SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. NAME OF THE MEDICINALPRODUCT

Afrab Loratadine tablet

2. QUALITATIVE AND QUANTITATIVECOMPOSITION

Each tablet contains 10mg of Loratadine.

{For a full list of excipients, see section 6.1}

3. PHARMACEUTICALFORM

Tablet.

A white round concave tablet with AFRAB inscribed on one side and a marked line on the other side.

4. Clinical particulars

4.1 Therapeutic indications

Loratadine 10mg Tablets is indicated for the symptomatic treatment of allergic rhinitis and chronic idiopathic urticaria.

4.2 Posology and method of administration

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:

Safety and efficacy of loratadine 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 10mg every other day is recommended for adults and children weighing more than 30kg.

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 mealtime.

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

Loratadine 10 mg Tablets should be administered with caution in patients with severe liver impairment (see section 4.2).

The administration of Loratadine 10 mg Tablets should be discontinued at least 48 hours before skin tests since antihistamines may prevent or reduce otherwise positive reactions to dermal reactivity index.

This medicinal product contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucosegalactose malabsorption should not take this medicine

4.5Interaction with other medicinal products and other forms of interaction

When administered concomitantly with alcohol, Loratadine 10 mg Tablets 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

4.6 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 10mg Tablets during pregnancy.

Breast-feeding

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. Loratadine has 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

Sedation and anti cholinergic effects are not likely. Headache, nausea and fatigue have been reported. Those that have been reported rarely include hair loss, changes in liver function and severe allergic reactions.

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%)

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 overdosage, 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 Pharmacodynamics properties

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

Mechanism of action

Loratadine, the active ingredient in Loratadine 10 mg Tablets, 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 electrocardiograms.

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 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 adult

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 major 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 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 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.

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 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 volunteers and in healthy geriatric volunteers

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.

6. PHARMACEUTICALPARTICULARS

6.1 List of excipients

Lactose Monohydrate
Corn starch
Pregel Starch
Magnesium Stearate
Aerosil

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3years.

6.4 Special precautions for storage

Store below 30 ° C.

6.5 Nature and contents of container

Alu PVC blister pack of 2 x 10 and 10 x 10 tablets

6.6 Special precautions for disposal

No special requirements for disposal

7. APPLICANT/MANUFACTURER

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