Summary of Product Characteristics
RUPANASE 10
(Rupatadine 10 mg tablets)

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1. Name of the medicinal product

RUPANASE 10 Tablets

2. Qualitative and quantitative composition

Each tablet contains rupatadine fumarate 12.80 mg, equivalent to 10 mg of rupatadine base.

Excipient with known effect:
Each tablet contains 61.1 mg of lactose monohydrate.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Tablet.

Round, biconvex, light salmon-pink tablets with no markings.

4. Clinical particulars

4.1 Therapeutic indications

Symptomatic treatment of allergic rhinitis and urticaria in adults and adolescents (over 12 years of age).

4.2 Posology and method of administration

Posology

Adults and adolescents (over 12 years of age): the recommended dose is 10 mg (one tablet) once a day.

Elderly

RUPANASE 10 should be used with caution in elderly patients (65 years and older).

Paediatric population

RUPANASE 10 is not recommended for use in children below 12 years of age, as safety has not been established.

Method of administration

For oral use. RUPANASE 10 can be taken with or without food.

4.3 Contraindications

- Hypersensitivity to rupatadine or to any of the excipients listed in section 6.1.
- Pregnancy and breast-feeding (see section 4.6).

4.4 Special warnings and precautions for use

As there is no clinical experience in patients with impaired kidney or liver function, the use of RUPANASE 10 is not recommended in these patients. The administration with grapefruit juice is not recommended (see section 4.5). The combination 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) may be required, as rupatadine may increase their plasma concentrations.

Cardiac safety

RUPANASE 10 should be used with caution in patients with known prolongation of the QT interval, uncorrected hypokalaemia, or ongoing prodysrhythmic conditions such as clinically significant bradycardia and acute myocardial ischaemia.

Lactose

This medicine contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Effects of other medicines on RUPANASE 10

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. The concomitant administration of RUPANASE 10 with ketoconazole or erythromycin increases the systemic exposure to rupatadine 10-fold and 2–3-fold respectively. Concomitant grapefruit juice increased the systemic exposure of rupatadine by 3.5-fold and should be avoided.

Effects of RUPANASE 10 on other medicines

Caution should be taken when RUPANASE 10 is co-administered with other metabolised medicines with narrow therapeutic windows. RUPANASE 10 should be used with caution when administered with alcohol; a 20 mg dose increased the impairment caused by alcohol. Asymptomatic creatine phosphokinase increases have been reported, and caution is advised with statins. RUPANASE 10 acts as a mild inhibitor of CYP3A4 (a mild increase in midazolam exposure was observed).

4.6 Fertility, pregnancy and lactation

Pregnancy

RUPANASE 10 is contraindicated during pregnancy.

Breast-feeding

Rupatadine is excreted in animal milk. Owing to potential harmful effects in neonates, the use of RUPANASE 10 should be avoided during breast-feeding.

Fertility

No human data on fertility are available.

4.7 Effects on ability to drive and use machines

At the recommended dose, RUPANASE 10 is not expected to influence the ability to drive or use machinery. Nevertheless, care should be taken before driving or using machinery until the patient's individual reaction to RUPANASE 10 has been established.

4.8 Undesirable effects

The adverse reactions are listed below by System Organ Class and frequency, defined as: common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100) and not known (cannot be estimated from the available data). Reactions with frequency ‘not known’ are derived from post-marketing experience.

System Organ Class	Frequency	Adverse reaction
Infections and infestations	Uncommon	Pharyngitis, rhinitis
Metabolism and nutrition disorders	Uncommon	Increased appetite

System Organ Class	Frequency	Adverse reaction
Nervous system disorders	Common	Somnolence, headache, dizziness
	Uncommon	Disturbance in attention
Respiratory, thoracic and mediastinal disorders	Uncommon	Epistaxis, nasal dryness, upper respiratory tract disorder, cough, dry throat
Gastrointestinal disorders	Common	Dry mouth
	Uncommon	Nausea, upper abdominal pain, diarrhoea, dyspepsia, vomiting, abdominal pain, constipation
Skin and subcutaneous tissue disorders	Uncommon	Rash
Musculoskeletal and connective tissue disorders	Uncommon	Back pain, arthralgia, myalgia
General disorders and administration site conditions	Common	Fatigue, asthenia
	Uncommon	Thirst, malaise, pyrexia, irritability
Investigations	Uncommon	Increased blood creatine phosphokinase, increased alanine aminotransferase, increased aspartate aminotransferase, abnormal liver function test, weight increase
Cardiac disorders	Not known	Tachycardia, palpitations
Immune system disorders	Not known	Hypersensitivity reactions (including anaphylactic reactions, angioedema and urticaria)

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to the National Regulatory Authority.

4.9 Overdose

Should overdose occur, treatment should be symptomatic and supportive, taking into account any concomitantly ingested medicines.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihistamines for systemic use, other antihistamines for systemic use. ATC code: R06AX28.

Mechanism of action

Rupatadine is a non-sedating, long-acting histamine antagonist with selective peripheral H1-receptor antagonist activity. At the recommended dose of 10 mg, the onset of antihistamine activity is at 30 minutes and the effect lasts for 24 hours. Rupatadine also inhibits the degranulation of mast cells induced by immunological and non-immunological stimuli and inhibits the release of cytokines, particularly TNF-alpha, in human mast cells and monocytes. Some of its metabolites (desloratadine and its hydroxylated metabolites) retain antihistaminic activity and may contribute to the overall efficacy.

5.2 Pharmacokinetic properties

Absorption

Rupatadine is rapidly absorbed after oral administration, with a Tmax of approximately 0.75 hours. The mean Cmax was 2.6 ng/mL after a single 10 mg dose and 3.8 ng/mL after 10 mg/day for 7 days. Intake of food increased systemic exposure (AUC) to rupatadine by about 23% and delayed Tmax by 1 hour, without clinical significance.

Distribution

Rupatadine is 98% to 99% bound to human plasma proteins.

Biotransformation

Rupatadine is extensively metabolised, mainly by oxidative processes; CYP3A4 is the main isoenzyme responsible, with CYP2C9, CYP2C19 and CYP2D6 also involved. Some metabolites retain antihistaminic activity and contribute to the overall efficacy and long duration of action.

Elimination

The plasma concentration exhibits a bi-exponential decay with a mean elimination half-life of 5.9 hours. After a 40 mg dose of 14C-rupatadine, 34.6% of the radioactivity was recovered in urine and 60.9% in faeces over 7 days; biliary excretion is the most important elimination route. The amounts of unchanged active substance in urine and faeces were insignificant.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated-dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction and development.

6. Pharmaceutical particulars

6.1 List of excipients

- Microcrystalline cellulose
- Lactose monohydrate
- Magnesium stearate
- Pregelatinised maize starch
- Red iron oxide (E172)
- Yellow iron oxide (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at or below 30°C. Keep the blister in the outer carton in order to protect from light. Keep out of the reach and sight of children.

6.5 Nature and contents of container

PVC-PVDC/aluminium blister packs, in pack sizes of 10 (1 strip of 10 tablets), 20 (2 strips of 10 tablets) or 30 (2 strips of 15 tablets) in a cardboard carton. Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorisation Holder

iNova Pharmaceuticals (Pty) Ltd, 15e Riley Road, Bedfordview, South Africa.

8. Marketing Authorisation Number

H2019/1243/654ER

9. Date of first authorisation / renewal of the authorisation

10. Date of revision of the text