APPROVED
By OLOPEZL at 1:20 pm, Aug 29, 2023

SUMMARY PRODUCT OF CHARACTERISTICS

Rupafin 10 mg Tablets

Rupatadine

1. NAME OF THE MEDICINAL PRODUCT

Rupafin 10 mg Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
10 mg of rupatadine (as fumarate)
Excipients: lactose 57.57 mg as lactose monohydrate
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.
Round, light salmon coloured tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and method of administration

Adults and adolescents (over 12 years of age)
The recommended dose is 10 mg (one tablet) once a day, with or without food.

Elderly
Rupatadine should be used with caution in elderly people (see section 4.4).

Patients with renal or hepatic insufficiency
As there is no clinical experience in patients with impaired kidney or liver functions, the use of Rupatadine 10 mg Tablets is at present not recommended in these patients.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Concomitant use with ketokonazole and antibiotic macrolides is contraindicated.

4.4 Special warnings and precautions for use

The administration of rupatadine with grapefruit juice is not recommended (see section 4.5).
The combination of rupatadine with potent CYP3A4 inhibitors should be avoided and with moderate CYP3A4 inhibitors should be administered with caution (see section 4.5).
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 concentration of these drugs (see section 4.5).

Cardiac safety of rupatadine was assessed in a Thorough QT/QTc study. Rupatadine up to 10 times therapeutic dose did not produce any effect on the ECG and hence raises no cardiac safety concerns. However 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 10 mg Tablets should be used with caution in elderly patients (65 years and older). Although no overall differences in effectiveness or safety were observed in clinical trials, higher sensitivity of some older individuals cannot be excluded due to the low number of elderly patients enrolled (see section 5.2).

Regarding use in patients with renal or hepatic impairment, see section posology and method of administration (see section 4.2).

Due to the presence of lactose monohydrate in rupatadine 10 mg tablets, patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Interaction studies have only been performed in adults and adolescent (over 12 years of age) with rupatadine 10 mg tablets.

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.

Interaction with ketoconazole or erythromycin: The concomitant administration of rupatadine 20 mg and ketoconazole or erythromycin increases the systemic exposure to rupatadine 10 times and 2-3 times respectively. These modifications were not associated with an effect on the QT interval or with an increase of the adverse reactions in comparison with the drugs when administered separately. However, rupatadine should not be used when it is administered concomitanly with these drug substances.
Rupatadine should be used with caution when it is administered concomitanly with other inhibitors of the isozyme CYP3A4.

Interaction with 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 since knowledge of the effect of rupatadine on other drugs is limited.

Interaction with alcohol: After administration of alcohol, a dose of 10 mg of rupatadine produced marginal effects in some psychomotor performance tests although they were not significantly different from those induced by intake of alcohol only. A dose of 20 mg increased the impairment caused by the intake of alcohol.

Interaction with CNS depressants: As with other antihistamines, interactions with CNS depressants cannot be excluded.

Interaction with 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 coadministered with statins.

4.6 Fertility, Pregnancy, and lactation

Pregnancy:
There are limited amount of data from the use of rupatadine in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development (see section 5.3). As a precautionary measure, it is preferable to avoid the use of rupatadine during pregnancy.

Breastfeeding
Rupatadine is excreted in animal milk. It is unknown whether rupatadine is excreted into breast milk. A decision must be made whether to discontinue breastfeeding or to discontinue/abstain from rupatadine therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman.

Fertility
There are no clinical data on fertility. Studies in animal have shown a significant reduction of fertility at exposure levels higher than those observed in humans at the maximum therapeutic dose (see section 5.3).

4.7 Effects on the ability to drive and use machines

Rupatadine 10 mg had no influence on the ability to drive and use machines. Nevertheless, care should be taken before driving or using machinery until the patient's individual reaction on rupatadine has been established.

4.8 Undesirable effects

Rupatadine 10 mg has been administered to over 2025 adult and adolescent patients in clinical studies, 120 of whom received rupatadine for at least 1 year.

The most common adverse reactions in controlled clinical studies were somnolence (9.5%), headache (6.9%) and fatigue (3.2%).

