

**IPAR**



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

---

Natures Aid Premeze Agnus Castus hard capsules  
Agnus Castus Fruit

TR0126/312/001  
TR Holder Clonmel Healthcare Ltd

**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 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 Clonmel Healthcare Limited a Certificate of Traditional Use Registration for Natures Aid Premeze Agnus Castus hard capsules, containing powdered Agnus castus fruit.

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 available on the HPRA's website.

## II. QUALITY ASPECTS

This application is for Natures Aid Premeze Agnus Castus hard capsules. The active ingredient of Natures Aid Premeze Agnus Castus hard capsules is obtained from *Vitex agnus-castus* L., fructus (Agnus castus fruit).

### II.1 S.1 Herbal Substance

The herbal substance is *Vitex agnus-castus* L., fructus (Agnus castus fruit), described in the European Pharmacopoeia, and is produced in accordance with the principles of good agricultural and collection practice (GACP).

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

### II.2 S.2 Herbal preparation

The herbal preparation is powdered agnus castus fruit and 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 have 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 suitably qualified manufacturing sites.

The manufacturing process is considered to be sufficiently validated.

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

All ingredients comply with Ph. Eur. The capsule shells 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 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(s) 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 materials comply with Ph. Eur. and/or EU legislation on materials intended 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.

## 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 Natures Aid Premeze Agnus Castus hard capsules.

## III. NON-CLINICAL ASPECTS

The HPRA has been assured that good laboratory practice (GLP) standards were followed in an appropriate manner in the studies conducted.

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. Information presented demonstrating 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.

A GLP compliant Ames test has been submitted which did not reveal a risk of genotoxicity associated with Agnes Castus powder. Carcinogenicity and reproductive toxicity testing has not been conducted.

An environmental risk assessment is not required for herbal medicinal products according to guidance CPMP/SWP/4447/00

## IV. CLINICAL ASPECTS

Natures Aid Premeze Agnus Castus hard capsules is a traditional herbal medicinal product used 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 Natures Aid Premeze Agnus Castus hard 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 Natures Aid Premeze Agnus Castus hard capsules 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.

This traditional herbal medicinal product is contraindicated in patients with hypersensitivity to Agnus Castus fruit or to any of the excipients listed in section 6.1 of the SmPC. It is also contraindicated in patients with a current pituitary disorder or in pregnancy or lactation.

Patients should not exceed the stated dose.

Patients who suffer from or suffered from an oestrogen-sensitive cancer should consult their doctor before using Natures Aid Premeze Agnus Castus Capsules.

Patients who are using dopamine agonists, oestrogens and antioestrogens should consult their doctor before using Natures Aid Premeze Agnus Castus Capsules.

The use in children and adolescents under 18 years of age has not been established due to lack of adequate data.

If the symptoms persist, or worsen during the use of the product, or do not improve after 3 months of using the product, a qualified healthcare professional e.g. a doctor or pharmacist should be consulted.

Vitex agnus-castus fruits are thought to act on the pituitary-hypothalamic axis and therefore patients with a history of a pituitary disorder should consult with a doctor before using this product. In cases of prolactin secreting tumours of the pituitary gland, the intake of Vitex agnus-castus fruits can mask symptoms of the tumour.

Immune system disorders (severe allergic reactions with face swelling, dyspnoea and swallowing difficulties), skin and subcutaneous tissue disorders (allergic skin reactions such as rash and urticaria, acne), nervous system disorders (headache, dizziness), gastrointestinal disorders (nausea, abdominal pain), and reproductive system disorders (menstrual disorders) have been reported.

No studies on the effect on the ability to drive and use machines have been performed.

In the event of an overdose, patients are advised to contact a doctor, pharmacist or healthcare professional.

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 Natures Aid Premeze Agnus Castus hard capsules.

The HPRA, on the basis of the data submitted, considered that Natures Aid Premeze Agnus Castus hard capsules demonstrated adequate evidence of traditional use for the approved indication(s) and no new non-clinical or clinical safety concerns have been identified.

A Certificate of Traditional Use Registration for Natures Aid Premeze Agnus Castus hard capsules is granted.

## **VI. REVISION DATE**