National Agency for Food & Drug Administration & Control (NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. NAME OF THE MEDICINAL PRODUCT
Avrotyn 10mg Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains 10mg Loratadine.
For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM
White, round, biconvex tablets.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
Avrotyn is indicated for the relief of symptoms associated with allergic rhinitis (hay fever) such as sneezing, runny or itchy nose and burning or itchy eyes in adults and children over the age of 2 years.
It may also be used to help relieve symptoms of urticaria (itching and redness, which is often known as hives) and other allergic skin disorders.

4.2 Posology and method of administration
Posology

Adults and children over 12 years of age:
1 tablet (10 mg) once daily. The tablet may be taken without regard to mealtime.

Children 6 years and older (who weigh more than 30kg):
1 tablet (10mg) once daily.

Body weight 30 kg or less: These tablets are not suitable in children with a body weight less than 30 kg.

Efficacy and safety of Avrotyn Tablets in children under 2 years of age has not been established.

Dose may be taken with or without food.

Note**:** Geriatric patients may be more sensitive to the effects of the adult dose.

Do not exceed the recommended dose. If symptoms persist, consult your doctor.

Patients with severe liver impairment should be administered a lower initial dose because they may have reduced clearance of loratadine. An initial dose of 10 mg every other day is recommended for adults and children weighing more than 30 kg, and for children weighing 30 kg or less, 5 ml (5 mg) every other day is recommended.
No dosage adjustments are required in the elderly or in patients with renal insufficiency.

Method of administration
For oral administration.

4.3 Contraindications
The product should not be used in the following conditions:

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 and other antihistamines of similar chemical structure.
- Pregnancy or breastfeeding
- Children under the age of 2 due to its antihistamine properties, which may cause CNS stimulation or seizures in young patients.

4.4 Special warnings and precautions for use

Avrotyn Tablets should be administered with caution in patients with severe liver impairment (see 4.2) as the liver extensively metabolizes Loratadine, and dose adjustments are necessary per healthcare guidelines. Similarly, individuals with kidney failure or renal impairment should be cautious as such patients will have elevated Loratadine concentrations, requiring dose adjustments.

The administration of Avrotyn Tablets should be discontinued at least 48 hours before skin tests since antihistamines may prevent or reduce otherwise positive reactions to dermal reactivity index.

This medication requires cautious use in asthmatic or COPD patients due to its anticholinergic effects, which may cause a flare-up.

At the recommended dose, Loratadine is not expected to cause drowsiness or less alertness. However, very rarely some people experience drowsiness, which may affect their ability to drive or use machines.

Consult your doctor before taking this product if you are pregnant or breast feeding.

4.5 Interaction with other medicinal products and other forms of interaction

When administered concomitantly with alcohol, Avrotyn Tablets have 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.These include such drugs as cimetidine, erythromycin, ketoconazole, quinidine, fluconazole and fluoxetine.
Antihistamines may suppress cutaneous histamine response to allergen extracts. Its therapy should be stopped several days before skin testing.

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 (see section 5.3). 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.

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 experienced drowsiness, which may affect their ability to drive or use machines.

4.8 Undesirable effects

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 AR and 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%). Other adverse reactions reported very rarely during the post-marketing period are listed in the following table.

Immune system disorders	Hypersensitivity reactions (including angioedema and anaphylaxis)
Nervous system disorders	Dizziness, convulsion
Cardiac disorders	Tachycardia, palpitation
Gastrointestinal disorders	Nausea, dry mouth, gastritis
Hepato-biliary disorders	Abnormal hepatic function
Skin and subcutaneous tissue disorders	Rash, alopecia
General disorders and administration site conditions	Fatigue
Adverse reactions with frequency 'not known':	
Investigations	Weight increased

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 – H_1 antagonist, ATC code: R06A X13.
Loratadine, the active ingredient in Loratadine Tablets, 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 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
Lactose monohydrate
Microcrystalline cellulose
Sodium starch glycolate
Maize starch
Magnesium stearate.

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
3 years

6.4 Special precautions for storage
No special precautions for storage.

6.5 Nature and contents of container
10 Alu-PVC blisters containing 10 tablets each, packed in a printed clinical carton.
Pack sizes: 100

6.6 Special precautions for disposal and other handling
No special requirements.

7. APPLICANT

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