165mm

155mm

Statins
Asymptomatic CPK increases have been uncommonly reported in Rupatadine clinical trials. The risk of interactions with statins, some of which are also metabolised by the cytochrome P450 CYP3A4 isoenzyme,is unknown. For these reasons, Rupatadine should be used with caution when it is co-administered with statins.

Midazolam
After the administration of 10mg Rupatadine in combination with 7.5mg midazolam, an increase of exposure (Cmax and AUC) of midazolam was mildly higher observed. For this reason, Rupatadine acts as a mild inhibitor of CYP3A4.

OVERDOSAGE
The most common adverse reaction was somnolence. If accidental ingestion of very high doses occurs symptomatic treatment together with the required supportive measures should be given.

HOW SUPPLIED
Rupaler (Rupatadine) 1mg /ml Oral Soultion is available in bottle of 60ml and 120ml.
Rupaler (Rupatadine) Tablets 10mg are available in blister pack of 10's, 20's and 30's.

DOSAGE:
As directed by the physician.

Instructions:
Store below 30°C, protect from light.
To be dispensed on the prescription of a registered medical practitioner only. Keep cap tightly closed.
Keep out of the reach of children.

خوراک : ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایات : دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر روشنی سے بچا کر جگہ پر رکھیں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے پر ہی فروخت کریں۔
ڈھکن کو اچھی طرح بند رکھیں۔ بچوں کی پہنچ سے دور رکھیں۔

Kaizen Pharmaceuticals (Pvt.) Ltd.

Manufactured by:
Kaizen Pharmaceuticals (Pvt.) Ltd.
E-127-129, North Western Industrial Zone,
Bin Qasim, Karachi-75020, Pakistan.

Rupaler

(Rupatadine Fumarate)

1mg /ml Oral Soultion & 10mg Tablet

روپالر

(روپاٹاڈین فیومیریٹ)

ایم ایل گرام / ملی لیٹر اورل سلوشن اور ۱۰ ایم ایل گرام گولی

Description:
Rupaler (Rupatadine) is a powerful medication used to treat various allergic conditions. It is an antihistamine with platelet-activating factor (PAF) antagonist activity.

Composition:
Each ml contains
Rupatadine as Fumerate……1mg

Each tablet contains
Rupatadine as Fumerate……10mg

CLINICAL PHARMACOLOGY
Mechanism of Action:
Rupatadine is a second-generation antihistamine, long-acting histamine antagonist with selective peripheral H1-receptor and platelet activating factor (PAF) antagonistic activities. Some of the metabolites (desloratadine and its hydroxylated metabolites) retain an antihistaminic activity and may partially contribute to the overall efficacy of the drug, maintaining activity for up to 24 hours.

PHARMACOKINETICS
Absorption
Rupatadine is rapidly absorbed after oral administration, with a Tmax of approximately 0.75 hours after intake. The mean Cmax was 2.6ng/ml after a single oral dose of 10mg and 4.6ng/ml after a single oral dose of 20mg. Pharmacokinetics of Rupatadine was linear for a dose between 10mg and 20mg after single and repeated doses. After a dose of 10mg once a day for 7 days, the mean Cmax was 3.8ng/ml. The plasma concentration followed a bi-exponential drop-off with a mean elimination half-life of 5.9 hours. The binding-rate of Rupatadine to plasma proteins was 98.5-99%.

Effect of Food
Intake of food increased the systemic exposure (AUC) to Rupatadine by about 23%. The exposure to one of its active metabolites and to the main inactive metabolite was practically the same (reduction of about 5% and 3% respectively). The time taken to reach the maximum plasma concentration (Tmax) of Rupatadine was delayed by 1 hour.

Distribution
Plasma protein binding is 98.5-99.0% and apparently concentration-independent in the range studied. Metabolites did not exert any displacing effect. Rupatadine

has a large apparent volume of distribution in healthy volunteers. The apparent volume of distribution (Vd/F) obtained after a repeated administration of a 10mg dose was 9799L.

Metabolism
The main biotransformation pathways of Rupatadine identified were different oxidative processes, namely oxidation of the pyridine methyl group to the carboxylic acid, hydroxylation in the 3, 5 and 6 positions in the tricyclic ring system and N-dealkylation of the piperidine nitrogen. In vitro metabolism studies in the human liver microsomes indicate that Rupatadine is mainly metabolized by the cytochrome P450 (CYP 3A4), with other CYP isoenzymes less involved, e.g., CYP2C9, CYP2C19 and CYP2D6.

