Public Assessment Report

Decentralised Procedure

DESLORATADINE GLENMARK 5 MG TABLETS

UK/H/3054/001/DC
UK Licence No: PL 25258/0052

GLENMARK GENERICS (EUROPE) LIMITED
On 4th April 2012, the UK granted Glenmark Generics (Europe) Limited a Marketing Authorisation (licence) for Desloratadine Glenmark 5 mg Tablets.

Desloratadine Glenmark 5 mg Tablets contain the active ingredient desloratadine.

Desloratadine is a long-acting anti-histamine medicine.

This medicine is used to:

- Relieve symptoms associated with **allergic rhinitis**, such as inflammation of the nasal passages caused by an allergy to pollen or dust mites for example. Other symptoms include sneezing, runny or itchy nose, itchy palate, and itchy, red or watery eyes.

- Relieve symptoms of **urticaria**, which is a skin condition caused by an allergy. Symptoms include itching and hives (nettle rash). Relief can last a full day and help you to resume your normal daily activities and sleep.

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of taking Desloratadine Glenmark 5 mg Tablets outweigh the risks and a Marketing Authorisation was granted.
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## Module 1

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<td><strong>Type of Application</strong></td>
<td>Generic application, Article 10.1</td>
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<td>Desloratadine</td>
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<td><strong>Form</strong></td>
<td>Tablets</td>
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<td><strong>Strength</strong></td>
<td>5 mg</td>
</tr>
<tr>
<td><strong>MA Holder</strong></td>
<td>Glenmark Generics (Europe) Limited Laxmi House, 2B Draycott Avenue Harrow, Middlesex HA3 0BU, UK</td>
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<td><strong>Reference Member State (RMS)</strong></td>
<td>The United Kingdom (UK)</td>
</tr>
<tr>
<td><strong>Concerned Member States (CMS)</strong></td>
<td>Denmark (DK), Finland (FI), France (FR), Germany (DE), Greece (EL), Spain (ES), Hungary (HU), Ireland (IE), the Netherlands (NL), Poland (PL), Portugal (PT), Romania (RO) and Sweden (SE)</td>
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</table>
Module 2
Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT
Desloratadine Glenmark 5 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains 5mg desloratadine.
Excipients: 98.80mg lactose monohydrate.
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Tablet.
Off white to light pink, circular, biconvex with ‘L5’ debossed on one side and plain on the other side.
Diameter: approximately 10.5mm

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Desloratadine Glenmark 5mg Tablets are indicated for the relief of symptoms associated with:
- allergic rhinitis (See section 5.1)
- urticaria (see section 5.1)

4.2 Posology and method of administration
Method of administration:
For oral use.
The tablet should be swallowed with a sufficient amount of fluid (e.g. one glass of water).

Posology
Adults and adolescents (12 years of age and over): one tablet once a day, with or without a meal for the relief of symptoms associated with allergic rhinitis (including intermittent and persistent allergic rhinitis) and urticaria (see section 5.1).

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 4 days or more per week and for more than 4 weeks), continued treatment may be proposed to the patients during the allergen exposure periods.

Paediatric population
There is limited clinical trial efficacy experience with the use of desloratadine in adolescents aged 12 to 17 years of age (see sections 4.8 and 5.1).
The safety and efficacy of Desloratadine Glenmark 5mg Tablets in children under 12 years of age has not been established.

Patients with renal impairment
Desloratadine Glenmark 5mg Tablets should be used with caution in patients with severe renal insufficiency.

4.3 Contraindications
Hypersensitivity to the active substance, to any of the excipients, or to loratadine.

4.4 Special warnings and precautions for use
Efficacy and safety of Desloratadine Glenmark 5mg Tablets in children under 12 years of age have not been established.

In the case of severe renal insufficiency, Desloratadine Glenmark 5mg Tablets should be used with caution (see section 5.2).
This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction
No clinically relevant interactions were observed in clinical trials with desloratadine in which erythromycin or ketoconazole were co-administered (see section 5.1).

In a clinical pharmacology trial desloratadine taken concomitantly with alcohol did not potentiate the performance impairing effects of alcohol (see section 5.1).

