LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Amorolfin Apofri
(amorolfine hydrochloride)

Asp no: 2011-1032

This module reflects the scientific discussion for the approval of Amorolfin Apofri. The procedure was finalised at 2012-12-14. For information on changes after this date please refer to the module 'Update'.

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.mpa.se E-mail: registrator@mpa.se

I. INTRODUCTION

The application for Amorolfin Apofri, 5%, medicated nail lacquer, is a hybrid application made according to Article 10(3) of Directive 2001/83/EC. The applicant, Evolan Pharma AB, applies through the Swedish National Procedure.

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Loceryl, 5%, medicinskt nagellack, authorised in Sweden since 1993, with Galderma Nordic AB as marketing authorisation holder.

Amorolfin Apofri and the reference product Loceryl nail lacquer are pharmaceutically essentially similar.

For approved indications, see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

Amorolfin Apofri is presented in the form of a medicated nail lacquer containing 55.7 mg/ml of amorolfine hydrochloride which corresponds to 50 mg/ml of amorolfine. The excipients included in the product are anhydrous ethanol, ethyl acetate, butyl acetate, triacetin and ammonio methacrylate co-polymer. The medicated nail lacquer is filled in amber glass bottles equipped with HDPE caps.

II.2 Drug Substance

Amorolfine hydrochloride does not have a monograph in the Ph Eur.

Amorolfine hydrochloride is a white, crystalline powder which is easily soluble in ethanol, soluble in methylene chloride and slightly to very slightly soluble in water. The structure of amorolfine hydrochloride has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on polymorphism and chirality has been presented. The amorolfine hydrochloride is a racemic mixture. 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 under ICH conditions have been conducted and the data provided are sufficient to confirm the applied retest period.

II.3 Medicinal Product

Amorolfin Apofri medicated nail lacquer is formulated using excipients described in the current Ph Eur, except for butyl acetate which is controlled according to acceptable in house

specifications. For all raw materials used in the product are 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) has been demonstrated.

The product development has taken into consideration the physico-chemical characteristics of the active substance.

The manufacturing process has been sufficiently well 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 of 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.

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

This is a hybrid application for a locally applied, locally acting product for which bioequivalence cannot be demonstrated through bioavailability studies. Amorolfin Apofri and the reference product Loceryl nail lacquer are pharmaceutically essentially similar. No clinical studies are included in the dossier, but an *in vitro* transungual delivery study has been performed in order to compare the reference product and the product applied for. The clinical part of the dossier consists of a clinical overview based on bibliographic references and the results of the *in vitro* permeation study.

The results of the study indicate that the test product Amorolfine nail lacquer and the reference product Loceryl behave similarly *in vitro* and can be considered equivalent on a model of human nail (cow horn samples mounted in static Franz diffusion cells). The *in vitro* permeation study supports similarity of Amorolfin Apofri with Loceryl. However, the assessment of similarity is mainly based on the fact that the qualitative and quantitative compositions are identical and the products can be considered pharmaceutically essentially similar.

IV.2 Discussion on the clinical aspects

No specific efficacy studies were submitted in support of this application. The applicant summarized published studies demonstrating the effect of topical amorolfine in the treatment of onychomycosis.

With respect to clinical safety, no clinical studies were submitted in this application, but in the published clinical trials, topical amorolfine is shown to be well tolerated with mainly local reactions (burning, erythema, pruritus, scaling and local pain). Some cases of allergic contact dermatitis due to amorolfine have been reported. As absorption of amorolfine to the systemic circulation through the nail is negligible, systemic side effects are not expected to occur.

In conclusion, the data presented are considered sufficient to give an overview of the efficacy and safety of Amolorfine 5% Nail Lacquer in patients with onchomycosis and no further data are necessary.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

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 Amorolfine ADOH, SE/H/1006/01/DC for the content and Ibuprofen Apofri, national procedure 111:2007/37918 for the lay-out. The bridging report submitted by the applicant has been found acceptable.

The risk/benefit ratio is considered positive and Amorolfin Apofri, 5%, medicated nail lacquer is recommended for approval.

VI. APPROVAL

Amorolfin Apofri, 5%, medicated nail lacquer was approved in the national procedure on 2012-12-14.

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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)

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
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