8026222-9093

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

ALLENIL

(Olopatadine Hydrochloride Tablets)

Composition

Each film coated tablet contains :

Olopatadine Hydrochloride U.S.P.	5 mg
Excipients	q.s.

Colours : Red Oxide of Iron & Titanium Dioxide I.P.

Dosage Form

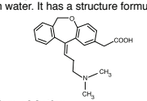
Tablet

Clinical Pharmacology

Olopatadine is an antihistaminic and antiallergic agent.

Description

Olopatadine Hydrochloride is the hydrochloride salt of (11Z)-11-[3-(Dimethyl-amino)propylidene]-6,11-dihydrodibenzo[*b*,*e*]oxepin-2-yl-acetic acid. It has empirical formula $C_{21}H_{23}NO_3 \cdot HCl$; and has a molecular weight 373.87. Olopatadine Hydrochloride is soluble in water. It has a structure formula :



Mechanism of Action

Olopatadine is a selective histamine H_1 receptor antagonist possessing inhibitory effects on the release of inflammatory lipid mediators such as leukotrienes, thromboxane, platelet activating factor (PAF), etc., from human polymorphonuclear leukocytes and eosinophils. It also inhibits the tachykininergic contraction in the bronchi of allergen model by prejunctional inhibition of peripheral sensory nerves.

Pharmacokinetics

After single oral administration of olopatadine hydrochloride 5mg and 10mg under fasting conditions to healthy adults, olopatadine was absorbed rapidly and reached the maximum concentration C_{max} (107.66 ± 22.01 ng/ml for 5 mg and 191.78 ± 42.99 ng/ml for 10 mg) in about 0.5 to 2 hour (T_{max} - 1.00 ± 0.32 hr for 5 mg and 0.92 ± 0.47 hr for 10 mg). The elimination half life $t_{½}$ for 5 mg and 10 mg olopatadine tablet are 8.75 ± 4.63 hr and 7.13 ± 2.21 hr respectively while the AUC parameter for 5 mg and 10 mg olopatadine tablet is 326 ± 83 ng.hr/ml and 638 ± 136 ng.hr/ml respectively.

After repeated oral administration of olopatadine hydrochloride 10 mg, 2 times a day for 6 days and 1 time on 7th day, (total 13 times), C_{max} approaches to 1.14 times as that of oral single administration.When 10 mg of olopatadine hydrochloride is given orally once after breakfast to patients with low kidney function whose creatinine clearance was 2.3 to 34.4mL/min, blood plasma concentration shows C_{max} in 1.0 to 8.0 hours after administration and it vanishes monophasically. Compared to healthy adult, C_{max} of patients with low kidney function is 2.3 times higher and AUC is about 8 times higher. In elderly subjects (above 70 years age), the concentration change is high compared to healthy adults. C_{max} is about 1.3 times higher, AUC is about 1.8 times higher while $t_{½}$ is mostly 10 to 11 hours in both the cases. The protein binding ratios in human plasma are in a range of 54.7-55.2%, and the main binding protein is human albumin.

In plasma after oral administration at a dose of 80 mg, the N-oxide form (M3) and N-monodesmethyl form (M1) were detected at amounts of about 7% and 1% of the unchanged drug, respectively. The plasma concentrations of both metabolites decreased in parallel to the decrease of the unchanged drug. The N-didesmethyl form (M2) was not detected in the plasma.When olopatadine hydrochloride 5 mg and 10 mg is given orally to healthy adults once, the accumulated urine excretion percentage till 48 hours was in the range of 63.0 to 71.6% of administered amount. Further if 10 mg of olopatadine is given orally for 2 times a day for 6 days and once on 7th day (total 13 times) the excretion percentage was shown to be similar to that after one single oral administration.

Indications

ALLENIL is indicated for allergic rhinitis, urticaria and itching accompanied by skin diseases (eczema, dermatitis, pruritus cutaneous, psoriasis vulgaris and erythema exudativum multiforme).

Contra-indications

Hypersensitivity to olopatadine or any other ingredients of this formulation.

Warnings and Precautions

Caution is advised while administering olopatadine to patients with impaired renal function, liver malfunction and the elderly. In patients with renal dysfunction, there is a risk of increased blood levels of the drug. There is a risk of degeneration of liver function, if olopatadine is administered to patients with impaired liver function. A higher blood plasma concentration and increase in other pharmacokinetic parameters is observed in elderly patients compared to healthy adults.

