IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Finovare 20 mg/g Cream
Fusidic acid
PA23214/001/001

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation for a specific medicinal product for human use. It is made available by the HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of Directive 2001/83/EC, as amended. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the medicinal product for marketing in Ireland.

CONTENTS

I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the HPRA has granted a marketing authorisation for Finovare 20 mg/g cream, from Citrine Healthcare Limited on 31st of March 2023 for the topical antibiotic treatment of infections, including impetigo, caused by sensitive micro-organisms, in particular *Staphylococcus aureus*.

This was a national marketing authorisation application according to Article 10.3 of Directive 2001/83/EC, as amended (A so called "Hybrid" application)

This medicinal product is subject to medical prescription which may not be renewed.

No scientific advice was sought by the applicant for this procedure.

The Summary of Product Characteristics for (SmPC) for this medicinal product is available on the HPRA's website at www.hpra.ie

Name of the product	Finovare 20 mg/g Cream
Name(s) of the active substance(s) (INN)	Fusidic acid
Pharmacotherapeutic classification (ATC code)	D06AX01
Pharmaceutical form and strength(s)	20 milligrams/gram , Cream
Marketing Authorisation Number(s) in Ireland (PA)	PA23214/001/001
Marketing Authorisation Holder	Citrine Healthcare Limited
Procedure No.	CRN00CCXZ

II. QUALITY ASPECTS

II.1. Introduction

This application is for Finovare 20 mg/g Cream

II.2 Drug substance

The active substance is fusidic acid, an established active substance described in the European/British Pharmacopoeia, and is manufactured in accordance with the principles of Good Manufacturing Practice (GMP)

The active substance specification is considered adequate to control the quality and meets current pharmacopoeial requirements. Batch analytical data demonstrating compliance with this specification has been provided.

II.3 Medicinal product

P.1 Composition

Each gram of cream contains 20 mg fusidic acid.

The excipients in the medicinal product are listed in section 6.1 of the SmPC.
A visual description of the product is included in section 3 of the SmPC.

P.2 Pharmaceutical Development

The product is an established pharmaceutical form, and its development is adequately described in accordance with the relevant European guidelines.

P.3 Manufacture of the Product

The product is manufactured in accordance with the principles of good manufacturing practice (GMP) at suitably qualified manufacturing sites.

The manufacturing process has been validated according to relevant European/ICH guidelines and the process is considered to be sufficiently validated.

P.4 Control of Other Substances (Excipients/*Ancillary Substances*)

All ingredients comply with Ph. Eur. or are adequately controlled by the manufacturer's specifications.

P.5 Control of Finished Product

The Finished Product Specification is based on the pharmacopoeial monograph for the dosage form, and the tests and control limits are considered appropriate for this type of product.

The analytical methods used are described in sufficient detail and are supported by validation data.

Batch analytical data for a number of batches from the proposed production site(s) have been provided, and demonstrate the ability of the manufacturer to produce batches of finished product of consistent quality.

P.6 Packaging material

The approved packaging for this product is described in section 6.5 of the SmPC.

Evidence has been provided that the packaging complies with Ph. Eur./EU legislation for use with foodstuffs requirements.

P.7 Stability of the Finished Product

Stability data on the finished product in the proposed packaging have been provided in accordance with EU guidelines and support the shelf-life and storage conditions listed in sections 6.3 and 6.4 of the SmPC.

II.4 Discussion on Chemical, Pharmaceutical and Biological Aspects

The important quality characteristics of the product are well-defined and controlled. Satisfactory chemical and pharmaceutical documentation has been provided, assuring consistent quality of Finovare 20mg/g Cream.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This national procedure concerns a hybrid application claiming essential similarity with the innovator product Fucidin 20 mg/g Cream which has been registered in Denmark by Leo Pharma AS since 4 May 1962 (original product). In Ireland, the reference product is Fucidin cream 20 mg/g, cream, which has been registered since 13th October, 1980 via a national procedure. No new preclinical data have been submitted. As such, no pre-clinical assessment has been made on the application. This is acceptable for this type of application.

