IPAR

Public Assessment Report for a
Traditional Herbal Medicinal Product for Human Use
Prostasan Soft Capsules
Extract (as soft extract) from Saw Palmetto fruit
TR 2309/002/001
A. Vogel Ireland Limited

Date of registration: 25th May 2012

CONTENTS

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 Prostasan soft capsules, containing 320 mg of extract (as soft extract) from saw palmetto fruit (*Serenoa repens* (Bartram) Small, fructus (9-12:1).

This application is for a traditional herbal medicinal product as defined by Article 16a(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 vailable on the HPRA's website.

II. QUALITY ASPECTS

This application is for Prostasan soft capsules. The active ingredient of Prostasan soft capsules is obtained from saw palmetto fruit.

III.1.1 S.1 Herbal Substance

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

III.1.2 S.2 Herbal preparation

The herbal preparation is a soft extract from saw palmetto fruit (*Serenoa repens* (Bartram) Small, fructus (syn. *Sabal serrulata* (Michaux)) 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.

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's 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 satisfactory process validation results have been provided for production batches.

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 and tests and control limits are considered appropriate for this type of product.
The analytical methods used are described in sufficient detail and the methods are considered valid.
Batch analytical data have been provided and support the specifications.

P.6 Packaging material

The approved packaging for this product is described in section 6.5 of the SmPC.
It has been confirmed that the packaging complies with Ph. Eur. or relevant legislation for use with foodstuffs.

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.

III.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 Prostasan soft capsules.

III. NON-CLINICAL ASPECTS

Prostasan soft capsule 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 Saw Palmetto are acceptable to the standards of today's Good Laboratory Practice GLP and safety testing requirements. However, for those studies that have been submitted in support of this application, the HPRA has been assured that GLP standards were followed and the studies were conducted in an appropriate manner.
A number of new non-clinical studies have been submitted with respect to potential pharmacokinetic drug interactions and genotoxicity. An expert report on safety has also been provided with respect to these studies but also includes an appropriate review of the available literature. Of the data presented, no safety concern was identified. Overall, the information presented demonstrating traditional use is acceptable and thus the lack of provision of a complete standard safety package is acceptable and 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 A. Vogel Ireland Limited to the Traditional Herbal Medicinal Product Registration Scheme under Article 16c of Directive 2001/83/EC, as amended.

The proposed indication for this traditional herbal medicinal product is in the relief of lower urinary tract symptoms in men who have a confirmed diagnosis of benign prostatic hypertrophy (BPH). This is based on traditional use only. Prior to treatment other serious conditions should have been ruled out by a doctor.

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 with this application 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 Prostasan 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.

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

Prostasan is intended for use in men only. It is not suitable for patients under 18 years of age.

Patients shouldn't take more than the recommended dose of Prostasan.

It is strongly advised that patients see a doctor before taking this product as the urinary symptoms Prostasan is used to treat may be due to a serious underlying condition which requires investigation by a doctor.

This product is solely intended for use in men who have had benign prostatic hypertrophy (BPH) already diagnosed by a medical practitioner.

If patients notice blood in their urine, back pain, groin pain or if they have a fever, it is recommended that medical advice be sought immediately.

It is recommended that if symptoms worsen during use or persist longer than 8 weeks a qualified health care professional, such as a doctor or pharmacist should be consulted.

The possible side effects that may occur after taking Prostasan include belching, stomach discomfort and allergic reactions such as skin rashes.

Patients with intolerance to fructose (a type of sugar) should not take this medicine.

The safety of Saw palmetto has not been studied in patients with liver or kidney problems.

No studies on the effects of Prostasan on the ability to drive and use machines have been performed.

A PSA test is a blood test that doctors may do in men with urinary symptoms.
Saw palmetto is unlikely to have an effect on levels of PSA (Serum Prostate Specific Antigen).

Due to one case of bleeding during surgery associated with the use of Saw palmetto, it is recommended that Saw palmetto should be discontinued and a platelet blood test taken prior to patients undergoing surgery.

Patients taking other medication for Benign Prostatic Hypertrophy should consult their doctor before using Prostasan capsules.
It should be noted that long-term safety data for Saw palmetto is lacking.
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.

III.3.3 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 Prostasan soft capsules.

The HPRA, on the basis of the data submitted, considered that Prostasan soft capsules demonstrated adequate evidence of traditional use for the approved indications and no new non-clinical or clinical safety concerns have been identified.

A Certificate of Traditional Use Registration for Prostasan soft capsules is granted.