LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

# Public Assessment Report
# Scientific discussion

# Gabapentin Brown, capsule, hard, (gabapentin)

# SE/H/1003/01-03/DC

**This module reflects the scientific discussion for the approval of Gabapentin Brown. The procedure was finalised at 2011-10-11. For information on changes after this date please refer to the module 'Update'.**

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# I. INTRODUCTION

Brown&Burk UK Ltd has applied for a marketing authorisation for Gabapentin Brown, 100 mg, 300 mg and 400 mg, capsule, hard, claiming essential similarity to Neurontin, 100 mg, 300 mg and 400 mg, capsule, hard, marketed in Sweden by Pfizer AB. The product contains gabapentin as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bio-equivalence study is Neurontin, 400 mg, capsule, hard, marketed by Pfizer Ltd in UK.

# II. QUALITY ASPECTS

## II.1 Introduction

Gabapentin Brown is presented in the form of hard capsules containing 100 mg, 300 mg or 400 mg of gabapentin. The excipients are maize starch, talc, gelatine, sodium laurilsulfate and titanium dioxide. In addition, the 300 mg capsules contain yellow iron oxide and the 400 mg capsules contain red and yellow iron oxide. The capsules are packed in PVC/PVdC/aluminium blisters or in polypropylene containers.

## II.2 Drug Substance

Gabapentin has a monograph in the Ph Eur.

Gabapentin is a white, crystalline powder which is freely soluble in water and in alkaline and acidic solutions. The structure of gabapentin has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on polymorphism 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

Gabapentin Brown hard capsules are formulated using excipients described in the current Ph Eur. All raw materials used in the product are of vegetable origin/chemical origin or 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.

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, when stored below 30°C.

# 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 randomised, single-dose, two-way crossover study conducted in 36 healthy volunteers, comparing Gabapentin Brown, 400 mg, capsules with Neurontin, 400 mg, capsules under fasting conditions. The study was conducted at Accutest Research Laboratories Private Limited, Navi-Mumbai, India between 10 July 2009 and 06 August 2009. Blood samples were collected pre-dose and up to 48 hours post-dose. The study design is considered acceptable. Plasma concentrations of gabapentin were determined with an adequately validated HPLC/MS/MS method. For $AUC_{0-t}$ and $C_{max}$ the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80-125%.

Gabapentin has dose dependent absorption, possibly because of a saturable transport mechanism through the L-amino acid transport system. Available data indicate that the 400 mg strength is in the lower part of the non-linear dose-range., and a study at 400 mg is sufficient for extrapolating bioequivalence over the whole therapeutic dose range and absence of studies with the lower strengths of 100 mg and 300 mg are considered 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 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 results of the conducted bioequivalence study can be extrapolated to other strengths 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 Gabapentin Brown, 100 mg, 300 mg and 400 mg, capsule, hard, is recommended for approval.

# VI. APPROVAL

The Decentralised procedure for Gabapentin Brown, 100 mg, 300 mg and 400 mg, capsule, hard, was successfully finalised on 2011-10-11.

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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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