LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Ursosan
(ursodeoxycholic acid)

Asp no: 2013-0528

This module reflects the scientific discussion for the approval of Ursosan. The procedure was finalised at 2014-04-03. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Ursosan, 500 mg, film-coated tablets, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Evolan 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 Ursofalk, 250 mg, hard capsules, authorised in Sweden since 1995, with Dr Falk Pharma GmbH, Germany as marketing authorisation holder.
The reference product used in the bioequivalence study is Ursofalk, 500 mg, film-coated tablets, from Germany with Dr Falk Pharma GmbH as marketing authorisation holder.

For approved indications, see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

Ursosan is presented in the form of tablets containing 500 mg of ursodeoxycholic acid. The excipients are maize starch maize starch, pregelatinized, sodium starch glycollate A, silica colloidal anhydrous, magnesium stearate , hypromellose, titanium dioxide and macrogol 400.

The tablets are packed in clear PVC/PVDC/Al blisters.

II.2 Drug Substance

Ursodeoxycholic acid. has a monograph in the Ph Eur.

Ursodeoxycholic acid. is a white or almost white powder which is very slightly soluble in water . The structure of ursodeoxycholic acid 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

Ursosan filmcoated tablet 500 mg is formulated using excipients described in the current Ph Eur, All raw materials used in the product has 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, such as poor aqueous solubility.
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

Bioequivalence was evaluated in one single-dose, two-way crossover study conducted in 44 healthy volunteers, comparing Ursosan, 500 mg, film-coated tablets with Ursofalk, 500 mg, film-coated tablets under fasting conditions. The study was conducted at the Clinical Hospital of the Ministry of Health of the Republic of Moldova between 15 Oct and 15 Dec 2011. Blood-samples were collected pre-dose and up to 72 hours post-dose. In addition blood samples for base line correction were collected at eight occasions during the 24 hours preceding drug administration. The study design is considered acceptable. Plasma concentrations of ursodeoxycholic acid were determined with a validated LC/MS/MS method. There is one issue regarding the bioanalysis that need to be resolved. For base line corrected AUC_{0-72} 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%. Based on the submitted bioequivalence study, Ursosan 500 mg film-coated tablet is considered bioequivalent with Ursofalk 500 mg film-coated tablet.

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 Ursosan 250mg hard

capsules SE/H996/01/MR.The bridging report submitted by the applicant has been found acceptable.

The risk/benefit ratio is considered positive and Ursosan, 500 mg, film-coated tablets, is recommended for approval.

VI. APPROVAL

Ursosan, 500 mg, film-coated tablets, was approved in the national procedure on 2014-04-03.

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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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