PREMHERB FILM-COATED TABLETS

THR 23056/0002

UKPAR

TABLE OF CONTENTS

PREMHERB FILM-COATED TABLETS

THR 23056/0002

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted M H Pharma (UK) Ltd a Traditional Herbal Registration Certificate for the traditional herbal medicinal product PremHerb Film-coated Tablets (Traditional Herbal Registration number: 23056/0002). This product is available without prescription and can be bought from pharmacies and other outlets.

PremHerb Film-coated Tablets are used for the relief of premenstral symptoms. The tablets' active ingredient comes from the fruit of the plant *Vitex agnus castus L.*, also known as the chaste tree. This registration is based exclusively upon evidence of traditional use of Agnus castus fruit as a herbal medicine and not upon data generated from clinical trials. There is no requirement under the Traditional Herbal Registration scheme to prove scientifically that the product works.

No new or unexpected safety concerns arose from this application and it was, therefore, decided that a Traditional Herbal Registration Certificate could be granted.

PREMHERB FILM-COATED TABLETS

THR 23056/0002

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

INTRODUCTION

The MHRA granted a Traditional Herbal Registration Certificate for the traditional herbal remedy PremHerb Film-coated Tablets to M H Pharma (UK) Ltd, trading as Medic Herb, on 16 October 2007. This product is on the general sales list (GSL).

The application was submitted under Article 16.c of Directive 2001/83 EC, as amended, as part of the Traditional Herbal Medicines Registration Scheme.

This product consists of film-coated tablets containing 4 mg of Agnus castus fruit extract. The product is used for the relief of premenstral symptoms.

This THR is based exclusively on evidence of traditional use of Agnus castus fruit. The recommended dose is one tablet daily.

The data supplied by the applicant demonstrate 30 years of traditional use of Agnus castus fruit in the European Community. A satisfactory review of the available safety data on Agnus castus fruit has also been provided, together with an expert safety report supporting the proposed product.

PHARMACEUTICAL ASSESSMENT REPORT

HERBAL SUBSTANCE

Manufacture

The herbal substance is the fruit of the plant, *Vitex agnus castus* L., which belongs to the Verbenaceae family. This plant is indigenous to the whole of the Mediterranean region as far as Western Asia. The fruit is collected from the wild, mainly from Morocco.

Ripe fruits are collected manually from August to September and dried under natural conditions before being stored protected from light.

The information provided on the collection of the plant starting material is considered to be acceptable and assurance has been given that cultivation and harvesting are performed according to Good Agricultural and Collection Practice (GACP).

Characterisation

The fruits are globular to oblong 4-seeded drupes, black-brown to olive-black, with a diameter of 3 – 5 mm. The fruit is surrounded two-thirds to three-quarters in a cup-like fashion by the greenish-grey fine-tomentose calyx. The calyx ends up in 4 – 5 short three-cornered teeth. Some of the fruits still have the fruit stalk, which is about 1 mm long. The fruit is quadrilocular and each loculus contains an oblong adipose seed. The fruits have an aromatic sage-like odour and a sharp pepper-like taste.

Control of Herbal Substance

The starting material is stated to comply with the monograph "Agnus-castus-Früchte" DAC (Deutscher Arzneimittel-Codex i.e. the German Pharmaceutical Codex, a supplementary pharmacopoeia to the European and German Pharmacopoeia). The DAC specifications are comparable to the Pharmaeuropa monograph.

There is now a monograph for Agnus castus fruit in the Ph Eur (5^{th} Edition) and all future batches of herbal substance will be tested to this monograph.

Satisfactory certificates of analysis for the herbal substance have been provided.

HERBAL PREPARATION

General information

Herbal preparation: chaste tree fruits dry extract
Scientific name of the plant: *Vitex agnus-castus* L.
Synonyms of the herbal substance: *Agnus-castus vulgaris* Carr., *Vitex verticillata* Lam., chaste tree, hemp tree, wild lavender, monk's pepper tree, keuschlamm or mönchspfeffer.
Parts of the plant used: dried fruits
Name of the herbal substance: chaste tree fruits (*Agni casti fructus*)
Ratio of the herbal substance to the herbal preparation (native): 7 - 13:1
Extraction solvent: ethanol 60 % (m/m)

The dry extract preparation is a pale brown, flowable powder with a characteristic aromatic odour and slightly bitter taste. It consists of 10 % native extract and 90 % liquid glucose (dry substance). The particle size of the dry extract is at least 80 % < 0.1 mm.