4.6 Fertility, pregnancy and lactation
Desloratadine was not teratogenic in animal studies. The safe use of the medicinal product during pregnancy has not been established. The use of desloratadine during pregnancy is therefore not recommended.

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

4.7 Effects on ability to drive and use machines
Desloratadine has no or negligible influence on the ability to drive and use machines, as assessed in clinical trials.

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 range of indications including allergic rhinitis and chronic idiopathic urticaria, at the recommended dose of 5 mg daily, undesirable effects with desloratadine were reported in 3 % of patients in excess of those treated with placebo. The most frequent adverse events reported in excess of placebo were fatigue (1.2 %), dry mouth (0.8 %) and headache (0.6 %). In a clinical trial with 578 adolescent patients, 12 through 17 years of age, the most common adverse event was headache; this occurred in 5.9 % of patients treated with desloratadine and 6.9 % of patients receiving placebo. Other undesirable effects reported very rarely (<1/10,000) during the post-marketing period are listed in the following table.

<table>
<thead>
<tr>
<th>Psychiatric disorders</th>
<th>Hallucinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous system disorders</td>
<td>Dizziness, somnolence, insomnia, psychomotor hyperactivity, seizures</td>
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<tr>
<td>Cardiac disorders</td>
<td>Tachycardia, palpitations</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Abdominal pain, nausea, vomiting, dyspepsia, diarrhoea</td>
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<tr>
<td>Hepatobiliary disorders</td>
<td>Elevations of liver enzymes, increased bilirubin, hepatitis</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>Myalgia</td>
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<tr>
<td>General disorders</td>
<td>Hypersensitivity reactions (such as anaphylaxis, angioedema, dyspnoea, pruritus, rash and urticaria)</td>
</tr>
</tbody>
</table>

4.9 Overdose
Symptoms
Based on a multiple dose clinical trial, in which up to 45 mg of desloratadine was administered (nine times the clinical dose), no clinically relevant effects were observed.

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.
5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Other antihistamines for systemic use
ATC code: R06A X27

Desloratadine in a non-sedating, long-acting histamine antagonist with selective peripheral H1-receptor antagonist activity. After oral administration, desloratadine selectively blocks peripheral histamine H1-receptors because the substance is excluded from entry to the central nervous system.

Desloratadine has demonstrated antiallergic properties from in vitro studies. These include inhibiting the release of proinflammatory cytokines such as IL-4, IL-6, IL-8, and IL-13 from human mast cells/basophils, as well as inhibition of the expression of the adhesion molecule P-selectin on endothelial cells. The clinical relevance of these observations remains to be confirmed.

In a multiple dose clinical trial, in which up to 20 mg of desloratadine was administered daily for 14 days, no statistically or clinically relevant cardiovascular effect was observed. In a clinical pharmacology trial, in which desloratadine was administered at a dose of 45 mg daily (nine times the clinical dose) for ten days, no prolongation of QTc interval was seen.

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

Desloratadine does not readily penetrate the central nervous system. In controlled clinical trials, at the recommended dose of 5 mg daily, there was no excess incidence of somnolence as compared to placebo. Desloratadine given at a single daily dose of 7.5 mg did not affect psychomotor performance in clinical trials. In a single dose study performed in adults, desloratadine 5 mg did not affect standard measures of flight performance including exacerbation of subjective sleepiness or tasks related to flying.

In clinical pharmacology trials, co-administration with alcohol did not increase the alcohol-induced impairment in performance or increase in sleepiness. No significant differences were found in the psychomotor test results between desloratadine and placebo groups, whether administered alone or with alcohol.

In patients with allergic rhinitis, desloratadine was effective in relieving symptoms such as sneezing, nasal discharge and itching, as well as ocular itching, tearing and redness, and itching of palate. Desloratadine effectively controlled symptoms for 24 hours. The efficacy of desloratadine has not been clearly demonstrated in trials with adolescent patients 12 through 17 years of age.

