

Public Assessment Report

Scientific discussion

Virafosc

(foscarnet sodium hexahydrate)

SE/H/2229/01/DC

This module reflects the scientific discussion for the approval of Virafosc. The procedure was finalised on 2022-11-29. For information on changes after this date please refer to the module ‘Update’.

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, a marketing authorisation has been granted for Virafosc 24 mg/ml solution for infusion.

The active substance is foscarnet sodium hexahydrate. A comprehensive description of the indication and posology is given in the SmPC.

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

The application for Virafosc 24 mg/ml solution for infusion is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Campus Pharma AB, applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and DK, FI, NO as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Foscavir 24 mg/ml Solution for infusion authorised in NL since 1989, with Clinigen Healthcare B.V. as marketing authorisation holder.

European Reference Product (ERP)

A European Reference Product is used in CMS DK, NO: Foscavir 24 mg/ml solution for infusion authorised in SE since 1989, with AstraZeneca AB as marketing authorisation holder.

The justification to use this product is based on RMS's own files. The ERP information was circulated during the validation period.

Potential similarity with orphan medicinal products

According to the application form and a check of the Community Register of orphan medicinal products the following medicinal products have been designated as orphan medicinal products, but not yet been granted a marketing authorisation in the EU: EU/3/12/999, EU/3/15/1439, EU/3/16/1773.

Having considered the arguments presented by the applicant and with reference to Article 8 of Regulation (EC) No 141/2000, Virafosc is considered not similar (as defined in Article 3 of Commission Regulation (EC) No. 847/2000) to Livtency (EU/3/13/1133).

Therefore, with reference to Article 8 of Regulation (EC) No. 141/2000, the existence of any market exclusivity for Livtency in the treatment of cytomegalovirus disease in patients with impaired cell mediated immunity, does not prevent the granting of the marketing authorisation of Virafosc. This finding is without prejudice to the outcome of the scientific assessment of the marketing authorisation application.

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

Pharmacology/Pharmacokinetics/Toxicology

Pharmacodynamic, pharmacokinetic and toxicological properties of foscarnet sodium hexahydrate are well known. As foscarnet sodium hexahydrate 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)

Since Virafosc is a generic product, it will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

IV. CLINICAL ASPECTS

Pharmacokinetics

To support the marketing authorisation application the applicant has not conducted any bioequivalence studies.

The applicant claims that a bioequivalence study is not necessary according to the Guideline on the investigation of Bioequivalence (CHMP/QWP/EWP/1401/98 Rev. 1) since the product is an aqueous parenteral solution with the same concentration of active substance as the reference product and with the same qualitative composition regarding excipients.

Discussion and overall conclusion

The applied product is to be administered as an aqueous intravenous solution containing the same active substance as the currently authorised product. None of the excipients are known to interact with the drug substance. For this type of product, no bioequivalence studies are required according to the Guideline on the investigation of Bioequivalence (CHMP/QWP/EWP/1401/98 Rev. 1).

The absence of bioequivalence studies is acceptable.

Pharmacodynamics/Clinical efficacy/Clinical safety

No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted. Provided that bioequivalence with the originator product is demonstrated, additional data is not necessary.

Pharmacovigilance system

The Applicant has submitted a signed Summary of the Applicant's/Proposed Future MAH's Pharmacovigilance System. Provided that the Pharmacovigilance System Master File fully complies with the new legal requirements as set out in the Commission Implementing Regulation and as detailed in the GVP module, the RMS considers the Summary acceptable.

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, characterise, prevent or minimise risks relating to Virafosc.

Safety specification

The MAH has submitted the version 1.1 RMP dated 2022-05-05 and proposed the following summary safety concerns:

Summary of safety concerns	
Important identified risks	• None
Important potential risks	• None
Missing information	• None

Pharmacovigilance Plan

Routine pharmacovigilance is suggested and no additional pharmacovigilance activities are proposed.

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 submitted Risk Management Plan, version 1.1 signed 2022-05-05 is considered acceptable. The MAH has satisfactorily responded to the questions raised and updated the RMP accordingly.

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 (PL) has been performed on the basis of a bridging report making reference to Foscavir 24 mg/ml solution for infusion (UK PL 31644/0001).

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, Virafosc, is found adequate. There are no objections to approval of, Virafosc, from a non-clinical and clinical point of view. The product information is acceptable. The benefit/risk is considered positive, and the application is therefore recommended for approval.

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

N/A

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

N/A

VII. APPROVAL

The decentralised procedure for Virafosc 24 mg/ml solution for infusion was positively finalised on 2022-11-29.

Public Assessment Report – Update

Procedure number*	Scope	Product Information affected (Yes/No)	Date of end of procedure	Approval/non approval	Summary/Justification for refuse

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