COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Gabapentine Mylan 600 mg and 800 mg, tablets

(gabapentin)

NL/H/5084/001-002/DC

Date: 25 November 2019

This module reflects the scientific discussion for the approval of Gabapentine Mylan. The procedure was finalised on 7 June 2011 with Germany as RMS (DE/H/2828/001-002/DC). The current RMS is the Netherlands (NL/H/5084/001-002/DC). For information on changes after this date please refer to the 'steps taken after finalisation' at the end of this PAR.

List of abbreviations

ASMF	Active Substance Master File
CMD(h)	Coordination group for Mutual recognition and Decentralised procedure for human medicinal products
CMS	Concerned Member State
EDMF	European Drug Master File
ICH	International Conference of Harmonisation
MAH	Marketing Authorisation Holder
PL	Package Leaflet
RH	Relative Humidity
SmPC	Summary of Product Characteristics

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have granted a marketing authorisation for Gabapentine Mylan 600 mg and 800 mg, tablets from Mylan B.V.

The product is indicated for:

Epilepsy
Gabapentin is indicated as adjunctive therapy in the treatment of partial seizures with and without secondary generalization in adults and children aged 6 years and above (see section 5.1 of the SmPC).
Gabapentin is indicated as monotherapy in the treatment of partial seizures with and without secondary generalization in adults and adolescents aged 12 years and above.

Peripheral neuropathic pain
Gabapentin is indicated for the treatment of peripheral neuropathic pain such as painful diabetic neuropathy and post-herpetic neuralgia in adults.

A comprehensive description of the indications and posology is given in the SmPC.

This decentralised procedure concerns a generic application claiming essential similarity with the innovator product Neurontin 600 and 800 mg tablets, which was first authorised within the EU in the UK on 5 February 1993. Neurontin 600 and 800 mg film-coated tablets (NL License RVG 25247-25248) have been authorised in the Netherlands by Pfizer B.V. since 27 November 2000 through MRP DE/H/0899/004-005.

The marketing authorisation has been granted pursuant to Article 10(1) of Directive 2001/83/EC.

The concerned member states (CMS) involved in this procedure are Belgium, Portugal and the United Kingdom. The role of RMS was transferred to the Netherlands on 25 November 2019. Subssequently, the MA in Germany was withdrawn.

II. QUALITY ASPECTS

II.1 Introduction

Gabapentine Mylan 600 mg is a white to off-white, oval, biconvex, uncoated, bevelled edged tablet, debossed with “MYLAN” on one side and “G” to the left of the score and “24” to the right of the score on the other side. The tablet can be divided into equal doses.

Gabapentine Mylan 800 mg is a white to off-white, oval, biconvex, uncoated, bevelled edged tablet, debossed with “MYLAN” on one side and “G” to the left of the score and “25” to the right of the score on the other side. The tablet can be divided into equal doses.

The tablets are packed in white opaque HDPE bottle with white opaque polypropylene (PP) cap containing desiccant (silica gel), OPA/Al/PVC - Al blisters or OPA/Al/PVC – Al perforated unit dose blisters.

The excipients are: hydroxypropylcellulose, mannitol, poloxamer, crospovidone, talc, magnesium stearate.

II.2 Drug Substance

The active substance is gabapentin, an established active substance. A draft monograph for gabapentin is published in Pharmeuropa 21.3 dated July 2009. The chemical-pharmaceutical documentation and Expert Report in relation to Gabapentin are of sufficient quality in view of the present European regulatory requirements

Manufacturing process
The Active Substance Master File (ASMF) procedure is used for the active substance. The main objective of the ASMF procedure, commonly known as the European Drug Master File (EDMF) procedure, is to allow valuable confidential intellectual property or ‘know-how’ of the manufacturer of the active substance (ASM) to be protected, while at the same time allowing the applicant or marketing authorisation holder (MAH) to take full responsibility for the medicinal product, the quality and quality control of the active substance. Competent Authorities/EMA thus have access to the complete information that is necessary to evaluate the suitability of the use of the active substance in the medicinal product.

Quality control of drug substance
The control tests and specifications for drug substance product are adequately drawn up and sufficient batch results are presented.

Stability of drug substance
Stability studies have been performed with three consecutive production scale batches. No significant changes in any parameters were observed.

II.3 Medicinal Product

Pharmaceutical development
The product development is adequately described in accordance with the relevant European guidelines. The choice of excipients is justified and their functions explained.