Manufacture

Description of Manufacturing Process and Process Controls

A satisfactory description of the manufacturing process and flow diagram have been provided.

Control of Materials

Certificates of analysis for all materials used in the manufacture of the herbal preparation are provided. Excipients described in a pharmacopeia are tested and released according to their Ph. Eur. monograph. The excipient water is tested according to the manufacturer's monograph, which is satisfactory.

Controls of Critical Steps and Intermediates

There are no critical steps identified as the manufacture of the herbal preparation is considered to be a standard procedure.

Process Validation and/or Evaluation

The applicant has provided a satisfactory process validation report for batches of herbal preparation.

Control of Herbal Preparation

Specification

A satisfactory specification with appropriate tests and limits has been provided for the herbal preparation

Analytical Procedures

Satisfactory analytical procedures are used to control the herbal preparation.

Validation of Analytical Procedures

All analytical procedures have been appropriately validated.

Batch Analyses

Certificates of analysis (CoA) have been provided for production batches of the herbal preparation, demonstrating satisfactory compliance with the proposed specification.

Justification of Specification

The proposed specification has been justified satisfactorily.

Container Closure System

Satisfactory specifications have been provided by the supplier, together with the declaration of compliance with Directive 90/128 EC, as amended. The primary packaging materials also comply with Directive 2002/72/EC, relating to foodstuffs.

Stability

Batches were packed in the final container closure system and stored under ICH real time, and accelerated conditions. The data support the proposed retest period of 24 months. Based on the results, no specific declaration of storage is applicable, although it is recommended that the dry extract is stored protected from light, heat and moisture. This is acceptable.

HERBAL PRODUCT

Description and Composition of the Herbal Product

Qualitative composition of the product

Component	Ref standard	Function
Drug substance Dry extract of Chaste tree fruits (7 - 13:1) Extraction solvent: ethanol 60 % (m/m) *, **		
Other constituents **Tablet core:** Liquid glucose (dry substance) Silica, colloidal anhydrous Lactose monohydrate Magnesium stearate Maize starch Cellulose, microcrystalline Sodium starch glycolate (type A)	 Ph Eur Ph Eur Ph Eur Ph Eur Ph Eur Ph Eur Ph Eur	 for extract manufacture;desiccant increases flowability, anti-adhesive binding agent "outer" lubricant disintegrant binding agent for tabletting disintegrant
Film coating: Lactose monohydrate Hydroxypropylmethylcellulose Macrogol 4000 Titanium dioxide E 171 Iron (III)-oxide E 172 (= red iron oxide)	 Ph Eur Ph Eur Ph Eur Ph Eur HSE	 binding agent binding agent for film coating for spray solution manufacture colouring agent colouring agent
Purified water*, **		

* The water used for the manufacture of the extraction solvent corresponds to the monograph

** Not contained in the drug product.

Manufacture

Description of Manufacturing Process and Process Controls

Manufacture of the herbal product is by the standard direct tabletting method. The components for the tablet mixture are weighed and sieved before being mixed homogenously in a mixing barrel. The mixed tablet mass is then pressed to form tablet cores on a rotary pelleting machine before being coated. The film-coated tablets are then sealed into mono blisters. The blisters are packaged into folding cartons and equipped with the package leaflet.

A satisfactory flow diagram outlining the various stages of the manufacturing process and the in-process controls is provided.

Control of Critical Steps and Intermediates

A number of in-process control tests are performed during the manufacturing process. All are considered adequate.

Process Validation and/or Evaluation

Process validation results show that the production process provides a reproducible product of satisfactory quality and consistency. All results were within the release specification.

Control of Excipients

All the excipients and analytical procedures are as specified by the pharmacopoeia monographs. The colouring agents, titanium dioxide E 171 and iron (III) oxide E 172, comply with Directive

2001/50/EC (amending Directive 95/45/EC) and, in the case of titanium dioxide, the Ph. Eur. monograph.

Certificates of analysis of the excipients have been provided by the suppliers. The only excipients not described in a pharmacopoeia are iron (III) oxide E 172 and water used in the manufacture of the herbal extract. The Certificates of analysis for the iron (III) oxide E 172 and water confirm that these excipients are of satisfactory quality.

