Summary of Product Characteristic

Contents

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1. Name of the Medicinal Product:

ROTAFLU (Loratadine 5 mg and Pseudoephedrine HCL 120 mg Tablets)

2. Quality and Quantitative Composition:

2.1 Qualitative Declaration

Each SR Tablet Contains:
Loratadine USP 5 mg
Pseudoephedrine HCL 120 mg
Excipients Q.S.

2.2 Quantitative Declaration

Components	Amount / Unit (mg)	Reference
Pseudoephedrine HCL	120	In-House
HPMC K-100 M	120	In-House
Microcrystalline cellulose	13	Ph Eur (BP)
Ethyl cellulose N-100	21	Ph Eur (BP)
Povidone K-30%	12	Ph Eur (BP)
Magnesium Stearate	3	Ph Eur (BP)
Colloidal Silicon Dioxide	3	Ph Eur (BP)
Purified Talc	3	Ph Eur (BP)
Loratadine	5	USP (NF)
Purified water	q.s	Ph Eur (BP)
Ready Mix of pure coat aqua white (FC)	5.5	In-House
Isopropyl Alcohol	q.s	Ph Eur (BP)

3. Pharmaceutical Form:

Tablets (Sustained release)

4. Clinical Particulars:

4.1 Therapeutic indications

Loratadine and pseudoephedrine is a combination medicine used to treat sneezing, runny or stuffy nose, itchy or watery eyes, hives, skin rash, itching, and other symptoms of allergies and the common cold.

4.2 Posology and method of administration

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Administer ROTAFLU SR Tablets by the oral route only. Do not break, chew, or crush the tablet. Swallow the tablet whole. Recommended route of administration: Oral.

Method of administration
Adults and children 12 years of age and older- One tablet every 12 hours each tablets contains 5 mg of Loratadine and 120 mg pseudoephedrine 120 mg. Do not take more than 2 tablets in 24 hours.

4.3 Contraindications

ROTAFLU SR Tablets are contraindicated in:
- Patients with hypersensitivity to any of its ingredients, or to loratadine
- Patients with narrow-angle glaucoma
- Patients with urinary retention
- Patients receiving monoamine oxidase (MAO) inhibitor therapy or within fourteen (14) days of stopping such treatment [see Drug Interactions (7.1)]
- Patients with severe hypertension or severe coronary artery disease

4.4 Special warning and precautions for use

Cardiovascular and Central Nervous System Effects: The pseudoephedrine contained in ROTAFLU SR Tablets, like other sympathomimetic amines, can produce cardiovascular and central nervous system (CNS) effects in some patients such as insomnia, dizziness, weakness, tremor, or arrhythmias. In addition, central nervous system stimulation with convulsions or cardiovascular collapse with accompanying hypotension has been reported. Therefore, ROTAFLU SR Tablets should be used with caution in patients with cardiovascular disorders, and should not be used in patients with severe hypertension or severe coronary artery disease.

Coexisting Conditions : ROTAFLU SR Tablets contain pseudoephedrine sulfate, a sympathomimetic amine, and therefore should be used with caution in patients with diabetes and hyperthyroidism. Also use with caution in patients with prostatic hypertrophy or increased intraocular pressure, as urinary retention and narrow-angle glaucoma may occur

Co-Administration with Monoamine : Oxidase (MAO) Inhibitors ROTAFLU SR Tablets should not be used in patients receiving monoamine oxidase (MAO) inhibitor therapy or within fourteen (14) days of stopping such treatment as an increase in blood pressure or hypertensive crisis, may occur
Hypersensitivity Reactions : Hypersensitivity reactions including rash, pruritus, urticaria, edema, dyspnea, and anaphylaxis have been reported after administration of desloratadine a component of ROTAFLU SR Tablets. If such a reaction occurs, therapy with ROTAFLU SR Tablets should be stopped and alternative treatment should be considered

Renal Impairment : ROTAFLU SR Tablets should generally be avoided in patients with renal impairment

Hepatic Impairment : ROTAFLU SR Tablets should generally be avoided in patients with hepatic impairment

Ask a doctor or pharmacist if it is safe for you to take this medication if you have:

- kidney disease;
- glaucoma;
- heart disease or high blood pressure;
- diabetes;
- thyroid disorder; or
- bladder obstruction or other urination problems.

4.5 Interaction with other medicinal products and other forms of interaction

Monoamine Oxidase Inhibitors: ROTAFLU SR Tablets should not be used in patients receiving monoamine oxidase (MAO) inhibitor therapy or within fourteen (14) days of stopping such treatment because the action of pseudoephedrine a component of ROTAFLU SR Tablets on the vascular system may be potentiated by these agents.

