP caps, packed in labeled carton along with package insert.

LEVOZIN Tablets 5 mg (Levocetirizine Dihydrochloride Tablets):
Blister of 10 tablets, 5 or 20 such blisters are packed in a printed carton along with the package insert

MAL10100016AZ
MAL11030093AZ

Date of preparation: January 2022

Manufactured in India by:
Tablet manufactured at:
FDC Ltd,
L-121/B, Phase III/A, Verna Industrial Estate,
Verna - 403 722, Salcete, Goa.

Solution manufactured at:
FDC Limited,
B-8, MIDC Industrial Area, Waluj,
Aurangabad - 431 136, Maharashtra.

SAP CODE

FDC Limited	LEAFLET	Std. Pharma Code No.: **Front: 196 / Back: 197**
Size	110 mm x 280 mm - Artwork Same Size	
FoldedSize		UnfoldedSize
No. of Folds		
GSM	60 GSM	
Paper	Maplitho Paper	
Specifican No.		
Colour	■ PANTONE Process Black	
SAP Code :		Supercedes SAP Code: 2000005554
Location : Goa III - Country: Malaysia		Prepared On: 28-09-2021

Reason for Change: 1) Brand Name added.
2) USP add in generic name.
3) Instruction for use added.