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Evaluation of Medicines for Human Use

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FINAL

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

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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]

Well-established use	Traditional use
With regard to the marketing authorisation application of Article 10a of Directive 2001/83/EC as amended *Valeriana officinalis* L., radix (valerian root) • Herbal substance *not covered* • Herbal preparations - extracts prepared with ethanol/water (ethanol 40 -70 % (V/V))	With regard to the registration application of Article 16d(1) of Directive 2001/83/EC as amended *Valeriana officinalis* L., radix (valerian root) • 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

Well-established use	Traditional use
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

Well-established use	Traditional use
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

Well-established use	Traditional use
Posology Oral use *Adolescents over 12 years of age, adults, elderly* 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 *Adolescents over 12 years of age, adults, elderly* 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

Well-established use	Traditional use
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

Well-established use	Traditional use
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

Well-established use	Traditional use
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

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.

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

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
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-HT1A receptor.	Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended.

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 as amended.

5.3 Preclinical safety data[4]

Well-established use	Traditional use
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

Well-established use	Traditional use
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.