IPAR

Public Assessment Report for a Traditional Herbal Medicinal Product for Human Use

Venaforce Varicose Veins gastro-resistant tablets
Dry extract from fresh *Aesculus hippocastanum* L., semen (Horse Chestnut seed)

TR 2309/011/001

TR holder A. Vogel Ireland Limited

CONTENTS

I. INTRODUCTION

II. QUALITY ASPECTS

III. NON-CLINICAL ASPECTS

IV. CLINICAL ASPECTS

V. OVERALL CONCLUSIONS

VI. REVISION DATE

VII. UPDATE

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 Venaforce Varicose Veins gastro-resistant tablets.

This application was submitted as a standard application according to Article 16a(1) of Directive 2001/83 EC, as amended as part of the Traditional Herbal Medicinal Product Registration Scheme.

About the product

The genus *Aesculus* belongs to the family *Sapindaceae*. The active ingredient of Venaforce Varicose Veins gastro-resistant tablets is a dry extract obtained from *Aesculus hippocastanum* L. seeds. The product is a yellowish beige coated tablet for oral use.

Venaforce Varicose Veins gastro-resistant tablets is a traditional herbal medicinal product used for relieving the symptoms of varicose veins such as tired, aching or heavy legs, exclusively based on long-standing use. There is no requirement under the Traditional Herbal Registration scheme to prove scientifically that the product is efficacious, the registration is based exclusively upon the longstanding use of Venaforce Varicose Veins gastro-resistant tablets as a traditional herbal medicine and not upon data generated from clinical trials.

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 Venaforce Varicose Veins gastro-resistant tablets.

II.1.1 S.1 Herbal Substance

The herbal substance is fresh Horse Chestnut seeds (*Aesculus hippocastanum* L., semen).
The herbal substance specification is considered adequate to control the quality and meets current appropriate requirements.

II.1.2 S.2 Herbal preparation

The herbal preparation is an extract (as dry extract) from fresh *Aesculus hippocastanum* L., semen (Horse Chestnut seeds) and is manufactured in accordance with the principles of Good Manufacturing Practice (GMP).

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

II.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.

P.3 Manufacture of the Product

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

The manufacturing process is standard and has been appropriately validated.

P.4 Control of Other Substances (Excipients)

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 tablets 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 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 components 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.

II.1.4 Discussion on Chemical, Pharmaceutical and Biological Aspects

The important quality characteristics of the product are well-defined and controlled. Satisfactory pharmaceutical documentation has been provided, assuring consistent quality of Venaforce Varicose Veins gastro-resistant tablets.

II.1.5 Other information

Not applicable.

II.1.6 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 Venaforce Varicose Veins gastro-resistant tablets.

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 Venaforce Varicose Veins are acceptable to 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. A more comprehensive review has been performed by the Herbal Medicinal Products Committee of the EMA (*EMEA/HMPC/225304/2008)*. Overall the information presented is considered to be acceptable and demonstrates that 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. Specific genotoxicity studies for Venaforce Varicose Veins have not been performed, however, on the basis of the data presented it is considered that there is no concern regarding genotoxicity. Appropriate carcinogenicity and reproductive toxicity studies have not been submitted. However, the product is for short term use and is contraindicated in pregnancy.

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 by Directive 2004/24/EC.

The proposed indication for this traditional herbal medicinal product is in the relief of symptoms of varicose veins such as tired, aching or heavy legs, exclusively based on long-standing use.

IV.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 with this application and is satisfactory and in accordance with Article 16c1(c).
The efficacy of the traditional herbal medicinal product is plausible on the basis of long-standing use and experience.

The indication proposed for Venaforce Varicose Veins gastro-resistant tablets is in line with traditional indications recorded and hence, compatible with the requirements of the Traditional Herbal Medicinal Products Directive 2004/24/EC

IV.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.
Venaforce Varicose Veins gastro-resistant tablets should not be used by patients who have an allergy or are hypersensitive to horse chestnut seed or any of the other ingredients.

This product is recommended for oral short-term use only.

It is recommended that if symptoms worsen or persist for more than two weeks medical advice should be sought.

This product should not be given to children and adolescents under the age of 18 years.

If there is inflammation of the skin, hardening of the affected veins, hardening of the surrounding skin, severe pain in the legs, ulcers or sudden swelling of one or both legs, a doctor should be consulted.

Patients who have developed ulcers on their legs should not use this product if they are not receiving medical care for these ulcers. If a patient develops a leg ulcer while using this product they should immediately seek medical treatment for the ulcer.

This product contains soya oil polysaccharide and should not be used by patients who are allergic to peanut or soya.
Venaforce Varicose Veins gastro-resistant tablets should not be used by women who are pregnant or breast-feeding.
No studies on the effect on the ability to drive have been performed on this product.
The possible side effects that may occur after using this product include feeling sick, stomach discomfort, wind, diarrhoea, itching or rash. Headaches and dizziness may also occur.
In conclusion, this product proves not to be harmful in the specified conditions of use based on the review of safety data, expert report and additional data provided.

IV.3.3 Pharmacovigilance

It should be noted that in accordance with Article 16g of Directive 2004/24/EC, 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 Venaforce Varicose Veins gastro-resistant tablets.

The HPRA, on the basis of the data submitted, considered that Venaforce Varicose Veins gastro-resistant tablets demonstrated adequate evidence of traditional use for the approved indication and no new non-clinical or clinical safety concerns have been identified.

A Certificate of Traditional Use Registration for Venaforce Varicose Veins gastro-resistant tablets is granted.

VI. REVISION DATE

November 2018