LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Prednisolon Pilum
(prednisolone)

Asp no: 2013-0498

This module reflects the scientific discussion for the approval of Prednisolon Pilum. The procedure was finalised at 2014-05-08. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Prednisolon Pilum, 5 mg, tablets, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Pilum 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 Prednisolon Pfizer, 5 mg, tablets, authorised in Sweden since 1996, with Pfizer AB as marketing authorisation holder.
The applicant has submitted a BCS-based biowaiver application for Prednisolon Pilum, 5 mg, tablets.

For approved indications, see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

Prednisolon Pilum is presented in the form of tablets containing 5 mg of prednisolone. The excipients are lactose monohydrate, maize starch and magnesium stearate. The tablets are packed in blisters.

II.2 Drug Substance

Prednisolone is described in a monograph in Ph.Eur.

Prednisolone is a white or almost white, crystalline, hygroscopic powder which is very slightly soluble in water, soluble in ethanol (96 per cent) and in methanol, sparingly soluble in acetone, slightly soluble in methylene chloride. The structure of prednisolone has been adequately proven and its physico-chemical properties sufficiently described. Relevant information 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/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.

II.3 Medicinal Product

Prednisolon Pilum, 5 mg, tablets is formulated using excipients described in the current Ph Eur. All raw materials used in the product have 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.

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, with no special storage precautions.

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 applicant applied for a biowaiver based on the Biopharmaceutics Classification System (BCS).

Absolute bioavailability ranging from 92 to106 % was reported in three literature references. Of these, a study by Ferry et al was a well-designed study using a specific bioanalytical method and is considered to be a strong support of complete absorption. Although a study by Bergem et al suggest a somewhat lower bioavailability at higher doses; 77.6% after 20 mg compared to 84.5% after 10 mg, the overall data indicate that prednisolone is completely absorbed.

The excipients are not identical in the test and reference product, but none of the excipients are known to affect drug bioavailability.

Prednisolone is not considered to be a narrow therapeutic index drug.

In conclusion, a BCS class I-based biowaiver is acceptable from a pharmacokinetic perspective.

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

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 Prednisolon Alternova, tablet, 2,5 and 5 mg. The user test of the Prednisolon Alternova leaflet was assessed and accepted in 111:2011/1592, 2011-11-18. The bridging report submitted by the applicant has been found acceptable.

The risk/benefit ratio is considered positive and Prednisolon Pilum, 5 mg, tablets, is recommended for approval.

VI. APPROVAL

Prednisolon Pilum, 5 mg, tablets, was approved in the national procedure on 2014-05-08.

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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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