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Committee on Herbal Medicinal Products (HMPC)

European Union herbal monograph on *Arctostaphylos uva-ursi* (L.) Spreng., folium

Draft

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Adoption by HMPC • Monograph (EMA/HMPC/573460/2009 Rev. 1) • AR (EMA/HMPC/573462/2009 Rev. 1) • List of references (EMA/HMPC/573461/2009 Rev. 1) • Overview of comments received during public consultation (EMA/HMPC/46410/2011 Rev. 1) • HMPC Opinion (EMA/HMPC/888910/2011)	24 January 2012
Second revision	
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Start of public consultation	12 April 2017
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BG (bulgarski): Мечо грозде, лист CS (čeština): medvědicový list DA (dansk): Melbærrisblad DE (Deutsch): Bärentraubenblätter EL (elliniká): Φύλλο αρκτοκομάρου EN (English): bearberry leaf ES (español): gayuba, hoja de ET (eesti keel): leesikaleht FI (suomi): sianpuolukka, lehti FR (français): busserole (feuille de) HR (hrvatski): medvjetkin list HU (magyar): orvosi medveszőlő levél IT (italiano): uva ursina foglia	LT (lietuvių kalba): Meškauogių lapai LV (latviešu valoda): Miltenes lapas MT (Malti): werqa ta' l-ulva ursi NL (Nederlands): beredruif PL (polski): liść mącznicy PT (português): uva-ursina, folha RO (română): frunză de strugurii ursului SK (slovenčina): list medvedice SL (slovenščina): list vednozelenega gornika SV (svenska): mjölon, blad IS (íslenska): NO (norsk): melbærblad

European Union herbal monograph on *Arctostaphylos uva-ursi* (L.) Spreng., folium

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 registration application of Article 16d(1) of Directive 2001/83/EC *Arctostaphylos uva-ursi* (L.) Spreng., folium (bearberry leaf) i) Herbal substance Not applicable ii) Herbal preparations a) Comminuted herbal substance b) Powdered herbal substance c) Dry extract (DER 3.5-5.5:1), extraction solvent ethanol 60% V/V, containing 23.5-29.3% of hydroquinone derivatives calculated as anhydrous arbutin (spectrophotometry) d) Dry extract (DER 2.5-4.5:1), extraction solvent water, containing 20-28% of hydroquinone derivatives calculated as anhydrous arbutin (spectrophotometry) e) Liquid extract (DER 1:1), extraction solvent ethanol 25% V/V

3. Pharmaceutical form

Well-established use	Traditional use
	Comminuted herbal substance as herbal tea for oral use. Herbal preparations in liquid or solid dosage forms

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

[2] The material complies with the Ph. Eur. monograph (ref.: 1054)

Well-established use	Traditional use
	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
	Traditional herbal medicinal product used for treatment of symptoms of mild recurrent lower urinary tract infections such as burning sensation during urination and/or frequent urination in women, after serious conditions have been excluded by a medical doctor. The product is a traditional herbal medicinal product for use in the specified indication exclusively based upon long-standing use.

4.2. Posology and method of administration[3]

Well-established use	Traditional use
	Posology *Adults and elderly* a) Comminuted herbal substance Herbal tea: 1.5-4 g of the comminuted herbal substance in 150 ml of boiling water as a herbal infusion or in 150 ml of water as a macerate 2 to 4 times daily Maximum daily dose: 8 g b) Powdered herbal substance Single dose: 700 mg (2x350 mg) twice daily Maximum daily dose:1.75 g (5x350 mg) c) and d) Dry extracts Single dose: the dose corresponding to 100–210 mg of hydroquinone derivatives calculated as anhydrous arbutin (spectrophotometry) 2–4 times daily

[3] For guidance on herbal substance/herbal preparation administered as herbal tea or as infusion/decoction/macerate preparation, please refer to the HMPC 'Glossary on herbal teas' (EMA/HMPC/5829/2010 Rev.1).

Well-established use	Traditional use
	Daily dose: 200–840 mg e) Liquid extract Single dose: 1.5–4 ml up to three times daily Maximum daily dose: 8 ml The use in children and adolescents under 18 years of age is not recommended (see section 4.4 'Special warnings and precautions for use'). The use in men is not recommended (see section 4.4 'Special warnings and precautions for use'). **Duration of use** Not to be used for more than one week. If the symptoms persist for more than 4 days during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted. **Method of administration** Oral use The macerate should be used immediately after preparation.

4.3. Contraindications

Well-established use	Traditional use
	Hypersensitivity to the active substance. Kidney disorders

4.4. Special warnings and precautions for use

Well-established use	Traditional use
	The use in children and adolescents under 18 years of age is not recommended because of concerns requiring medical advice. The use in men is not recommended because of concerns requiring medical supervision. If the symptoms worsen or if complaints such as fever, dysuria, spasms, or blood in urine occur during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

Well-established use	Traditional use
	Uvae ursi folium may cause a greenish-brown coloration of the urine. 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.

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
	No fertility data available. Safety during pregnancy and lactation has not been established. The use should be avoided during pregnancy (see section 5.3 'Preclinical safety data'). In absence of sufficient data, the use during lactation is not recommended.

4.7. Effects on ability to drive and use machines

Well-established use	Traditional use
	No studies on the effect on the ability to drive and use machines have been performed.

4.8. Undesirable effects

Well-established use	Traditional use
	Nausea, vomiting, stomach-ache have been reported. 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
	No case of overdose has been reported.

5. Pharmacological properties

5.1. Pharmacodynamic properties

Well-established use	Traditional use
	Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC.

5.2. Pharmacokinetic properties

Well-established use	Traditional use
	Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC.

5.3. Preclinical safety data

Well-established use	Traditional use
	Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC, unless necessary for the safe use of the product. Available tests on genotoxicity of water and ethanolic extracts of Uvae ursi folium are inadequate. Reproductive toxicity has not been studied. Available carcinogenicity studies have been negative. Arbutin, the main component of Uvae ursi folium, displayed some maternal and fetal toxicity in rats after subcutaneous administration of 400 mg/kg per day. No effect on reproduction has been observed at doses of 100 mg/kg per day. Toxicity tests with hydroquinone, a hydrolysis product of arbutin, have demonstrated some evidence of genotoxicity and carcinogenicity. Risks posed by the exposure of hydroquinone during the short-term treatment with Uvae ursi folium preparations are considered minimal.

6. Pharmaceutical particulars

Well-established use	Traditional use
	Not applicable

7. Date of compilation / last revision

28 March 2017