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EMA/HMPC/606742/2017
Committee on Herbal Medicinal Products (HMPC)

European Union herbal monograph on *Vitex agnus-castus* L., fructus

Final

Initial assessment	
Discussion in Working Party on European Union monographs and list (MLWP)	March 2009 May 2009 July 2009 September 2009
Adoption by Committee on Herbal Medicinal Products (HMPC) for release for consultation	17 September 2009
End of consultation (deadline for comments)	15 February 2010
Re-discussion in MLWP	May 2010 July 2010 September 2010 November 2010
Adoption by HMPC Monograph (EMA/HMPC/144006/2009) AR (EMA/HMPC/144003/2009) List of references (EMA/HMPC/144004/2009) Overview of comments received during public consultation (EMA/HMPC/278781/2010) HMPC Opinion (EMA/HMPC/756507/2010)	25 November 2010
First systematic review	
Discussion in MLWP	September 2017 November 2017 January 2018
Adoption by HMPC	27 March 2018

Keywords	Herbal medicinal products; HMPC; European Union herbal monographs; well-established medicinal use; traditional use; <i>Vitex agnus-castus</i> L., fructus; Agni casti fructus; agnus castus fruit
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BG (bългарski): Аврамово дърво, плод	LT (lietuvių kalba): Tikrųjų skaistminių vaisiai
CS (čeština): drmkový plod	LV (latviešu valoda): Viteksa augļi
DA (dansk): Kyskhedstræfrugt	MT (malti): frotta tas-Sigret il-Virgi
DE (Deutsch): Mönchspfefferfrüchte	NL (nederlands): Monnikspeper, Kuisboom
EL (elliniká): καρπός λυγαριάς	PL (polski): Owoc niepokalanka zwyczajnego
EN (English): agnus castus fruit	PT (português): anho-casto, fruto
ES (español): sauzgatillo, fruto de	RO (română): fruct de scai de tufă mare
ET (eesti keel): mungapipravili	SK (slovenčina): plod vitexu jahňacieho
FI (suomi): siveydenpuu, hedelmä	SL (slovenščina): plod navadne konopljike
FR (français): gattilier (fruit de)	SV (svenska): munkpeppar, frukt
HR (hrvatski): konopljikin plod	IS (íslenska):
HU (magyar): barátcserje termés	NO (norsk): agnocastofrukt
IT (italiano): Agnocasto frutto	

European Union herbal monograph on *Vitex agnus-castus* L., fructus

1. Name of the medicinal product

To be specified for the individual finished product.

2. Qualitative and quantitative composition^{1, 2}

Well-established use	Traditional use
<p>With regard to the marketing authorisation application of Article 10(a) of Directive 2001/83/EC</p> <p><i>Vitex agnus-castus</i> L., fructus (agnus castus fruit)</p> <p>i) Herbal substance</p> <p>Not applicable</p> <p>ii) Herbal preparations</p> <p>Dry extract (DER 6-12:1), extraction solvent ethanol 60% m/m</p>	<p>With regard to the registration application of Article 16d(1) of Directive 2001/83/EC</p> <p><i>Vitex agnus-castus</i> L., fructus (agnus castus fruit)</p> <p>i) Herbal substance</p> <p>Not applicable</p> <p>ii) Herbal preparations</p> <p>a) Powdered herbal substance</p> <p>b) Tincture (ratio of herbal substance to extraction solvent 1:5), extraction solvent ethanol 68-70% V/V</p> <p>c) Dry extract (DER 7-13:1), extraction solvent ethanol 60% m/m</p> <p>d) Dry extract (DER 10.0-18.5:1), extraction solvent ethanol 50-52% m/m</p>

3. Pharmaceutical form

Well-established use	Traditional use
<p>Herbal preparation in solid dosage form for oral use.</p> <p>The pharmaceutical form should be described by the European Pharmacopoeia full standard term.</p>	<p>Herbal preparation in solid or liquid dosage forms for oral use.</p> <p>The pharmaceutical form should be described by the European Pharmacopoeia full standard term.</p>

¹ The declaration of the active substance(s) for an individual finished product should be in accordance with relevant herbal quality guidance.

² The material complies with the Ph. Eur. monograph (ref.: 01/2015: 2147)

4. Clinical particulars

4.1. Therapeutic indications

Well-established use	Traditional use
Herbal medicinal product for the treatment of premenstrual syndrome	Traditional herbal medicinal product for the relief of minor symptoms in the days before menstruation (premenstrual syndrome) The product is a traditional herbal medicinal product for use in the specified indication exclusively based upon long-standing use.

4.2. Posology and method of administration

Well-established use	Traditional use
<p>Posology</p> <p><i>Female adults</i></p> <p>Daily dose:</p> <p>Once daily 20 mg dry extract</p> <p>There is no relevant indication in prepubertal children.</p> <p>The use in pubertal children and adolescents under 18 years of age is not recommended due to lack of adequate data (see section 4.4).</p> <p>Duration of use</p> <p>To achieve an optimal treatment effect, continued use over three months is recommended.</p> <p>If the symptoms persist after a continued use over three months, a doctor should be consulted.</p> <p>Method of administration</p> <p>Oral use</p>	<p>Posology</p> <p><i>Female adults</i></p> <p>Herbal preparation a)</p> <p>Single dose: 400 mg 2 times daily</p> <p>Daily dose: 800mg</p> <p>Herbal preparation b)</p> <p>Single dose: 165 mg once daily</p> <p>Daily dose: 165 mg</p> <p>Herbal preparation c)</p> <p>Single dose: 4 mg once daily</p> <p>Daily dose: 4 mg</p> <p>Herbal preparation d)</p> <p>Single dose: 2-3 mg once daily</p> <p>Daily dose: 2-3 mg</p> <p>There is no relevant indication in prepubertal children.</p> <p>The use in pubertal children and adolescents under 18 years of age is not recommended due to lack of adequate data (see section 4.4).</p> <p>Duration of use</p> <p>If the symptoms persist after a continued use over three months, a doctor or a qualified health care practitioner should be consulted.</p>

Well-established use	Traditional use
	Method of administration Oral use

4.3. Contraindications

Well-established use	Traditional use
Hypersensitivity to the active substance.	Hypersensitivity to the active substance.

4.4. Special warnings and precautions for use

Well-established use	Traditional use
<p>Patients who suffer or suffered from an oestrogen-sensitive cancer should consult their doctor before using agnus castus fruit.</p> <p>Patients who are using dopamine agonists, dopamine antagonists, oestrogens and antioestrogens should consult their doctor before using agnus castus fruit (see section 4.5).</p> <p>The use in children and adolescents under 18 years of age has not been established due to lack of adequate data.</p> <p>If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.</p> <p>Agnus castus fruit is thought to act on the pituitary-hypothalamic axis and therefore patients with a history of a pituitary disorder should consult a doctor before use.</p> <p>In cases of prolactin secreting tumours of the pituitary gland the intake of agnus castus fruit can mask symptoms of the tumour.</p>	<p>Patients who suffer or suffered from an oestrogen-sensitive cancer should consult their doctor before using agnus castus fruit.</p> <p>Patients who are using dopamine agonists, dopamine antagonists, oestrogens and antioestrogens should consult their doctor before using agnus castus fruit (see section 4.5).</p> <p>The use in children and adolescents under 18 years of age has not been established due to lack of adequate data.</p> <p>If the symptoms worsen during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.</p> <p>Agnus castus fruit is thought to act on the pituitary-hypothalamic axis and therefore patients with a history of a pituitary disorder should consult a doctor before use.</p> <p>In cases of prolactin secreting tumours of the pituitary gland the intake of agnus castus fruit can mask symptoms of the tumour.</p> <p>For tinctures containing ethanol, the appropriate labelling for ethanol, taken from the 'Guideline on excipients in the label and package leaflet of medicinal products for human use', must be included.</p>

4.5. Interactions with other medicinal products and other forms of interaction

Well-established use	Traditional use
<p>None reported</p> <p>Because of the possible dopaminergic and oestrogenic effects of agnus castus fruit interactions with dopamine agonists, dopamine antagonists, oestrogens and antioestrogens cannot be excluded.</p>	<p>None reported</p> <p>Because of the possible dopaminergic and oestrogenic effects of agnus castus fruit interactions with dopamine agonists, dopamine antagonists, oestrogens and antioestrogens cannot be excluded.</p>

4.6. Fertility, pregnancy and lactation

Well-established use	Traditional use
<p>There is no indication for the use during pregnancy.</p> <p><i>Pregnancy</i></p> <p>There are no data from the use of agnus castus fruit in pregnant women available. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3). The use is not recommended during pregnancy.</p> <p><i>Lactation</i></p> <p>It is unknown whether agnus castus fruit or its metabolites are excreted in human milk. Data from reproductive studies suggest that agnus castus fruit may affect lactation. A risk to the suckling child cannot be excluded. The use during lactation is not recommended.</p> <p><i>Fertility</i></p> <p>No fertility data are available.</p>	<p>There is no indication for the use during pregnancy.</p> <p><i>Pregnancy</i></p> <p>There are no data from the use of agnus castus fruit in pregnant women available. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3). The use is not recommended during pregnancy.</p> <p><i>Lactation</i></p> <p>It is unknown whether agnus castus fruit or its metabolites are excreted in human milk. Data from reproductive studies suggest that agnus castus fruit may affect lactation. A risk to the suckling child cannot be excluded. The use during lactation is not recommended.</p> <p><i>Fertility</i></p> <p>No fertility data are available.</p>

4.7. Effects on ability to drive and use machines

Well-established use	Traditional use
<p>No studies on the effect on the ability to drive and use machines have been performed.</p>	<p>No studies on the effect on the ability to drive and use machines have been performed.</p>

4.8. Undesirable effects

Well-established use	Traditional use
<p>Immune system disorders (severe allergic reactions with face swelling, dyspnoea and</p>	<p>Immune system disorders (severe allergic reactions with face swelling, dyspnoea and</p>

Well-established use	Traditional use
<p>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.</p> <p>The frequency is not known.</p> <p>If other adverse reactions not mentioned above occur, a doctor or a pharmacist should be consulted.</p>	<p>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.</p> <p>The frequency is not known.</p> <p>If other adverse reactions not mentioned above occur, a doctor or a pharmacist should be consulted.</p>

4.9. Overdose

Well-established use	Traditional use
No case of overdose has been reported.	No case of overdose has been reported.

5. Pharmacological properties

5.1. Pharmacodynamic properties

Well-established use	Traditional use
<p>Pharmacotherapeutic group: Other gynaecologicals</p> <p>Proposed ATC code: G02CX03</p> <p>The mode of action is not known.</p> <p>Inhibitory influences on prolactin release and dopaminergic (dopamine-agonistic) effects were seen in preclinical studies by different working groups. In human pharmacology a reduction of elevated prolactin levels by agnus castus fruit has not been conclusively proven.</p> <p>There are contradictory results concerning binding to oestrogen receptor in general and the preferential binding to β- or α-receptors. Furthermore, there are some references concerning β-endorphin-like activity (possibly via μ-opiate receptor binding).</p>	<p>Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC</p>

5.2. Pharmacokinetic properties

Well-established use	Traditional use
No data available	Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC

5.3. Preclinical safety data

Well-established use	Traditional use
<p>There are only limited preclinical safety data for agnus castus fruit or preparations thereof.</p> <p>Tests on mutagenicity and carcinogenicity have not been performed.</p> <p>In two repeat-dose toxicity studies in rats (4 weeks, 26 weeks) signs of liver toxicity have been observed.</p> <p>Adequate tests on reproductive toxicity have not been performed.</p>	<p>Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC, unless necessary for the safe use of the product</p> <p>Tests on mutagenicity and carcinogenicity have not been performed.</p> <p>Adequate tests on reproductive toxicity have not been performed.</p>

6. Pharmaceutical particulars

Well-established use	Traditional use
Not applicable	Not applicable

7. Date of compilation/last revision

27 March 2018