Excipients of Human or Animal Origin
A satisfactory declaration has been provided by the supplier of lactose monohydrate that this excipient is sourced from healthy animals suitable for human consumption. The applicant confirms that the magnesium stearate used is of vegetable origin.

Control of Herbal Product
Specification
The finished product specifications at release and end of shelf life are detailed and the tests and limits used were found to be satisfactory for a product of this nature.

Analytical Procedures / Validation of Analytical Procedures
Satisfactory details have been provided on all analytical procedures and these analytical procedures are valid.

Batch Analyses
Certificates of Analysis have been presented for batches of the drug product demonstrating little inter-batch variation.

Characterisation of Impurities
No toxic degradation products are known to come from this herbal preparation.

Reference Standards or Materials
Certificates of Analysis for all the markers, including the reference substance, have been provided by the finished product manufacturer.

Container Closure System
The film-coated tablets are sealed into polypropylene mono blisters. Specifications have been provided by the suppliers. The components of the primary packaging system, including the sealing layer, comply with Directive 2002/72 relating to contact with foodstuffs.

Stability
Stability studies were conducted under ICH conditions (longterm and accelerated) on product batches in the container type proposed for marketing.

Based on the results a proposed shelf life of 3 years with no special storage conditions is justified.

PRODUCT LITERATURE

The product literature (Summary of Product Characteristics, Patient Information Leaflet and labelling) for this product are pharmaceutically satisfactory.

A package leaflet has been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC. The

results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

ASSESSOR'S OVERALL CONCLUSIONS ON QUALITY

This product is satisfactory and a Traditional Herbal Registration can be granted.

NON-CLINICAL ASSESSMENT

NONCLINICAL ASPECTS

The Expert Safety Report submitted by the applicant lists relevant references to published work studying the toxicology of Agnus castus fruit.

NONCLINCIAL OVERVIEW

The applicant has submitted a good literature review with this application. An Expert Report on Safety was provided which included reviews of some non-clinical data. The Expert Safety Report was written by a pharmacist with expertise in herbal medicines, and is dated 28 December 2005.

The overview submitted in support of this application is satisfactory.

Due to a shortage of published data on Agnus castus fruit, it is not possible to assess if the safety package for the phytochemical constituents of Agnus castus fruit is acceptable to the standards of today's GLP and safety testing requirements. However, the information supplied demonstrating traditional use is acceptable and thus the lack of provision of a complete standard safety package may be acceptable and in compliance with guideline EMEA/HMPC/32116/05.

Data in the literature for genotoxic and carcinogenic potential of the product is still deficient as basic genotoxicity tests have not been conducted. The company have provided their assurance that they will address this lack of data before renewal of their licence.

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

The SPC for this product is satisfactory.

ENVIRONMENTAL RISK ASSESSMENT

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

CONCLUSION

The information supplied demonstrating traditional use of Agnus castus fruit is acceptable. An adequate literature review of Agnus castus fruit has been carried out by the applicant and no new non-clinical data was submitted for assessment with this application. Granting of a THR is acceptable.

CLINICAL ASSESSMENT REPORT

PROPOSED INDICATION

The applicant has submitted the following therapeutic indication:

"A traditional herbal medicinal product that has been used to help relieve the symptoms associated with premenstrual syndrome, based on traditional use only."

It is to be noted that the recommended dose of the product under application is one tablet per day (each tablet contains 4mg of extract) containing the equivalent of 40mg of dried herb per tablet.

POSOLOGY AND METHOD OF ADMINISTRATION

The Applicant has submitted the following:

"For oral use only.
For women experiencing premenstrual symptoms, take 1 tablet daily. Tablets should be taken at the same time of day if possible (morning or evening) and swallowed whole with plenty of liquid. Some individuals may need to take PremHerb for up to 3 months for maximum benefit to occur.
Women suffering from a current pituitary disorder should not take PremHerb.
Not for children and adolescents under 18 years."

EFFICACY

No clinical efficacy data is required for registration of Traditional Herbal Medicinal Products (THMP).

EVIDENCE OF TRADITIONAL USE

Agnus castus fruit is generally accepted to have a tradition of use as an herbal medicine.

Article 16 c 1 (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.

Information has been provided in support of the medicinal use of Agnus castus fruit. within the EU for a period exceeding 30 years.

One Agnus castus fruit product has been licensed in the UK since November 1994. Prior to this the same product is stated to have been marketed under the automatic Product Licence of Rights since April 1973. The product is indicated as a traditional herbal remedy to help restore normal fluid balance and relieve occasional bloating in women.

