LORATADINE
(June 2010)

SUMMARY OF PRODUCT CHARACTERISTICS
(IN CONSIDERATION OF THE PHARMACEUTICAL FORM SECTIONS MARKED BY
<> MAY BE DELETED AS APPROPRIATE. SECTIONS MARKED BY [ ] ARE TO BE
COMPLETED NATIONALLY)
1. NAME OF THE MEDICINAL PRODUCT

<(Invented) name strength pharmaceutical form>

<(Invented) name and associated names (see Annex I) strength pharmaceutical form>
[See Annex I - To be completed nationally]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

<Each <tablet><coated tablet><film-coated tablet><effervescent tablet><soluble tablet><oral lyophilisate><oral dispersible tablet> contains 10 mg loratadine.>
<Each ml of <syrup><oral solution><oral suspension> contains 1 mg loratadine.>
<Each 5 ml of <syrup><oral solution><oral suspension> contains 5 mg loratadine.>
<The quantity of lactose monohydrate in the loratadine 10 mg tablet composition is 71.3 mg.>
<The quantity of sucrose in the loratadine syrup composition is 600 mg/ml. The amount of sucrose per 5 ml (5 mg) dose is 3 grams.>

For a full list of excipients, see section 6.1.
[To be completed nationally]

3. PHARMACEUTICAL FORM

<Tablet>:<White, to off-white, oval tablet with flask and bowl, score and “10” on one side, plain on the other side.>
<Coated tablet> <Film-coated tablet>:<The scoreline of the <tablet> is only to facilitate breaking for ease of swallowing and not to divide into equal doses.>
<Effervescent tablet> <Soluble tablet>
<Oral lyophilisate> <Oral dispersible tablet>
<Syrup> <Oral solution> <Oral suspension>

<Visual description of product to be completed nationally>
[To be completed nationally]

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

<(Invented) name> is indicated for the symptomatic treatment of allergic rhinitis and chronic idiopathic urticaria.

4.2 Posology and method of administration

Adults and children over 12 years of age: 10 mg once daily (<one <tablet> <coated tablet> <film-coated tablet><effervescent tablet><soluble tablet><oral lyophilisate><oral dispersible tablet>><10 ml (10 mg) of the <syrup><oral solution><oral suspension>> once daily). The {pharmaceutical form} may be taken without regard to mealtime.

Children 2 to 12 years of age are dosed by weight:
Body weight more than 30 kg: 10 mg once daily (<one <tablet> <coated tablet> <film-coated tablet><effervescent tablet><soluble tablet><oral lyophilisate><oral dispersible tablet>><10 ml (10 mg) of the <syrup><oral solution><oral suspension>> once daily).
<Body weight 30 kg or less: 5 ml (5 mg) of the <syrup><oral solution> <oral suspension> once daily.>

<The 10 mg strength <tablet><coated tablet> <film-coated tablet> <effervescent tablet> <soluble tablet><oral lyophilisate> <oral dispersible tablet> is not appropriate in children with a body weight less than 30 kg.>

[To be completed nationally]

Efficacy and safety of X in children under 2 years of age has not been established.

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<, and for children weighing 30 kg or less, 5 ml (5 mg) every other day is recommended>. No dosage adjustments are required in the elderly or in patients with renal insufficiency.

4.3 Contraindications

X is contraindicated in patients who are hypersensitive to the active substance or to any of the excipients in these formulations.

4.4 Special warnings and precautions for use

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

<Tablet
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.>

<<Syrup><oral solution>
This medicinal product contains sucrose; thus patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase isomaltase insufficiency should not take this medicine.>

<<Effervescent tablet><soluble tablet>
This medicinal product contains lactose, sorbitol and sucrose; thus patients with rare hereditary problems of fructose, galactose intolerance, the Lapp lactase deficiency, glucose-galactose malabsorption or sucrase isomaltase insufficiency should not take this medicine.>

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.>

[To be completed nationally]

The administration of X 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, X 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.
4.6 Pregnancy and lactation

Loratadine was not teratogenic in animal studies. The safe use of loratadine during pregnancy has not been established. The use of X during pregnancy is therefore not recommended.

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

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

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%).

In clinical trials involving adults and adolescents in a range of indications including AR and 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%). Other adverse reactions reported very rarely during the post-marketing period are listed in the following table.

<table>
<thead>
<tr>
<th>Immune system disorders</th>
<th>Anaphylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous system disorders</td>
<td>Dizziness</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td>Tachycardia, palpitation</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Nausea, dry mouth, gastritis</td>
</tr>
<tr>
<td>Hepatobiliary disorders</td>
<td>Abnormal hepatic function</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Rash, alopecia</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>Fatigue</td>
</tr>
</tbody>
</table>

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 – H₁ antagonist, ATC code: R06A X13.

Loratadine, the active ingredient in X, is a tricyclic antihistamine with selective, peripheral H₁-receptor activity.

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 H₂-receptor activity. It does not inhibit norepinephrine uptake and has practically no influence on cardiovascular function or on intrinsic cardiac pacemaker activity.

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 % to 99 %) and its active metabolite 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. 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.

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 active form, as loratadine or DL.

The bioavailability parameters of loratadine and of 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 the clinical effect.

In patients with chronic renal impairment, both the AUC and peak plasma levels (C_max) increased for loratadine and its 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 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 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 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 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.

<No evidence of mucous membrane irritation was observed after daily administration of up to 12 tablets (120 mg) of oral lyophilisates into the hamster cheek pouch for five days.>

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

<Tablet: lactose monohydrate, maize starch, magnesium stearate.>

<<Effervescent tablet<soluble tablet>: >

<Oral lyophilisate: >

<<Syrup<oral solution>: >

[To be completed nationally]

6.2 Incompatibilities

[To be completed nationally]

6.3 Shelf life

<Tablet: 36 months>
<<Effervescent tablet<soluble tablet>: >
<Oral lyophilisate: 2 years<24 months>
<<Syrup<oral solution>: >

[To be completed nationally]

6.4 Special precautions for storage
[For Storage condition statements see Appendix III]

<Tablet: This medicinal product does not require any special storage conditions.>
<<Effervescent tablet<soluble tablet>: >
<Oral lyophilisate<oral dispersible tablet: Store in the original package in order to protect from moisture.>
<Syrup<oral solution<oral suspension>: Store in the original package in order to protect from light.>

[To be completed nationally]
6.5 Nature and contents of container

<Tablet: Blister strip consisting of a 20 µm aluminum foil with vinyl heat coating and a 250 µm clear, transparent polyvinylchloride film.>
<Pack sizes of 2, 5, 7, 10, 14, 15, 20, 21, 28, 30, 50, or 100 tablets.>

<Not all pack sizes may be marketed.>

[To be completed nationally]

6.6 Special precautions for disposal

[To be completed nationally]

7. MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

{Name and address}
<{tel}>
<{fax}>
<{e-mail}>

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

[To be completed nationally]