PROFESSIONAL INFORMATION

SCHEDULING STATUS:

S2

PROPRIETARY NAME AND DOSAGE FORM:

NEOCLARITYNE ™TABLETS

COMPOSITION:

Active ingredient: 5.0 mg desloratadine.

Inactive ingredients: Calcium phosphate, maize starch, microcrystalline cellulose, purified water and talc.

Contains sugar: Lactose monohydrate.

CATEGORY AND CLASS

A.5.7.1 Antihistaminics

PHARMACOLOGICAL ACTION:

Desloratadine is a non-sedating long-acting histamine antagonist with selective peripheral H_1-receptor antagonist activity. Desloratadine has demonstrated anti-allergic, antihistaminic, and anti-inflammatory activity.

Clinical Pharmacology

Pharmacodynamic Properties:

After oral administration, desloratadine selectively blocks peripheral histamine H_1-receptors. It does not readily penetrate into the central nervous system.

In addition to antihistaminic activity, desloratadine has demonstrated anti-allergic and anti-inflammatory activity from numerous *in vitro* (mainly conducted on cells of human origin) and *in vivo* studies. These studies have shown that desloratadine inhibits the broad cascade of events that initiate and propagate allergic inflammation.

Pharmacokinetic Properties:

Desloratadine plasma concentrations can be detected within 30 minutes of desloratadine administration. Desloratadine is well absorbed with maximum concentration achieved after approximately 3 hours; the terminal phase half-life is approximately 27 hours. The degree of accumulation of desloratadine was consistent with its half-life (approximately 27 hours) and a once daily dosing frequency. The bioavailability of desloratadine was dose proportional over the range of 5 mg to 20 mg.

Desloratadine is moderately bound (83 % - 87 %) to plasma proteins. There is no evidence of clinically relevant drug accumulation following once daily dosing of desloratadine (5 mg to 20 mg) for 14 days.

The enzyme responsible for the metabolism of desloratadine has not been identified yet, and therefore some interactions with other drugs cannot be fully excluded. *In-vivo*

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studies with specific inhibitors of CYP3A4 and CYP2D6 have shown that these enzymes are not important in the metabolism of desloratadine. Desloratadine does not inhibit CYP3A4 or CYP2D6 and is neither a substrate nor an inhibitor of P-glycoprotein.

In a single dose trial using a 7.5 mg dose of desloratadine, there was no effect of food (high-fat, high caloric breakfast) on the disposition of desloratadine. In another study, grapefruit juice had no effect on the disposition of desloratadine.

INDICATIONS:

NEOCLARITYNE TABLETS are indicated for the relief of symptoms associated with allergic rhinitis. NEOCLARITYNE TABLETS are also indicated for the short-term relief of symptoms associated with chronic idiopathic urticaria.

CONTRAINDICATIONS:

Hypersensitivity to the active substance or to any of the excipients.

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WARNINGS AND SPECIAL PRECAUTIONS:

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose galactose malabsorption should not take NEOCLARITYNE TABLETS.

Desloratadine should be administered with caution in patients with a medical or family history of seizures. In particular, young children may be more susceptible to developing new seizures under desloratadine treatment. Healthcare providers may consider discontinuing desloratadine in patients who experience a seizure while on treatment.

Special Precautions

Safety and efficacy of NEOCLARITYNE TABLETS in children under 12 years of age have not been established.

Safety and efficacy of desloratadine have not been established for treatment periods in excess of 4 weeks.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take NEOCLARITYNE TABLETS.

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Effects on ability to drive and use machines

NEOCLARITYNE TABLETS lacks significant sedative effects. Patients should, however be warned that a small number of individuals may experience sedation. It is therefore advisable to determine individual response before driving or performing complicated tasks.

INTERACTIONS:

There was no effect of food or grapefruit juice on the disposition of desloratadine.

Co-administration of desloratadine, as contained in NEOCLARITYNE, with ketoconazole increases the maximum desloratadine concentration (C_{max}) by 45 % and the area under the time concentration curve (AUC) by 37 %. Co-administration of desloratadine with erythromycin increased the C_{max} of desloratadine by 24 % and the AUC by 14 %.

