



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Committee on Herbal Medicinal Products (HMPC)

## Community herbal monograph on *Capsicum annum* L. var. *minimum* (Miller) Heiser and small fruited varieties of *Capsicum frutescens* L., fructus

### Draft

Discussion in Working Party on Community monographs and Community list (MLWP)	November 2013 January 2014 March 2014 May 2014
Adoption by Committee on Herbal Medicinal Products (HMPC) for release for consultation	1 July 2014
End of consultation (deadline for comments). Comments should be provided using this <a href="#">template</a> to <a href="mailto:hmpc.secretariat@ema.europa.eu">hmpc.secretariat@ema.europa.eu</a>	15 December 2014
Rediscussion in Working Party on Community monographs and Community list (MLWP)	
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Keywords	Herbal medicinal products; HMPC; Community herbal monographs; well-established medicinal use; traditional use; <i>Capsicum annum</i> L. var. <i>minimum</i> (Miller) Heiser and small fruited varieties of <i>Capsicum frutescens</i> L., fructus; Capsici fructus; Capsicum
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BG (bulgarski): Люти пиперки, плод CS (čeština): paprikový plod DA (dansk): Cayennepeber DE (Deutsch): Cayennepfeffer EL (elliniká): Καπνικού καρπός EN (English): Capsicum ES (español): Cápsico, fruto de ET (eesti keel): kajenni paprika FI (suomi): espanjanpippuri FR (français): Piment de Cayenne (fruit de) HR (hrvatski): paprikin plod HU (magyar): Paprikatermés IT (italiano): Peperoncino frutto	LT (lietuvių kalba): Paprikų vaisiai LV (latviešu valoda): Paprikas augļi MT (Malti): Bżar NL (Nederlands): Spaanse peper PL (polski): Owoc pieprzowca PT (português): Pimento de Caiena RO (română): SK (slovenčina): Paprikový plod SL (slovenščina): plod paprike SV (svenska): Spanskpeppar <i>IS (íslenska):</i> <i>NO (norsk):</i> Spansk pepper
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# Community herbal monograph on *Capsicum annuum* L. var. *minimum* (Miller) Heiser and small fruited varieties of *Capsicum frutescens* L., fructus

## 1. Name of the medicinal product

To be specified for the individual finished product.

## 2. Qualitative and quantitative composition<sup>1,2</sup>

Well-established use <sup>3</sup>	Traditional use
<p>With regard to the marketing authorisation application of Article 10(a) of Directive 2001/83/EC as amended</p> <p><i>Capsicum annuum</i> L. var. <i>minimum</i> (Miller) Heiser and small fruited varieties of <i>Capsicum frutescens</i> L., fructus (Capsicum)</p> <p>i) Herbal substance</p> <p>Not applicable.</p> <p>ii) Herbal preparations</p> <p>a) Soft extract (DER 4-7:1), standardised to 2.0–2.78% total capsaicinoids, extraction solvent ethanol 80% (V/V)</p> <p>b) Soft extract (DER 1.5–2.5:1), extraction solvent ethanol 96% (V/V)</p> <p>c) Soft extract (DER 11-30:1), extraction solvent propan-2-ol</p>	

## 3. Pharmaceutical form

Well-established use	Traditional use
<p>Herbal preparation in a medicated plaster or in semi-solid dosage forms for cutaneous use.</p> <p>The pharmaceutical form should be described by the European Pharmacopoeia full standard term.</p>	

<sup>1</sup> The material complies with the Ph. Eur. monograph (ref.: 01/2014:1859).

<sup>2</sup> The declaration of the active substance(s) for an individual finished product should be in accordance with relevant herbal quality guidance.

<sup>3</sup> Contact with the national agencies before starting an application procedure is advised in order to address the need to provide equivalence data (National Scientific Advice).

## 4. Clinical particulars

### 4.1. Therapeutic indications

Well-established use	Traditional use
Herbal medicinal product for the relief of muscle pain such as lower back pain.	

