LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Latanoprost/Timolol Tubilux Pharma
(latanoprost and timolol maleate)

SE/H/1303/01/DC

This module reflects the scientific discussion for the approval of Latanoprost/Timolol Tubilux Pharma. The procedure was finalised at 2013-12-11. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Latanoprost/Timolol Tubilux Pharma, eye drops solution, latanoprost 50 micrograms/ml and timolol 5 mg/ml (as timolol maleate), is a hybrid application made according to Article 10(3) of Directive 2001/83/EC. The applicant, Tubilux Pharma S.p.A applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and DE and UK as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Xalacom® Eye drops solution 50 micrograms Latanoprost + 5 mg Timolol per ml ,authorised in DE since 2001-12-06, with PHARMACIA GmbH as marketing authorisation holder.

II. QUALITY ASPECTS

II.1 Introduction

Latanoprost/Timolol Tubilux Pharma is presented in the form of an eye drops solution containing 0.05 mg/ml of latanoprost and 5 mg/ml of timolol (as maleate). The solution is filled into LDPE bottles with a dropper applicator and a screw cap.

II.2 Drug Substance

Latanoprost

Latanoprost does not have a monograph in the European Pharmacopeia (Ph. Eur.). The substance is a colorless to pale yellowish viscous oil which is practically insoluble in water.

The structure of latanoprost has been adequately proven and its physico-chemical properties sufficiently described. Latanoprost is a single stereoisomer. The route of synthesis has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

The specification for latanoprost 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 re-test period.

Timolol maleate

Timolol maleate is described in the Ph. Eur. The substance appears as a white to practically white, crystalline powder or colourless crystals. The (*2S)*-enantiomer of timolol is used in the formulation.

The manufacturer of timolol maleate holds a Certificate of Suitability (CEP) which verifies that the drug substance is suitably controlled by monograph no. 572 of the Ph. Eur.

The specification for timolol maleate complies with the requirements of the Ph. Eur. The analytical methods applied are suitably described and validated.

The stability of the substance was evaluated by the EDQM prior to granting the CEP.

II.3 Medicinal Product

Latanoprost/Timolol Tubilux Pharma, eye drops solution is formulated using excipients described in the current Ph. Eur., except for sodium dihydrogen phosphate monohydrate which is controlled in accordance with the United States Pharmacopeia (USP). None of the raw materials are of human or animal origin.

The pharmaceutical development work has been sufficiently described. Pharmaceutical equivalence between the generic product and the reference product has been demonstrated. The efficacy of the preservative benzalkonium chloride has been verified and the potential of leaching into the solution has been addressed.

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. The analytical procedures have been validated.

Stability studies under ICH conditions have been performed and data presented support the shelf-life claimed in the SPC, when stored at 2-8 °C. The results of the photostability study show that the product should be protected from light. Additional studies have been performed in order to support the in-use period of four weeks after the first opening.

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

N/A

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 Latanoprost/Timolol Tubilux Pharma, eye drops solution, latanoprost 50 micrograms/ml and timolol 5 mg/ml, is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Latanoprost/Timolol Tubilux Pharma, eye drops solution, latanoprost 50 micrograms/ml and timolol 5 mg/ml, was successfully finalised on 2013-12-11.

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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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