LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Loratadin ABECE
(loratadine)

Asp no: 2017-0260

This module reflects the scientific discussion for the approval of Loratadin ABECE. The procedure was finalised on 2018-04-06. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Loratadin ABECE, 10 mg, tablet, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Evolan Pharma AB, applies for a marketing authorisation in Sweden through a National Procedure.

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Clarityn, 10 mg, tablet, authorised in Ireland since 1988, with Schering-Plough Limited as marketing authorisation holder.
The reference product used in the bioequivalence study is Clarityn, 10 mg, tablet, from UK with Schering-Plough Limited as marketing authorisation holder.

For approved indications, see the Summary of Product Characteristics.

For recommendations to the marketing authorisation not falling under Article 21a/22 of Directive 2001/83/EC and conditions to the marketing authorisation pursuant to Article 21a or 22 of Directive 2001/83/EC to the marketing authorisation, please see section VI.

II. QUALITY ASPECTS

II.1 Drug Substance

The structure of the drug substance has been adequately proven and its physico-chemical properties are sufficiently described.

The manufacture of the drug substance has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

The drug substance specification includes relevant tests and the limits for impurities and degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies confirm the retest period.

II.2 Medicinal Product

The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

The tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

III. NON-CLINICAL ASPECTS

III.1 Discussion on the non-clinical aspects

Since this product has been shown to be essentially similar and refer to a product approved based on a full application with regard to preclinical data, no further such data have been submitted or are considered necessary.

IV. CLINICAL ASPECTS

IV.1 Pharmacokinetics

Bioequivalence was evaluated in one single-dose, two-way crossover study conducted in 51 healthy volunteers, comparing Loratadin ABECE, 10 mg, tablet with Clarityn, 10 mg, tablet under fasting conditions. The study was conducted between 4th February and 4th March 2008. Blood samples were collected pre-dose and up to 72 hours post-dose. The study design is considered acceptable. Plasma concentrations of loratadine and desloratadine were determined with an LC-MS/MS method. Evaluation of bioequivalence was based upon measured concentrations of the parent compound loratadine. Metabolite data is considered as supportive data. The justification for absence of ISR data was acceptable. For AUC_{0-t} and C_{max} the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%.

Based on the submitted bioequivalence study, Loratadin ABECE is considered bioequivalent with Clarityn.

IV.2 Discussion on the clinical aspects

Since this product has been shown to be essentially similar and refer to a product approved based on a full application with regard to clinical efficacy/safety data, no further such data have been submitted or are considered necessary.

IV.3 Risk Management Plan

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Loratadin ABECE. The submitted Risk Management Plan, version 1.0 signed 30 Sep 2017 is considered acceptable.

Safety specification

Important identified risks	Hypersensitivity (including anaphylaxis, angioedema, dyspnea, pruritus, rash and urticaria) Abnormal hepatic function (including hepatitis and elevated hepatic enzymes and bilirubin) Convulsion Supraventricular tachyarrythmia

Important potential risks	Movement disorder (including psychomotor hyperactivity and restlessness) Hallucinations Abnormal behaviour in paediatric patients (including anger, agitation and aggression) Eye disorders including eye swelling, ocular dryness and vision impairment Skin disorders including Stevens-Johnson syndrome/Toxic Epidermal Necrolysis Interaction with CYP3A4/CYP2D6 inhibitors
Missing information	Use in children less than 2 years of age Use in lactation

Pharmacovigilance Plan
Routine pharmacovigilance is suggested and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

Risk minimisation measures
Routine risk minimisation is suggested and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the MPA;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

V. USER CONSULTATION

A user consultation with target patient groups on the package information leaflet (PIL) has been performed on the basis of a bridging report making reference to the user test for Loratadin Sandoz, NL/H/0693/DC. Regarding layout the applicant has proposed a bridging to the product Loratadin Apofri, approved in the national procedure 111:2011/40875.
The bridging report submitted by the applicant has been found acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the generic product, Loratadin ABECE, is found adequate. There are no objections to approval of Loratadin ABECE, from a non-clinical and clinical point of view. Bioequivalence between the test and reference product has been adequately demonstrated. The product information is acceptable.
The application is therefore recommended for approval.

List of recommendations not falling under Article 21a/22 of Directive 2001/83/EC in case of a positive benefit risk assessment

N/A

List of conditions pursuant to Article 21a or 22 of Directive 2001/83/EC

N/A

VII. APPROVAL

Loratadin ABECE, 10 mg, tablet was approved in the national procedure on 2018-04-06.

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Public Assessment Report – Update

Procedure number*	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse

*Only procedure qualifier, chronological number and grouping qualifier (when applicable)

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