III.2 Pharmacology

Pharmacodynamic properties of fucidic acid are well known. As fucidic acid is a widely used, well-known active substance, the applicant has not provided additional non-clinical studies and further studies are not required. A non-clinical overview based on literature review has been provided and is acceptable for this type of application.

III.3 Pharmacokinetics

A nonclinical overview of the pharmacokinetic properties of fucidic acid has not been provided as there are no published preclinical data on systemic absorption of fusidic acid from a topical preparation. This is acceptable as fucidic acid is a well-know, widely used active substance and preclinical data have been superseded by clinical experience.

III.4 Toxicology

Toxicological properties of fucidic acid are well known. As fucidic acid is a widely used, well-known active substance, the applicant has not provided additional non-clinical studies and further studies are not required. A non-clinical overview based on literature review has been provided and is acceptable for this type of application.

III.5 Ecotoxicity/environmental risk assessment

A rationale for the absence of ERA studies has been provided. Approval of Fucitrine 20mg/g will not lead to an increased exposure to the environment.

III.6 Discussion on the non-clinical aspects

There are no objections to approval of Fucitrine 20mg/g cream from a non-clinical point of view.

IV. CLINICAL ASPECTS

IV.1 Introduction

Fusidic acid is a well-known active substance with established efficacy and tolerability.

The content of the SmPC approved during the national procedure is in accordance with that accepted for the reference product Fucidin Cream marketed by Leo Laboratories Limited, and the clinical data presented by the applicant.

This product is indicated for the topical antibiotic treatment of infections, including impetigo, caused by sensitive micro-organisms, in particular *Staphylococcus aureus*.

This national procedure concerns a hybrid application claiming essential similarity with the innovator product Fucidin 20 mg/g Cream which has been registered in Denmark by Leo Pharma AS since 4 May 1962 (original product). In Ireland, the reference product is Fucidin cream 20 mg/g, cream, which has been registered since 13th October, 1980 via a national procedure.

The marketing authorisation has been granted pursuant to Article 10.3 of Directive 2001/83/EC, a hybrid application. As required by article 10.3 a comparative clinical trial was performed to demonstrate therapeutic equivalence, as showing bioequivalence by pharmacokinetics is not possible.

This product has previously been authorised in the EU by another MAH, with the UK, (then NL following Brexit) as RMS and Belgium, Germany, Luxembourg, Spain and Poland as CMS. The design and methodology of the clinical study was discussed and accepted during these Article 10.3 EU procedures.

The HPRA has been assured that GCP standards were followed in an appropriate manner in the study conducted.

IV.2 Pharmacokinetics

No new pharmacokinetic data were provided by the applicant and this is acceptable in keeping with the legal basis of this application.

IV.3 Pharmacodynamics

No new pharmacodynamic data were provided by the applicant and this is acceptable in keeping with the legal basis of this application.

IV.4 Clinical Efficacy

The MAH provided one clinical study in support of this hybrid application. It was a multicentre, randomised, 2-arm, double-blind, parallel clinical study. The study compared the efficacy and safety of the test product Fusidic acid 20 mg/g cream against that of the innovator product, Fucidin Cream 20 mg/g (Leo Pharma) in adults and children older than 18 months who had a clinical diagnosis of localised impetigo contagiosa.

Subjects were randomised to one of the two treatments. The dose of cream applied (to fully disinfected lesions) was dependent on the location of the lesions and the age of the patient. Treatment was followed for a maximum period of 14 days, or until the lesions disappeared. The primary endpoint was rate of "cure" at one week. "Cure" was defined as the complete absence of lesions or the lesions having become dry and without crusts; remaining local erythema of the intact skin is acceptable, or such progress that no further antibiotic therapy was necessary. Non-inferiority was assumed if the 95% CI were within a pre-specified 20% limit.

