IPAR

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

Menoforce Sage Tablets
Dry extract of sage leaf

TR2309/004/001

TR holder: A. Vogel Ireland Limited

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CONTENTS

I. INTRODUCTION

II. QUALITY ASPECTS

III. NON-CLINICAL ASPECTS

IV. CLINICAL ASPECTS

V. OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

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 HPRA has established the Traditional Herbal Medicinal Products Registration Scheme.

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 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 Bioforce UK Ltda Certificate of Traditional Use Registration for Menoforce Sage tablets, containing dry extract from the leaves of *Salvia officinalis* L. (Sage).

This application was submitted as a standard application according to Article 16a of Directive 2001/83/EC, as amended, 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 Menoforce Sage tablets. The active ingredient of Menoforce Sage tablets is an extract obtained from *Salvia officinalis* L. (Sage).

One tablet contains 51 mg of dry extract from fresh Sage (Salvia officinalis L.) leaves (equivalent to 795-1370 mg of fresh herb). Extraction solvent: ethanol 68% v/v.

II.1 S.1 Herbal Substance

The herbal substance specification is considered adequate to control the quality and meets appropriate current requirements. Satisfactory batch analytical data has been provided.

II.2 S.2 Herbal preparation

The herbal preparation is a tincture (dried during manufacture) from fresh leaves of *Salvia officinalis* L. (Sage) and is manufactured in accordance with the principles of Good Manufacturing Practice (GMP)

The specification for the tincture is considered adequate to control the quality and batch analytical data demonstrating satisfactory compliance with this specification has been provided.

II.3 Medicinal product

P.1 Composition

The compositionof the medicinal product is stated in section 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 and the process provides a product of satisfactory quality.

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 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 from the proposed production sitet 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 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.4 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 Menoforce Sage tablets

III. NON-CLINICAL ASPECTS

Menoforce Sage tablets is a traditional herbal medicinal product as defined by Article 16a(1) of Directive 2001/83/EC as amended. Given the type of application and limited data available, it is not possible to assess if the safety standards for the phytochemical constituents of Menoforce Sage tablets are acceptable to the standards of today's GLP and safety testing requirements.

A single study was presented with respect to genotoxicity and this study was considered to be performed to acceptable standards and demonstrated no genotoxic potential. An expert report on safety has also been provided which includes an appropriate review of the available literature. No safety concern was identified however limited data was available with respect to the carcinogenicity and reproductive toxicity potential of Menoforce Sage tablets.

Overall the information presented demonstrating traditional use is considered to be acceptable and the lack of provision of a complete standard safety package is in line with the EMA 'Guideline on Non-clinical Documentation for Herbal Medicinal Products in Applications for Marketing Authorisation (bibliographical and mixed applications) and in Applications for Simplified Registration' (EMEA/HMPC/32116/05).

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 Bioforce (UK) Ltd to the Traditional Herbal Medicines Registration Scheme under Article 16a of Directive 2001/83/EC, as amended.

The proposed indication for this traditional herbal medicinal product is in the relief of menopausal hot flushes and excessive perspiration, exclusively based on long-standing use.

IV.1 Clinical Efficacy

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 Menoforce Sage tablets as a traditional herbal medicine and not upon data generated from clinical trials.

Article 16c1(c) of Directive 2001/83/EC 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. With regard to this traditional use data, the requirements of Article 16c1(c) have been met.

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

The indication proposed for Menoforce Sage 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.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.

Menoforce is not recommended for use in persons under 18 years of age.

It is recommended that if symptoms worsen during the use of Menoforce or if they do not improve after 12 weeks, a qualified healthcare professional such as a doctor or pharmacist should be consulted.

Enough data has not been gathered to establish the safety of this product for long term use.

The use of Menoforce should be avoided in those who are allergic to sage or any of the other ingredients of this product.

Menoforce should not be used during pregnancy and breast-feeding.

It is noted that sweating can be a symptom of a more serious underlying condition and it is therefore recommended that patients seek medical advice if they are worried about their symptoms.

It is advised that this product contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

The intake of sage preparations might influence the effect of medicinal products acting via the GABA receptor (e.g. barbiturates, benzodiazepines), even if not noticed clinically. Therefore the use of Menoforce with such medicinal products is not recommended.

Menoforce may impair the ability to drive and use machines. Affected patients should not drive or operate machinery.

No side effects to Menoforce have been reported. If side effects occur, a doctor or pharmacist should be consulted.

Overdose has been reported after intake of more than 15 g of sage leaves with a sense of heat, fast heart rate, vertigo and seizures.

In conclusion, the 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 Pharmacovigilance

It should be noted that in accordance with Article 16g of Directive 2001/83/EC, as amended, 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 Menoforce Sage tablets.

The HPRA, on the basis of the data submitted, considered that Menoforce Sage tablets demonstrated adequate evidence of traditional use for the approved indications and no new preclinical or clinical safety concerns have been identified.

A certificate of traditional use registration for Menoforce Sage tablets is granted.

VI. REVISION DATE

April 2019

VII. UPDATES

Scope	Procedure number	Product Information affected	Date of start of procedure	Date of end of procedure	Approval/non approval
2010 - National Variation Type II (60 day)- **B.II.b.3.A, B.II.b.5.E, B.II.c.1.A, B.II.c.1.B, B.II.c.1.C x 2, B.II.c.1.z, B.II.c.2.A, B.II.c.2.D, B.II.d.1.E, B.II.d.1.z x 2, B.II.c.2.A, B.II.e.1.A.1, B.II.e.2.B x 8, B.II.e.2.C x 8, B.II.f.1.A.2, B.II.f.1.D, B.II.f.1.z, B.III.2.B & C.I.z**	CRN 2186673	SPC sections 3, 4.8, 4.9, 6.3 **IPAR** **IPA II Quality Aspects** II.3 P1 & II.3 P7	12/12/16	12/07/17	Approved