The majority of adverse reactions observed in clinical trials were mild to moderate in severity and usually did not require cessation of therapy.
The frequencies of adverse reactions are assigned as follows:
Common (≥ 1/100 to < 1/10)
Uncommon (≥ 1/1000 to < 1/100)
Rare (≥1/10,000 to <1/1,000)

The frequencies of adverse reactions reported in patients treated with rupatadine 10 mg tablets during clinical trials and spontaneous reporting were as follows:

Infections and infestations
Uncommon: Pharyngitis, Rhinitis

Immune system disorders
Rare: Hypersensitivity reactions (including anaphylactic reactions, angioedema and urticaria)*

Metabolism and nutrition disorders
Uncommon: Increased appetite

Nervous system disorders:
Common: Somnolence, Headache, Dizziness
Uncommon: Disturbance in attention

Cardiac disorders
Rare: tachycardia and palpitations*

Respiratory, thoracic, and mediastinal disorders
Uncommon: Epistaxis, Nasal dryness, Cough, Dry throat, Oropharyngeal pain

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Gastrointestinal disorders
Common: Dry mouth
Uncommon: Nausea, Abdominal pain upper, Diarrhoea, Dyspepsia, Vomiting, Abdominal pain, Constipation

Skin and subcutaneous tissue disorders
Uncommon: Rash

Musculoskeletal, connective tissues and bone disorders
Uncommon: Back pain, arthralgia, myalgia

General Disorders and administration site condition
Common: Fatigue, Asthenia
Uncommon: Thirst, Malaise, Pyrexia, Irritability

Investigations
Uncommon: Blood creatine phosphokinase increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Liver function test abnormal, Weight increased

* tachycardia and palpitations and hypersensitivity reactions (including anaphylactic reactions, angioedema and urticarial) have been reported in post-marketing experience with rupatadine 10 mg tablets.

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.

4.9 Overdose
No case of overdose has been reported. In a clinical safety study rupatadine at daily dose of 100 mg during 6 days was well tolerated. 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: other antihistamines for systemic use, ATC code: R06A X28.

Rupatadine is a second generation antihistamine, long-acting histamine antagonist, with selective peripheral H1-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.

In vitro studies with rupatadine at high concentration have shown an inhibition of the degranulation of mast cells induced by immunological and non-immunological stimuli as well as the release of cytokines, particularly of the TNFα in human mast cells and monocytes. The clinical relevance of the observed experimental data remains to be confirmed.

Clinical trials in volunteers (n= 375) and patients (n= 2429) with allergic rhinitis did not show significant effect on the electrocardiogram when rupatadine was administered at doses ranging from 2 mg to 100 mg.

5.2 Pharmacokinetic properties

Absorption and bioavailability
Rupatadine is rapidly absorbed after oral administration, with a t_{max} of approximately 0.75 hours after intake. The mean C_{max} was 2.6 ng/ml after a single oral dose of 10 mg and 4.6 ng/ml after a single oral dose of 20 mg. Pharmacokinetics of rupatadine was linear for a dose between 10 and 20 mg after single and repeated dose. After a dose of 10 mg once a day for 7 days, the mean C_{max} was 3.8 ng/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%.

As rupatadine has never been administered to humans by intravenous route, no data is available on its absolute bioavailability.

Effect of the intake 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. The maximum plasma concentration (C_{max}) was not affected by food intake. These differences had no clinical significance.

Metabolism and elimination
In a study of excretion in humans (40 mg of ^{14}C-rupatadine), 34.6% of the radioactivity administered was recovered in urine and 60.9% in faeces collected over 7 days. Rupatadine undergoes considerable pre-systemic metabolism when administered by oral route. The amounts of unaltered active substance found in urine and faeces were insignificant. This means that rupatadine is almost completely metabolised. Roughly, the active metabolites desloratadine and other hydroxylated derivatives accounted for 26% and 48% respectively of the total systemic exposure of the active substances. In vitro metabolism studies in human liver microsomes indicate that rupatadine is mainly metabolised by the cytochrome P450 (CYP 3A4).

Specific patient groups
In a study on healthy volunteers to compare the results in young adults and elderly patients, the values for AUC and C_{max} for rupatadine were higher in the elderly than in young adults. This is probably due to a decrease of the first-pass hepatic metabolism in the elderly. These differences were not observed in the metabolites analysed. The mean elimination half-life of rupatadine in elderly and young volunteers was 8.7 hours and 5.9 hours respectively. As these results for rupatadine and for its metabolites were not clinically significant, it was concluded that it is not necessary to make any adjustment when using a dose of 10 mg in the elderly.

5.3 Preclinical safety data
Preclinical data reveal no special hazard for humans based on conventional studies of pharmacology, repeated dose toxicity, genotoxicity, and carcinogenic potential.

More than 100 times the clinically recommended dose (10 mg) of rupatadine did neither extend the QTc or QRS interval nor produce arrhythmia in various species of animals such as rats, guinea pigs and dogs. Rupatadine and one of its main active metabolites in humans, 3-hydroxydesloratadine, did not affect the cardiac action potential in isolated dog Purkinje fibres at concentrations at least 2000 times greater than the C_{max} reached after the administration of a dose of 10 mg in humans. In a study that evaluated the effect on cloned human HERG channel, rupatadine inhibited that channel at a concentration 1685 times greater than the C_{max} obtained after the administration of 10 mg of rupatadine. Desloratadine, the metabolite with the greatest activity, had no effect at a 10 micromolar concentration. Studies of tissue distribution in rats with radiolabelled rupatadine showed that rupatadine does not accumulate in heart tissue.

