LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report

Scientific discussion

Noepix
(levetiracetam)

SE/H/1143/01/DC

This module reflects the scientific discussion for the approval of Noepix. The procedure was finalised at 21th of September 2011. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Sigillata Limited has applied for a marketing authorisation for Noepix, oral solution, 100 mg/ml, claiming essential similarity to Keppra, 100 mg/ml, oral solution marketed in the EU since 2000 by UCB SA Pharma Sector. The product contains levetiracetam as active substance. For approved indications see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

Noepix is presented in the form of oral solution containing 100 mg/ml of levetiracetam. The excipients are sodium citrate, citric acid monohydrate, methyl parahydroxybenzoate (E218), propyl parahydroxybenzoate (E216), ammonium glycyrrhizate, glycerol (E422), maltitol liquid (E965), acesulfame potassium (E950), grape flavour and purified water. The oral solution is filled in amber glass bottles.
Three presentations are available:

- A 300 ml bottle with a 10 ml oral syringe graduated every 0.25 ml.
- A 300 ml bottle with a 3 ml oral syringe graduated every 0.1 ml.
- A 300 ml bottle with a 1 ml oral syringe graduated every 0.05 ml.

For the 1 ml and 3 ml syringes an adaptor is also provided.

II.2 Drug Substance

Levetiracetam has a monograph in the Ph Eur.

Levetiracetam is a white or almost white powder which is very soluble in water, soluble in acetonitrile and practically insoluble in hexane. The structure of levetiracetam has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on chirality is presented. The route of synthesis has been described and 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

Levetiracetam oral solution is formulated using excipients described in the current Ph Eur, except for ammonium glycyrrhizate solution and grape flavour which are controlled according to acceptable specifications. 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. Selection of the excipients was based on the reference product labelling. The absence of a bioequivalence study is deemed acceptable from a chemical-pharmaceutical point of view; it is in line with the statements in the guideline on the investigation of bioequivalence.

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. The medicinal product does not require any special storage conditions.

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 has not submitted any bioequivalence studies to support this application. According to the Guideline on the investigation of Bioequivalence (CHMP/QWP/EWP/1401/98 Rev. 1), bioequivalence studies may be waived if the test product is an aqueous oral solution at time of administration and contains an active substance in the same concentration as an approved oral solution. However, if the excipients may affect gastrointestinal transit, absorption, solubility or stability, a bioequivalence study should be conducted, unless the difference in these excipients can be adequately justified. Noepix oral solution has the same concentration of active substance as Keppra oral solution and contains the same excipients as Keppra oral solution in very similar amounts. Thus, the waiving of bioequivalence studies is acceptable.

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 PL is harmonised with the originator. Therefore, a full user test is not considered necessary. 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 Noepix, oral solution, 100 mg/ml, is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Noepix, oral solution, 100 mg/ml, was successfully finalised on 2011-09-21.

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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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