IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Diclofenac 140 mg medicated plaster
Diclofenac epolamine
PA1104/005/001

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 Diclofenac 140 mg medicated plaster, from Regiomedica GmbH on 28th October 2022 for local symptomatic treatment of pain in epicondylitis and ankle sprain in adolescents from 16 years of age and adults.

This application for a marketing authorisation was submitted in accordance with Article 10c of Directive 2001/83/EC and is referred to as an 'informed consent' application. This means that the Marketing Authorisation Holder for Flector Tissugel 140 mg Medicated Plaster (PA1104/004/001), an authorised medicinal product in Europe, has permitted the applicant to refer to their dossier to obtain an authorisation for Diclofenac 140 mg medicated plaster. Diclofenac 140 mg medicated plaster has the same qualitative and quantitative composition in terms of active substances and the same pharmaceutical form as Flector Tissugel 140 mg Medicated Plaster.

The applicant did not seek national or European scientific advice for this medicinal product.

The authorised method of sale and supply for this medicinal product is in line with that of the reference product, Flector Tissugel 140 mg Medicated Plaster. The product is designated a "Product subject to medical prescription which may be renewed". Supply is through pharmacies only and promotion is to healthcare professionals only.

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	Diclofenac 140 mg medicated plaster
Name(s) of the active substance(s) (INN)	Diclofenac sodium (as diclofenac epolamine)
Pharmacotherapeutic classification (ATC code)	M02AA15
Pharmaceutical form and strength(s)	Medicated plaster, 140 milligrams
Marketing Authorisation Number(s) in Ireland (PA)	PA1104/005/001
Marketing Authorisation Holder	IBSA Farmaceutici Italia S.r.l, Via Martiri di Cefalonia 2, 26900 Lodi (LO), Italy
Procedure No.	CRN00DCQQ

II. QUALITY ASPECTS

II.1. Introduction

This application is for Diclofenac 140 mg medicated plaster.

II.2 Drug substance

The active substance is diclofenac sodium (as diclofenac epolamine), an established active substance not described in the European 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 regulatory requirements. Batch analytical data demonstrating compliance with this specification has been provided under the dossier of Flector Tissugel 140 mg Medicated Plaster.

II.3 Medicinal product

P.1 Composition

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 as provided for under the dossier of Flector Tissugel 140 mg Medicated Plaster.

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 as provided for under the dossier of Flector Tissugel 140 mg Medicated Plaster.

P.4 Control of Other Substances (Excipients)

All ingredients comply with Ph. Eur. or are adequately controlled by the manufacturer's specifications as provided for under the dossier of Flector Tissugel 140 mg Medicated Plaster.

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 based on the reference to the dossier of Flector Tissugel 140 mg Medicated Plaster.

The analytical methods used are described in sufficient detail and are supported by validation data as provided for under the dossier of Flector Tissugel 140 mg Medicated Plaster.

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 as provided for under the dossier of Flector Tissugel 140 mg Medicated Plaster.

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 as provided for under the dossier of Flector Tissugel 140 mg Medicated Plaster.

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 under the dossier of Flector Tissugel 140 mg Medicated Plaster and support the shelf-life and storage conditions listed in sections 6.3 and 6.4 of the SmPC.

Adventitious Agent Safety

Certificates of suitability issued by EDQM have been provided for excipients and compliance with the Note For Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Medicinal Products has been satisfactorily demonstrated.

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 Diclofenac 140 mg medicated plaster PA1104/005/001

III. NON-CLINICAL ASPECTS

III.1 Introduction

This active substance is the same as that present in Flector Tissugel 140 mg Medicated Plaster, IBSA Farmaceutici Italia srl, on the European market. 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.5 Ecotoxicity/environmental risk assessment

An ERA has been submitted for Diclofenac 140 mg medicated plaster. The ERA indicates a log K_{OW} value in the region of 4.5-4.8 for diclofenac. As diclofenac has a reported log K_{OW} > 4.5 for the neutral diclofenac species this consequently triggers a step-wise screening for persistence, bioaccumulation and toxicity. In addition, the PEC surface water is 0.7 µg/L, which is above the trigger value of 0.01 µg/L triggering a Phase II assessment.
The literature suggests that based on the low BCF of 3-5 found in the standard OECD 305 fish bioconcentration study, the phrase "diclofenac has low potential for bioaccumulation" is justified, and diclofenac is therefore not a PBT substance.
An assessment factor of 10 and a NOEC of 0.32 mg/l from a chronic fish toxicity study are used to compute the PNEC. The PEC/PNEC ratio obtained for the active ingredient, diclofenac is 0.0025, which is less than 1 and as such further testing in the aquatic compartment will not be necessary, and it can be concluded that usage of Diclofenac medicated plaster is unlikely to represent a risk to the aquatic environment.

III.6 Discussion on the non-clinical aspects

The pharmacodynamic, pharmacokinetic and toxicological properties of diclofenac are well known. As this is an "Informed consent" Marketing Authorisation Application according to Article 10c of Directive 2001/83/EC, 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. The usage of Diclofenac 140 mg medicated plaster is unlikely to represent a risk to the environment.

IV. CLINICAL ASPECTS

IV.1 Introduction

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

This medicinal product is the same as Flector Tissugel 140 mg Medicated Plaster already on the European market.

The content of the SmPC approved during the national procedure is in accordance with that accepted for the reference product Flector Tissugel 140 mg Medicated Plaster marketed by IBSA Farmaceutici Italia S.r.l.

As this is an "Informed consent" Marketing Authorisation Application according to Article 10c of Directive 2001/83/EC, no clinical studies have been submitted by the applicant. This is deemed acceptable by the HPRA.

IV.2 Pharmacokinetics

N/A "Informed consent" Marketing Authorisation Application

IV.3 Pharmacodynamics

N/A "Informed consent" Marketing Authorisation Application

IV.4 Clinical Efficacy

N/A "Informed consent" Marketing Authorisation Application

IV.5 Clinical Safety

A Risk Management Plan, version 1.1, has been submitted, 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 Diclofenac 140mg medicated plaster. It is concluded that routine pharmacovigilance and risk minimisation measures are sufficient.

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.

IV.6 Discussion on the clinical aspects

As this is an "Informed consent" Marketing Authorisation Application according to Article 10c of Directive 2001/83/EC, no clinical studies have been submitted by the applicant. This is deemed acceptable by the HPRA.

This medicinal product is the same as Flector Tissugel 140 mg Medicated Plaster already on the European market.

The content of the SmPC approved during the national procedure is in accordance with that accepted for the reference product Flector Tissugel 140 mg Medicated Plaster marketed by IBSA Farmaceutici Italia S.r.l.

A Risk Management Plan has been submitted and PSURs shall be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list).

V. OVERALL CONCLUSIONS

Diclofenac 140 mg Medicated Plaster is the same as Flector Tissugel 140 mg Medicated Plaster. Flector Tissugel 140 mg Medicated Plaster is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

The HPRA, on the basis of the data submitted considered that Diclofenac 140 mg Medicated Plaster was the same as the reference product and therefore granted a Marketing Authorisation.

VI. REVISION DATE

January 2023

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	28th October 2022	27th October 2027
Transfer	N/A	SmPC sections 7, 8, 10 Package Leaflet New MA Holder: IBSA Farmaceutici Italia S.r.l New PA number: PA1104/005/001	N/A	13th January 2023