The applicant has also provided a literature review demonstrating the use of Agnus castus fruit in Germany for more than 30 years. The indications listed included hypermenorrhoea, menstrual disorders due to corpus luteum insufficientcy, premenstrual syndrome and deficient milk secretion.

The applicant has also provided information from a survey of 280 registered medical herbalists carried out in 1997 to estimate the traditional medicinal use of Agnus castus fruit. Ninty-four per cent of the 153 respondents indicated that they used the extracts to treat their patients for premenstrual symptoms. The preparations used included tincture, fluid extract, solid and powdered extracts.

Assessor's Comments
There is sufficient evidence of traditional use of Agnus castus fruit for a period of at least 30 years, including evidence for the treatment of symptoms associated with premenstrual syndrome at the same dose. Therefore a traditional herbal registration can be granted for this indication.

SAFETY REVIEW

Article 16 c 1 (d) requires the applicant to provide a bibliography of the safety data together with an expert report.

A safety review has been provided, as well as an expert report written by a pharmacist with expertise in herbal medicines. His CV has been included.

The Clinical Review of Safety submitted in the dossier outlined adverse events from controlled, and uncontrolled studies and spontaneous reports relevant to the safety Agnus castus fruit.

Assessor's Comments
The Safety Review is comprehensive and reveals the main safety issues associated with treatment with Agnus castus fruit; the adverse effects appear to be mild and self-limiting, and include gastro-intestinal disturbances, acne, menstrual disorders, pruritis and rashes. There is a theoretical risk of an interaction with other medicinal products that contain hormones. As the herb may have an effect on pituitary function, the product should not be used by women with a previous history of pituitary disorders (such as prolactinoma).

SUMMARY OF PRODUCT CHARACTERISTICS

The SPC for this product is satisfactory.

PATIENT INFORMATION LEAFLET

The PIL for this product is satisfactory.

LABELLING

All labelling is satisfactory.

ASSESSMENT OF SUITABILITY FOR GENERAL SALES LIST (GSL) STATUS

Section 51 of the Medicines Act 1968 states that "GSL may be appropriate for medicines which can, with reasonable safety, be sold or supplied otherwise than by or under the supervision of a pharmacist". The term "reasonable safety" may usefully be defined as "Where the hazard to health

and the risk of misuse and the need for special precautions in handling are small, and where wider sale would be a convenience to the purchaser".

1. Hazard to health: there appears to be a minimal risk of hazard to health.
2. Risk of misuse: in essence the risk of misuse of this product is felt to be low.
3. Need to take special precautions in handling: none needed
4. Wider sales are convenient to the purchaser

In summary, it is considered that the four criteria for GSL status have been met and this product should have a GSL status.

DISCUSSION

This is an application for registration under the Traditional Herbal Medicinal Products Directive. The data supplied by the Applicant are sufficient to demonstrate 30 years of traditional use within the European Community. A satisfactory review of the available safety data relating to Agnus castus fruit has been provided.

RECOMMENDATIONS

A Traditional Registration may be granted.

OVERALL CONCLUSION AND RISK ASSESSMENT

QUALITY

The quality data submitted with this application are satisfactory.

PRECLINICAL

No new preclinical data were submitted and none are required for an application of this type.

EFFICACY AND SAFETY

No clinical efficacy data are required for registration of Traditional Herbal Medicinal Products (THMP).

The Applicant has provided a bibliographic review which shows ample evidence for the use of Agnus castus fruit within the EU for a period exceeding 30 years.

A satisfactory review of the safety data has been provided.

The SPC, PIL and labelling are satisfactory.

RISK ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified.

PREMHERB FILM-COATED TABLETS

THR 23056/0002

STEPS TAKEN FOR ASSESSMENT

1	The MHRA received the Traditional Herbal Registration application on 20 January 2006
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 10 April 2006
3	Following assessment of the application the MHRA requested further information relating to the quality dossier on 17 July 2006, the clinical dossier on 16 May 2007 and the preclinical dossier on 15 June 2007. The applicant responded to the MHRA's requests, providing further information on the quality dossier on 6 September 2006, the clinical dossier on 25 May 2007 and the preclinical dossier on 11 July 2007
4	Following assessment of the response the MHRA requested further information relating to the quality dossier on 6 August 2007 and the clinical dossier on 15 August 2007. The applicant responded to the MHRA's requests, providing further information on the quality dossier and clinical dossiers on 30 August 2007
5	A THR was granted on 16 October 2007