In addition to the established classifications of seasonal and perennial, allergic rhinitis can alternatively be classified as intermittent allergic rhinitis and persistent allergic rhinitis according to the duration of symptoms. Intermittent allergic rhinitis is defined as the presence of symptoms for less than 4 days per week or for less than 4 weeks. Persistent allergic rhinitis is defined as the presence of symptoms for 4 days or more per week and for more than 4 weeks.

Desloratadine was effective in alleviating the burden of seasonal allergic rhinitis as shown by the total score of the rhino-conjunctivitis quality of life questionnaire. The greatest amelioration was seen in the domains of practical problems and daily activities limited by symptoms.

Chronic idiopathic urticaria was studied as a clinical model for urticarial conditions, since the underlying pathophysiology is similar, regardless of etiology, and because chronic patients can be more easily recruited prospectively. Since histamine release is a causal factor in all urticarial diseases, desloratadine is expected to be effective in providing symptomatic relief for other urticarial conditions, in addition to chronic idiopathic urticaria, as advised in clinical guidelines.

In two placebo-controlled six week trials in patients with chronic idiopathic urticaria, desloratadine was effective in relieving pruritus and decreasing the size and number of hives by the end of the first dosing interval. In each trial, the effects were sustained over the 24 hour dosing interval. As with other antihistamine trials in chronic idiopathic urticaria, the minority of patients who were identified as non-responsive to antihistamines was excluded. An improvement in pruritus of more than 50 % was observed in 55 % of patients treated with desloratadine compared with 19 % of patients treated with
placebo. Treatment with desloratadine also significantly reduced interference with sleep and daytime function, as measured by a four-point scale used to assess these variables.

5.2 Pharmacokinetic properties
Desloratadine plasma concentrations can be detected within 30 minutes of 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.

In a pharmacokinetic trial in which patient demographics were comparable to those of the general seasonal allergic rhinitis population, 4% of the subjects achieved a higher concentration of desloratadine. This percentage may vary according to ethnic background. Maximum desloratadine concentration was about 3-fold higher at approximately 7 hours with a terminal phase half-life of approximately 89 hours. The safety profile of these subjects was not different from that of the general population.

Desloratadine is moderately bound (83% - 87%) to plasma proteins. There is no evidence of clinically relevant medicine 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 medicinal products can not be fully excluded. Desloratadine does not inhibit CYP3A4 in vivo, and in vitro studies have shown that the medicinal product does not inhibit 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.

5.3 Preclinical safety data
Desloratadine is the primary active metabolite of loratadine. Non-clinical studies conducted with desloratadine and loratadine demonstrated that there are no qualitative or quantitative differences in the toxicity profile of desloratadine and loratadine at comparable levels of exposure to desloratadine.

Non-clinical data with desloratadine reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, and toxicity to reproduction. The lack of carcinogenic potential was demonstrated in studies conducted with desloratadine and loratadine.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Microcrystalline Cellulose
Lactose Monohydrate
Maize Starch
Silica, Colloidal Anhydrous
Magnesium Stearate

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
2 years

6.4 Special precautions for storage
This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container
This medicinal product is packed in Aluminium/Aluminium blisters comprised of cold formable aluminium foil and hard tempered aluminium lidding foil.
Pack sizes: 7, 10, 14, 15, 20, 28, 30, 50 or 100 tablets.
Not all pack sizes may be marketed.
6.6 Special precautions for disposal
No special requirements.

7 MARKETING AUTHORISATION HOLDER
PL 25258/00052

8 MARKETING AUTHORIZATON NUMBER(S)
Glenmark Generics (Europe) Limited
Laxmi House, 2B Draycott Avenue
Harrow, Middlesex HA3 0BU,
UK

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
04/04/2012

10 DATE OF REVISION OF THE TEXT
04/04/2012

11 DOSIMETRY (IF APPLICABLE)

12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE)
Module 3
Patient Information Leaflet

PACKAGE LEAFLET: INFORMATION FOR THE USER
Desloratadine 5 mg tablets

Read all of this leaflet carefully before you start taking/using this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects which worry you, talk to your doctor, pharmacist or nurse.

