



6 June 2011
EMA/HMPC/585558/2007 *Corr.*¹
Committee on Herbal Medicinal Products (HMPC)

Community herbal monograph on *Valeriana officinalis* L., radix and *Humulus lupulus* L., flos

Final

Discussion in Working Party on Community monographs and Community list (MLWP)	January 2008 May 2008 March 2009 May 2009
Adoption by Committee on Herbal Medicinal Products (HMPC) for release for consultation	14 May 2009
End of consultation (deadline for comments). Comments should be provided using this template to hmpc.secretariat@ema.europa.eu	15 September 2009
Rediscussion in Working Party on Community monographs and Community list (MLWP)	4 May 2010
Adoption by Committee on Herbal Medicinal Products (HMPC)	6 May 2010

Keywords	Herbal medicinal products; HMPC; Community herbal monographs; well-established medicinal use; traditional use; <i>Valeriana officinalis</i> L.; <i>Humulus lupulus</i> L.; Valerianae radix; Lupuli flos; valerian root and hop strobiles
-----------------	---

BG (bългарски): Валериана, корен/Хмел, лист CS (čeština): Kozlíkový kořen/Chmelová šištice DA (dansk): Baldrianrod/Humlekopper DE (Deutsch): Baldrianwurzel/Hopfenzapfen EL (elliniká): Ρίζα Βαλεριανής και Άνθος Λυκίσκου EN (English): Valerian Root/Hop Strobile ES (español): Valeriana, raíz de/Lúpulo, flor de ET (eesti keel): Palderjanijuur/Humalakäbi FI (suomi): FR (français): Valériane (racine de)/Houblon (cône de) HU (magyar): Macskagyökér és Komlótoboz IT (italiano): Valeriana radice/Luppolo fiore LT (lietuvių kalba): Valerijonų šaknys ir apynių spurgai	LV (latviešu valoda): Baldriāna saknes/Apīņu ziedi MT (malti): Għeruq Tal-valerjana u fjuri tal-hops NL (nederlands): Valeriaanwortel/Hopbellen PL (polski): Korzeń kozłka/Szyszka chmielu PT (português): Valeriana, raiz/Lúpulo, cone RO (română): Rădăcină de valeriană și conuri de hamei SK (slovenčina): Valeriánový koreň/Chmeľový kvet SL (slovenščina): Korenina zdravilne špajke/Cvet navadnega hmelja SV (svenska): Vänderot/Humlekotte <i>IS (islenska):</i> <i>NO (norsk):</i> Valerianarot/Humle
---	--

¹ Changes introduced in June 2011 in substance names in EU languages and section 5.3.



Community herbal monograph on *Valeriana officinalis* L., radix and *Humulus lupulus* L., flos

1. Name of the medicinal product

To be specified for the individual finished product.

2. Qualitative and quantitative composition^{2,3}

Well-established use	Traditional use
<p>With regard to the marketing authorisation application of Article 10a of Directive 2001/83/EC as amended</p> <p>Fixed combinations of <i>Valeriana officinalis</i> L., radix (valerian root) and <i>Humulus lupulus</i> L., flos (hop strobiles)</p> <p>i) Herbal substances Not applicable</p> <p>ii) Herbal preparations used in fixed combinations of</p> <p>a) Dry extracts of valerian root (DER 4-8:1, methanol 45-51% m/m) and hop strobiles (DER 3-10:1, methanol 40-51% m/m)</p> <p>b) Dry extracts of valerian root (DER 4-7:1, ethanol 70% v/v) and hop strobiles (DER 4-8:1, methanol 40% v/v)</p>	<p>With regard to the registration application of Article 16d(1) of Directive 2001/83/EC as amended</p> <p>Fixed combinations of <i>Valeriana officinalis</i> L., radix (valerian root) and <i>Humulus lupulus</i> L., flos (hop strobiles)</p> <p>i) Herbal substances Not applicable</p> <p>ii) Herbal preparations used in fixed combinations of</p> <ul style="list-style-type: none"> - Liquid extract (DER 1:6.3) from a mixture of valerian root-hop strobiles (1:1), extraction solvent ethanol 40% v/v - Liquid extract from a mixture (1:1) of valerian root tincture (DER 1:10), extraction solvent ethanol 53% m/m and hop strobiles liquid extract (DER 1:2.2), extraction solvent ethanol 53% m/m - Dry extracts <p>a) Dry extracts of valerian root (DER 4-6:1), extraction solvent water and hop strobiles (DER 3-6:1), extraction solvent water</p> <p>b) Dry extracts of valerian root (DER 5-7:1), extraction solvent methanol 45% m/m and hop strobiles (DER 5-7:1), extraction solvent water</p> <p>c) Dry extracts of valerian root (DER 4-5:1), extraction solvent ethanol 60% v/v and hop strobiles (DER 5-9:1), extraction solvent water</p>

