

## **Public Assessment Report**

### **Scientific discussion**

**Ibuprofen Patheon Express mini 200 mg,  
soft capsules  
(ibuprofen)**

**NL/H/5368/001/DC**

**Date: 26 September 2024**

This module reflects the scientific discussion for the non-approval of Ibuprofen Patheon Express mini 200 mg, soft capsules. The procedure was finalised on 23 November 2022.

## I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have refused a marketing authorisation for Ibuprofen Patheon Express mini 200 mg, soft capsules, from Patheon Softgels B.V.

The indication applied for was:

This medical product is indicated in adults, adolescents and children weighing from 20 kg (6 years of age and above) for the short-term symptomatic treatment of mild to moderate pain such as headache, period pain, dental pain and fever and pain associated with the common cold.

The marketing authorisation was applied for pursuant to Article 10(3), hybrid of Directive 2001/83/EC, claiming essential similarity between the new product and the European Reference Product (ERP) Nurofen Express 400 mg soft capsules, which was initially registered in Bulgaria by Reckitt Benckiser Healthcare BG and is currently registered in the Netherlands through the decentralised procedure NL/H/4313/001 since 14 December 2011. The current Reference Member State (RMS) of the ERP is the Netherlands, justification to use this reference is based on RMS's own files. The ERP information was circulated during the validation period.

The concerned member states (CMS) involved in this procedure were Austria, Cyprus, Czechia, France, Germany, Greece, Hungary, Malta, Romania, Slovakia.

### General comments on the application

The initial application includes a second product strength (Nurofen Fastine Zavance 400 mg, soft capsules, NL/H/5368/002/DC) with Nurofen Express 400 mg soft capsules as reference product for both strengths. A bioequivalence study has been performed with the 400 mg strength and the reference. For the 200 mg strength, a biowaiver has been requested. See for more information the Public Assessment Report for NL/H/5368/002/DC.

The application was discussed in the board meeting of 20 October 2022. Furthermore, a breakout session (BOS) was held in November 2022.

## II. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The marketing authorisation could not be granted due to major objections qualifying as potential serious risk to public health as defined in the Guideline on the definition of a potential serious risk to public health in the context of Article 29(1) and (2) of Directive 2001/83/EC — March 2006 (2006/C 133/05):

### Overall benefit-risk

From a chemical/pharmacokinetic point of view, a marketing authorisation for the product Ibuprofen Patheon Express mini 200 mg could not be granted.

For this application, a bioequivalence study has been performed with the 400 mg strength and the reference. For the 200 mg strength, a biowaiver has been requested. To complement the bioequivalence study and to support the biowaiver, comparative dissolution studies were conducted at pH 1.2, 4.5, pH 6.8 and 7.2.

Bioequivalence with the reference has been demonstrated for the 400 mg strength. However, the similarity of the dissolution profiles of the 200 mg and 400 mg strengths at pH 6.8 was not proven. The conventional  $f_2$  calculations applied by the MAH and the conclusion that similarity has been demonstrated are considered inaccurate; as the  $f_2$  criteria were not met,  $f_2$  cannot be calculated.

Since similarity between the dissolution profiles of the 400 mg and 200 mg strengths was not demonstrated, the results of the bioequivalence study with the 400 mg strength cannot be extrapolated to the 200 mg strength according to the conditions in the Guideline on the Investigation of Bioequivalence CPMP/EWP/QWP/1401/98 Rev. 1/Corr\*, section 4.1.6. Overall, the biowaiver was not approved and the bioequivalence of the 200 mg strength with the reference has not been proven.

Therefore, the Board concluded that the marketing authorisation for Ibuprofen Patheon Express mini 200 mg, soft capsules cannot be granted. Agreement on this conclusion was reached with the concerned member states. The decentralised procedure was finalised with a negative outcome on 23 November 2022.