

# Rupataget™

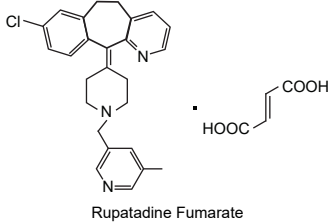
( R u p a t a d i n e )

روپیتاگیٹ

## Tablets 10mg

### DESCRIPTION

Rupataget (Rupatadine) is an antihistamine with platelet-activating factor (PAF) antagonist activity. Its chemical name 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  $C_{30}H_{30}ClN_5O_4$  and the structural formula is:



### QUALITATIVE & QUANTITATIVE COMPOSITION

Rupataget (Rupatadine) is available for oral administration as:

Rupataget Tablets 10mg

Each tablet contains:

Rupatadine fumarate BP equivalent to Rupatadine...10mg

### CLINICAL PHARMACOLOGY

#### Mechanism of Action

Rupatadine is a second-generation antihistamine, long-acting histamine antagonist, with selective peripheral  $H_1$ -receptor antagonist activity. Some of the metabolites (desloratadine and its hydroxylated metabolites) retain an antihistaminic activity and may partially contribute to the overall efficacy of the drug.

#### Pharmacokinetics

##### Absorption

Rupatadine is rapidly absorbed after oral administration, with a  $T_{max}$  of approximately 0.75 hours after intake. The mean  $C_{max}$  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  $C_{max}$  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 ( $T_{max}$ ) 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 ( $V_{dF}$ ) 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

Rupataget (Rupatadine) Tablet is indicated for symptomatic treatment of allergic rhinitis and urticaria in adults and adolescents (over 12 years of age).

### DOSAGE AND ADMINISTRATION

Adults and adolescents (over 12 years of age)

The recommended dose of Rupataget (Rupatadine) Tablet is 10mg once a day, with or without food.

### 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.

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

### CONTRAINDICATIONS

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

### 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.

### 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 and moisture.

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

## HOW SUPPLIED

Rupataget (Rupatadine) Tablets 10mg are available in blister pack of 14's.

**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.

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