² The material complies with the Ph. Eur. monograph (ref.: 01/2008:0453 and 01/2005:1222).

³ The declaration of the active substance(s) for an individual finished product should be in accordance with relevant herbal quality guidance.

	<p>d) Dry extracts of valerian root (DER 4-7:1), extraction solvent methanol 45% v/v and hop strobiles (DER 4-8:1), extraction solvent ethanol 40% v/v</p> <p>e) Dry extracts of valerian root (DER 3-7:1), extraction solvent ethanol 70% v/v and hop strobiles (DER 4-8:1), extraction solvent ethanol 40% v/v</p> <p>f) Dry extracts of valerian root (DER 6-7:1), extraction solvent ethanol 70% v/v and hop strobiles (DER 11-14:1), extraction solvent ethanol 96% v/v</p> <p>g) Dry extracts of valerian root (DER 5-8:1), extraction solvent ethanol 85% v/v and hop strobiles (DER 9-11:1), extraction solvent ethanol 90% v/v</p>
--	---

3. Pharmaceutical form

Well-established use	Traditional use
<p>Herbal preparation in solid dosage forms 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>

4. Clinical particulars

4.1. Therapeutic indications

Well-established use	Traditional use
<p>Indication 1)</p> <p>Herbal medicinal product for the relief of sleep disorders.</p>	<p>Indication 1)</p> <p>Traditional herbal medicinal product for relief of mild symptoms of mental stress.</p> <p>Indication 2)</p> <p>Traditional herbal medicinal product used to aid sleep.</p> <p>The product is a traditional herbal medicinal product for use in specified indications exclusively based on long-standing use.</p>

