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*Evaluation of Medicines for Human Use*

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**COMMITTEE ON HERBAL MEDICINAL PRODUCTS  
(HMPC)**

**DRAFT**

**COMMUNITY HERBAL MONOGRAPH ON  
VALERIAN ROOT (VALERIANA, RADIX)**

<b>DISCUSSION IN THE DRAFTING GROUP ON SAFETY &amp; EFFICACY</b>	May 2005 June 2005 September 2005
<b>ADOPTION BY HMPC FOR RELEASE FOR CONSULTATION</b>	September 2005
<b>END OF CONSULTATION (DEADLINE FOR COMMENTS )</b>	31 January 2006

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<b>KEYWORDS</b>	Herbal medicinal products; HMPC; Community herbal monograph; well-established use; traditional use.
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## COMMUNITY HERBAL MONOGRAPH ON VALERIAN ROOT (VALERIANA, RADIX)

### 1. NAME OF THE MEDICINAL PRODUCT

To be specified for the individual finished product.

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION<sup>1</sup>

<u>Well-established use</u>	<u>Traditional use</u>
With regard to the marketing authorisation application of Article 10(1)(a)(ii) of Directive 2001/83/EC as amended	With regard to the registration application of Article 16d(1) of Directive 2001/83/EC as amended
Valerian root <sup>2</sup> preparations	Herbal preparations
<ul style="list-style-type: none"> <li>- Extract prepared with water, ethanol/water (ethanol max. 70 % V/V)</li> <li>- Tinctures (1:5, ethanol max. 70 % V/V)</li> </ul>	<ul style="list-style-type: none"> <li>- Dried Valerian root<sup>2</sup></li> <li>- Fresh plant juice</li> <li>- Valerian root oil</li> </ul>

### 3. PHARMACEUTICAL FORM

<u>Well-established use</u>	<u>Traditional use</u>
Herbal preparation in solid or liquid dosage forms. The pharmaceutical form should be described according to the standard terms published by the European Pharmacopoeia.	Herbal preparation in solid or liquid dosage forms. The pharmaceutical form should be described according to the standard terms published by the European Pharmacopoeia.

### 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 difficulty in falling asleep (non-organic insomnia according to ICD-10, F51.0).	Traditional herbal medicinal product for support of mental relaxation and to aid natural sleep exclusively based on long-standing use.

#### 4.2 Posology and method of administration

<u>Well-established use</u>	<u>Traditional use</u>
<b>Posology</b> Oral use.	<b>Posology</b> Oral use.

<sup>1</sup> The declaration of all active substances should be done in accordance with the 'Guideline on quality of herbal medicinal products / traditional herbal medicinal products' (CPMP/QWP/2819/00 Rev.1, EMEA/CVMP/814/00 Rev.1).

<sup>2</sup> The herbal substance complies with the European Pharmacopoeia (monograph reference 01/2005:0453).

<p><i>Adolescents over 12 years of age, adults, elderly</i></p> <p>Single dose: Tincture (1:5, ethanol max. 70 % V/V) or extracts with water, ethanol/water (max. 70 % V/V) equivalent to 2 to 3 g of the drug. For nervous tension up to 3 times daily. As an aid to sleep, a single dose half to one hour before bedtime with an earlier dose during the evening if necessary.</p> <p>Maximum daily dose: 4 single doses.</p> <p><b>Method of administration</b> No special advice.</p> <p><b>Duration of use</b> Because of its gradual onset of efficacy Valerian root is not suitable for acute interventional treatment of stress symptoms or reactive sleep disturbances. To achieve an optimal treatment effect, continued use over 2 – 4 weeks is recommended.</p>	<p><i>Adolescents over 12 years of age, adults, elderly</i></p> <p>Single dose: - 0.3 to 1 g dried Valerian root (e.g. as powdered drug or as herbal tea, according to British Herbal Pharmacopoeia, 1976) - 15 ml of fresh plant juice - 15 mg of Valerian root oil For relaxation 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.</p> <p>Maximum daily dose: 4 single doses</p> <p><b>Method of administration</b> No special advice.</p> <p><b>Duration of use</b> To achieve optimal efficacy, continued use over 2 – 4 weeks is recommended.</p>
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#### 4.3. Contraindications

<u>Well-established use</u>	<u>Traditional use</u>
Patients with known hypersensitivity to Valerian should not use Valerian root preparations.	Patients with known hypersensitivity to Valerian should not use Valerian root preparations.