### 4.2. Posology and method of administration

Well-established use	Traditional use
<p><b>Posology</b></p> <p>Herbal preparation a)</p> <p><b>Medicated plaster</b></p> <p><i>Adolescents, adults, and elderly</i></p> <p>1 medicated plaster (22 x 14 cm) containing 390-552 mg of soft extract of <i>Capsici fructus</i>, corresponding to 11 mg capsaicinoids expressed as capsaicin (= 35 µg / cm<sup>2</sup>).</p> <p>1 medicated plaster (12 x 18 cm) containing 171-240 mg of soft extract of <i>Capsici fructus</i>, corresponding to 4.8 mg capsaicinoids expressed as capsaicin (= 22 µg / cm<sup>2</sup>).</p> <p>Daily dosage: A maximum of 1 plaster per day should be applied on the affected area for at least 4 and up to 12 hours. There should be an interval of at least 12 hours before a new plaster is applied at the same application area.</p> <p>The use in children under 12 years of age is not recommended (see section 4.4 'Special warnings and precautions for use').</p> <p><b>Semi-solid dosage forms</b></p> <p><i>Adults and elderly</i></p> <p>Semi-solid dosage forms containing 0.6-1.9 g soft extract corresponding to 40-53 mg capsaicinoids / 100 g.</p> <p>Apply 2-4 times daily. To be applied in a thin layer on the affected area.</p> <p>The use in children and adolescents under 18 years of age is not recommended (see section 4.4 'Special warnings and precautions for use').</p>	

Well-established use	Traditional use
<p>Herbal preparation b)</p> <p><i>Adults and elderly</i></p> <p>Semi-solid dosage forms containing 0.9-2.9 g soft extract corresponding to 50 mg capsaicinoids / 100 g.</p> <p>Apply 2-4 times daily. To be applied in a thin layer on the affected area.</p> <p>The use in children and adolescents under 18 years of age is not recommended (see section 4.4 'Special warnings and precautions for use').</p> <p>Herbal preparation c)</p> <p><i>Adults and elderly</i></p> <p>Semi-solid dosage forms containing 0.24-1.02 g soft extract corresponding to 53 mg capsaicinoids / 100 g.</p> <p>Apply 2-4 times daily. To be applied in a thin layer on the affected area.</p> <p>The use in children and adolescents under 18 years of age is not recommended (see section 4.4 'Special warnings and precautions for use').</p> <p><b>Duration of use</b></p> <p>If the symptoms persist during the use of the medicinal product, a doctor or a pharmacist should be consulted. The medication should be continued until relief of pain is achieved, if necessary up to 3 weeks. After 3 weeks of use a break of at least 2 weeks is required.</p> <p><b>Method of administration</b></p> <p>Cutaneous use.</p>	

### 4.3. Contraindications

Well-established use	Traditional use
<p>Hypersensitivity to the active substance or to other sources of capsaicinoids (e.g. paprika plants or chili).</p> <p>Broken skin or wounds.</p>	

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

Well-established use	Traditional use
<p><b>Medicated plaster</b></p> <p>The use is not recommended in children below 12 years of age due to a lack of data on safety and efficacy.</p> <p>If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.</p> <p>The plaster should not be applied near the eyes or to mucous membranes. It is recommended not to scratch the application site to avoid damage to the skin. Application of additional sources of heat during treatment should be avoided. Treatment should be discontinued if excessive warmth is experienced.</p> <p>A physician should be consulted in those acute cases when the condition is accompanied by reddening, swelling or hyperthermia of joints, ongoing joint trouble or severe back pain radiating into the legs and/or are associated with neurological syndromes (e.g. numbness, tingling).</p> <p><b>Semi-solid dosage forms</b></p> <p>The use in children and adolescents under 18 years of age has not been established due to lack of data on safety and efficacy.</p> <p>The medicinal product should not be applied near the eyes or to mucous membranes.</p> <p>Application of additional sources of heat during treatment should be avoided.</p> <p>If the symptoms worsen during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.</p>	

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

Well-established use	Traditional use
None reported.	

