

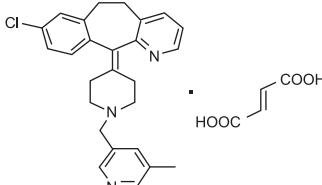
Rupataget™

(Rupatadine)

Oral Solution 1mg/mL

DESCRIPTION

Rupataget (Rupatadine) is an antihistamine with platelet-activating factor (PAF) antagonist activity. Chemically, it is 8-Chloro-11-[1-[(5-methyl-3-pyridyl)methyl]piperidin-4-ylidene]-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridine fumarate. Its molecular formula is $C_{30}H_{30}ClN_3O_4$ and the structural formula is:



Rupatadine Fumarate

QUALITATIVE AND QUANTITATIVE COMPOSITION

Rupataget (Rupatadine) is available for oral administration as:

Rupataget Oral Solution 1mg/mL

Each mL contains:

Rupatadine fumarate BP equivalent to Rupatadine ... 1mg

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

In children 2-5 and 6-11 years old, Rupatadine was rapidly absorbed and the mean C_{max} was of 1.9 and 2.5mg/mL after repeated oral dose, respectively. In term of exposition, the mean total area under the curve (AUC) value was 10.4ng·h/mL in children 2-5 years and 10.7ng·h/mL in children 6-11 years.

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 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 children 2-5 years was 15.9h and in children 6-11 years was 12.3h.

THERAPEUTIC INDICATIONS

Allergic Rhinitis

Rupataget (Rupatadine) is indicated for the symptomatic relief of nasal and non-nasal symptoms of seasonal allergic rhinitis (SAR) and perennial allergic rhinitis (PAR) in patients 2 years of age and older.

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Chronic Spontaneous Urticaria

Rupataget (Rupatadine) is indicated for the relief of the symptoms associated with chronic spontaneous urticaria (CSU), e.g., pruritus and hives, in patients 2 years of age and older.

Pediatrics (<2 years of age)

Rupataget (Rupatadine) has not been studied in children <2 years of age. Rupataget (Rupatadine) should not be administered in children <2 years of age.

DOSAGE AND ADMINISTRATION

Recommended Dosing

Children 2-11 years of age

Dosage in children weighing equal or more than 25kg

5mL (5mg of Rupatadine) Oral Solution once a day, with or without food.

Dosage in children weighing equal or more than 10kg upto less than 25kg
2.5mL (2.5mg of Rupatadine) Oral Solution once a day, with or without food.

Missed Dose

If a dose of Rupataget (Rupatadine) Oral Solution is missed, it should be taken as soon as possible, unless it is almost time for the next dose. A patient should not take two Rupataget (Rupatadine) Oral Solution doses at the same time to make up for a missed dose.

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, upper abdominal pain, diarrhea, dyspepsia, nausea, vomiting, constipation, rash, arthralgia, back pain, myalgia, malaise, pyrexia, thirst, irritability, alanine amino transferase increase, aspartate aminotransferase increase, blood creatinine phosphokinase increase, abnormal liver function test and weight increase.

Rare: Tachycardia and palpitations.

To report SUSPECTED ADVERSE REACTIONS to Getz Pharma's Pharmacovigilance Section, please contact at dsafety@getzpharma.com or +92-21-38636363

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.
- 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.

DRUG INTERACTIONS

Interaction studies have only been performed in adults and adolescents (over 12 years of age) with Rupatadine Tablets 10mg .

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 metabolized 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.

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 (C_{max} 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.

STORAGE

Do not store above 30°C.

Protect from light.

The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED

Rupatagel (Rupatadine) Oral Solution 1mg/mL is available in 60mL amber colored PET bottle packed with a package insert in a unit carton.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

Please read the contents carefully before use.

This package insert is continually updated from time to time.

Manufactured by:

Herbion Pakistan (Pvt.) Ltd.

Industrial Triangle, Kahuta Road, Islamabad, Pakistan.

Manufactured for:

 **Getz**
p h a r m a

29-30/27,
K.I.A., Karachi,
Pakistan

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