In this leaflet:
1. What Desloratadine 5 mg Tablets are and what they are used for
2. What you need to know before you take Desloratadine 5 mg Tablets
3. How to take Desloratadine 5 mg Tablets
4. Possible side effects
5. How to store Desloratadine 5 mg Tablets
6. Further information

1. What Desloratadine 5 mg Tablets are and what they are used for
Desloratadine is a long-acting anti-histamine medicine. This medicine is used to:
- relieve symptoms associated with allergic rhinitis, such as inflammation of the nasal passages caused by an allergy to pollen or dust mites for example. Other symptoms include sneezing, runny or itchy nose, itchy palate, and itchy, red or watery eyes.
- relieve symptoms of urticaria, which is a skin condition caused by an allergy. Symptoms include itching and hives (nettle rash).
Relief can last a full day and help you to resume your normal daily activities and sleep.

2. What you need to know before you take Desloratadine 5 mg Tablets
Do not take Desloratadine 5 mg Tablets if:
- you are allergic (hypersensitive) to desloratadine or any of the other ingredients of the medicine (see section 6) or loratadine.

Warnings - talk to your doctor, pharmacist or nurse
- If you have poor kidney function.

Taking other medicines
There are no known medicines which interfere with the way in which desloratadine works.

Pregnancy and breast-feeding
This medicine should not be taken if you are pregnant or breast-feeding. Always talk to your doctor or pharmacist before taking any medicine during pregnancy and breast-feeding.

Driving and using machines
Very rarely some people feel drowsy after taking this medicine. If you feel drowsy, you should not drive or use machinery.

Important information about some of the ingredients of this medicine
This medicine contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, talk to your doctor before taking this medicine.

3. How to take Desloratadine 5 mg Tablets
This medicine can only be given to adults and children aged 12 years and over.

Dosage:
Take one tablet once a day. Swallow the tablet whole with water. You can take this medicine with or without meals.

Duration of treatment:
- Allergic rhinitis:
  If your allergic rhinitis occurs for less than 4 days each week, or the condition lasts for less than 4 weeks, your doctor will give you a short course of medicine and then review your condition. They may decide that you do not need to take this medicine for a long time.
  If your allergic rhinitis lasts for 4 days or more each week, or for more than 4 weeks, your doctor may decide that you need to take the medicine for longer during the pollen season.
- Urticaria
  If you are taking this medicine for urticaria, follow your doctor’s instructions.
  If you are unsure of how to take the medicine talk to your doctor, pharmacist or nurse for further advice.

If you take more Desloratadine 5 mg Tablets than you should
Take the dose prescribed by the doctor. If you take too much medicine no serious problems are expected. However, if you do take more desloratadine than you
were told to, talk to your doctor or pharmacist.

If you forget to take Desloratadine 5 mg Tablets
If you forget to take your dose on time, take it as soon as you remember, then go back to your regular dosing schedule. If it is nearly time for your next dose do not take the missed dose. Do not take a double dose to make up for a forgotten dose.

4. Possible side effects
Like all medicines, desloratadine can cause side effects, although not everybody gets them.
Stop taking the medicine and see a doctor straight away if you experience any of the following serious side effects
• breathing difficulties, wheezing, itching, hives and swelling of the mouth and throat. These might be signs of a rare allergic reaction.
• palpitations, rapid heartbeat and fits. (Very rare side effects).

Other side effects which may happen include:
• fatigue
• dry mouth
• headache.

Very rarely some patients may suffer from the following:
• stomach pain
• nausea (feeling sick)
• vomiting
• upset stomach
• diarrhoea
• dizziness
• drowsiness
• inability to sleep
• muscle pain
• hallucinations
• restlessness (with increased body movement)
• liver inflammation and abnormal liver function tests.

