Drugfield **PHARMACEUTICALS LIMITED**

SUMMARY OF PRODUCT CHARACTERISTICS

Nosdrine Syrup

1. NAME OF THE MEDICINAL PRODUCT

Nosdrine® (Loratadine 5mg) Syrup

2. QUALITATIVE AND QUANTITATIVECOMPOSITION

Each 5ml syrup contains 5mg loratadine
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Liquid (Syrup)

4. Clinical particulars

4.1 Therapeutic indications

Nosdrine® (Loratadine) is indicated for the relief of sneezing, runny nose, itchy, watery eyes, itchy throat or nose. It is also indicated for the symptomatic treatment of allergic rhinitis and chronic idiopathic urticarial in adults.

4.2 Posology and method of administration

Posology

Important Dosage and Administration Instructions

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

Oral administration
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4.3 Contraindications

Loratadine is contraindicated in patients who are hypersensitive to the active substance.

4.4 Special warnings and precautions for use

Loratadine tablet should be administered with caution in patients with severe liver impairment this medicinal product contains sucrose; patients with rare hereditary problems of fructose intolerance, glucose-galactosemalabsorption or sucrase-isomaltase insufficiency should not take this medicine. The administration of Loratadine 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

Clinically Significant Drug Interactions with Loratadine

When administered concomitantly 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 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

Risk Summary

A large amount of data on pregnant women (more than 1000 exposed outcomes) indicates no

malformativenorfeto/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

Lactation

Risk Summary

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

Females and Males of Reproductive Potential

Infertility

There are no data available on male and female fertility.

Pediatric Use

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4.7 Effects on ability to drive and use of machines

In clinical studies that assessed driving ability, no impairment occurred in patients receiving loratadine. Loratidine 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

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%).

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%).

Other adverse effects that occur rarely are: dizziness, convulsions, tachycardia, palpitiations,Hypersensitivity reactions (including angioedema and anaphylaxis), nausea, dry mouth, gastritis, rash, alopecia, abnormal hepatic function, fatigue, and weight increase.

4.9 Overdose

Over dosage 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 PHARMACOLOGICALPROPERTIES

Mechanism of Action

Loratadine is a piperidine histamine H1-receptor antagonist with anti-allergic properties and without sedative effects. Loratadine blocks the H1 histamine receptor and prevents the symptoms that are caused by histamine activity on capillaries, bronchial smooth muscle, and gastrointestinal smooth muscle, including vasodilatation, increased capillary permeability, bronchoconstriction, and spasmodic contraction of gastrointestinal smooth muscle. Loratadine does not cross the blood-brain barrier and does not cause central nervous system effects.

5.1 Pharmacodynamics Properties

Loratadine is indicated for the symptomatic treatment of allergic rhinitis and chronic idiopathic urticarial in adults and children over the age of 2 years. Loratadine, the active ingredient in Nosdrine, 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 Cytochrome (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 Area under Curves (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

Non-clinical 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 10 times higher than those achieved with clinical doses.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Proplene Glycol
Sucrose
Sodium CMC (MV)
Aspartame
Methyl Paraben
Ethanol 96%
Raspberry Essence
Sunset yellow
Citric acid
Butylated Hydroxyanisole (BHA)
Purified water (to the volume)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store below 30ºC. Protect from light and moisture.

6.5 Nature and contents of container and special equipment for use, administration or implantation

Nosdrine® Syrup is presented in a 60ml amber bottle in a carton with leaflet enclosed

6.6 Special precautions for disposal and other handling

No special requirements.

7 APPLICANT/MANUFACTURER

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