As olopatadine can cause an increase in AST (GOT),

gamma-GTP, LDH, AI-P levels, etc. along with liver malfunction and jaundice, the patient should be carefully observed and in case of an abnormality, treatment should be stopped and proper measures should be taken. Since olopatadine causes drowsiness, patients should be asked to avoid driving an automobile or operating machinery, while taking the drug.

For patients receiving steroid treatment, the reduction in steroid intake with this drug should be carried out gradually under control. In case of administration to patients with seasonal allergic disease, treatment should be started at the beginning of and it is advisable to continue till end of the season.

Prolonged use of the drug should be avoided in patients in whom the therapy does not a show a positive effect.

Olopatadine interferes with allergic skin testing. Thus, the use of olopatadine tablet should be avoided before performing any such procedure.The relation is not clear but after intake of olopatadine, symptoms of myocardial infarction have been reported.

Pregnancy & Lactation

Safety of olopatadine in pregnant women is not established so olopatadine should be given to pregnant women or women with possibility of pregnancy, only if the benefit is greater than risk. Olopatadine has been reported to be excreted in the milk of lactating rats. Because of the potential for adverse effects on the nursing infant, a decision should be made whether to discontinue nursing or discontinuing the drug, taking into account the importance of the drug to the mother.

Drug Interactions

Olopatadine did not inhibit P450 activities when it was simultaneously incubated with substrates for different P450 isozymes. Also, P450 activities in human liver microsomes were unaffected by pretreatment with olopatadine or M1. Furthermore, spectral analysis revealed that neither olopatadine nor M1 formed an MIC (metabolic intermediate complex). Therefore, it is unlikely that olopatadine will cause drug-drug interactions involving P450 isozymes.

Side effects

The most commonly reported adverse effects with olopatadine are sleepiness, fatigue, dry mouth, stomach pain, discomfort in stomach, rise in AST(GOT), ALT(GPT), g-GTP, LDH, AI-P, etc., increase in W.B.C and eosinophils, occult blood, protein in urine, increased serum cholesterol and urine sugar positive. Other side effects of olopatadine include symptoms like redness, swelling of face or limbs etc, labored breathing, headache, heaviness, giddiness, numbness, less concentration, diarrhea, mouth ulcer, angular stomatitis, heartburn, hyperphagia, constipation, increase in total bilirubin, reduced lymphocyte & W.B.C.count, increased urinary creatinine and BUN, dysuria, rise in blood pressure, discomfort in chest, increase in body weight, involuntary movement of face or limbs, taste perversion, abnormal menstruation, burning, muscle pain and joint pain.

Overdosage

There is no information available on the overdose of olopatadine by oral administration.

Dosage and Administration

Dosage should be adjusted according to individual patient response and tolerability. The usually recommended dose of **ALLENIL** for adults is 5 mg twice a day, given in morning and in the night before sleeping.

Elderly : Since the elderly have a physiological hypofunction and a greater sensitivity to adverse effects, the administration of olopatadine should begin with a lower dose. Caution is advised throughout the treatment period.

Pediatric use : Safety of olopatadine in low birth weight infants, neonate, suckling infant and infants is not established so it should not be used for infants.

Hepatic impairment : There is a risk of degeneration of liver function, if olopatadine is administered to patients with impaired liver function. Therefore, caution is advised while administering olopatadine to patients with liver malfunction.

Renal impairment : In patients with renal dysfunction, there is a risk of increased blood levels of the drug. Thus, caution is advised while administering olopatadine to patients with impaired renal function.

Incompatibilities

None known.

Storage

Store below 25°C in a dry place, protected from light. Keep out of reach of children.

Expiry Date

Do not use later than expiry date.

Presentation

ALLENIL is available as 5 mg tablets in blister strip of 10's.

torrent

Marketed by :
TORRENT PHARMACEUTICALS LTD.
Indrad-382 721, Dist. Mehsana, INDIA.

Manufactured by :
Hetero Labs Limited,
Village : Kalyanpur, Chakkan Road, Baddi.
Tehsil : Nalagarh , Dist. Solan,
Himachal Pradesh - 173 205.