Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Lorat 10mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One tablet contains loratadine 10 mg.

Excipients with known effect: Also contains lactose monohydrate 69.175 mg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablets
White oval tablets, scored and marked ‘LT 10’ on one face. The tablets can be divided into equal halves.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Lorat is indicated for the symptomatic treatment of allergic rhinitis and chronic idiopathic uticaria.

4.2 Posology and method of administration

Route of Administration: Oral.

Adults and children over 12 years of age:
10 mg once daily (one tablet once daily). The tablet may be taken without regard for meal time.

Children 2 to 12 years of age with:
Body weight more than 30kg: 10mg once daily (one tablet once daily).

Body weight 30kg or less:
Once daily ½ tablet (equivalent to 5mg loratadine).

The safety and efficacy of Lorat in children under 2 years of age has not been established. No data are available.

Patients with hepatic impairment
Patients with severe liver impairment should be administered a lower initial dose because they may have reduced clearance of loratadine. An initial dose of 10mg every other day is recommended for adults and children weighing more than 30kg and for children weighing 30kg or less, 5mg (½ tablet) every other day is recommended.

Patients with renal impairment
No dosage adjustments are required in patients with renal insufficiency.

Elderly
No dosage adjustments are required in the elderly.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Lorat should be administered with caution in patients with severe liver impairment (see section 4.2).

The administration of Lorat should be discontinued at least 48 hours before skin tests since antihistamines may prevent or reduce otherwise positive reactions to dermal reactivity index.

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

When administered concomitantly with alcohol, Lorat has no potentiating effects as measured by psychomotor performance studies.

Potential interaction may occur with all known inhibitors of CYP3A4 or CYP2D6 resulting in elevated levels of loratadine (see section 5.2), which may cause an increase in adverse events.

Increase in plasma concentrations of loratadine has been reported after concomitant use with ketoconazole, erythromycin, and cimetidine in controlled trials, but without clinically significant changes (including electrocardiographic).

Paediatric population
Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

Pregnancy
A large amount of data on pregnant women (more than 1000 exposed outcomes) indicate no malformative nor feto/neonatal toxicity of loratadine. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of loratadine during pregnancy.

Breastfeeding
Loratadine is excreted in breast milk, therefore the use of loratadine is not recommended in breast feeding women.

Fertility
There are no data available on male and female fertility.

4.7 Effects on ability to drive and use machines

In clinical trials that assessed driving ability, no impairment occurred in patients receiving loratadine. However, patients should be informed that very rarely some people experience drowsiness, which may affect their ability to drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

In clinical trials involving adults and adolescents in a range of indications including AR and CIU, at the recommended dose of 10mg daily. Adverse reactions with loratadine were reported in 2% of patients in excess of those treated with placebo. The most frequent adverse reactions reported in excess of placebo were somnolence (1.2%), headache (0.6%), increased appetite (0.5%) and insomnia (0.1%).

Tabulated list of adverse reactions
The following adverse reactions reported during the post-marketing period are listed in the following table by System Organ Class. Frequencies are defined as very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (<1/10,000) and not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

System Organ Class	Frequency	Adverse Experience Term
Immune system disorders	Very rare	Hypersensitivity reactions (including angioedema and anaphylaxis)
Nervous system disorders	Very rare	Dizziness, convulsion
Cardiac disorders	Very rare	Tachycardia, palpitation
Gastrointestinal disorders	Very rare	Nausea, dry mouth, gastritis
Hepato-biliary disorders	Very rare	Abnormal hepatic function
Skin and subcutaneous tissue disorders	Very rare	Rash, alopecia
General disorders and administration site conditions	Very rare	Fatigue
Investigations	Not known	Weight increased

Paediatric population
In clinical trials in a paediatric population children aged 2 through 12 years, common adverse reactions reported in excess of placebo were headache (2.7%), nervousness (2.3%) and fatigue (1%).

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 via HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Overdosage with loratadine increased the occurrence of anticholinergic symptoms. Somnolence, tachycardia and headache have been reported with overdose.

In the event of overdose, general symptomatic and supportive measures are to be instituted and maintained for as long as necessary. Administration of activated charcoal as a slurry with water may be attempted. Gastric lavage may be considered. Loratadine is not removed by haemodialysis and it is not known if loratadine is removed by peritoneal dialysis. Medical monitoring of the patient is to be continued after emergency treatment.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antihistamines – H_1 antagonist, ATC code: R06A X13.

Mechanism of action
Loratadine, the active ingredient in Lorat, is a tricyclic antihistamine with selective, peripheral H_1- receptor activity.

Pharmacodynamic effects
Loratadine has no clinically significant sedative or anticholinergic properties in the majority of the population and when used at the recommended dosage.