In the rat, a significant reduction of male and female fertility occurred at the high dose of 120 mg/kg/day, providing C_{max} 268 times those measured in humans at the therapeutic dose (10 mg/day). Foetal toxicity (growth delay, incomplete ossification, minor skeletal findings) was reported in rats at maternotoxic dose-levels only (25 and 120 mg/kg/day). In rabbits, no evidence of developmental toxicity was noted at doses up to 100 mg/kg. The developmental No Adverse Effect Levels were determined at 5 mg/kg/day in rats and 100 mg/kg/day in rabbits, yielding C_{max} 45 and 116 times higher, respectively, than those measured in humans at the therapeutic dose (10 mg/day).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Pregelatinised maize starch
Microcrystalline cellulose
Red iron oxide (E-172)
Yellow iron oxide (E-172)
Lactose monohydrate
Magnesium stearate

6.2 Incompatibilities
Not applicable

6.3 Shelf life
3 years

6.4 Special precautions for storage
Keep the blister in the outer carton in order to protect from light. Store below 30ºC.

6.5 Nature and content of the container
PVC/PVDC/aluminium blister.
Pack of 10 tablets.

6.6 Special precautions for disposal and other handling
No special requirements.
Any unused product or waste material should be disposed of in accordance with local requirements.

7. NAME AND ADDRESS OF MANUFACTURER

Noucor Health, S.A.
Avda. Camí Reial, 51-57
08184 Palau-Solità i Plegamans
Barcelona, Spain

8. NAME AND ADDRESS OF IMPORTER

P.T. Nicholas Laboratories Indonesia
Jln. Pulobuaran Raya Blok FF 12A Jakarta
Industrial Estate Pulogadung, Jakarta 13930
Indonesia

9. DATE OF REVISION OF THE TEXT

07/2022 (Based on EU SPC 04/2015)

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APPROVED
By OLOPEZL at 1:20 pm, Aug 29, 2023

INFORMASI PRODUK UNTUK PASIEN

Rupafin 10 mg Tablets

Rupatadine

Baca seluruh brosur ini hati-hati sebelum menggunakan obat ini.
- Simpan brosur ini. Anda mungkin perlu membacanya lagi.
- Jika anda mempunyai pertanyaan lebih lanjut, silahkan bertanya pada dokter atau apoteker anda.
- Obat ini diresepkan untuk anda. Jangan berikan kepada orang lain. Hal ini mungkin berbahaya bagi mereka meskipun gejala mereka sama dengan gejala anda
- Jika salah satu efek samping menjadi serius atau jika anda menemukan efek samping yang tidak tercantum pada brosur ini, mohon berikan informasi kepada dokter atau apoteker anda

Pada brosur ini :

1. APA DAN UNTUK APA RUPAFIN

Rupatadine adalah antihistamin

Rupafin mengatasi gejala rhinitis alergi pada remaja mulai usia 12 tahun ke atas dan dewasa.

2. SEBELUM ANDA MENGGUNAKAN RUPAFIN

Jangan gunakan Rupafin
- Jika anda alergi (Hipersensitif) terhadap rupatadine atau bahan lain pada Rupafin.
- Bersama dengan ketokonazole dan antibiotic golongan makrolida (erythromycin, clarithromycin, azitromycin dll)

Penggunaan Rupafin dengan hati-hati
Jika anda penderita insufisiensi ginjal dan hati, tanyakan pada dokter anda. Penggunaan Rupafin tablet, pada saat ini tidak dianjurkan untuk pasien dengan gangguan fungsi ginjal atau hati.
Obat ini tidak digunakan untuk anak usia di bawah 12 tahun. Jika anda berumur lebih dari 65 tahun, tanyakan kepada dokter atau apoteker anda.

Penggunaan Obat Lain
Beritahukan dokter atau apoteker anda jika anda menggunakan atau dalam waktu dekat menggunakan obat lain, termasuk obat yang diperoleh tanpa resep dokter.

Penggunaan Rupafin dengan makanan dan minuman.
Rupafin seharusnya tidak digunakan bersamaan dengan jus jeruk, karena dapat meningkatkan kadar/konsentrasi Rupafin dalam tubuh anda.

Kehamilan dan Menyusui
Jangan gunakan Rupafin selama kehamilan dan menyusui, kecuali diindikasikan/diresepkan oleh dokter anda.
Tanyakan kepada dokter atau apoteker anda sebelum menggunakan obat apapun.

