Summary of Product Characteristics

1-NAME OF THE MEDICINAL PRODUCT (FPP)

LORATOL

Loratadine

1.1 Strength

1 mg/ml

1.2 Pharmaceutical form

Oral suspension

2- QUALITATIVE AND QUANTITATIVE COMPOSITION

Loratol oral suspension contains 1 mg of loratadine per ml of suspension.

Excipients with known effect:

Sodium benzoate 2 mg/ml.

Propylene glycol 50 mg/ml.

Sucrose 300 mg/ml.

For the full list of excipients, see section 6.1

3- PHARMACEUTICAL FORM

Oral suspension

White coloured, cherry odour, homogeneous suspension.

4- CLINICAL PARTICULARS

4.1 Therapeutic indications

Loratol Oral Suspension is indicated for the symptomatic treatment of allergic rhinitis and chronic idiopathic urticaria.

4.2 Posology and mode of administration

4.2.1 Posology

Age	Dose in mg of Loratidine	Dose in ml of Loratol Oral Suspension
Adults and Children older than 12 years	10 mg once a day	10 ml once a day
Children between 2 and 12 years		
• Body weight more than 30 kg	10 mg once a day	10 ml once a day
• Body weight less than 30 kg	5 mg once a day	5 ml once a day

4.2.2 Special populations

- No dosage adjustments are required in the elderly.
- In patients with severe liver impairment the clearance of loratadine can be reduced. Therefore, the initial starting dose should be given every other day instead of every day. If the treatment is well tolerated and more efficacy is needed, every day dosing can be considered.
- No dosage adjustments are required in patients with renal insufficiency.

4.2.3 Paediatric population

Safety and effectiveness in children below the age of 2 is not established and therefore Loratol is not recommended under the age of 2 years.

4.2.4 Method of administration

Oral use.

The syrup may be taken without regard to mealtime.

4.3 Contraindications

Loratol Oral Suspension is contraindicated in patients who are hypersensitive to loratadine or to any of the ingredients listed in section 6.1.

4.4 Special warning and precautions for use

4.4.1 General information

Loratol Oral Suspension should be administered with caution in patients with severe liver impairment (see section 4.2.2).

Loratol Oral Suspension contains sucrose: patients with fructose intolerance, glucose-galactose malabsorption or sucrase / isomaltase deficiency should not take this medicine.

Loratol administration should be discontinued for at least 48 hours prior to skin testing for the diagnosis of allergy as antihistamines may inhibit or reduce the skin response.

Loratol oral suspension contains 10 mg sodium benzoate in each 5 ml dose.

Loratol oral suspension contains 250 mg propylene glycol in each 5 ml dose.

4.4.2 Paediatric population

Safety and effectiveness in children below the age of 2 years have not been established.

4.5 Interactions with other medicinal products and other forms of interactions

4.5.1 General information

When administered concurrently with alcohol, loratadine 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, which may cause an increase in adverse.

4.5.2 Additional information on special populations

None

4.5.3 Paediatric population

Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

4.6.1 Pregnancy

Loratadine should not be administered during pregnancy. There is no experience of the use of loratadine in human pregnancy.

4.6.2 Lactation

Since loratadine is excreted in breast milk it should not be administered to lactating women.

4.6.3 Fertility

There are no data available on male and female fertility.

4.7 Effects on the 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 studies in adults and adolescents with allergic rhinitis and chronic idiopathic urticaria at the recommended dose of 10 mg, adverse events with loratadine were reported in 2% more patients than those treated with placebo. The most frequently reported adverse reactions with greater frequency than placebo were: drowsiness (1.2%), headache (0.6%), increased appetite (0.5%) and insomnia (0.1%). %).

Other side effects reported very rarely (<1/10000) since marketing are listed in the following table.

System Organ Class	Very rare adverse events (<1/10000)
Immune System disorders	Hypersensitivity reactions (including angioedema and anaphylaxis)
Nervous system disorders	Dizziness, convulsion
Cardiac disorders	Tachycardia, palpitation
Gastrointestinal disorders	Nausea, dry mouth, gastritis
Hepatobiliary disorders	Abnormal hepatic function
Skin and subcutaneous tissue disorders	Rash, alopecia
General disorders and administration site conditions	Fatigue

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

Overdose with loratadine increases the occurrence of anticholinergic symptoms. Somnolence, tachycardia, and headache have been reported during loratadine overdoses.

Treatment in case of overdose.

- Symptomatic treatment and maintenance of vital functions.
- Activated charcoal suspended in water may possibly be administered.
- Gastric lavage may be considered.
- Loratadine is not removed by haemodialysis and it is not known if peritoneal dialysis eliminates it.
- The patient must remain under medical supervision after the emergency treatment.

5- PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group and ATC code: R06A X13 (Antihistamines – H1 antagonist).

Loratadine is a tricyclic antihistamine that selectively acts on peripheral H1 receptors. Loratadine does not have a significant sedative or anticholinergic effect in most of the population when used at the recommended dose. During long-term treatment, clinically significant changes in vital function, biological parameters, clinical examination, or electrocardiographic tracing were not observed. Loratadine has no significant action at H2 receptors. It does not inhibit norepinephrine uptake and has virtually no influence on cardiovascular function or 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.

5.2 Pharmacokinetic properties

Absorption

After oral administration, loratadine is rapidly and well absorbed and undergoes an extensive first pass metabolism, mainly by CYP3A4 and CYP2D6. 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 electrocardiographic). Concomitant ingestion of food can delay slightly the absorption of loratadine but without influencing the clinical effect.

Distribution

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

Linearity

The bioavailability parameters of Loratadine and of the active metabolite are dose proportional.

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.

Geriatric population

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

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 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.

Liver impairment

In patients with chronic alcoholic liver disease, the AUC and peak plasma levels (Cmax) 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.

5.3 Preclinical safety data

Preclinical data do not indicate a specific hazard for humans based on conventional studies of safety, pharmacology, repeated dose toxicity, genotoxicity, or carcinogenicity.

The study of reproductive functions revealed no teratogenic effects in animals. However, prolonged parturition and reduced viability of offspring were observed in rats exposed to plasma levels (AUC) 10-fold higher than those achieved with clinical doses.

6- PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Polysorbate 80
- Propylene glycol
- Sodium citrate
- Citric acid
- Microcrystalline cellulose & Carmellose sodium
- Sodium benzoate
- Sucrose
- Glycerol

- Xanthan gum
- Cherry essence
- Purified water

6.2 Incompatibilities

None known

6.3 Shelf life

Proposed shelf-life: 24 Months

Shelf-life after first opening of container: Liquid suitable for treatment of a period ranging from 10 to 20 days.

6.4 Special precautions for storage

Store below 30^{o}C.

6.5 Nature and contents of container

Amber coloured glass bottle, closed with a plastic (polyethylene) cap.

Content: 100 ml

The bottle is packed with a leaflet and a 5ml measuring device (polypropylene) in a carton box.

6.6 Special precautions for disposal and other handlings

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

7- MARKETING AUTHORISATION HOLDER AND MANUFACURING SITE ADDRESS

7.1 Marketing Authorisation Holder

Dafra Pharma GmbH,

Mühlenberg 7, 4052 Basel, Switzerland

7.2 Manufacturer

Nobel Ilaç, San. Ve. Tic. A.S. Sancaklar 81100 Düzce, Turkey.

8- MARKETING AUHORISATION NUMBER

See list of MAs per country

9- DATE OF FIRST REGISTRATION

See list of MAs per country

10- DATE OF REVISION OF TEXT

March 2019