During long-term treatment there were no clinically significant changes in vital signs, laboratory test values, physical examinations or electrocardiogram.

Loratadine has no significant H_2-receptor activity. It does not inhibit norepinephrine uptake and has practically no influence on cardiovascular function or on intrinsic cardiac pacemaker activity.

Human histamine skin wheal studies following a single 10mg dose has shown that the antihistamine effects are seen within 1-3 hours reaching a peak at 8-12 hours and lasting in excess of 24 hours. There was no evidence of tolerance to this effect after 28 days of dosing with loratadine.

Clinical efficacy and safety
Over 10,000 subjects (12 years and older) have been treated with loratadine 10mg tablets in controlled clinical trials. Loratadine 10mg tablets once daily was superior to placebo and similar to clemastine in improving the effects on nasal and non-nasal symptoms of AR. In these studies somnolence occurred less frequently with loratadine than with clemastine and about the same frequency as terfenadine and placebo.

Among these subjects (12 years and older), 1000 subjects with CIU were enrolled in placebo controlled studies. A once daily 10mg dose of loratadine was superior to placebo in the management of CIU as demonstrated by the reduction of associated itching, erythema and hives. In these studies the incidence of somnolence with loratadine was similar to placebo.

Paediatric population
Approximately 200 paediatric subjects (6 to 12 years of age) with seasonal allergic rhinitis received doses of loratadine syrup up to 10mg once daily in controlled clinical trials. In another study, 60 paediatric subjects (2 to 5 years of age) received 5mg of loratadine syrup once daily. No unexpected adverse events were observed.

The paediatric efficacy was similar to the efficacy observed in adults.

5.2 Pharmacokinetic properties

After oral administration, loratadine is rapidly and well absorbed and undergoes an extensive first pass metabolism, mainly by CYP3A4 and CYP2D6. The major metabolite-desloratadine (DL)- is pharmacologically active and responsible for a large part of the clinical effect. Loratadine and DL achieve maximum plasma concentrations (T_{max}) between 1-1.5 hours and 1.5 – 3.7 hours after administration, respectively.

Increase in plasma concentrations of loratadine has been reported after concomitant use with ketoconazole, erythromycin and cimetidine in controlled trials but without clinically significant changes (including electrocardiographic).

Loratadine is highly bound (97%-99%) and its active metabolite moderately bound (73%-76%) to plasma proteins.

In healthy subjects, plasma distribution half-lives of loratadine and its active metabolite are approximately 1 and 2 hours, respectively. The main elimination half-lives in healthy adult subjects were 8.4 hours (range = 3 to 20 hours) for loratadine and 28 hours (range= 8.8 – 9.2 hours) for the major active metabolite.

Approximately 40% of the dose is excreted in the urine and 42% in the faeces over a 10 day period and mainly in the form of conjugated metabolites. Approximately 27% of the dose is eliminated in the urine during the first 24 hours. Less than 1% of the active substance is excreted unchanged in its active form, as loratadine or DL.

The bioavailability parameters of loratadine and the active metabolite are dose proportional.
The pharmacokinetic profile of loratadine and its metabolites is comparable in healthy adult volunteers and in healthy geriatric volunteers.

Concomitant ingestion of food can delay slightly the absorption of loratadine but without influencing clinical effects.

In patients with chronic renal impairment, the AUC and peak plasma levels (C_{max}) increased for loratadine and its metabolite as compared to the AUC and peak plasma levels (C_{max}) of patients with normal renal function.

The mean elimination half-lives of loratadine and its metabolite were not significantly different from that observed in normal subjects. Haemodialysis does not have an effect on the pharmacokinetics of loratadine or its active metabolite in subjects with chronic renal impairment.

In patients with chronic alcohol liver disease, the AUC and peak plasma levels (C_{max}) of loratadine were double while the pharmacokinetic profile of the active metabolite was not significantly changed from that in patients with normal liver function. The elimination half-lives for loratadine and its metabolite were 24 hours and 37 hours, respectively, and increased with increasing severity of liver disease.

Loratadine and its active metabolite are excreted in the breast milk of lactating women.

5.3 Preclinical safety data

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

In reproductive toxicity studies, no teratogeneric effects were observed. However, prolonged parturition and reduced viability of offspring were observed in rats at plasma levels (AUC) 10 times higher than those achieved with clinical doses.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Magnesium stearate
Maize starch
Colloidal anhydrous silica

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage precautions.

6.5 Nature and contents of container

PVC/aluminium blisters containing 5, 7, 28 or 30 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Rowex Ltd.
Bantry
Co. Cork

8 MARKETING AUTHORISATION NUMBER

PA0711/088/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 23 September 2005

Date of last renewal: 23 September 2010

10 DATE OF REVISION OF THE TEXT

January 2018