If any of the side effects become serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. How to store Desloratadine 5 mg Tablets
Keep out of the reach and sight of children.
Do not use the medicine after the expiry date which is stated on the carton and blister. The expiry date refers to the last day of the month.
This medicine does not require any special storage conditions.
Tell your pharmacist if you notice any changes in the appearance of the tablets.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Further information
What Desloratadine 5 mg tablets contain
• The active substance is desloratadine. Each tablet contains 5 mg desloratadine
• The other ingredients of the tablet are Microcrystalline cellulose, Lactose monohydrate, Maize starch, Silica, colloidal anhydrous; Magnesium stearate

What Desloratadine 5 mg tablets look like and contents of the pack
Desloratadine tablets are off-white to light-pink, circular, biconvex tablets with ‘L5’ engraved on one side and plain on the other side.
The tablets are available in blister packs containing 7, 10, 14, 15, 20, 28, 30, 50 or 100 tablets. Not all pack sizes may be marketed.

Marketing Authorisation Holder:
Glenmark Generics (Europe) Limited
Laxmi House, 2B Draycott Avenue
Harrow, Middlesex HA3 8BU, UK

Manufacturers:
Glenmark Pharmaceuticals s.r.o
Fibichova 143,566 17 Vysoké Mýto, Czech Republic

Glenmark Generics (Europe) Limited
The Old Sawmill, Hatfield Park, Hattfield, Herts AL9 6FG, UK

This leaflet was last revised in 03/2012.
Module 4
Labelling
Module 5
Scientific discussion during initial procedure

I  INTRODUCTION
Based on the review of the data on quality, safety and efficacy, Denmark, Finland, France, Germany, Greece, Spain, Hungary, Ireland, the Netherlands, Poland, Portugal, Romania, Sweden and the UK considered that the application for Desloratadine Glenmark 5 mg Tablets could be approved. This prescription only medicine (POM) is indicated for:

• Allergic rhinitis
• Urticaria

This application for Desloratadine Glenmark 5 mg Tablets was submitted according to Article 10.1 of Directive 2001/83/EC, claiming to be a generic medicinal product of Neoclarityn 5 mg film-coated Tablets, authorised in the relevant European member states via the centralised procedure to Schering-Plough Europe on 15th January 2001.

Desloratadine is a non-sedating, long-acting histamine antagonist with selective peripheral H1-receptor antagonist activity. After oral administration, desloratadine selectively blocks peripheral histamine H1-receptors because the substance is excluded from entry to the central nervous system.

No new non-clinical studies were conducted, which is acceptable given that the product contains a widely-used, well-known active substance.

No clinical studies, with the exception of the bioequivalence study, have been performed and none are required for this application as the pharmacology of desloratadine is well-established.

For manufacturing sites within the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

For manufacturing sites outside the community, the RMS has accepted copies of current GMP Certificates or satisfactory inspection summary reports, ‘close-out letters’ or ‘exchange of information’ issued by the inspection services of the competent authorities (or those countries with which the EEA has a Mutual Recognition Agreement for their own territories) as certification that acceptable standards of GMP are in place at those non-Community sites.
II. ABOUT THE PRODUCT

<table>
<thead>
<tr>
<th>Name of the product in the Reference Member State</th>
<th>Desloratadine Glenmark 5 mg Tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name(s) of the active substance(s) (INN)</td>
<td>Desloratadine</td>
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<tr>
<td>Pharmacotherapeutic classification (ATC code)</td>
<td>Other antihistamines for systemic use (R06AX27)</td>
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<tr>
<td>Pharmaceutical form and strength(s)</td>
<td>5 mg Tablets</td>
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<tr>
<td>Reference numbers for the Decentralised Procedure</td>
<td>UK/H/3054/001/DC</td>
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<tr>
<td>Reference Member State</td>
<td>The United Kingdom (UK)</td>
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<td>Member States concerned</td>
<td>Denmark (DK), Finland (FI), France (FR), Germany (DE), Greece (EL), Spain (ES), Hungary (HU), Ireland (IE), the Netherlands (NL), Poland (PL), Portugal (PT), Romania (RO) and Sweden (SE)</td>
</tr>
<tr>
<td>Marketing Authorisation Number(s)</td>
<td>PL 25258/0052</td>
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<tr>
<td>Name and address of the authorisation holder</td>
<td>Glenmark Generics (Europe) Limited Laxmi House, 2B Draycott Avenue Harrow, Middlesex HA3 0BU, UK</td>
</tr>
</tbody>
</table>
III SCIENTIFIC OVERVIEW AND DISCUSSION
III.1 QUALITY ASPECTS
S. Active substance

INN name: Desloratadine
Chemical name: 8-chloro-6,11-dihydro-11-(4-piperidinylidene)-5H-benzo-[5,6]cyclohepta[1,2-b]pyridine

Structural formula:

Molecular formula: C₁₉H₁₉ClN₂

Appearance: White to off-white powder.