Beta-Adrenergic Blocking Agents: The antihypertensive effects of beta-adrenergic blocking agents, methyldopa, and reserpine, may be reduced by sympathomimetics such as pseudoephedrine. Exercise caution when using ROTAFLU SR Tablets with these agents.

Digitalis: Increased ectopic pacemaker activity can occur when pseudoephedrine is used concomitantly with digitalis. Exercise caution when using ROTAFLU SR Tablets with these agents.

Inhibitors of Cytochrome P450 3A4 : In controlled clinical studies co-administration of desloratadine with ketoconazole, erythromycin, or azithromycin resulted in increased plasma concentrations of desloratadine and 3-hydroxydesloratadine but there were no clinically relevant changes in the safety profile of desloratadine

Fluoxetine: In controlled clinical studies co-administration of desloratadine with fluoxetine, a selective serotonin reuptake inhibitor (SSRI), resulted in increased plasma concentrations of desloratadine and 3-hydroxydesloratadine but there were no clinically relevant changes in the safety profile of desloratadine.

Cimetidine: In controlled clinical studies co-administration of desloratadine with cimetidine a histamine H2-receptor antagonist resulted in increased plasma concentrations of desloratadine and 3-hydroxydesloratadine but there were no clinically relevant changes in the safety profile of desloratadine.

4.6 Pregnancy and lactation

Pregnancy

Pregnancy Category C: There are no adequate and well-controlled studies of desloratadine and pseudoephedrine in combination in pregnant women. Neither are there animal reproduction studies conducted with the combination of desloratadine and pseudoephedrine. Desloratadine was not teratogenic in rats or rabbits but affected implantation in rats. Because animal reproduction studies are not always predictive of human response, ROTAFLU SR Tablets should be used during pregnancy only if clearly needed. Desloratadine was not teratogenic in rats or rabbits at approximately 210 and

230 times, respectively, the AUC in humans at the recommended daily oral dose. An increase in pre-implantation loss and a decreased number of implantations and fetuses were noted, however, in a separate study in female rats at approximately

120 times the AUC in humans at the recommended daily oral dose. Reduced body weight and slow righting reflex were reported in pups at approximately 50 times or greater than the AUC in humans at the recommended daily oral dose. Desloratadine had no effect on pup development at approximately 7 times the AUC in humans at the recommended daily oral dose. The AUCs in comparison referred to the desloratadine exposure in rabbits and the sum of desloratadine and its metabolites exposures in rats, respectively.

Lactation
Desloratadine and pseudoephedrine both pass into breast milk; therefore, a decision should be made whether to discontinue nursing or to discontinue ROTAFLU SR Tablets, taking into account the benefit of the drug to the nursing mother and the possible risk to the child.

4.8 Undesirable effects

Signs of an allergic reaction, like rash; hives; itching; red, swollen, blistered, or peeling skin with or without fever; wheezing; tightness in the chest or throat; trouble breathing, swallowing, or talking; unusual hoarseness; or swelling of the mouth, face, lips, tongue, or throat. All drugs may cause side effects. However, many people have no side effects or only have minor side effects. Call your doctor or get medical help if any of these side effects or any other side effects bother you or do not go away:

- Dizziness.
- Feeling nervous and excitable.
- Not able to sleep.
- Feeling sleepy.

Nervous system
Nervous system side effects of loratadine have included headaches in approximately 7% of treated patients. Loratadine has not been shown to cause significant drowsiness, sedation, or impair psychomotor skills.
Nervous system side effects of pseudoephedrine have included nervous system stimulation, resulting in tremor, anxiety, and nervousness. Insomnia has been reported in up to 30% of pseudoephedrine-treated patients. Headache, somnolence, and dizziness have also occurred in patients receiving pseudoephedrine.

Cardiovascular
Cardiovascular side effects of loratadine have included at least one report of syncopal episodes, premature ventricular complexes, and a prolonged QT interval.
Pseudoephedrine causes vasoconstriction which generally does not produce hypertension, but may be problematic for patients with preexisting hypertension. Arrhythmias may be produced in predisposed patients. Rarely, pseudoephedrine has been reported to cause coronary artery spasm and chest pain.

Gastrointestinal
Gastrointestinal side effects have included anorexia and gastric irritation in approximately 5% of patients treated with pseudoephedrine. Dry mouth, nose, or throat have occurred in up to 15% of patients. Gastrointestinal effects of loratadine have been rare and included nausea and dry mouth. A

few cases of mechanical upper gastrointestinal tract obstruction have been reported with Claritin-D 24 Hour tablets (brand of loratadine-pseudoephedrine), primarily in patients who have difficulty swallowing tablets or in whom there is upper gastrointestinal tract narrowing or abnormal esophageal peristalsis. Ischemic colitis has been reported.