Co-administration of desloratadine, as contained in NEOCLARITYNE, with azithromycin resulted in an increase of both C_{max} (31 %) and AUC (12 %) of azithromycin.

The increase in C_{max} and AUC of desloratadine, as contained in NEOCLARITYNE, when co-administered with either ketoconazole or erythromycin did not cause any clinical relevant adverse events in the populations studied. Co-administration of cimetidine with desloratadine, as contained in NEOCLARITYNE, did not significantly affect the pharmacokinetics of desloratadine.

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Co-administration of fluoxetine with desloratadine, as contained in NEOCLARITYNE, caused an increase in the C_{max} of desloratadine by 15 % and an increase of 13 % in AUC and 17 % in C_{max} of 3-OH desloratadine respectively.

The C_{max} and AUC of fluoxetine were reduced by 9 % and 11 % respectively. The corresponding mean parameters of norfluoxetine increased by 23 % and 18 % respectively, with co-administration of desloratadine, as contained in NEOCLARITYNE, and fluoxetine.

No clinically relevant changes in desloratadine plasma concentrations were observed in multiple-dose ketoconazole, erythromycin, azithromycin, fluoxetine and cimetidine interaction trials.

HUMAN REPRODUCTION:

NEOCLARITYNE TABLETS were not found to be teratogenic in animal studies. The safe use of NEOCLARITYNE TABLETS during pregnancy has not been established. The use of NEOCLARITYNE TABLETS during pregnancy is therefore not recommended.

Desloratadine is excreted into breast milk, therefore the use of NEOCLARITYNE TABLETS is not recommended in breast-feeding women.

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DOSAGE AND DIRECTIONS FOR USE:

Adults and adolescents (≥ 12 years of age): One NEOCLARITYNE 5 mg film-coated tablet once a day regardless of mealtime for the relief of symptoms associated with allergic rhinitis (including intermittent and persistent allergic rhinitis) and chronic idiopathic urticaria. For oral use only.

Intermittent allergic rhinitis (presence of symptoms for less than 4 days per week or for less than 4 weeks) should be managed in accordance with the evaluation of patient's disease history and the treatment could be discontinued after symptoms are resolved and reinitiated upon their reappearance.

In persistent allergic rhinitis (presence of symptoms for more than 4 days or more per week and for more than 4 weeks), continued treatment may be proposed to the patients during allergen exposure periods).

Improvement of symptoms associated with seasonal allergic rhinitis usually becomes noticeable within 1 - 2 hours after administration of desloratadine.

SIDE EFFECTS

Table 1: The following side effects have been reported and the frequencies are unknown	
Immune system disorders	Hypersensitivity reactions (such as anaphylaxis, angioedema, dyspnoea, pruritus, rash and urticaria)
Metabolism and nutrition disorders	Increased appetite
Nervous system disorders	Dizziness, somnolence, insomnia, seizures, psychomotor hyperactivity and headache
Cardiac disorders	Tachycardia, palpitations.
Gastro-intestinal disorders	Abdominal pain, nausea, vomiting, dyspepsia, diarrhoea, and dry mouth.
Hepato-biliary disorders	Elevations of liver enzymes, increased bilirubin, hepatitis.
Musculoskeletal and connective tissue disorders	Myalgia.
General disorders and administrative site conditions	Fatigue.

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KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

In the event of overdose, consider standard measures to remove unabsorbed active substance. Symptomatic and supportive treatment is recommended.

Desloratadine is not eliminated by haemodialysis; it is not known if it is eliminated by peritoneal dialysis.

IDENTIFICATION:

Light blue round embossed tablets (embossed with the Schering-Plough

Logo .

PRESENTATION:

NEOCLARITYNE TABLETS are packed in blister packs.

Blisters are packed in cartons of 10 or 30 tablets.

STORAGE INSTRUCTIONS:

Store at or below 25 °C.

Protect from moisture.

Keep out of reach of children.

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REGISTRATION NUMBER:

35/5.7.1/0208

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Bayer (Pty) Ltd

27 Wrench Road

Isando, 1600

South Africa

1968/011192/07

DATE OF PUBLICATION OF THIS PROFESSIONAL INFORMATION:

Date on the registration certificate: 20 May 2002

Date of the most recently revised professional information as approved: 2 March 2012

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