NALIS® LORATADINE ORAL SYRUP.

(LORATADINE BP 5MG/5ML)

SUBMITTED BY: NALIS PHARMACEUTICALS LTD

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SUMMARY OF PRODUCT CHARACTERISTICS

(SmPC) .

1. NAME OF THE DRUG PRODUCT

Nalis® Loratadine oral syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

An orange coloured syrup.

Each 5ml contains:

Loratadine BP……. 5mg
Excipients……. q.s

3. PHARMACEUTICAL FORM

Oral syrup

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Nalis Loratadine is indicated for the symptomatic relief of allergy such as hay fever (allergic rhinitis), urticaria (hives), chronic idiopathic urticaria, and other skin allergies. For allergic rhinitis, loratadine is indicated for both nasal and eye symptoms - sneezing, runny nose, and itchy or burning eyes. For adult and children.

4.2 Posology and method of administration

Posology

Adults and children over 12 years of age:

10ml (10mg) of the syrup once daily.

Paediatric population

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

Body weight more than 30kg: 10ml (10mg) of the syrup once daily;

Body weight 30kg or less: 5ml (5mg) of the syrup once daily.

Efficacy and safety of Loratadine 5mg/5ml Syrup in children under 2 years of age has not been established.

Patients with severe liver 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, and for children weighing 30kg or less, 5ml (5mg) every other day is recommended.

Patients with severe renal impairment

No dosage adjustments are required in the elderly or in patients with renal insufficiency.

Elderly

No dosage adjustments are required in the elderly.

Method of administration

For oral administration.

4.3 Contradindications

Nalis Loratadine 5mg/5ml Syrup is contraindicated in patients who are hypersensitive to the active substance or to any of the excipients in this formulation.

4.4 Special warnings and precautions for use

Loratadine 5mg/5ml Syrup should be administered with caution in patients with severe liver impairment (see section 4.2).

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

The administration of Loratadine 5mg/5ml Syrup 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 drug products and other forms of interaction

When administered concomitantly with alcohol, Loratadine 5mg/5ml Syrup 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).

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 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 5mg/5ml Syrup 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 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

a. Summary of the safety profile

In clinical trials involving adults and adolescents in a range of indications including AR and CIU, at the recommended dose of 10mg daily, adverse reactions with loratadine were reported in 2% of patients in excess of those treated with the 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%).

b. 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 Reaction
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

c. 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 regulatory bodies such as NAFDAC.

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: anti histamines – H_1 antagonist,

ATC code: R06A X13.

Loratadine, the active ingredient in Loratadine 5mg/5ml Syrup, is a tricyclic antihistamine with selective, peripheral H_1-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 H_2-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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

S/N	Raw Material	Specification
1.	Sodium CMC	B.P
2.	Methyl paraben	B.P
3.	Propyl paraben	B.P
4.	Glycerine	B.P
5.	Sugar	B.P
6.	Orange flavour	B.P
8.	Sunset Yellow Colour	B.P
9.	Sodium benzoate	B.P
10	Xanthan gum	BP
11	Tween 80	BP
12	Treated water	B.P

6.2 Incompatibilities

None known

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Bottle made from Amber pet with a tamper evident child resistant closure having a polypropylene outer layer and a polyethylene inner layer. This product is provided with a measuring device (dispensing cup).

Pack Sizes: 100 ml.

6.6 Special precautions for disposal of used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7. APPLICANT/HOLDER OF CERTIFICATE OF PRODUCT REGISTRATION

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8. DRUG PRODUCT MANUFACTURER

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9. NAFDAC REGISTRATION NUMBER(S):

A11-100059