IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0577/046/002
Case No: 2045597

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

McDermott Laboratories Ltd t/a Gerard Laboratories

35/36 Baldoyle Industrial Estate, **Grange Road**, **Dublin 13**, **Ireland**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Histaclar Allergy 10mg Film Coated Tablets

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **04/04/2008**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Histaclar Allergy 10mg Film Coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 10mg Loratadine.

Each tablet also contains 84.5mg of Lactose Monohydrate.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablets

Film-coated white round biconvex tablets scored on one side and marked “LR 10” on the other side.
The tablets can be divided into equal halves.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Histaclar Allergy is indicated for the symptomatic treatment of allergic rhinitis (AR) and chronic idiopathic urticaria (CIU).

4.2 Posology and method of administration

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

Children 2 to 12 years of age with body weight more than 30 kg:
10mg once daily (one film-coated tablet once daily).

Body weight 30 kg or less:
The 10 mg strength film-coated tablet is not appropriate in children with a body weight less than 30 kg.

Efficacy and safety of Histaclar Allergy in children under 2 years of age has not been established.

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

4.3 Contraindications

Histaclar Allergy is contra-indicated in patients who are hypersensitive to the active substance or to any of the excipients.

4.4 Special warnings and precautions for use

Histaclar Allergy should be administered with caution in patients with severe liver impairment (see 4.2).

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

The administration of Histaclar Allergy 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

When administered concomitantly with alcohol Histaclar Allergy has no potentiating effects as measured by psychomotor performance studies.

Due to the wide therapeutic index of loratadine no clinically relevant interactions are expected and none were observed in the conducted clinical trials (see 5.2).

4.6 Pregnancy and lactation

Loratadine was not teratogenic in animal studies. The safe use of loratadine during pregnancy has not been established. The use of Histaclar Allergy during pregnancy is therefore not recommended.

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 experience 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 disorders	Anaphylaxis
Nervous system disorders	Dizziness
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

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: RO6A X13. Loratadine, the active ingredient in Histaclar Allergy, 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 no 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%-99%) and its active metabolite moderately bound (73%-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 the 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 may slightly delay the absorption of loratadine without influencing the clinical effect.

In patients with chronic renal impairment, the area under curve (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 doubled 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 substance 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.

No evidence of mucous membrane irritation was observed after daily administration of up to 12 tablets (120mg) or oral lyophilisates into the hamster cheek pouch for five days.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet Core
Lactose monohydrate
Microcrystalline cellulose
Maize starch
Pregelatinized maize starch
Hydrated colloidal silica
Magnesium stearate

Film coat
Hypromellose
Macrogol 400 and 6000

Polishing agents
Carnauba wax
Talc

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package.

6.5 Nature and contents of container

PVC/Aluminium blister packs.

Blister pack sizes of 5, 7 and 10.

Not all pack sizes may be marketed.

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

No special requirements

7 MARKETING AUTHORISATION HOLDER

McDermott Laboratories Ltd (T/A Gerard Laboratories)
35/36 Baldoyle Industrial Estate
Grange Road
Dublin 13
Ireland

8 MARKETING AUTHORISATION NUMBER

PA 577/46/2

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 4th April 2003
Date of last renewal: 4th April 2008

10 DATE OF REVISION OF THE TEXT

July 2008