

Revised in April 2020

## 1. NAME OF THE MEDICINAL PRODUCT

**LORASTINE® TABLETS**

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10 mg loratadine.

Excipients with known effect:

The quantity of lactose monohydrate in the loratadine 10 mg tablet composition is 71.3 mg.

For a full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

White to off-white, oval tablet with flask and bowl, score and “10” on one side, plain on the other side.

The score line of the tablet is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Lorastine tablets are indicated for:

Seasonal allergic rhinitis, perennial allergic rhinitis, chronic urticaria.

### 4.2 Posology and method of administration

#### Posology

##### *Adults:*

One tablet once daily.

##### *Paediatric population:*

Children 6 years of age and older with a body weight greater than 30 kg:

One tablet once daily.

For appropriate dosing in children younger than 6 years or with body weight of 30 kg or less, there are other formulations more suitable.

##### Children under 2 years of age:

The safety and efficacy of Lorastine Tablets have 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 10 mg every other day is recommended for adults and children weighing more than 30 kg.

##### *Patients with renal impairment*

No dosage adjustments are required in patients with renal insufficiency.

#### *Elderly*

No dosage adjustments are required in the elderly.

#### *Method of administration*

Oral use. The tablet may be taken without regard to meal time.

### **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**

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

This medicinal product contains lactose; thus patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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

### **4.5 Interaction with other medicinal products and other forms of interaction**

When administered concomitantly with alcohol, Lorastine Tablets have 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 lorastine (see Section 5.2), which may cause an increase in adverse events.

Increase in plasma concentrations of lorastine 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 fetoneonatal toxicity of lorastine. 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 Lorastine Tablets during pregnancy.

#### Breastfeeding

Lorastine is excreted in breast milk. Therefore, the use of Lorastine Tablets is not recommended in breastfeeding 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 was observed in patients receiving loratadine. Lorastine Tablets have no or negligible influence on the ability to drive and use machines. 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 allergic rhinitis (AR) and chronic idiopathic urticaria (CIU), at the recommended dose of 10 mg 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 ( $\geq 1/10$ ), common ( $\geq 1/100$  to  $< 1/10$ ), uncommon ( $\geq 1/1,000$  to  $< 1/100$ ), rare ( $\geq 1/10,000$  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
Hepatobiliary 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 increase

##### 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 to the Ministry of Health according to the National Regulation by using an online form

<https://sideeffects.health.gov.il>

## 4.9 Overdose

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

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<sub>1</sub> antagonist, ATC code: R06A X13.

#### Mechanism of action

Loratadine, the active ingredient in Lorastine tablets, is a tricyclic antihistamine with selective, peripheral H<sub>1</sub>-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 electrocardiograms.

Loratadine has no significant H<sub>2</sub>-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 10 mg 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 10 mg tablets in controlled clinical trials. Loratadine 10 mg 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 10 mg 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 10 mg once daily in controlled clinical trials. In another study, 60 paediatric subjects (2 to 5 years of age) received 5 mg 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

### Absorption

Loratadine is rapidly and well-absorbed. Concomitant ingestion of food can delay slightly the absorption of loratadine but without influencing the clinical effect. The bioavailability parameters of loratadine and of the active metabolite are dose proportional.

### Distribution

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

In healthy subjects, plasma distribution half-lives of loratadine and its active metabolite are approximately 1 and 2 hours, respectively.

### Biotransformation

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.

### Elimination

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 the active form, as loratadine or DL.

The mean elimination half-lives in healthy adult subjects were 8.4 hours (range = 3 to 20 hours) for loratadine and 28 hours (range = 8.8 to 92 hours) for the major active metabolite.

### Renal impairment

In patients with chronic renal impairment, both the AUC and peak plasma levels ( $C_{max}$ ) increased for loratadine and its active metabolite as compared to the AUCs and peak plasma levels ( $C_{max}$ ) of patients with normal renal function. The mean elimination half-lives of loratadine and its active 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.

### Hepatic impairment

In patients with chronic alcoholic 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 active metabolite were 24 hours and 37 hours, respectively, and increased with increasing severity of liver disease.

### Elderly

The pharmacokinetic profile of loratadine and its active metabolite is comparable in healthy adult volunteers and in healthy geriatric volunteers.

## 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 and carcinogenic potential.

In reproductive toxicity studies, no teratogenic 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, maize starch, magnesium stearate.

### **6.2 Incompatibilities**

Not applicable

### **6.3 Shelf life**

The expiry date of the product is indicated on the packaging materials.

### **6.4 Special precautions for storage**

Store below 25°C.

### **6.5 Nature and contents of container**

Blister strip consisting of aluminium foil with vinyl heat seal coating and a clear, transparent polyvinylchloride (PVC) film or polyvinylchloride (PVC) film with polyvinylidenechloride (PVDC) coating.

Pack sizes of 7, 10, 20, tablets.

Not all pack sizes may be marketed.

### **6.6 Special precautions for disposal**

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

#### **Manufacturer:**

Schering-Plough Labo. NV Belgium

#### **Marketing Authorisation Holder:**

Bayer Israel Ltd. 36 Hacharash St., Hod Hasharon 45240