LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

# Public Assessment Report
# Scientific discussion

# Naprocur
# 250 mg and 500 mg gastro-resistant tablet
# (naproxen)

# Asp no: 2012-0603--0604

**This module reflects the scientific discussion for the approval of Naprocur The procedure was finalised on 14 March 2013. For information on changes after this date please refer to the module 'Update'.**

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# I. INTRODUCTION

Evolan Pharma AB has applied for a marketing authorisation for Naprocur gastro-resistant tablet, 250 mg and 500 mg claiming essential similarity to Naprosyn Entero gastro-resistant tablet 250 mg and 500 mg marketed in Sweden by Roche AB. The product contains naproxen as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bioequivalence study is Naprosyn EC 500 mg tablet from the United Kingdom with Roche Product Limited as marketing authorisation holder.

# II. QUALITY ASPECTS

## II.1 Introduction

Naprocur is presented in the form of gastro-resistant tablets containing 250 mg or 500 mg of naproxen. The excipients are croscarmellose sodium, magnesium stearate, povidone, methacrylic acid- ethyl acrylate copolymer, polysorbate 80, sodiumlaurilsulfate, simethicone emulsion, talc and triethyl citrate. The gastro-resistant tablets are packed in PVC/Al-blisters.

## II.2 Drug Substance

Naproxen has a monograph in the Ph Eur.

Naproxen is practically insoluble in water but is soluble in ethanol and methanol. The structure has been adequately proven and its physico-chemical properties sufficiently described. 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

Naprocur gastro-resistant tablet is formulated using excipients described in the current Ph Eur, except for trace amounts of simethicone emulsion which is controlled according to USP. All raw materials used in the product are of vegetable origin.

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.

# 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

Bioequivalence was evaluated in one single-dose, four-period, 4-way crossover study conducted in 30 healthy volunteers, comparing Naproxen, 500 mg, gastro-resistant tablets with Naprosyn EC tablets, 500 mg under fasting and fed conditions. The study was conducted at Lambda Therapeutic Research Sp. z o.o., Centrum Badań Klinicznych NZOZ, Warszawa, Poland between 31st August and 24th September 2011. Blood samples were collected pre-dose and up to 72 hours post-dose. The study design is considered acceptable. Plasma concentrations of naproxen were determined with an adequately validated LC-MS/MS method. For $AUC_{0-t}$ , $AUC_{0-\infty}$ and $C_{max}$ the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%.

## 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 Portuguese.
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 results of the conducted bioequivalence study can be extrapolated to the lower strength of 250 mg since the criteria for biowaiver for additional strengths are fulfilled according to the Note for Guidance on the Investigation of Bioavailability and Bioequivalence.

The risk/benefit ratio is considered positive and Naprocur gastro-resistant tablet, 250 mg and 500 mg is recommended for approval.

# VI. APPROVAL

Naprocur gastro-resistant tablet, 250 mg and 500 mg was approved in the national procedure on 14 March 2013.

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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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