

Public Assessment Report

Scientific discussion

Etrilect

(bromhexine hydrochloride and

ephedrine hydrochloride)

SE/H/1624/01/DC

This module reflects the scientific discussion for the approval of Etrilect. The procedure was finalised on 2017-06-13. For information on changes after this date please refer to the module ‘Update’.

I. INTRODUCTION

The application for Etrilect 0.5 mg/ml + 1 mg/ml oral solution, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Applicant is Actavis Group PTC ehf., applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and IS as concerned member states (CMS). However, the application was withdrawn from IS during clock stop.

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Mollipect 0.5 mg/ml + 1 mg/ml oral solution authorised in SE since 1974, with BioPhausia AB 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 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

No bioequivalence study comparing Etrilect with the reference product has been conducted. According to the Guideline on the investigation of Bioequivalence (CHMP/QWP/EWP/1401/98 Rev. 1), bioequivalence studies may be waived if the test product is an aqueous oral solution at time of administration and contains an active substance in the same concentration as an approved oral solution. However, if the excipients may affect gastrointestinal transit, absorption, solubility or stability, a bioequivalence study should be conducted, unless the differences in the amounts of these excipients can be adequately justified by reference to other data.

The excipients used in Etrilect are in general the same and in similar amounts as in the reference product Mollipsect. The only exception is that potassium sorbate is present in the reference product. None of the excipients are known to affect bioavailability. Waiving bioequivalence studies is therefore acceptable.

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 revised risk management plan in response to questions raised in the first round, 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 Etrilect.

Safety specification

The summary of safety specification is presented in the table below. This list is acceptable.

Summary of safety concerns	
Important identified risks	Dependence when used in high doses and after prolonged use Safety in patients with underlying severe heart disease Hypersensitivity including severe cutaneous adverse reactions
Important potential risks	NA
Missing information	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.

Summary of the RMP

The RMP is approved.

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 RMS;
- 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

The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PIL was English.

The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the generic product, Etrilect, is found adequate. There are no objections to approval of Etrilect, from a non-clinical and clinical point of view. 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 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

The Decentralised procedure for Etrilect, 0.5 mg/ml + 1 mg/ml oral solution was positively finalised on 2017-06-13.

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)