4.2. Posology and method of administration

Well-established use	Traditional use
<p>Posology</p> <p><i>Adolescents over 12 years of age, adults, elderly</i></p> <p>Single dose</p> <p>Herbal preparation a): Fixed combinations of 187 mg/28 mg - 500 mg/65 mg dry extracts of valerian root and hop strobiles, respectively</p> <p>1-2 doses half to one hour before bedtime, not exceeding 500 mg of valerian extract.</p> <p>Herbal preparation b): Fixed combination of 200 mg/45-mg - 350 mg/70 mg of dry extracts of valerian root and hop strobiles, respectively</p> <p>1-2 doses half to one hour before bedtime, not exceeding 500 mg of valerian extract.</p> <p>The use in children below the age of 12 years is not recommended (see 4.4. 'Special warning and precautions for use').</p> <p>Duration of use</p> <p>Because of its gradual onset of efficacy fixed combinations of valerian root and hops are not suitable for acute interventional treatment of mild nervous tension or sleep disorders. To achieve an optimal treatment effect, the continued use over 4 weeks is recommended.</p> <p>If symptoms persist or worsen after 4 weeks of continued use, a doctor should be consulted.</p> <p>Method of administration</p> <p>Oral use.</p>	<p>Posology</p> <p><i>Adolescents over 12 years of age, adults, elderly</i></p> <p>Liquid extracts:</p> <ul style="list-style-type: none"> - Liquid extract (DER 1:6.3): single dose 20 ml - Liquid extract (DER 1:1): 40 or 75 drops in a half glass of water <p>Dry extracts:</p> <ul style="list-style-type: none"> a) Fixed combinations of 80 mg/20 mg or 160 mg/40 mg dry extracts of valerian root and hop strobiles, respectively Daily dosage: 3 x 3 doses or 3 x 2 doses for indication 1 and 3 x 1 or 2 x 1 doses 1 hour before bedtime for indication 2 b) Fixed combination of 187 mg/45 mg dry extracts of valerian root and hop strobiles, respectively Daily dosage: up to 3 x 1 doses for indication 1 and 1 dose 1 hour before bedtime for indication 2 c) Fixed combinations of 100 mg/30 mg of dry extracts of valerian root and hop strobiles, respectively Daily dosage: 2-3 doses for indication 1 and 2 doses 1 hour before bedtime for indication 2 d) Fixed combinations of 125 mg/25 mg of dry extracts of valerian root and hop strobiles, respectively Daily dosage: up to 3 x 2 doses for indication 1 and 2 doses 1 hour before bedtime for indication 2 e1) Fixed combinations of 100 mg/24 mg - 32 mg dry extracts of valerian root and hop strobiles, respectively Daily dosage: 3 x 2 doses for indication 1 and 2 doses 1 hour before bedtime for indication 2 e2) Fixed combinations of 68 mg/16 mg of dry extracts of valerian root and hop strobiles, respectively Daily dosage: 3 x 3 doses for indication 1 and 3 doses 1 hour before bedtime for indication 2 f) Fixed combinations of 225 mg/30 mg dry

	<p>extracts of valerian root and hop strobiles, respectively</p> <p>Daily dosage: 3x1 doses for indication 1 and 1-2 doses 1 hour before bedtime for indication 2</p> <p>g) Fixed combinations of 77 mg/18.8 mg of dry extracts of valerian root and hop strobiles, respectively</p> <p>Daily dosage: 3 x 2 doses for indication 1 and 2 doses 1 hour before bedtime for indication 2</p> <p>The use in children below the age of 12 years is not recommended (see 4.4. 'Special warning and precautions for use').</p> <p>Duration of use</p> <p>If the symptoms persist longer than 4 weeks of continued use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.</p> <p>Method of administration</p> <p>Oral use.</p>
--	---

4.3. Contraindications

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

4.4. Special warnings and precautions for use

Well-established use	Traditional use
The use of these fixed combinations is not recommended in children below the age of 12 years, due to lack of adequate data.	<p>The use of these fixed combinations is not recommended in children below the age of 12 years, due to lack of adequate data.</p> <p>For extracts 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
Only limited data on pharmacological interactions with other medicinal products are available.	Only limited data on pharmacological interactions with other medicinal products are available.

Clinically relevant interaction with drugs metabolised by the CYP 2D6, CYP 3A4/5, CYP 1A2 or CYP 2E1 pathway has not been observed. Combination with synthetic sedatives requires medical diagnosis and supervision.	Clinically relevant interaction with drugs metabolised by the CYP 2D6, CYP 3A4/5, CYP 1A2 or CYP 2E1 pathways has not been observed. Combination with synthetic sedatives is not recommended.
--	---

4.6. Pregnancy and lactation

Well-established use	Traditional use
Safety during pregnancy and lactation has not been established. As a precautionary measure, because of lack of data, use during pregnancy and lactation is not recommended.	Safety during pregnancy and lactation has not been established. As a precautionary measure, because of lack of data, use during pregnancy and lactation is not recommended.

4.7. Effects on ability to drive and use machines

Well-established use	Traditional use
May impair ability to drive and use machines. Affected patients should not drive or operate machinery.	May impair ability to drive and use machines. Affected patients should not drive or operate machinery.

