LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

# Public Assessment Report
# Scientific discussion

# Prednisolon EQL Pharma
# (prednisolone)

# Asp no: 2017-0477

**This module reflects the scientific discussion for the approval of Prednisolon EQL Pharma. The procedure was finalised on 2018-04-06. For information on changes after this date please refer to the module 'Update'.**

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# I. INTRODUCTION

The application for Prednisolon EQL Pharma, 5 mg, tablet, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, EQL Pharma AB applies for a marketing authorisation in Sweden through a National Procedure.

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Prednisolon Pfizer, 5 mg, tablet authorised in Sweden since 1973, with Pfizer AB as marketing authorisation holder.

For approved indications, see the Summary of Product Characteristics.

For recommendations to the marketing authorisation not falling under Article 21a/22 of Directive 2001/83/EC and conditions to the marketing authorisation pursuant to Article 21a or 22 of Directive 2001/83/EC to the marketing authorisation, please see section VI.

# II. QUALITY ASPECTS

## II.1 Drug Substance

The structure of the drug substance has been adequately proven and its physico-chemical properties are sufficiently described.

The manufacture of the drug substance has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

The drug 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 confirm the retest period.

## II.2 Medicinal Product

The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

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 have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

# 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 applies for a biowaiver based on the Biopharmaceutics Classification System (BCS). From a pharmacokinetic point of view, a BCS-class I based biowaiver is acceptable for an immediate release drug product if the drug substance has proven to exhibit complete absorption and the excipients that might affect bioavailability are quantitatively and qualitatively the same. It should also be confirmed that the substance is not a narrow therapeutic index drug.

The Applicant has submitted literature references to support the claim that the abruption of prednisolone is complete. In all but one of the studies referred to, the absolute bioavailability of orally administered prednisolone was within the range of 78 to106% (Al-Habet et al, Ferry et al, Bergrem et al and Täuber et al). The study by Ferry et al, in which the absolute bioavailability was determined to 92%, was a well-designed study using a specific bioanalytical method and is considered to be a strong support of complete absorption. The study by Bergrem et al, may suggest a somewhat lower bioavailability at higher doses; 78% after 20 mg compared to 85% after 10 mg. On the contrary, the results from Täuber et al, indicated a slightly higher bioavailability for a 20 mg dose (F=89%) compared to a 10 mg dose (F=78%). The differences between doses in these studies are likely a result of normal variability. Taken together, the data are not entirely conclusive but the overall data do indicate that the absorption of prednisolone is complete, i.e. ≥85%, which is the guideline requirement for classification as BCS class 1.

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-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.

## IV.3 Risk Management Plan

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Prednisolone EQL Pharma.

Safety specification

**Table 1 Summary of safety concerns**

| | |
|---|---|
| **Important identified risks** | None |
| **Important potential risks** | None |
| **Missing information** | None |

Pharmacovigilance Plan

Routine pharmacovigilance is suggested and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

Risk minimisation measures

Routine risk minimisation is suggested and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

Summary of the RMP

The submitted Risk Management Plan, version 0.2 signed 24-11-2017 is considered acceptable.

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the MPA;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

# V. 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 2.5 mg, 5 mg and 10 mg and Acetazolamid EQL Pharma 250 mg. The user test of the Prednisolon Alternova leaflet was assessed and accepted in the national procedure (111:2011/1592). The bridging report submitted by the applicant has been found acceptable.

# VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the generic product, Prednisolon EQL Pharma, is found adequate. There are no objections to approval of Prednisolon EQL Pharma, from a non-clinical and clinical point of view. The product information is acceptable.

The application is therefore recommended for approval.

**List of recommendations not falling under Article 21a/22 of Directive 2001/83/EC in case of a positive benefit risk assessment**

N/A

**List of conditions pursuant to Article 21a or 22 of Directive 2001/83/EC**

N/A

# VII. APPROVAL

Prednisolon EQL Pharma, 5 mg, tablet was approved in the national procedure on 2018-04-06.

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# Public Assessment Report – Update

| Procedure number* | Scope | Product Information affected | Date of end of procedure | Approval/ non approval | Summary/ Justification for refuse |
|---|---|---|---|---|---|
| | | | | | |

*Only procedure qualifier, chronological number and grouping qualifier (when applicable)

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