Excretion
The mean elimination half-life of Rupatadine in elderly and young volunteers was 8.7 hours and 5.9 hours respectively.

THERAPEUTIC INDICATIONS
Rupaler (Rupatadine) is an antihistamine used to relieve allergy symptoms such as watery eyes, runny nose, itching eyes/nose, and sneezing. It is also used to relieve itching and hives. It works by blocking a certain natural substance (histamine) that your body makes during an allergic reaction.

DOSAGE & ADMINISTRATION
Adults and adolescents (over 12 years of age): The recommended dose of Rupaler (Rupatadine) Tablet is 10mg once a day, with or without food.

Adults and children over 12 years: Take 10ml (10mg) once daily.
Children aged 6-12 years: Take 5ml (5mg) once daily.

• Do not exceed the recommended dosage unless directed by a healthcare professional.

ROUTE OF ADMINISTRATION
Oral

ADVERSE REACTIONS
Common

Dizziness, headache, somnolence, dry mouth, asthenia and fatigue.

Uncommon
Pharyngitis, rhinitis, increase appetite, disturbance in attention, cough, dry throat, epistaxis, nasal dryness, oropharyngeal pain, abdominal pain, abdominal pain upper, diarrhea, dyspepsia, nausea, vomiting, constipation, rash, arthralgia, back pain, myalgia, malaise, pyrexia, thirst, irritability, alanine aminotransferase increased, aspartate aminotransferase increased, blood creatine phosphokinase increased, liver function test abnormal and weight increase.

Rare or very rare
Palpitations and tachycardia

CONTRAINDICATIONS
Rupatadine is contraindicated in patients with hypersensitivity to the active substance or to any of the excipient of the product.

WARNINGS AND PRECAUTIONS
The administration of Rupatadine with grapefruit juice is not recommended.
- The combination of Rupatadine with potent CYP3A4 inhibitors should be avoided and with moderate CYP3A4 inhibitors should be administered with caution.
- Dose adjustment of sensitive CYP3A4 substrates (e.g. simvastatin, lovastatin) and CYP3A4 substrates with a narrow therapeutic index (e.g. ciclosporin, tacrolimus, sirolimus, everolimus, cisapride) could be required as Rupatadine may increase plasma concentrations of these drugs.
- Rupatadine should be used with caution in patients with known prolongation of the QT interval, patients with uncorrected hypokalemia, patients with ongoing proarrhythmic conditions, such as clinically significant bradycardia, acute myocardial ischemia.
- Rupatadine should be used with caution in elderly patients (65 years and older).
- Due to the presence of lactose monohydrate in Rupatadine tablets, patients with rare hereditary problems of galactose intolerance, the total lactase deficiency or glucose-galactose malabsorption should not take this medicine.
- The use of Rupatadine in patients with renal impairment or hepatic impairment is not recommended.
- Rare hypersensitivity reactions (including anaphylactic reactions, angioedema and urticaria) have been reported in post-marketing experience with Rupatadine.
- Effects on skeletal muscle such as myalgia, and muscle weakness have been reported in patients treated with Rupatadine. Use caution when co-administer with statins.

Pregnancy
There are no adequate and well controlled studies in pregnant women. As a precautionary measure, Rupatadine should be avoided during pregnancy unless advised by a physician.

Nursing Mothers
Rupatadine is excreted in animal milk. It is unknown whether Rupatadine is excreted into breast milk. The use of Rupatadine in nursing mothers is not recommended unless advised by a physician.

DRUG INTERACTIONS
Effects of other drugs on Rupatadine
Co-administration with potent CYP3A4 inhibitors (e.g. itraconazole,ketoconazole, voriconazole, posaconazole, HIV protease inhibitors,clarithromycin, nefazodone) should be avoided and co-medication with moderate CYP3A4 inhibitors (erythromycin, fluconazole, diltiazem) should be used with caution.

Grapefruit
The concomitant administration of grapefruit juice increased 3.5 times the systemic exposure of Rupatadine. Grapefruit juice should not be taken simultaneously.

Effects of Rupatadine on other drugs
Caution should be taken when Rupatadine is co-administered with other metabolised drugs with narrow therapeutic windows.

Alcohol
In sensitive patients, concurrent use of Rupatadine with alcohol may cause additional reduction in alertness and impairment of performance.
CNS Depressants
As with other antihistamines, interactions with CNS depressants cannot be excluded.