IPAR

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

Name of Product: Urostemol Prosta capsules

TR 1186/004/001

TR holder: Chefaro Ireland Limited

October 2016

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 Chefaro Ireland Ltd a Certificate of Traditional Use Registration for Urostemol Prosta capsules. Each capsule contains 500 mg of extract (as soft extract) from *Cucurbita pepo* L. convar. *citrullina* I. Greb. var. *styriaca* I. Greb., semen (pumpkin seed) (15-25 : 1). Extraction solvent: ethanol 92% m/m.

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 Urostemol Prosta capsules. The active ingredient of Urostemol Prosta is an extract obtained from pumpkin seed.

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II.1 S.1 Herbal Substance

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

II.2 S.2 Herbal preparation

The herbal preparation is a soft extract from pumpkin seed. It 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 pharmacopoeial requirements. Batch analytical data demonstrating compliance with this specification has been provided.

II.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 GMP at a suitably qualified manufacturing site.

The manufacturing process has been validated according to relevant European guidelines and the process is considered to be sufficiently validated.

P.4 Control of Other Substances (excipients)

All ingredients comply with a relevant monograph of the European Pharmacopoeia 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 hard capsules, 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 blister strip complies with EU legislation for plastic materials intended to come into contact with food.

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 Urostemol Prosta capsules.

III NON-CLINICAL ASPECTS

Urostemol Prosta is a traditional herbal medicinal product as defined by *Article 16a of Directive 2001/83/EC* as amended.

An expert report on safety has been provided which includes an appropriate review of the available literature.

No genotoxic potential was observed in the AMES test for this specific product formulation. No other new preclinical studies have been submitted. Given the type of application and limited data available, it is not possible to assess if the safety package for the phytochemical constituents of Urostemol Prosta are acceptable to the standards of today's GLP and safety testing requirements.

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 Chefaro Ireland Ltd under Article 16c of Directive 2001/83/EC, as amended.

Urostemol Prosta is a traditional herbal medicinal product used for the relief of lower urinary tract symptoms in men related to an overactive bladder or who have a confirmed diagnosis of benign prostatic hyperplasia (BPH), such as urgency to urinate, frequent urination day and night, incomplete emptying of the bladder and weak or interrupted urinary flow. This is exclusively based on long-standing use.
Prior to treatment, other serious conditions should have been ruled out by a doctor.

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 long standing use of Urostemol Prosta capsules 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 Urostemol Prosta caspulses 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.

It is strongly advised that you see a doctor before taking this product as urinary symptoms may be due to a serious underlying condition which only your doctor can diagnose.

Patients with confirmed benign prostatic hyperplasia (BPH)

This product is intended for men who have had benign prostatic hyperplasia (BPH) already diagnosed by a medical practitioner. Patients taking medication for benign prostatic hyperplasia (BPH) should consult their doctor before taking this product.

This medicinal product may alleviate the discomfort caused by an enlarged prostate but will not reverse the enlargement itself. Therefore, the patient should visit his doctor regularly.

If symptoms such as pyrexia, spasms, haematuria, urinary retention, painful urination, loin pain, abdominal or back pain are present or develop during use, medical advice must be sought.

If symptoms persist beyond 4 weeks or worsen during use a qualified healthcare professional should be consulted.

Due to a lack of data, the safety of this product for long term use has not been established.

The use in children and adolescents under 18 years of age is not recommended, because lower urinary tract symptoms in these populations require medical supervision.

Urostemol Prosta capsules should not be used by those allergic to the active substances, to other members of the Cucurbitaceae family (such as watermelon, courgettes etc.), or to any of the excipients listed in the SmPC.

The following adverse reactions have been commonly reported: mild gastrointestinal complaints (abdominal pain, dyspepsia, nausea, vomiting, stomach discomfort, dysphagia, oesophageal pain and diarrhoea).

Hypersensitivity reactions (rash, urticaria, erythema, pruritus, oedema and anaphylactic shock) have also been reported, the frequency is not known.

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 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 Urostemol Prosta.

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

A certificate of traditional use for Urostemol Prosta is granted.