LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Amorolfine Pierre Fabre
(Amorolfine hydrochloride)

This module reflects the scientific discussion for the approval of Amorolfine Pierre Fabre. Please note that the marketing authorisation was first approved with the name "Amorolfine ADOH" and therefore this name is used throughout the document. The procedure was finalised at 2011-02-02. 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

ADOH B. V. has applied for a marketing authorisation for Amorolfine ADOH, medicated nail laquer 5% claiming essential similarity to Loceryl 5% nail lacquer marketed in Sweden by Galderma. The product contains Amorolfine hydrochloride as active substance. For approved indications see the Summary of Product Characteristics. This product is intended for topical application on the nails for the treatment of onychomycosis, and thus, conventional pharmacokinetic bioequivalence studies cannot be performed.

II. QUALITY ASPECTS

II.1 Introduction

Amorolfine ADOH is presented in the form of medicated nail lacquer containing 55.7 mg of amorolfine hydrochloride which corresponds to 50 mg of the amorolfine. The excipients are ethanol anhydrous, ethyl acetate, butyl acetate, triacetin (glycerine triacetate) and ammonio methacrylate copolymer (type A). The medical nail lacquer is filled in glass bottles.

II.2 Drug Substance

Amorolfine hydrochloride is not monographed in the Ph Eur.

Amorolfine hydrochloride is a white to almost white solid powder which is soluble in water, freely soluble in methanol and ethanol, sparingly soluble in 2-propanol, slightly soluble in acetone and toluene, practically insoluble in n-heptane.

The structure of amorolfine hydrochloride has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on polymorphism and chirality is presented. 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 and 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 retest period of 2 years.

II.3 Medicinal Product

Amorolfine ADOH 5 % 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 specification. All raw materials used in the product are of vegetable origin.

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

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 of 2 year before opening of the finished product. The in-use shelf-life is 6 months after opening of the container for the drug product.

III. NON-CLINICAL ASPECTS

III.1 Discussion on the non-clinical aspects

This is a hybrid application referring to a product approved based on a full application with regard to non-clinical data. The qualitative and quantitative composition of the proposed medicated nail lacquer is strictly identical to that of the reference product Loceryl®. The risk for toxicity of Amorolfine 5% ADOH nail lacquer formulation due to systemic exposure is low. The product has shown skin-irritant and skin-sensitising properties, however, this is adequately addressed in the SmPC.

IV. CLINICAL ASPECTS

IV.1 Pharmacokinetics

No human pharmacokinetic studies or clinical studies have been conducted for this hybrid application. This is supported by the fact that the qualitative and quantitative composition of the proposed medicated nail lacquer is strictly identical to that of the reference product Loceryl®. An *in vitro* study, using bovine hoof membrane as a model for the human nail, demonstrated similar nail penetration of the Amorolofine ADOH nail laquer as for the reference product Loceryl®.

IV.2 Discussion on the clinical aspects

The approach not to perform any specific clinical studies with the product is endorsed based on the fact that this is a locally applied, locally acting product with a qualitative and quantitative composition identical to that of the reference product. Hence, it is considered reasonable to extrapolate efficacy and safety from the originator product to Amorolofine ADOH.

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 Amorolfine ADOH 5% nail laquer is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Amorolfine ADOH 5% nail laquer was successfully finalised on 2011-02-02.

LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

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
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