Molecular weight: 310.83
Solubility: Freely soluble in methanol, soluble in ethanol, very slightly soluble in acetone and insoluble in water.

The source of desloratadine used in the product complies with in-house specifications.

Synthesis of the active substance from the designated starting materials has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specification tests are in place for all starting materials and reagents and these are supported by relevant Certificates of Analysis.

Appropriate proof-of-structure data have been supplied for the active substance. All potential known impurities have been identified and characterised.

An appropriate specification is provided for the active substance. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications. Batch analysis data are provided and comply with the proposed specification.

Satisfactory Certificates of Analysis have been provided for all working standards.

Suitable specifications have been provided for all packaging used. The primary packaging has been shown to comply with current guidelines.

Stability studies have been performed with the active substance and no significant changes of the parameters were observed. On the basis of the results, a suitable re-test period could be approved.
P. Medicinal Product

Other Ingredients
Other ingredients in the tablets consist of the pharmaceutical excipients microcrystalline cellulose, lactose monohydrate, maize starch, silica, colloidal anhydrous and magnesium stearate.

All excipients comply with their respective European Pharmacopoeia monographs.

With the exception of lactose monohydrate, none of the excipients used contain material of animal or human origin.

The applicant has provided a declaration that the milk used in the production of the lactose monohydrate is sourced from healthy animals under the same conditions as those intended for human consumption. Confirmation has been provided that the magnesium stearate used in this product is of vegetable origin.

No genetically modified organisms (GMO) have been used in the preparation of this product.

Pharmaceutical Development
The objective of the development programme was to produce a safe, efficacious product containing desloratadine that could be considered a generic medicinal product of Neoclarityn 5 mg film-coated Tablets.

The applicant has provided suitable product development information. Valid justification for the use and amount of each excipient has been provided.

Comparative in-vitro impurity and dissolution profiles have been provided for the proposed and reference products.

The reference product used in the bioequivalence study was Neoclarityn 5 mg film-coated Tablets, sourced from Belgium.

Manufacturing Process
A satisfactory batch formula has been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results. Satisfactory process validation data on batches have been provided. The applicant has committed to perform process validation on future commercial-scale batches.

Finished Product Specification
The finished product specification is acceptable. Test methods have been described and adequately validated, as appropriate. Batch data have been provided and comply with the release specifications. Certificates of Analysis have been provided for any working standards used.

Container-Closure System
This product is packaged in blisters comprised of cold formable aluminium foil and hard tempered aluminium lidding foil. Pack sizes are 7, 10, 14, 15, 20, 28, 30, 50 and 100 tablets. Not all pack sizes may be marketed.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary product packaging complies with relevant EU directives.
Stability of the product
Stability studies were performed on batches of the finished products in the packaging proposed for marketing and in accordance with current guidelines. These data support a shelf-life of 2 years with no special storage conditions. This is satisfactory.

Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labelling
The SmPC, PIL and labelling are pharmaceutically acceptable. A representative sample of the UK SmPC, PIL and label mock-ups are included in modules 2, 3 and 4 of this report.

User testing results have been submitted for the PIL for this product. The results indicate that the PIL is in accordance with Article 59 of Council Directive 2001/83/EC, as amended and is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

MAA form
The MAA form is pharmaceutically satisfactory.

Quality Overall Summary
The quality overall summary has been written by an appropriately qualified person and is a suitable summary of the pharmaceutical dossier.

Conclusion
It is recommended that a Marketing Authorisation is granted for this application from a quality point of view.
III.2 NON-CLINICAL ASPECTS

The pharmacodynamics, pharmacokinetics and toxicological properties of desloratadine are well-known. As desloratadine is a widely used, well-known active substance, the applicant has not provided any new non-clinical data and none are required. An overview based on literature review is appropriate.