176 subjects were enrolled (85 on the test preparation and 91 on the reference preparation). The intention to treat (ITT) population at week 1 was 172 and at week 2 was 173 subjects. The week one and two per protocol (PP) populations were 169 subjects, in both cases. The subject demographic characteristics (age, height, body weight) and the distributions of the clinical characteristics of the impetiginous lesions were well-matched between the two groups, with the exception of there being more males in the reference group.

The results for the primary endpoint in the ITT population are presented below.

Table 1. Clinical efficacy of the intended to treat population after 1 week.

Clinical efficacy parameter	Fusidic acid 20 mg/g (test) N=85	Fucidin 20 mg/g (reference) N=87	Total N=172
Cured	55 (64.7%)	54 (62.1%)	109 (63.4%)

The difference is 2.6% in favour of the test product with a 95% confidence interval of -11.6 to 16.7% which is within the pre-specified 20% clinically significant difference between the two products.

Therefore, the study met its primary endpoint.

The week 2 efficacy analysis for the ITT population are presented in Table 2 below.

Table 2 Efficacy analysis at week 2 of treatment (ITT population)

	Test	Reference	Totals
No. of subjects	85	88	173
Cured	74 (87.1%)	77 (87.5%)	151 (87.3%)
Improved	5 (5.9%)	7 (8%)	12 (6.9%)
Failed	6 (7.1%)	4 (4.5%)	10 (5.8%)

The difference in cure rates at week 2 of treatment shows that the proportions for test and reference are 87.1% and 87.5%, respectively. The inter-treatment difference (test-reference) is -0.4% (95% CI -9.8 to 8.9%), again supporting the primary efficacy analysis of equivalence between the two products.

IV.5 Clinical Safety

With the exception of the data generated during the therapeutic equivalence study, no new safety data were submitted and none were required for this hybrid application. The safety population included 175 patients. No new or unexpected safety issues were raised by the therapeutic equivalence study data.

Risk Management Plan

The applicant 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 Finovare 20 mg/g cream.

The RMP (version 0.2, signed 8th July 2021) is acceptable. Routine pharmacovigilance and routine risk minimisation activities are considered sufficient.

The applicant is requested to ensure it maintains the RMP in line with the latest SmPC updates and maintains regular reviews.

Summary of Safety Concerns	
Important identified risks	None
Important potential risks	Hypersensitivity reactions
Missing Information	None

Periodic Safety Update Report (PSUR)
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.

IV.6 Discussion on the clinical aspects

For this authorisation, reference is made to the clinical studies and clinical experience with the innovator product, Fucidin Cream by Leo Pharma. The proposed product is a locally applied medicinal product and therefore a traditional bioequivalence study is not deemed appropriate in this setting. Instead, the applicant demonstrated through a therapeutic equivalence study that the efficacy and safety profile of the proposed product is similar to the efficacy and safety profile of the reference product.

V. OVERALL CONCLUSIONS

Finovare 20 mg/g cream is a generic form of Fucidin Cream by Leo Pharma. Fucidin Cream is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

Therapeutic equivalence has been shown to be in compliance with CHMP guidance documents. The SmPC is consistent with that of the reference product.

The MAH has provided written confirmation that systems and services are in place to ensure compliance with their pharmacovigilance obligations.

The HPRA, on the basis of the data submitted, considered that Finovare 20 mg/g cream demonstrated therapeutic equivalence with the reference product as well as a satisfactory risk/benefit profile and therefore granted a marketing authorisation.

VI. REVISION DATE

5 years from the finalisation of the procedure.

VII. UPDATES

This section reflects the significant changes following finalisation of the initial procedure.

SCOPE	**PROCEDURE NUMBER**	**PRODUCT INFORMATION AFFECTED**	**DATE OF START OF PROCEDURE**	**DATE OF END OF PROCEDURE**
New National	N/A	SmPC Sections 1 to 9	31st March 2023	30th March 2028