



Loratadine (Micronized)

1. Name of the medicinal product

Mosedin® 10 mg Tablets.

Mosedin® 5 mg/5 ml Syrup.

2. Qualitative and quantitative composition

Each Tablet contains 10 mg loratadine micronized

Each 5 ml Oral Solution contains 5 mg loratadine micronized

Excipient(s) with known effect

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Tablet & Syrup.

Syrup: Clear colourless to slightly yellow syrup with cherry flavour.

Tablet: White to off white pentagonal biconvex tablet bisected from one side and embossed by amoun logo on the other side.

The scoring line is not to divide the tablet into two equal doses.

4. Clinical particulars

4.1 Therapeutic indications

This medicine is indicated for the symptomatic treatment of allergic rhinitis and chronic idiopathic urticaria in adults and children over the age of 2 years.

4.2 Posology and method of administration

Posology

Adults and children over 12 years of age:

10 mg once daily (one tablet once daily) or 10ml (10mg) of the oral solution once daily.

Paediatric population

Children 2 to 12 years of age are dosed by weight.

Children 2 to 12 years of age are dosed by weight. An initial dose of 10 mg every other day is recommended for adults and children weighing more than 30 kg, and for children weighing 30kg or less, 5ml oral solution (5mg) every other day is recommended

No dosage adjustments are required in patients with renal insufficiency.

Olderly:

No dosage adjustments are required in the elderly.

Method of administration

Oral use: The tablet or the syrup solution may be taken without regard to mealtime.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Mosedin® syrup contains 550 mg propylene glycol / 5 ml.

This medicine should be administered with caution in patients with severe liver impairment (see 4.2).

Mosedin® tablet contains lactose; thus patients with rare hereditary problems of galactose intolerance, the lapp lactase deficiency or glucose-galactose malsorption should not take this medicine.

The administration of this medicine 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, this medicine 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 ketconazole, erythromycin, and cimetidine in controlled trials, but without clinically significant changes (including electrocardiographic).

Discontinue consumption of alcohol or products containing propylene glycol during and for at least three days after therapy with metronidazole. Use of oral metronidazole is associated with a disulfiram-like reaction to alcohol, including abdominal cramps, nausea, vomiting, headaches, and flushing.

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 foeto/neonatal toxicity of loratadine. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of loratadine during pregnancy.

Breast-feeding

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 studies that assessed driving ability, no impairment was observed in patients receiving loratadine. This medicine 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

Summary of the safety profile:

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 allergic rhinitis (AR) and chronic idiopathic urticarial (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 (≥ 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 Egyptian pharmacovigilance center:

pv.followup@edagovpt.gov.eg

www.esa.moh.gov.eg

5. Pharmacological properties

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.

Mechanism of action

Loratadine the active ingredient in this medicine is a tricyclic antihistamine with selective, peripheral H1 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 H2-receptor activity. It does not inhibit norepinephrine uptake and has practically no influence on cardiovascular function or on intrinsic cardiac pacemaker activity.

Loratadine Tablets: 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.

5.2 Pharmacokinetic properties

Biotransformation

After oral administration, loratadine is rapidly and well absorbed and undergoes an extensive first pass metabolism, mainly by CYP 3A4 and CYP 2D6. The major metabolite – desloratadine (DL) – is pharmacologically active and responsible for a large part of 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.

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.

Elimination

Approximately 40% of the dose is excreted in the urine and 42% in the faeces over a 10-day period (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.

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.

Renal impairment

In patients with chronic renal impairment, both the AUC and the 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 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.

Olderly

The pharmacokinetic profile of loratadine and its metabolites is comparable in healthy volunteers and in healthy geriatric volunteers.

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

6. Pharmaceutical particulars

6.1 List of excipients

Tablet: Dibasic calcium phosphate anhydrous, Lactose Monohydrate, Avicel PH102, Povidone XL (Crospovidone), Povidone K30, Magnesium stearate, Tak purified Aerosol 200.

Syrup: Propylene glycol, Sorbitol 70%, Sucrose, Citric acid Monohydrate, Benzoic acid, Sucralose, Carboxy methyl cellulose sodium, Ammonium glycyrrhizinate, Disodium edetate, Cherry Flavor liquid, Purified water.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

See outer pack

6.4 Special precautions for storage

Syrup:Store at temperature not exceeding 25°C.

Tablet: Store at temperature not exceeding 30°C, in a dry place.

6.5 Nature and contents of container

Tablet: Carton Box containing Strips (AL/Transparent Colorless PVC) each of 10 tablet + insert leaflet. For the number of strips, refer to the outer pack.

Syrup: Carton Box containing amber colored PET bottle of 60 ml syrup with white cap and plastic measuring cup and an inner leaflet

EDA revision date: 22/6/2023

Manufacturer & license holder: Amoun Pharmaceutical company

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