Non-Clinical Overview
The non-clinical overview has been written by an appropriately qualified person and is a suitable summary of the non-clinical aspects of the dossier.

Environmental Risk Assessment
An Environmental Risk Assessment has not been provided and is not required for an application of this type.

Conclusion
It is recommended that a Marketing Authorisation is granted for this application from a non-clinical point of view.
III.3  CLINICAL ASPECTS
CLINICAL PHARMACOLOGY

With the exception of the following bioequivalence study, no new pharmacokinetic or pharmacodynamic data were submitted with this application and none were required.

Pharmacokinetics
A open-label, single-dose, randomised, two-way crossover study to compare the pharmacokinetics of the test product Desloratadine 5 mg Tablets versus the reference product Neoclarityn (desloratadine) 5 mg film-coated Tablets (Schering-Plough Europe, Belgium) in healthy subjects under fasting conditions.

Blood samples were taken pre- and up to 96 hours post dose. There was a washout period of 16 days between each treatment period. Pharmacokinetic parameters were measured from the plasma and statistically analysed.

Results for desloratadine are presented below as log-transformed values:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>AUC(_{0-t}) (pg.hr/mL)</th>
<th>AUC(_{0-\infty}) (pg.hr/mL)</th>
<th>C(_{\text{max}}) (pg/mL)</th>
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</thead>
<tbody>
<tr>
<td>Test (T)</td>
<td>43050.22</td>
<td>46200.56</td>
<td>2627.02</td>
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<tr>
<td>Reference (R)</td>
<td>42613.75</td>
<td>45691.52</td>
<td>2713.64</td>
</tr>
<tr>
<td>T/R Ratio (90 % CI)</td>
<td>101.02</td>
<td>101.11</td>
<td>96.81</td>
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<td></td>
<td>95.57 – 106.79</td>
<td>95.77 – 106.76</td>
<td>90.86 – 103.14</td>
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</table>

AUC\(_{0-\infty}\) area under the plasma concentration-time curve from time zero to infinity
AUC\(_{0-t}\) area under the plasma concentration-time curve from time zero to t hours
C\(_{\text{max}}\) maximum plasma concentration

The results for the primary variables indicate that the 90 % confidence intervals for the test/reference ratio of geometric means for AUC\(_{0-t}\), AUC\(_{0-\infty}\) and C\(_{\text{max}}\) for desloratadine lie within the acceptance criteria of 80.00 -125.00 %. Thus, bioequivalence has been shown between the test and reference products in this study.

Efficacy
No new efficacy data were submitted with this application and none were required.

Safety
With the exception of the data submitted during the bioequivalence study, no new safety data were submitted with this application and none were required. No new or unexpected safety concerns were raised during the bioequivalence study.

The Pharmacovigilance System and Risk Management Plan
The RMS considers that the pharmacovigilance system as described by the applicant fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

A satisfactory justification has been provided for the absence of a Risk Management Plan.
Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labelling
The SmPC, PIL and labelling are clinically satisfactory and consistent with those for the reference product.

Clinical Overview
The clinical overview has been written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.

MAA Form
The MAA form is clinically satisfactory.

Conclusion
It is recommended that a Marketing Authorisation is granted for this application from a clinical point of view.
IV OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

QUALITY
The important quality characteristics of Desloratadine Glenmark 5 mg Tablets are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit-risk balance.

NON-CLINICAL
No new non-clinical data were submitted and none are required for an application of this type.

EFFICACY
Bioequivalence has been demonstrated between the applicant’s Desloratadine Glenmark 5 mg Tablets and the reference product Neoclarityn 5 mg film-coated Tablets.

No new or unexpected safety concerns arose from this application.

The SmPC, PIL and labelling are satisfactory and consistent with those for the reference product.

BENEFIT-RISK ASSESSMENT
The quality of the product is acceptable and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with desloratadine is considered to have demonstrated the therapeutic value of the compound. The benefit-risk balance is therefore considered to be positive.
Module 6

STEPS TAKEN AFTER INITIAL PROCEDURE - SUMMARY

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<thead>
<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
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