#### 4.6. Fertility, pregnancy and lactation

Well-established use	Traditional use
<p><b>Medicated plaster</b></p> <p>There are no data from the use of the plaster in pregnant women. Animal studies have shown reproductive toxicity after high subcutaneous doses of capsaicin. Capsaicin crosses the placenta and may pass into breast milk.</p> <p>Although, prenatal and neonatal effects of capsaicin occurred at doses in excess of the maximum clinical dose of plaster, the plaster should only be used during pregnancy and lactation after a careful risk-benefit assessment.</p> <p>No fertility data available.</p>	
<p><b>Semi-solid dosage forms</b></p> <p>Animal studies have shown reproductive toxicity after high subcutaneous doses of capsaicin. Capsaicin crosses the placenta and may pass into breast milk.</p> <p>Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.</p> <p>No fertility data available.</p>	

#### 4.7. Effects on ability to drive and use machines

Well-established use	Traditional use
Not relevant.	

#### 4.8. Undesirable effects

Well-established use	Traditional use
<p><b>Medicated plaster</b></p> <p>The active ingredient causes increased local blood circulation with marked reddening of the skin and a sensation of warmth. This reaction is part of the normal pharmacological action of the preparation and subsides as a rule within a short time after removal of the plaster.</p> <p>In rare cases (<math>\sim 1 / 10,000</math> to <math>&lt; 1 / 1,000</math>): Skin</p>	

Well-established use	Traditional use
<p>hypersensitivity and allergic reactions (e.g. urticaria, blisters or vesiculation at the application site) may occur. The treatment is to be stopped in such cases immediately. Especially during the first days of treatment a burning sensation or stinging or itching may occur. If, in individual cases, the side effects are experienced as excessive, treatment should be discontinued.</p> <p><b>Semi-solid dosage forms</b></p> <p>The active ingredient causes increased local blood circulation with marked reddening of the skin and a sensation of warmth. This reaction is part of the normal pharmacological action of the herbal preparation.</p> <p>Skin hypersensitivity and allergic reactions (e.g. urticaria, blisters or vesiculation at the application site) may occur. The frequency is not known.</p> <p>The treatment is to be stopped in such cases immediately.</p> <p>If, in individual cases, burning sensation or stinging or itching are experienced as excessive, treatment should be discontinued.</p>	

#### 4.9. Overdose

Well-established use	Traditional use
No case of overdose has been reported.	

## 5. Pharmacological properties

### 5.1. Pharmacodynamic properties

Well-established use	Traditional use
<p>Pharmacotherapeutic group: Capsicum preparations and similar agents</p> <p>Proposed ATC code: M02AB</p> <p>Capsaicin is the primary pungent principle in the fruit of capsicum plants. The precise mechanism of action has not been fully elucidated. Topically applied capsaicin triggers local irritation, which manifests symptomatically as erythema and a burning, sometimes itchy, sensation. This is</p>	

Well-established use	Traditional use
<p>generally attributed to a neurogenic inflammatory process and explained by the release of the neurotransmitter substance P. The second stage of the capsaicin action is associated with antinociceptive effects, the duration of which ranges from hours to weeks. Substance P depletion of the neuron following repeated application leads to a long-term desensitisation to burning and pain.</p>	

### 5.2. Pharmacokinetic properties

Well-established use	Traditional use
<p>Capsaicin is absorbed percutaneously. The absorbed capsaicin is metabolised mainly in the liver and eliminated in the form of metabolites in the urine and faeces.</p>	

### 5.3. Preclinical safety data

Well-established use	Traditional use
<p>No data on acute toxicity of the herbal preparations are available. Adequate tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed with herbal preparations.</p> <p>Acute toxicity of capsaicin in mice was in the order intravenous &gt; intraperitoneal &gt; subcutaneous &gt; oral &gt; dermal indicating that systemic absorption and toxicity following dermal application were lower than after an oral dose. High subcutaneous doses of capsaicin were not teratogenic in rats. However, there was evidence that capsaicin crosses the placenta and exerts a toxic effect on the peripheral nerves of foetuses, provoking extensive depletion of substance P from immunoreactive nerve fiber from the dorsal horn of the spinal cord. Prenatal treatment of rats with high subcutaneous doses of capsaicin (50 mg/kg) caused functional neuronal defects; whereas neonatal treatment retarded body growth and sexual maturation, decreased mating frequency and reduced gestations.</p> <p>Published data on potential mutagenicity and</p>	

<b>Well-established use</b>	<b>Traditional use</b>
carcinogenicity of capsaicin were inconclusive.	

## **6. Pharmaceutical particulars**

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

## **7. Date of compilation/last revision**

1 July 2014