

# **Public Assessment Report**

## **Scientific discussion**

### **Diklofenak Apofri** **(diclofenac diethylamine)**

**2016-2028**

**This module reflects the scientific discussion for the approval of Diklofenak Apofri. The procedure was finalised on 2017-09-29. For information on changes after this date please refer to the module 'Update'.**

## **I. INTRODUCTION**

The application for Diklofenak Apofri, gel, 23,2 mg/g is a hybrid application made according to Article 10(3) of Directive 2001/83/EC. The applicant, Apofri 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 Voltaren, 11,6 mg/g, gel authorised in Sweden since 2005, with GlaxoSmithKline Consumer Healthcare A/S as marketing authorisation holder.

The reference product used to establish therapeutic equivalence is Voltadol Forte, 23,2 mg/g, gel, from Spain with Novartis Consumer Health, S.A. as marketing authorisation holder.

## **II. QUALITY ASPECTS**

### **II.1 Drug Substance**

The structure of the drug substance has been adequately proven and its physico-chemical properties are sufficiently described.

The manufacture of the drug substance has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

The drug substance specification includes relevant tests and the limits for impurities and degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies confirm the retest period.

### **II.2 Medicinal Product**

The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

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 have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

### **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 amount of diclofenac absorbed systemically from the gel is proportional to the size of the treated area and depends on the applied dose and the skin moisture. The relative bioavailability of diclofenac between diclofenac 23.3 mg/g gel and diclofenac tablets was 4.5% after 7 days. The terminal half-life in plasma is 1-2 hours.

The applicant has not submitted any pharmacokinetic studies. For locally applied products, bioequivalence is generally not a suitable way to show therapeutic equivalence, since plasma levels are not relevant for local efficacy, although they may play a role with regard to safety. The applicant has not submitted any pharmacokinetic studies. Thus, it is not known if the systemic exposure is different following topical application of the applied product compared to the reference product. However, since the composition is identical to that of the reference product (with the exception of the fragrance), it is not considered likely that the systemic exposure should differ considerably. The absence of pharmacokinetic studies is acceptable.

#### **IV.2 Discussion on the clinical aspects**

No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted. Because efficacy and safety is unlikely to differ considerably compared to the reference product due to near identical composition, additional data is not necessary.

#### **IV.3 Risk Management Plan**

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterize, prevent or minimise risks relating to Diklofenak Apofri.

##### Safety specification

Summary table of safety concerns as approved in RMP

|                            |                                                                                 |
|----------------------------|---------------------------------------------------------------------------------|
| Important identified risks | Hypersensitivity such as asthma, angiooedema and urticaria.<br>Photosensitivity |
| Important potential risks  | Systemic adverse drug reactions (GI, CV, Hepatic, Renal)                        |
| Missing information        | Pregnancy and lactation<br>Pediatric population                                 |

#### Pharmacovigilance Plan

Routine pharmacovigilance is suggested and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

#### Risk minimisation measures

Routine risk minimisation is suggested and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

#### Summary of the RMP

The RMP is approved.

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the RMS;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

## **V. 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 Diklofenak Apofri 11,6 mg/g, approved in procedure 111:2011/63373, 2012-09-27. The bridging report submitted by the applicant has been found acceptable.

## **VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION**

The benefit/risk ratio is considered positive and Diklofenak Apofri, gel, 23,2 mg/g is recommended for approval.

**List of recommendations not falling under Article 21a/22 of Directive 2001/83 in case of a positive benefit risk assessment**

N/A

**List of conditions pursuant to Article 21a or 22 of Directive 2001/83/EC**

N/A

## **VII. APPROVAL**

Diklofenak Apofri, gel, 23,2 mg/g was approved in the national procedure on 2017-09-27.

## Public Assessment Report – Update

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

\*Only procedure qualifier, chronological number and grouping qualifier (when applicable)