4.9 Overdose and treatment

In the event of overdose, consider standard measures to remove any unabsorbed drug. Symptomatic and supportive treatment is recommended. Desloratadine and 3-hydroxydesloratadine are not eliminated by hemodialysis.

Desloratadine : Information regarding acute overdosage with desloratadine is limited to experience from post-marketing adverse event reports and from clinical trials conducted during the development of the ROTAFLU product. In the reported cases of overdose, there were no significant adverse events that were attributed to desloratadine. In a dose-ranging trial, at doses of 10 mg and 20 mg/day, somnolence was reported. Lethality occurred in rats at oral doses of 250 mg/kg or greater (estimated desloratadine and desloratadine metabolite exposures were approximately 120 times the AUC in humans at the recommended daily oral dose). The oral median lethal dose in mice was 353 mg/kg (estimated desloratadine exposure was approximately 290 times the human daily oral dose on an mg/m2 basis). No deaths occurred at oral doses up to 250 mg/kg in monkeys (estimated desloratadine exposure was approximately 810 times the human daily oral dose on an mg/m2 basis).

Sympathomimetics : In large doses, sympathomimetics such as pseudoephedrine may give rise to giddiness, headache, nausea, vomiting, sweating, thirst, tachycardia, precordial pain, palpitations, difficulty in micturition, muscle weakness and tenseness, anxiety, restlessness, and insomnia. Many patients can present a toxic psychosis with delusions and hallucinations. Some may develop cardiac arrhythmias, circulatory collapse, convulsions, coma, and respiratory failure

5. Pharmacological Properties:

5.1 Pharmacodynamic Properties

Wheal and Flare: Human histamine skin wheal studies following single and repeated 5 mg doses of desloratadine have shown that the drug exhibits an antihistaminic effect by 1 hour; this activity may persist for as long as 24 hours. There was no evidence of histamine-induced skin wheal tachyphylaxis within the desloratadine 5 mg group over the 28-day treatment period. The clinical relevance of histamine wheal skin testing is unknown.

Effects on QTc: In clinical trials for ROTAFLU SR Tablets,, ECGs were recorded at baseline and endpoint within 1 to 3 hours after the last dose. The majority of ECGs were normal at both baseline and endpoint. No clinically meaningful changes were observed following treatment with ROTAFLU SR Tablets, for any ECG parameter, including the QTc interval. An increase in the ventricular rate of 7.1 and 6.4 bpm was observed in the ROTAFLU SR Tablets, and pseudoephedrine groups, respectively, compared to an increase of 3.2 bpm in subjects receiving desloratadine alone. Single daily doses of ROTAFLU SR Tablets 45 mg were given to normal male and female volunteers for 10 days.

All ECGs obtained in this study were manually read in a blinded fashion by a cardiologist. In the ROTAFLU -treated subjects, there was a mean increase in the maximum heart rate of 9.2 bpm relative to placebo. The QT interval was corrected for heart rate (QTc) by both Bazett's and Fridericia methods. Using the QTc (Bazett), there was a mean increase of 8.1 msec in the ROTAFLU -treated subjects

relative to placebo. Using QTc (Fridericia) there was a mean increase of 0.4 msec in ROTAFLU - treated subjects relative to placebo. No clinically relevant adverse events were reported.

5.2 Pharmacokinetic Properties

Pharmacokinetics:

Absorption: In a single dose pharmacokinetic study, the mean time to maximum plasma concentrations (Tmax) for desloratadine occurred at approximately 4 to 5 hours post dose and mean peak plasma concentrations (Cmax) and area under the concentration-time curve (AUC) of approximately hr/mL, respectively, were observed. In another pharmacokinetic study, food and grapefruit juice had no effect on the 1.09 ng/mL and 31.6 ng bioavailability (Cmax and AUC) of desloratadine.

For pseudoephedrine, the mean Tmax occurred at 6 to 7 hours post dose and mean peak plasma concentrations (Cmax) and area under the hr/mL, respectively, were observed. Food had no effect on the bioavailabilityconcentration-time curve (AUC) of approximately 263 ng/mL and 4588 ng (Cmax and AUC) of pseudoephedrine.