Quality control of drug product

The product specifications cover appropriate parameters for this dosage form. Validations of the analytical methods have been presented. Batch analysis has been performed on three pilot scale batches of each strength used for stability and process validation. The batch analysis results show that the finished products meet the specifications proposed.

Stability of drug product

The conditions used in the stability studies are according to the ICH stability guideline. Results of bulk stability studies on three batches of each strength for 24 weeks at 25° C/60 % RH have been presented. No changes were observed. The proposed storage period of 12 months for bulk tablets stored in the proposed bulk package when stored below 25°C is accepted.

Stability testing of the finished product was carried out with three pilots scale batches of each strength packed both in HDPE bottles and blisters under long term and accelerated conditions for six month. A shelf life of 24 months with a storage condition of "Store below 25°C" for the product packed in bottle and blister pack is accepted.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Based on the submitted dossier, the member states consider that Gabapentine Mylan has a proven chemical-pharmaceutical quality. Sufficient controls have been laid down for the active substance and finished product.

III. NON-CLINICAL ASPECTS

III.1 Discussion on the non-clinical aspects

This product is a generic formulation of Neurontin, which is available on the European market. Reference is made to the preclinical data obtained with the innovator product. A non-clinical overview on the pharmacology, pharmacokinetics and toxicology has been provided, which is based on up-to-date and adequate scientific literature. The overview justifies why there is no need to generate additional non-clinical pharmacology, pharmacokinetics and toxicology data. Therefore, the member states agreed that no further non-clinical studies are required.

IV. CLINICAL ASPECTS

IV.1 Introduction

Gabapentin is a well-known active substance with established efficacy and tolerability. A clinical overview has been provided, which is based on scientific literature. The overview

justifies why there is no need to generate additional clinical data. Therefore, the member states agreed that no further clinical studies are required.

IV.2 Pharmacokinetics

Two bioequivalence studies were conducted in fasting state, in healthy volunteers, compared the Gabapentine Mylan 800 mg and 600 mg tablets with the innovator product Neurontin 800 mg and 600 mg tablets of Pfizer Holding France.

The submitted documentation indicates that the intended Gabapentine Mylan 800 and 600 mg tablets are bioequivalent with the reference product, Neurontin 800 and 600 mg tablets.

IV.3 Pharmacovigilance system

The Pharmacovigilance system as described by the MAH fulfils the requirements and provides adequate evidence that the MAH has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

IV.4 Discussion on the clinical aspects

For this authorisation, reference is made to the clinical studies and experience with the innovator product Neurontin. No new clinical studies were conducted. The MAH demonstrated through a bioequivalence study that the pharmacokinetic profile of the product is similar to the pharmacokinetic profile of this reference product. This generic medicinal product can be used instead of the reference product.

V. USER CONSULTATION

The content of the package leaflet (PL) has been prepared in accordance with Article 30 of Directive 2001/83/EC, as amended. As the product information, including the leaflet text has been harmonised with the brand leader Neurontin, it is reasonable to assume that the appropriate key messages are present and written in suitably patient-friendly terms to ensure the safe and effective use of the product.

The evaluation of the study was performed in accordance with: European Commission's "A Guideline on the Readability of the Label and Package Leaflet of Medicinal Products for Human use" and "Guidance concerning consultation with target patient groups for the package leaflet" (May 2006), EFPIA "General Recommendations for Readability User Testing of Package Leaflets for Medicinal Products for Human Use Submitted or Approved under the European Centralized Procedure" (March 2003), Annex to the EFPIA document (March 2002), MHRA "Guidance on the user testing of Patient Information Leaflets" (July 2005).

The results of the test indicate that the PIL is well structured and organized, easy to understand and written in a comprehensible manner. The test shows that the leaflet is readable and patients/users are able to act upon the information that it contains.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

Gabapentine Mylan 600 mg and 800 mg tablets have a proven chemical-pharmaceutical quality and are generic forms of Neurontin 600 and 800 mg tablets. Neurontin 6 is a well-known medicinal product with an established favourable efficacy and safety profile.

Bioequivalence has been shown to be in compliance with the requirements of European guidance documents.

There was no discussion in the CMD(h). Agreement between member states was reached during a written procedure. The member states, on the basis of the data submitted, considered that essential similarity has been demonstrated for Gapentine Mylan with the reference product, and have therefore granted a marketing authorisation. The decentralised procedure was finalised with a positive outcome on 7 June 2011.

STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

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