IPAR

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

TR Holder

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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 IMB has established the Traditional Herbal Medicinal Products Registration Scheme.

The Public Assessment Report reflects the scientific conclusion reached by the Irish Medicines Board (IMB) 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 IMB 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 IMB 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 IMB has granted NBTY Europe Ltd.,a Certificate of Traditional Use Registration for Nature's Bounty Agnus Castus PMS relief tablets containing dry extract from the fruit of *Vitex agnus castus L.* Plant.

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

The Summary of Product Characteristics (SmPC) for these traditional herbal medicinal products is available on the IMB's website.

II. QUALITY ASPECTS

This application is for Nature's Bounty Agnus Castus PMS Relief film-coated tablets. The active ingredient of Nature's Bounty Agnus Castus PMS Relief film-coated tablets is a dry extract obtained from the fruit of the *Vitex agnus castus L.*plant.

Each tablet contains:
3.9 mg of extract (as dry extract) from *Vitex agnus castus* L. fructus (equivalent to 23.4 – 31.2 mg of agnus castus fruit).
Extraction solvent : Ethanol 75% v/v

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 Vitex agnus castus fruit dry extract which 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 product is a clear film coated, speckled brown, round tablet, plain on both sides.

The product contains 3.9 mg of dry extract from agnus castus fruit (*Vitex agnus castus L.* fructus).

The tablet also contains the following inactive ingredients: maltodextrin, anhydrous colloidal silica, hydrated colloidal silica, microcrystalline cellulose, croscarmellose sodium, magnesium stearate, hypromellose and glycerol.

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 has been validated and the process provides a product of satisfactory quality and consistency.

P.4 Control of Other Substances (Excipients/*Ancillary Substances)*

All ingredients comply with Ph. Eur. or U.S.P. 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 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 product is presented as tablets in green polyethylene terephthalate (PET) bottles with a polypropylene cap and an inner seal liner made up of polyester, polymer adhesive layer, polyolefin foam and aluminium foil.
Bottles contain 30 or 60 tablets

Evidence has been provided that blister complies with the requirements of EU directive 2008/39/EC for plastic materials and articles intended to come in contact with foodstuffs and that the bottle complies with the Ph. Eur. standards.

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 demonstrating the stability of the product for 3 years when stored in line with the conditions "Do not store above 25°C. Store in the original package. Keep the bottle tightly closed in order to protect from light and moisture".

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 Nature's Bounty Agnus Castus PMS Relief film-coated tablets.

III. NON-CLINICAL ASPECTS

Agnus Castus PMS relief tablets is a traditional herbal medicinal product as defined by Article 16a(1) of Directive 2001/83/EC as amended.
No 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 Agnus Castus PMS relief tablets are acceptable to the standards of today's GLP and safety testing requirements.

An expert report on safety has been provided which includes an appropriate review of the available literature.
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 NBTY Europe Ltd under Article 16c of Directive 2001/83/EC, as amended.

Nature's Bounty Agnus Castus PMS relief tablets is a traditional herbal medicinal product used for for the relief of minor symptoms of premenstrual syndrome, exclusively based upon 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 Agnus Castus PMS relief 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 forAgnus Castus PMS relief 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.
Please see the SmPC for Agnus Castus PMS relief tablets (available on the IMB website) for details of contraindications, warnings for use and possible adverse events.

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 Nature's Bounty Agnus Castus film-coated tablets.

The IMB, on the basis of the data submitted, considered that Agnus Castus PMS relief tablets 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 Agnus Castus PMS relief tablets is granted.

VI. REVISION DATE

February 2021

VII. UPDATES

Procedure number	Product Information affected	Date of start of procedure	Date of end of procedure	Approval/non approval
CRN00C3LX TR Transfer	SPC section 7, 8 Package Leaflet New TR Holder: Holland & Barrett Limited, Cedar Drive, Dublin Airport Logistics Park, Saint Margarets, Co Dublin, K67 E0C5, Ireland New TR number: TR23157/012/001	26/02/2021	26/02/2021	Approved