LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Aciklovir Apofri
(aciclovir)

Asp no: 2017-0772

This module reflects the scientific discussion for the approval of Aciklovir Apofri. The procedure was finalised on 2018-06-25. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Apofri AB has applied for marketing authorisation for Aciklovir Apofri 50 mg/g, cutaneous stick. The active substance is aciclovir.

For approved indications, see the Summary of Product Characteristics.

The marketing authorisation has been granted pursuant to Article 10(3) of Directive 2001/83/EC.

For recommendations to the marketing authorisation not falling under Article 21a/22 of Directive 2001/83 and conditions to the marketing authorisation pursuant to Article 21a or 22 of Directive 2001/83/EC to the marketing authorisation, please see section VI.

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

Pharmacodynamic, pharmacokinetic and toxicological properties of active substance are well known. As active substance is a widely used, well-known active substance, no further studies are required and the applicant provides none. Overview based on literature review is, thus, appropriate.

Environmental Risk Assessment (ERA)
Aciclovir 50 mg/g cutaneous stick is intended for substitution, this will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

There are no objections to approval of Aciklovir Apofri from a non-clinical point of view.

IV. CLINICAL ASPECTS

IV.1 Pharmacokinetics

No pharmacokinetic studies have been performed for this product. Aciklovir Apofri is a product for topical application. Hence, conventional pharmacokinetic bioequivalence studies are not relevant due to low systemic exposure to aciklovir and the absence of pharmacokinetic studies is acceptable.

IV.2 Pharmacodynamics/Clinical efficacy/Clinical safety

An updated Clinical Overview has been submitted which addresses differences/similarities regarding efficacy and safety between the proposed product and the reference product Zovirax 5% cream. The Clinical Overview is now considered acceptable.

Two clinical studies have been performed in support of this application, one against the active comparator, Zovirax 5% cream and one against placebo formulation (cutaneous stick).

The performed studies are assessed as small. However, non-inferiority was shown against Zovirax cream, while most important, superiority was demonstrated against the placebo cutaneous stick. The efficacy of aciclovir containing products in reducing time to healing in comparison to time healing in the natural healing process, is assessed as marginal. However, aciclovir containing topical products against Herpes simplex infections have a favourable safety profile, and moreover, the clinical experience is extensive.

IV.3 Risk Management Plans

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, characterise, prevent or minimise risks relating to Aciklovir Apofri.

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

Summary of the RMP
The submitted Risk Management Plan, version 1.0 signed 18-05-2017 is considered acceptable.

Summary table of Safety concerns

Summary of safety concerns	
Important identified risks	• None
Important potential risks	• None
Missing information	• Pregnancy, lactation and fertility

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 MPA;
- 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.

Periodic Safety Update Report (PSUR)

Active substance is currently listed in the published EURD list

With regard to PSUR submission, the MAH should take the following into account:

- PSURs shall be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal. Marketing authorisation holders shall continuously check the European medicines web-portal for the DLP and frequency of submission of the next PSUR.

- For medicinal products authorized under the legal basis of Article 10(1) or Article 10a of Directive 2001/83/EC, no routine PSURs need to be submitted, unless otherwise specified in the EURD list.

- In case the active substance will be removed in the future from the EURD list because the MAs have been withdrawn in all but one MS, the MAH shall contact that MS and propose DLP and frequency for further PSUR submissions together with a justification.

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 Herpirax 50 mg/g, huidstift (NL/H/3877/001). The bridging report submitted by the applicant has been found acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the generic product, Aciklovir Apofri is found adequate. There are no objections to approval of Aciklovir Apofri from a non-clinical and clinical point of view. The product information is acceptable. The application is therefore recommended for approval.

VII. APPROVAL

Aciklovir Apofri, 50 mg/g, cutaneous stick, was approved in the national procedure on 2018-06-25.

LÄKEMEDELSVERKET
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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)

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