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

PremHerb Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains: 4.0 mg of extract (as dry extract) from Agnus castus fruit (*Vitex agnus castus* L.) (7-13:1)(equivalent to 28-52 mg of Agnus castus).
Extraction solvent: Ethanol 60% m/m.
Excipients: 1 film-coated tablet contains 124 mg of lactose monohydrate and 36 mg of liquid glucose.
For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film-coated tablet.
Salmon pink, round, convex, scored tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

A traditional herbal medicinal product that has been used to help relieve the symptoms associated with premenstrual syndrome, based on traditional use only.

4.2 Posology and method of administration

For oral use only.
For women experiencing premenstrual symptoms, take 1 tablet daily. Tablets should be taken at the same time of day if possible (morning or evening) and swallowed whole with plenty of liquid. Some individuals may need to take PremHerb for up to 3 months for maximum benefit to occur.
Women suffering from a current pituitary disorder should not take PremHerb.
Not for children and adolescents under 18 years.

4.3 Contraindications

Hypersensitivity to dry extract of Agnus castus fruit, or any of the other ingredients in the drug.
This product is not recommended for use in children, adolescents under 18 years or for patients with a current pituitary disorder.

4.4 Special warnings and precautions for use

Agnus castus is 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.
This product contains glucose:
1 film-coated tablet contains max. 36 mg
This product contains lactose:
1 film-coated tablet contains max. 124 mg lactose.
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

There are no published data available on drug interactions with extracts of Agnus castus.

Animal experiments have shown that that the drug has a dopaminergic effect and so, theoretically, there could be a reduction in the effectiveness of dopamine-receptor antagonists, and/or a potentiation of dopamine-receptor agonists.

4.6 Pregnancy and lactation

The safety of the product during pregnancy and lactation has not been established, therefore it should be avoided during pregnancy or while breastfeeding. Additionally, because of the potential for the product to have hormone-like actions the product should also be avoided by women who are trying to become pregnant.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Mild and reversible, transient side-effects are associated with Agnus castus use. Postmarketing surveillance studies suggest that the approximate incidence of adverse effects is between 1.9 - 5 %. Most frequently these are:

- Nausea
- Stomach disturbances
- Headache
- Diarrhoea
- Allergic skin reactions.

If there are signs of an allergic reaction the product should be withdrawn.

4.9 Overdose

In the event of an overdose, patients are advised to contact a doctor, pharmacist or healthcare professional. A small overdose (up to 8 tablets) may not cause any symptoms. In the event of a large overdose (more than 8 tablets), advice should be sought from a doctor. Management of an overdose should include appropriate symptomatic and supportive treatment as warranted by the clinical situation.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

No pharmacodynamic studies have been undertaken with Premherb and the pharmacodynamic properties are unknown.

5.2 Pharmacokinetic properties

Pharmacokinetic studies have not been conducted with Premherb or its active constituents.

5.3 Preclinical safety data

The non-clinical toxicology data available are limited. Tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Liquid glucose (dry substance**)**
Silica, colloidal anhydrous
Lactose monohydrate
Magnesium stearate

Maize starch
Cellulose, microcrystalline
Sodium starch glycolate (Type A)
Film coating:
Lactose monohydrate
Hypromellose
Macrogol 4000
Titanium dioxide E171
Iron(III)-oxide E172 (==red iron oxide)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The shelf life is 3 years

6.4 Special precautions for storage

This product does not require any special storage instructions

6.5 Nature and contents of container

Original packages containing 30 or 60 film-coated tablets
PremHerb® film-coated tablets are packed in PVC/ PVDC aluminium blisters and inserted into a carton.

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

M H Pharma (UK) Ltd
T/a Medic Herb
PO Box 2835
Brewery Courtyard
Draymans Lane
Marlow
Buckinghamshire
SL7 2XG

8 MARKETING AUTHORISATION NUMBER(S)

THR 23056/0002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

16/10/2007

10 DATE OF REVISION OF THE TEXT

16/10/2007

PATIENT INFORMATION LEAFLET

Patient Information Leaflet

PremHerb® film-coated tablets

MedicHerb

Agnus castus fruit extract 4mg

Please read this leaflet carefully before you start taking these tablets.
It contains some important information about PremHerb®.