4.8. Undesirable effects

Well-established use	Traditional use
Gastrointestinal symptoms (e.g. nausea, abdominal cramps) may occur after ingestion of valerian root preparations. The frequency is not known. If other adverse reactions not mentioned above occur, a doctor or a pharmacist should be consulted.	Gastrointestinal symptoms (e.g. nausea, abdominal cramps) may occur after ingestion of valerian root preparations. The frequency is not known. If other adverse reactions not mentioned above occur, a doctor or a qualified health care practitioner should be consulted.

4.9. Overdose

Well-established use	Traditional use
Valerian root at a dose of approximately 20 g caused benign symptoms (fatigue, abdominal cramp, chest tightness, lightheadedness, hand tremor and mydriasis), which disappeared within 24 hours. If symptoms arise, treatment should be supportive.	Valerian root at a dose of approximately 20 g caused benign symptoms (fatigue, abdominal cramp, chest tightness, lightheadedness, hand tremor and mydriasis), which disappeared within 24 hours. If symptoms arise, treatment should be supportive.

5. Pharmacological properties

5.1. Pharmacodynamic properties

Well-established use	Traditional use
<p>Pharmacotherapeutic group: Hypnotics and sedatives.</p> <p>ATC Code: N05CM09.</p> <p>The sedative effects of preparations of valerian root and hop strobiles have been long recognised empirically and have been confirmed for valerian root preparations in preclinical tests and controlled clinical studies. So far no clinical studies have been conducted with hop extracts alone as active drug for insomnia, but at least four randomized, placebo- or reference-controlled prospective clinical studies have been carried out with fixed combinations of dry extracts prepared from valerian root and hop strobiles with methanol 45% (m/m).</p> <p>Orally administered fixed combinations of these extracts in the recommended dosage have been shown to improve sleep latency and sleep quality. These effects cannot be attributed with certainty to any known constituents. Several mechanisms of action possibly contributing to the clinical effect have been identified for diverse constituents of valerian root (sesquiterpenoids, lignans, flavonoids) and include interactions with the GABA-system, agonism at the A-1 adenosine receptor and binding to the 5-HT_{1A} receptor. Also several mechanisms of action have been identified for diverse constituents of hop strobiles (bitter acids, flavonoids) and include interactions with the GABA-system, agonism at the melatonin receptors (ML1 and ML2) and binding to serotonin receptor subtypes (5-HT_{4e}, 5-HT₆ and 5-HT₇). Whether hop strobile extract acts either as a mild sedative independently or as a synergist for valerian root extract, is not yet known.</p>	<p>Not required as per Article 16c (1)(a)(iii) of Directive 2001/83/EC as amended.</p>

5.2. Pharmacokinetic properties

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

5.3. Preclinical safety data

Well-established use	Traditional use
<p>Extracts with ethanol and the essential oil of valerian root have shown low toxicity in solvents during acute tests and from repeated dose toxicity over periods of 4-8 weeks.</p> <p>Tests on reproductive toxicity, genotoxicity and carcinogenicity of valerian root preparations have not been performed.</p> <p>Tests on genotoxicity of water/ethanolic extracts of hop strobiles were negative.</p> <p>Tests on genotoxicity were not performed for water extracts of hops.</p> <p>Tests on reproductive toxicity and carcinogenicity of hop preparations have not been performed.</p>	<p>Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended, unless necessary for the safe use of the product.</p> <p>Extracts with ethanol and the essential oil of valerian root have shown low toxicity in rodents during acute tests and from repeated dose toxicity over periods of 4-8 weeks.</p> <p>Tests on reproductive toxicity, genotoxicity and carcinogenicity of valerian root preparations have not been performed.</p> <p>Tests on genotoxicity of water/ethanolic extracts of hop strobiles were negative.</p> <p>Tests on genotoxicity were not performed for water extracts of hops.</p> <p>Tests on reproductive toxicity and carcinogenicity of hop preparations have not been performed.</p>

6. Pharmaceutical particulars

Well-established use	Traditional use
Not applicable.	Not applicable.

7. Date of compilation/last revision

6 June 2011