#### 4.4. Special warnings and precautions for use

<u>Well-established use</u>	<u>Traditional use</u>
Because there is no experience available, use of this product is not recommended in children below the age of 12 years. If symptoms worsen after 2 weeks of continued use, a physician should be consulted.	Because there is no experience available, use of this product is not recommended in children below the age of 12 years. If symptoms persist during the use of the medicinal product or if adverse effects not mentioned in the package leaflet occur, a doctor or a qualified health care practitioner should be consulted.

#### 4.5. Interactions 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 or CYP 3A4 pathway is unlikely.	Only limited data on pharmacological interactions with other medicinal products are available. Clinically relevant interaction with drugs metabolised by the CYP 2D6 or CYP 3A4 pathway is unlikely.

<p>An additive effect with barbiturates is possible and could result in excessive sedation. Co-medication with barbiturates is therefore not recommended.</p> <p>Since additive effects with other sedatives cannot be excluded, co-medication is not recommended as a general precaution.</p> <p>The effect of Valerian preparations may be potentiated by alcohol. Excessive concomitant consumption of alcohol should therefore be avoided.</p>	<p>An additive effect with barbiturates is possible and could result in excessive sedation. Co-medication with barbiturates is therefore not recommended.</p> <p>Since additive effects with other sedatives cannot be excluded, co-medication is not recommended as a general precaution.</p> <p>The effect of Valerian preparations may be potentiated by alcohol. Excessive concomitant consumption of alcohol should therefore be avoided.</p>
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#### 4.6. Pregnancy and lactation

<p><u>Well-established use</u></p> <p>Safety during pregnancy and lactation has not been established definitely. No adverse effects have been reported from the common use of Valerian root as a medicinal product. As a precautionary measure, because of lack of data, use during pregnancy and lactation is not recommended.</p>	<p><u>Traditional use</u></p> <p>Safety during pregnancy and lactation has not been established definitely. No adverse effects have been reported from the common use of Valerian root as a medicinal product. As a precautionary measure, because of lack of data, use during pregnancy and lactation is not recommended.</p>
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#### 4.7. Effects on ability to drive and use machines

<p><u>Well-established use</u></p> <p>[Preparation] should not be taken up to 2 hours before driving or operating machinery.</p>	<p><u>Traditional use</u></p> <p>[Preparation] should not be taken up to 2 hours before driving or operating machinery.</p>
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#### 4.8. Undesirable effects

<p><u>Well-established use</u></p> <p>Very rarely (<math>\leq 1:10000^3</math>) gastro-intestinal symptoms (e.g. nausea, abdominal cramps) may occur after ingestion of Valerian root preparations.</p>	<p><u>Traditional use</u></p> <p>Very rarely (<math>\leq 1:10000^4</math>) gastro-intestinal symptoms (e.g. nausea, abdominal cramps) may occur after ingestion of Valerian root preparations.</p>
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#### 4.9. Overdose

<p><u>Well-established use</u></p> <p>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.</p> <p>After intake of very high doses of Valerian root over several years (daily consumption corresponding to approximately 30 g of the drug) withdrawal symptoms (delirium) have been</p>	<p><u>Traditional use</u></p> <p>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.</p> <p>After intake of very high doses of Valerian root over several years (daily consumption corresponding to approximately 30 g of the drug) withdrawal symptoms (delirium) have been</p>
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reported.	reported.
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## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

<u>Well-established use</u>	<u>Traditional use</u>
<p>Hypnotics and sedatives, ATC code: N05C M09</p> <p>The sedative and anxiolytic effects of preparations of Valerian root, which have long been recognised empirically, have been confirmed in preclinical trials and controlled clinical studies. Orally administered dry extracts of Valerian root prepared with water or water/ethanol up to 70 % ethanol (V/V) in the recommended dosage have been shown to improve sleep latency, sleep quality and daytime wellbeing in man. 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.</p>	<p>Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended.</p>

### 5.2 Pharmacokinetic properties

<u>Well-established use</u>	<u>Traditional use</u>
<p>No pharmacokinetic 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<sup>5</sup>

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

## 6. DATE OF COMPILATION

20 September 2005

<sup>5</sup> In case of Valerian root used as powder, the total exposure to valepotriates and baldrinals should not exceed the maximum exposure with herbal tea. 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 baldrinals are found. Where the applicant cannot demonstrate the absence of valepotriates in the finished product, he has to provide data on determination of the threshold of toxicological concern compatible with the safe use of the preparation.