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FINAL

**COMMUNITY HERBAL MONOGRAPH ON
VALERIANA OFFICINALIS L., RADIX**

DISCUSSION IN THE DRAFTING GROUP ON SAFETY & EFFICACY	May 2005 June 2005 September 2005
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**COMMUNITY HERBAL MONOGRAPH ON
VALERIANA OFFICINALIS L., RADIX**

1. NAME OF THE MEDICINAL PRODUCT

To be specified for the individual finished product.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION^{1, 2}

<u>Well-established use</u>	<u>Traditional use</u>
With regard to the marketing authorisation application of Article 10a of Directive 2001/83/EC as amended	With regard to the registration application of Article 16d(1) of Directive 2001/83/EC as amended
<i>Valeriana officinalis</i> L., radix (valerian root)	<i>Valeriana officinalis</i> L., radix (valerian root)
- Herbal substance <i>not covered</i> - Herbal preparations - extracts prepared with ethanol/water (ethanol 40 -70 % (V/V))	- Herbal substance - dried valerian root - Herbal preparations - dry extracts prepared with water - valerian tincture - expressed juice from fresh root - valerian root oil

3. PHARMACEUTICAL FORM

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

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

<u>Well-established use</u>	<u>Traditional use</u>
Herbal medicinal product for the relief of mild nervous tension and sleep disorders.	Traditional herbal medicinal product for relief of mild symptoms of mental stress and to aid sleep. The product is a traditional herbal medicinal product for use in specified indications exclusively based on long-standing use.

¹ The material complies with the Ph. Eur. monographs.

² The declaration of the active substance(s) should be in accordance with relevant herbal quality guidance.

4.2. Posology and method of administration

<u>Well-established use</u>	<u>Traditional use</u>
Posology Oral use <i>Adolescents over 12 years of age, adults, elderly</i> Single dose: - extracts prepared with ethanol/water (ethanol max. 40 - 70 % V/V) equivalent to 2 to 3 g of the herbal substance For relief of mild nervous tension up to 3 times daily. For relief of sleep disorders, a single dose half to one hour before bedtime with an earlier dose during the evening if necessary. Maximum daily dose: 4 single doses. Method of administration No special advice. Duration of use Because of its gradual onset of efficacy valerian root is not suitable for acute interventional treatment of mild nervous tension or sleep disorders. To achieve an optimal treatment effect, continued use over 2 – 4 weeks is recommended. If symptoms persist or worsen after 2 weeks of continued use, a doctor should be consulted.	Posology Oral use <i>Adolescents over 12 years of age, adults, elderly</i> Single dose: - 0.3 to 1 g dried valerian root (e.g. as powdered herbal substance) - 1 to 3 g dried valerian root for preparation of a tea - dry extracts prepared with water corresponding to 1 to 3 g of the herbal substance - valerian tincture corresponding to 0.3 to 1 g of the herbal substance - 15 ml of expressed juice - 15 mg of valerian root oil For relief of mild symptoms of mental stress up to 3 times daily. To aid sleep, a single dose half to one hour before bedtime with an earlier dose during the evening if necessary. Maximum daily dose: 4 single doses Method of administration No special advice. Duration of use If symptoms persist during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

4.3. Contraindications

<u>Well-established use</u>	<u>Traditional use</u>
Patients with known hypersensitivity to the active substance should not use valerian root preparations.	Patients with known hypersensitivity to the active substance should not use valerian root and its preparations.

4.4. Special warnings and precautions for use

<u>Well-established use</u>	<u>Traditional use</u>
The use of this product is not recommended in children below the age of 12 years. For valerian preparations containing ethanol the appropriate labelling for ethanol, taken from the guideline ³ on excipients, must be included.	The use of this product is not recommended in children below the age of 12 years. For valerian tincture the appropriate labelling for ethanol, taken from the guideline ³ on excipients, must be included.

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

<u>Well-established use</u>	<u>Traditional use</u>
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.	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 is not recommended.

4.6. Pregnancy and lactation

<u>Well-established use</u>	<u>Traditional use</u>
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

<u>Well-established use</u>	<u>Traditional use</u>
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

<u>Well-established use</u>	<u>Traditional use</u>
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.

³ 'Guideline on excipients in the label and package leaflet of medicinal products for human use' (Notice to Applicants, Volume 3B)

4.9. Overdose

<u>Well-established use</u>	<u>Traditional use</u>
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

<u>Well-established use</u>	<u>Traditional use</u>
Pharmacotherapeutic group: Hypnotics and sedatives, ATC code: N05C M09 The sedative effects of preparations of valerian root, which have long been recognised empirically, have been confirmed in preclinical tests and controlled clinical studies. Orally administered dry extracts of valerian root prepared with ethanol/water (ethanol max. 70 % (V/V)) 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 A1 adenosine receptor and binding to the 5-HT_{1A} receptor.	Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended.

5.2 Pharmacokinetic properties

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

5.3 Preclinical safety data⁴

<u>Well-established use</u>	<u>Traditional use</u>
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. Tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed.	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. Tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed.

6. PHARMACEUTICAL PARTICULARS

<u>Well-established use</u>	<u>Traditional use</u>
Not applicable.	Not applicable.

7. DATE OF COMPILATION/LAST REVISION

26 October 2006

⁴ Where valerian root is used as powder, the total exposure to valepotriates and degradation products such as baldrinals should not exceed the maximum exposure with herbal tea (prepared infusion). Alkylating and cytotoxic properties of valepotriates and baldrinals are normally not relevant for finished products because valepotriates decompose rapidly and only traces of valepotriates or their degradation products such as baldrinals are found. Where the applicant cannot demonstrate that the total exposure to valepotriates with the finished product does not exceed the maximum exposure with herbal tea, he has to provide data on determination of the threshold of toxicological concern compatible with the safe use of the preparation.