Following oral administration of ROTAFLU SR Tablets twice daily for 14 days in healthy volunteers, steady-state conditions were reached on Day 10 for desloratadine, 3-hydroxydesloratadine and pseudoephedrine. For desloratadine, mean steady-state peak plasma concentrations (Cmax) and area under the concentration-time curve AUC 0-12 hrs of approximately 1.7 ng/mL and 16 ng•hr/mL were observed, respectively. For pseudoephedrine, mean steady-state peak plasma concentrations (Cmax) and AUC 0-12 hrs of 459 ng/mL and 4658 ng•hr/mL were observed.

Distribution: Desloratadine and 3-hydroxydesloratadine are approximately 82% to 87% and 85% to 89%, bound to plasma proteins, respectively. Protein binding of desloratadine and 3-hydroxydesloratadine was unaltered in subjects with impaired renal function.

Metabolism: Desloratadine (a major metabolite of loratadine) is extensively metabolized to 3-hydroxydesloratadine, an active metabolite, which is subsequently glucuronidated. The enzyme(s) responsible for the formation of 3-hydroxydesloratadine have not been identified. Data from clinical trials with desloratadine indicate that a subset of the general population has a decreased ability to form 3-hydroxydesloratadine, and are poor metabolizers of desloratadine. In pharmacokinetic studies (n=3748), approximately 6% of subjects were poor metabolizers of desloratadine (defined as a subject with an AUC ratio of 3-hydroxydesloratadine to desloratadine less than 0.1, or a subject with a desloratadine half-life exceeding 50 hours). These pharmacokinetic studies included subjects between the ages of 2 and 70 years, including 977 subjects aged 2 to 5 years, 1575 subjects aged 6 to 11 years, and 1196 subjects aged 12 to 70 years. There was no difference in the prevalence of poor metabolizers across age groups. The frequency of poor metabolizers was higher in Blacks (17%, n=988) as compared to Caucasians (2%, n=1462) and Hispanics (2%, n=1063). The median exposure (AUC) to desloratadine in the poor metabolizers was approximately 6-fold greater than in the subjects who are not poor metabolizers. Subjects who are poor metabolizers of desloratadine cannot be prospectively identified and will be exposed to higher levels of desloratadine following dosing with the recommended dose of desloratadine.

Pseudoephedrine alone is incompletely metabolized (less than 1%) in the liver by N-demethylation to an inactive metabolite. The drug and its metabolite are excreted in the urine. About 55% to 96% of an administered dose of pseudoephedrine hydrochloride is excreted unchanged in the urine.

Elimination: Following single dose administration of ROTAFLU SR Tablets, the mean plasma elimination half-life of desloratadine was approximately 27 hours. In another study, following administration of single oral doses of desloratadine 5 mg, Cmax and AUC values increased in a dose proportional manner following single oral doses between 5 and 20 mg. The degree of accumulation after 14 days of dosing was consistent with the half-life and dosing frequency. A human mass balance study documented a recovery of approximately 87% of the 14C-desloratadine dose, which was equally distributed in urine and feces as metabolic products. Analysis of plasma 3-hydroxydesloratadine showed similar Tmax and halflife values compared to desloratadine.

The mean elimination half-life of pseudoephedrine is dependent on urinary pH. The elimination half-life is approximately 3 to 6 or 9 to 16 hours when the urinary pH is 5 or 8, respectively.

5.3Preclinical safety Data

Not available

6. Pharmaceutical Particulars:

6.1 List of excipients

HPMC K-100 M
Microcrystalline cellulose
Ethyl cellulose N-100
Povidone K-30%
Isopropyl Alcohol
Magnesium Stearate
Colloidal Silicon Dioxide
Purified Talc
Purified water BP
Ready Mix of pure coat aqua white (FC) IHS
Isopropyl Alcohol BP

6.2 Incompatibilities
None known

6.3 Shelf life
36 months

6.4 Special precautions for storage
Store below 25°C, in a dry place and away from children

6.5 Nature and contents of container
10 tablets packed in blister and such 1 blisters are packed in a printed carton with insert.

7. Marketing Authorization Holder:

NAME: NOVOPHARM FORMULATIONS (P) LTD.
ADDRESS:105.Rajmandir , 62- Alkapuri Society,
R.C Dutt Road, Vadodara – 390007,
GUJARAT, INDIA.
COUNTRY: INDIA
TELEPHONE: +91– 265–2342033
E-MAIL:novopharm.export@gmail.com

8. Marketing Authorization Number (s):

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9. Product license / registration Number (s)

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10. Manufacturer Name:

Name:NOVOPHARM FORMULATIONS (P) LTD.
C/O RELAX BIOTECH PVT. LTD.
Address:862/1 G.I.D.C, Industrial Estate, Makarpura,
Vadodara-390010, Gujarat, India.

11. Date of first authorization/renewal of the authorization:

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12. Date of revision of the text:

May 2023