LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Bromhexin Apofri, 0.8 mg/ml and 1.6 mg/ml, oral solution
(bromhexine hydrochloride)

Asp. no: 2011-0232 – 0233

This module reflects the scientific discussion for the approval of Bromhexin Apofri. The procedure was finalised at 2012-05-24. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Evolan Pharma AB has applied for a marketing authorisation for Bromhexin Apofri, 0.8 mg/ml and 1.6 mg/ml, oral solution claiming essential similarity to Tosseque, 0.8 mg/ml, syrup marketed in Portugal by Laboratório Medinfar–Produtos Farmacêuticos, S.A. The product contains bromhexine hydrochloride as active substance. For approved indications see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

Bromhexin Apofri is presented in the form of oral solutions containing 0.8 mg/ml and 1.6 mg/ml of bromhexine hydrochloride respectively. The excipients are sorbitol, propylene glycol, saccharin sodium, methyl parahydroxybenzoate, propyl parahydroxybenzoate, cherry flavour and purified water. The oral solutions are filled in glass bottles with polyethylene caps.

II.2 Drug Substance

Bromhexine hydrochloride has a monograph in the Ph Eur.

Bromhexine hydrochloride is a white or almost white, crystalline powder. It is very slightly soluble in water, slightly soluble in alcohol and in methylene chloride. The structure of bromhexine hydrochloride has been adequately proven and its physico-chemical properties sufficiently described. The route of synthesis has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

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

Stability studies have been conducted and the data provided are sufficient to confirm the retest period.

II.3 Medicinal Product

Bromhexin Apofri oral solution is formulated using excipients described in the current Ph Eur, except for the cherry flavour which is controlled according to an acceptable in house specification. All raw materials used in the product are of vegetable origin/has demonstrated compliance with Commission Directive 2003/63/EC and the NfG on Minimising the risk of transmitting Animal Spongiform Encephalopathy Agents via human and veterinary medicinal products (EMEA/410/01).

The product development has taken into consideration the physico-chemical characteristics of the active substance, such as poor aqueous solubility.

The manufacturing process has been sufficiently described and critical steps identified. Results from the process validation studies confirm that the process is under control and ensure both batch to batch reproducibility and compliance with the product specification.

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 under ICH conditions have been performed and data presented support the shelf life claimed in the SPC, when stored in the original package in order to protect from light.

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

The composition of Bromhexin Apofri 0.8 mg/ml is different compared to the reference product Tosseque 0.8 mg/ml. Both formulations contain sorbitol, but in different amounts. Bromhexin Apofri also contains the co-solvent propylene glycol which is not present in the reference formulation, which contains alcohol and glycerine as solvent instead. The difference in excipients is however not expected to have a clinical relevant effect on bromhexine bioavailability. The lack of bioequivalence studies with bromhexine 0.8 mg/ml is therefore acceptable. The absence of studies with the higher strength of 1.6 mg/ml is also acceptable as the compositions of the two strengths are identical, except for the amount of active substance, and the pharmacokinetics of bromhexine is linear.

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.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

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.

The risk/benefit ratio is considered positive and Bromhexin Apofri, 0.8 mg/ml and 1.6 mg/ml, oral solution is recommended for approval.

VI. APPROVAL

Bromhexin Apofri, 0.8 mg/ml and 1.6 mg/ml, oral solution was approved in the national procedure on 2012-05-24.

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Public Assessment Report – Update

Scope	Procedure number	Product Information affected	Date of start of the procedure	Date of end of procedure	Approval/ non approval	Assessment report attached
						Y/N (version)

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