Keep this leaflet with the tablets.
You may want to read it again or show it to your doctor, pharmacist or healthcare practitioner.

What is in this leaflet

1: What this product is and what it is used for

This product is a traditional herbal medicinal product containing Agnus castus fruit. Each film-coated tablet contains 4mg of extract (as dry extract) from Agnus castus fruit (*Vitex agnus castus L.*) (7-13:1) (equivalent to 28-52mg of Agnus castus). Extraction solvent: Ethanol 60% v|v.

PremHerb is a traditional herbal medicinal product used to help relieve the symptoms associated with premenstrual syndrome. This usage is based on traditional use only.

2: Before you take this product

DO NOT TAKE this product if you are:
- **lactose-intolerant** (react badly to lactose or milk)
- **pregnant** or **trying to become pregnant**
- **breastfeeding**
- **allergic to any of the ingredients** (see section 6)
- **suffering from a pituitary disorder**
- **under 18 years of age**

Tell your doctor before taking this product if you have:
- **an intolerance to some sugars** (see section 6)
- **had a pituitary disorder in the past**

If you are taking a dopamine-receptor antagonist or agonist-type drug, there is a theoretical risk that this product may affect the way they work.

3: How to take this product

For women experiencing premenstrual symptoms
Take 1 tablet daily.
Try to take the tablets at the same time each day, either in the morning or evening. Swallow the tablets whole with some water or other liquid. Do not chew the tablets. You can take the tablets with or without food. The maximum beneficial effect of this product may take up to 3 months to develop in some women.

Do not exceed the stated dose.
Do not give to children or adolescents under 18 years old.

If you take too much of this product (overdose)
If you take more than the recommended dose, speak to a doctor, pharmacist or healthcare practitioner and take this leaflet with you. A small overdose (up to 8 tablets) may not cause any symptoms. In the event of a large overdose (more than 8 tablets) advice should be sought from a doctor.

If you forget to take this product
Continue to take your usual dose at the usual time, it does not matter if you have missed a dose.

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If you have any questions, or are unsure about anything, please ask your doctor, pharmacist or healthcare practitioner.

4: Side-effects

Like all medicines this product can have side-effects. Any side-effects are usually mild and disappear in a few days. Side-effects that have been reported are listed below:

Side-effects	
• **nausea** or feeling sick • **indigestion** • **digestive upsets** such as wind, bloating or diarrhoea • **headache**	If these persist for more than a few days, or become troublesome, stop taking this product. These common side-effects are often only temporary.
• **allergic skin reactions** itching and/or rash of the skin	Stop taking this product immediately if you experience any allergic skin reaction.
Other side-effects	
Tell your doctor or pharmacist if you notice any other side-effect.	

5: After taking this product

Do not use your tablets after the expiry date.
Return any out-of-date tablets to your pharmacist who will dispose of them for you. The expiry date is printed on the box and the blister pack.

This medicinal product does not require any special storage conditions.

Keep the tablets out of the reach and sight of children.

Keep your tablets in the blister pack until it is time to take them.

6: Product description

Each film-coated tablet contains 4mg of extract (as dry extract) from Agnus castus fruit (*Vitex agnus castus L.*) (7-13:1) (equivalent to 28-52mg of Agnus castus). Extraction solvent: Ethanol 60% v|v.

This product also contains the following ingredients:
Tablet core: Liquid glucose, silica colloidal anhydrous, lactose monohydrate, magnesium stearate, maize starch, cellulose microcrystalline, sodium starch glycolate (type A).

Film-coating: lactose monohydrate, hypromellose, macrogol 4000, titanium dioxide (E 171), iron (III)-oxide (E 172).

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this product. Each film-coated tablet contains 124mg of lactose and 36mg of liquid glucose.

Each pack contains 30 or 60 film-coated tablets.