Mengendarai dan menggunakan mesin
Pada dosis yang direkomendasikan, Rupafin tidak mempengaruhi kemampuan anda mengendarai atau menggunakan mesin. Tetapi bagaimanapun, ketika anda menggunakan Rupafin pertama kali, sebaiknya anda berhati-hati untuk melihat bagaimana pengobatan berefek pada anda sebelum anda mengendarai atau menggunakan mesin.

Informasi penting mengenai bahan-bahan Rupafin.
Obat ini mengandung laktosa.
Jika anda telah diberitahukan dokter anda bahwa anda mempunyai intoleransi terhadap beberapa gula, hubungi dokter anda sebelum anda menggunakan obat ini.

3. CARA/BAGAIMANA MENGGUNAKAN RUPAFIN

Selalu gunakan Rupafin sesuai petunjuk dokter anda. Anda sebaiknya menanyakan kepada dokter atau apoteker anda jika anda tidak yakin.

Rupafin untuk remaja mulai usia 12 tahun ke atas dan dewasa. Dosis umumnya, sehari 1 tablet (10 mg Rupatadine) dengan atau tanpa makanan. Minum tablet dengan jumlah cairan/minum yang cukup (misal 1 gelas air minum)

Dokter akan memberitahukan anda berapa lama pengobatan dengan Rupafin akan berakhir

Jika anda menggunakan Rupafin melebihi dari seharusnya.
Jika anda secara tidak sengaja meminum dosis tinggi dari obat anda, segera beritahukan dokter atau apoteker anda.

Jika anda lupa meminum Rupafin
Minumlah secepatnya dan lanjutkan dengan penggunaan tablet anda sesuai pada waktunya. Jangan meminum dosis ganda untuk mengganti dosis yang terlewat.

4. EFEK SAMPING YANG MUNGKIN TERJADI

Seperti obat lain, Rupafin dapat mengakibatkan efek samping walaupun tidak semua orang mengalaminya.

Frekuensi efek samping yang dinyatakan pada daftar dibawah menggunakan ketentuan sebagai berikut:
umum (terjadi kurang dari 1 pada 10, tapi lebih dari 1 pada 100 pasien)
tidak umum (terjadi kurang dari 1 pada 100, tapi lebih dari 1 pada 1000 pasien)

Efek samping yang umum terjadi:
- Mengantuk
- Sakit kepala
- Pusing
- Mulut kering
- Lemas dan lelah.

Efek samping yang tidak umum terjadi:

- Peningkatan nafsu makan
- Sifat lekas marah
- Kesulitan konsentrasi
- Mimisan
- Hidung kering
- Sakit tenggorokan
- Rhinitis
- Mual, sakit pada bagian perut , diare, gangguan pencernaan, muntah, konstipasi
- Kemerahan pada kulit
- Nyeri punggung, nyeri sendi, nyeri otot
- Haus, ketidaknyamanan, demam
- Tes fungsi hati yang tidak normal
- Kenaikan berat badan.

Jika ada efek samping yang menjadi serius atau anda menyadari ada efek samping yang tidak tercantum pada leaflet ini, beritahukan pada dokter atau apoteker anda.

5. BAGAIMANA MENYIMPAN RUPAFIN

Jauhkan dari jangkauan dan pandangan anak-anak
Jangan gunakan Rupafin setelah tanggal kadaluarsa yang tercantum pada kemasan box dan blíster. Tanggal kadaluarsa menunjukkan hari terakhir pada bulan tersebut.

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Simpan blíster dalam box untuk melindungi dari cahaya.
Obat ini seharusnya tidak dimusnahkan melalui pembuangan air limbah atau pembuangan rumah tangga. Tanyakan pada apoteker anda, bagaimana memusnahkan obat yang tidak dibutuhkan lagi. Hal ini dapat membantu melindungi lingkungan.

6. INFORMASI TAMBAHAN

Apa kandungan Rupafin

- Zat aktifnya adalah rupatadine. Setiap tablet mengandung 10 mg rupatadine (sebagai fumarate).
- Bahan lainnya adalah pregelatinised maize starch, microcrystalline cellulose, red iron oxide (E-172), yellow iron oxide (E-172), lactose monohydrate dan magnesium stearate.

Bagaimana penampakan Rupafin dan kemasannya

Rupafin adalah tablet berbentuk bulat, berwarna salmon muda dan dikemas dalam blister isi 10 tablet.

Diproduksi oleh:

Noucor Health, S.A.
Avda. Camí Reial, 51-57
08184 Palau-Solità i Plegamans
Barcelona, Spain

Diimpor oleh:
P.T.Nicholas Laboratories Indonesia
Jln. Pulobuaran Raya Blok FF 12 A
Kawasan Industri Pulogadung, Jakarta 13930
Indonesia

Leaflet ini disetujui terakhir pada:
25/07/2014 (berdasarkan EU SPC 02/2010)

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