IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

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.

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I. INTRODUCTION

Specific provisions were introduced for traditional herbal medicinal products (THMPs) in accordance with the Traditional Herbal Medicinal Products Directive (2004/24/EC).The national regulations, the Medicinal Products (Control of Placing on the Market) Regulations 2007 (S.I. No. 540 of 2007) which implement this Directive came into force on 23rd July 2007. Consequently the Health Products Regulatory Authority (HPRA) has established the Traditional Herbal Medicinal Products Registration Scheme.

The Public Assessment Report reflects the scientific conclusion reached by the HPRA at the end of the evaluation process and provides a summary of the grounds for approval of a Certificate of Traditional Use Registration for a specific traditional herbal 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 EC Directive 2001/83/EC, as amended by Directive 2004/27/EC and Directive 2004/24/EC. 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 traditional herbal medicinal product for marketing in Ireland.

Based on the review of the data on quality, safety and traditional use, the HPRA has granted A. Vogel Ireland Limited a Certificate of Traditional Use Registration for Atrogel Arnica Gel, containing an ethanolic tincture of fresh Arnica flowers (*Arnica montana* L., flos).

This application is for a traditional herbal medicinal product as defined by Article 16(a)1 of Directive 2001/83 EC, as amended, and was submitted as part of the Traditional Herbal Medicinal Product Registration Scheme.
The Summary of Product Characteristics (SmPC) for this traditional herbal medicinal product is available on the HPRA's website.

II. QUALITY ASPECTS

This application is for Atrogel Arnica Gel. The active ingredient of Atrogel Arnica Gel is a tincture obtained from the fresh flowers of *Arnica montana* L.

III.1.1 S.1 Herbal Substance

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

III.1.2 S.2 Herbal preparation

The herbal preparation is an ethanolic tincture of fresh Arnica flowers (*Arnica montana* L., flos) and is manufactured in accordance with the principles of Good Manufacturing Practice (GMP).

The herbal preparation specification is considered adequate to control the quality and meets current appropriate requirements. Batch analytical data demonstrating compliance with this specification have been provided.

III.1.3 Medicinal product

P.1 Composition

The composition of the medicinal product is stated in sections 2 and 6.1 of the SmPC. A 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 the 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 the Finished Product

The Finished Product Specification is based on the pharmacopoeial monograph for 'semi-solid preparations for cutaneous application' 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 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 materials comply with Ph. Eur. or EU food-contact legislation 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.

Conclusion on quality
The important quality characteristics of the product are well-defined and controlled. Satisfactory pharmaceutical documentation has been provided, assuring consistent quality of Atrogel Arnica Gel.

III. NON-CLINICAL ASPECTS

Due to the nature of the application it is not possible to assess if the safety standards for the phytochemical constituents of Atrogel Arnica Gel are acceptable by the standards of today's GLP and safety testing requirements.

The product is a traditional herbal medicinal product as defined by Article 16a(1). No new non-clinical studies have been submitted. An expert report on safety has been provided which includes an appropriate review of the available literature. Information presented demonstrating traditional use is acceptable and thus the lack of provision of a complete standard safety package is acceptable in compliance with guideline EMEA/HMPC/32116/05.

Genotoxicity testing did not reveal any safety concerns. Carcinogenicity and reproductive toxicity testing is considered to be insufficient and has not been performed to current standards. Due to the lack of data, the use of the product during pregnancy and lactation should be avoided unless under the guidance of a medical practitioner.

An environmental risk assessment is not required for herbal medicinal products according to guidance CPMP/SWP/4447/00.

IV. CLINICAL ASPECTS

This is a national application submitted by A. Vogel Ireland Limited under Article 16c of Directive 2001/83 EC, as amended (Traditional Herbal Medicines Registration Scheme).

The proposed indication is: A traditional Herbal Medicinal Product for the symptomatic relief of muscular aches, pains and stiffness, sprains, bruises and swelling after contusions, exclusively based on long standing use.

III.3.1 Clinical Efficacy

No clinical efficacy data is required for registration of Traditional Herbal Medicinal Products (THMP). However, Article 16c1(c) requires the applicant to provide bibliographic or expert evidence to show that the medicinal product in question, or a corresponding product, has been in medicinal use throughout a period of at least 30 years, including at least 15 years within the Community. This traditional use data has been submitted and is satisfactory and is in accordance with Article 16c1(c)

The efficacy of this traditional herbal medicinal product is plausible on the basis of long standing use and experience.

The indication proposed for Atrogel Arnica Gel is in line with traditional indications recorded and hence, compatible with the requirements of the Traditional Herbal Medicinal Products Directive 2004/24/EC.

III.3.2 Clinical Safety
In accordance with Article 16c1(d) the Applicant has provided a bibliographic review of the safety data together with an expert report.

Atrogel Arnica Gel is intended for external topical use only, the amount of gel to be applied is dependent on the size of the area of injury.

Idiosyncratic skin sensitivity or skin allergies to Arnica herb in susceptible individuals would appear to be the most prominent type of adverse reaction seen**.** The use of Atrogel Arnica Gel should be avoided in those with a known sensitivity to plants in the Compositae (Asteraceae) family and should not be applied to broken or irritated skin.

There is no evidence that this topical treatment could interact with medicines taken orally**.**
There is little safety data available on the use of Atrogel Arnica Gel in pregnancy or lactation,therefore it should only be used under the supervision of a doctor in these situations.
If symptoms worsen during the use of Atrogel Arnica Gel or persist for longer than 1 week a doctor should be consulted.

In conclusion; This product proves not to be harmful in the specified conditions of use based on the bibliographic review of safety data, expert report and additional data provided.

III.3.3 Pharmacovigilance

It should be noted that in accordance with Article 16g of Directive 2004/24, the pharmacovigilance requirements described in Articles 101- 108 of Directive 2001/83 EC as amended also apply in respect of traditional herbal medicinal products.

V. OVERALL CONCLUSIONS

The important quality characteristics of the product are well-defined and controlled. Satisfactory pharmaceutical documentation has been provided, assuring consistent quality of Atrogel Arnica Gel.

The HPRA, on the basis of the data submitted, considered that Atrogel Arnica Gel demonstrated adequate evidence of traditional use for the approved indication(s) and no new non-clinical or clinical safety concerns have been identified.

A Certificate of Traditional Use Registration for Atrogel Arnica Gel is granted.

VI. REVISION DATE

April 2019