Registration holder for this product
M H Pharma (UK) Ltd, t/a MedicHerb, PO Box 2835,
Brewery Courtyard, Draymans Lane,
Marlow, Bucks SL7 2XG

Manufacturer of this product
Wiewelhove GmbH, Gildestrasse 39, 49477 Ibbenbüren, Germany

Traditional herbal registration number: THR 23056/0002

If you would like further information about this product, please contact:
M H Pharma (UK) Ltd, PO Box 2835, Marlow, Bucks SL7 2XG

Telephone: 01628 488487
Email: info@medicherb.co.uk

This leaflet was prepared in May 2007

For a large print, Braille or audio version of this leaflet, call 01628 488487

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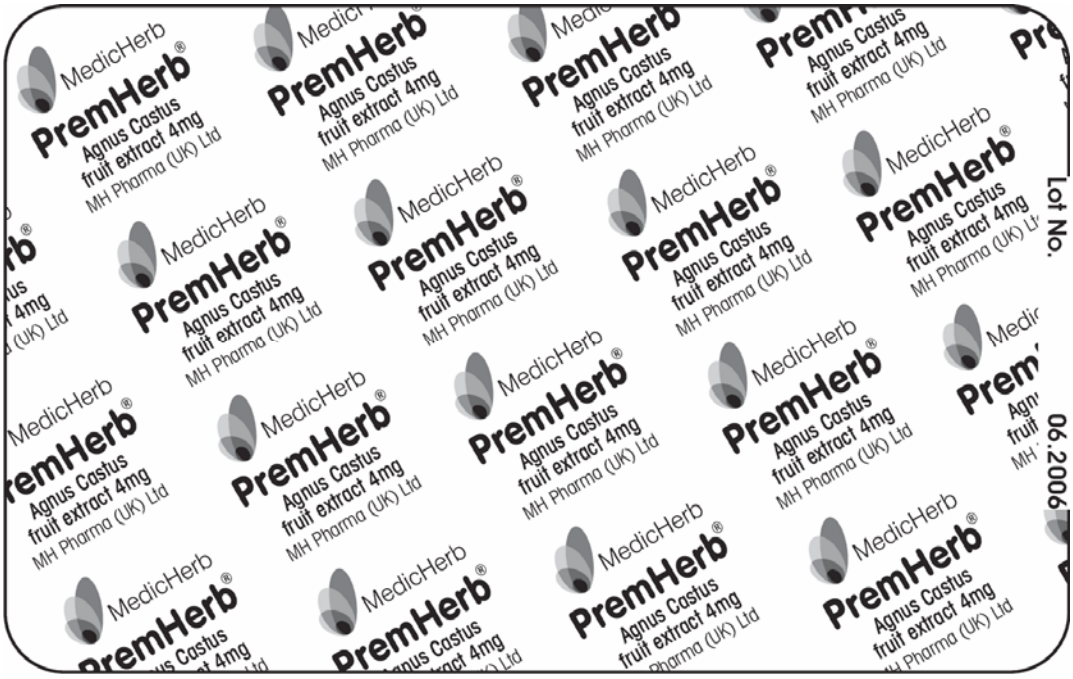
LABELLING

Blister foil:



Carton:


MedicHerb
PremHerb® 30 tablets
NEW
MedicHerb
PremHerb®
film-coated tablets
Agnus castus fruit extract 4mg
A traditional herbal medicinal product used to help relieve symptoms associated with
premenstrual syndrome
based on traditional use only
30 tablets
MedicHerb
PremHerb®
30 tablets
NEW
MedicHerb
PremHerb®
A traditional herbal medicinal product used to help relieve symptoms associated with premenstrual syndrome, based on traditional use only.
Active ingredients: Each PremHerb® tablet contains 4mg of extract (as dry extract) from Agnus castus fruit (Vitex agnus castus L.) (7-13:1) (equivalent to 28-52mg of Agnus castus). Extraction solvent ethanol 60% v/v.
This product contains lactose monohydrate and liquid glucose.
Dosage: For oral use. For women experiencing premenstrual symptoms, take one tablet daily. The tablets should be taken at the same time of day if possible (morning or evening). Swallow the tablet whole with some water or other liquid.
Warning: Do not exceed the stated dose
Do not use if you are:
allergic to any of the ingredients
pregnant or trying to become pregnant
breastfeeding
under 18
suffering from a pituitary disorder
Please read the enclosed information leaflet before taking these tablets. Keep out of sight and reach of children.
Store in the original packaging THR 23056/0002
This medicinal product does not require any special storage conditions
Expiry date: see base
Manufactured in Germany
THR holder: M H Pharma (UK) Ltd (trading as MediceHerb)
PO Box 2835, Marlow, Bucks SL7 2XG
Telephone: 01628 488487 Email: info@medicherb.co.uk
30 tablets PremHerb® MedicHerb
30 tablets PremHerb® MedicHerb
Batch No:
Expiry date:
5 060067 790110

Carton with Braille: