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

## Initial assessment

<table>
<thead>
<tr>
<th>Event</th>
<th>Dates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adoption by Committee on Herbal Medicinal Products (HMPC) for release for consultation</td>
<td>17 September 2009</td>
</tr>
<tr>
<td>End of consultation (deadline for comments)</td>
<td>15 February 2010</td>
</tr>
<tr>
<td>Re-discussion in MLWP</td>
<td>May 2010, July 2010, September 2010, November 2010</td>
</tr>
<tr>
<td>Adoption by HMPC</td>
<td>25 November 2010</td>
</tr>
<tr>
<td>Monograph (EMA/HMPC/144006/2009)</td>
<td></td>
</tr>
<tr>
<td>AR (EMA/HMPC/144003/2009)</td>
<td></td>
</tr>
<tr>
<td>List of references (EMA/HMPC/144004/2009)</td>
<td></td>
</tr>
<tr>
<td>Overview of comments received during public consultation (EMA/HMPC/278781/2010)</td>
<td></td>
</tr>
<tr>
<td>HMPC Opinion (EMA/HMPC/756507/2010)</td>
<td></td>
</tr>
</tbody>
</table>

## First systematic review

<table>
<thead>
<tr>
<th>Event</th>
<th>Dates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discussion in MLWP</td>
<td>September 2017</td>
</tr>
<tr>
<td></td>
<td>November 2017</td>
</tr>
<tr>
<td></td>
<td>January 2018</td>
</tr>
<tr>
<td>Adoption by HMPC</td>
<td>27 March 2018</td>
</tr>
</tbody>
</table>

## Keywords

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

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

3. **Pharmaceutical form**

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

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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

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

4.2. Posology and method of administration

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Posology</strong></td>
<td><strong>Posology</strong></td>
</tr>
<tr>
<td><em>Female adults</em></td>
<td><em>Female adults</em></td>
</tr>
<tr>
<td>Daily dose:</td>
<td>Daily dose:</td>
</tr>
<tr>
<td>Once daily 20 mg dry extract</td>
<td>400 mg 2 times daily</td>
</tr>
<tr>
<td>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).</td>
<td></td>
</tr>
<tr>
<td>If the symptoms persist after a continued use over three months, a doctor should be consulted.</td>
<td>If the symptoms persist after a continued use over three months, a doctor or a qualified health care practitioner should be consulted.</td>
</tr>
<tr>
<td><strong>Method of administration</strong></td>
<td><strong>Method of administration</strong></td>
</tr>
<tr>
<td>Oral use</td>
<td>Oral use</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### 4.3. Contraindications

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypersensitivity to the active substance.</td>
<td>Hypersensitivity to the active substance.</td>
</tr>
</tbody>
</table>

### 4.4. Special warnings and precautions for use

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients who suffer or suffered from an oestrogen-sensitive cancer should consult their doctor before using agnus castus fruit.</td>
<td>Patients who suffer or suffered from an oestrogen-sensitive cancer should consult their doctor before using agnus castus fruit.</td>
</tr>
<tr>
<td>Patients who are using dopamine agonists, dopamine antagonists, oestrogens and antioestrogens should consult their doctor before using agnus castus fruit (see section 4.5).</td>
<td>Patients who are using dopamine agonists, dopamine antagonists, oestrogens and antioestrogens should consult their doctor before using agnus castus fruit (see section 4.5).</td>
</tr>
<tr>
<td>The use in children and adolescents under 18 years of age has not been established due to lack of adequate data.</td>
<td>The use in children and adolescents under 18 years of age has not been established due to lack of adequate data.</td>
</tr>
<tr>
<td>If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.</td>
<td>If the symptoms worsen during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.</td>
</tr>
<tr>
<td>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.</td>
<td>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.</td>
</tr>
<tr>
<td>In cases of prolactin secreting tumours of the pituitary gland the intake of agnus castus fruit can mask symptoms of the tumour.</td>
<td>In cases of prolactin secreting tumours of the pituitary gland the intake of agnus castus fruit can mask symptoms of the tumour.</td>
</tr>
</tbody>
</table>

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

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

4.6. Fertility, pregnancy and lactation

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td>There is no indication for the use during pregnancy.</td>
<td>There is no indication for the use during pregnancy.</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Pregnancy</td>
</tr>
<tr>
<td>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.</td>
<td>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.</td>
</tr>
<tr>
<td>Lactation</td>
<td>Lactation</td>
</tr>
<tr>
<td>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.</td>
<td>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.</td>
</tr>
<tr>
<td>Fertility</td>
<td>Fertility</td>
</tr>
<tr>
<td>No fertility data are available.</td>
<td>No fertility data are available.</td>
</tr>
</tbody>
</table>

4.7. Effects on ability to drive and use machines

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td>No studies on the effect on the ability to drive and use machines have been performed.</td>
<td>No studies on the effect on the ability to drive and use machines have been performed.</td>
</tr>
</tbody>
</table>

4.8. Undesirable effects

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune system disorders (severe allergic reactions with face swelling, dyspnoea and</td>
<td>Immune system disorders (severe allergic reactions with face swelling, dyspnoea and</td>
</tr>
</tbody>
</table>
Well-established use

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.

The frequency is not known.

If other adverse reactions not mentioned above occur, a doctor or a pharmacist should be consulted.

Traditional use

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.

The frequency is not known.

If other adverse reactions not mentioned above occur, a doctor or a pharmacist should be consulted.

---

### 4.9. Overdose

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td>No case of overdose has been reported.</td>
<td>No case of overdose has been reported.</td>
</tr>
</tbody>
</table>

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### 5. Pharmacological properties

#### 5.1. Pharmacodynamic properties

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacotherapeutic group: Other gynaecologicals</td>
<td>Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC</td>
</tr>
<tr>
<td>Proposed ATC code: G02CX03</td>
<td></td>
</tr>
<tr>
<td>The mode of action is not known.</td>
<td></td>
</tr>
<tr>
<td>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.</td>
<td></td>
</tr>
<tr>
<td>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).</td>
<td></td>
</tr>
</tbody>
</table>
5.2. *Pharmacokinetic properties*

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td>No data available</td>
<td>Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC</td>
</tr>
</tbody>
</table>

5.3. *Preclinical safety data*

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

6. *Pharmaceutical particulars*

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not applicable</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

7. *Date of compilation/last revision*

27 March 2018