30 May 2017
EMA/HMPC/464684/2016
Committee on Herbal Medicinal Products (HMPC)

European Union herbal monograph on *Vitis vinifera* L., folium

Final

Initial assessment	
Discussion in Working Party on European Union monographs and list (MLWP)	March 2009 July 2009 September 2009
Adoption by Committee on Herbal Medicinal Products (HMPC) for release for consultation	12 November 2009
End of consultation (deadline for comments[1])	15 April 2010
Re-discussion in MLWP	May 2010 July 2010
Adoption by HMPC Monograph (EMA/HMPC/16635/2009) AR (EMA/HMPC/16633/2009) List of references (EMA/HMPC/16634/2009) List entry (EMA/HMPC/5816/2010) Overview of comments received during public consultation (EMA/HMPC/276427/2010) HMPC List entry Opinion (EMA/457286/2010) HMPC Opinion (EMA/HMPC/457286/2010)	15 July 2010 *Corr.* 24 November 2015
First systematic review	
Discussion in Working Party on European Union monographs and list (MLWP)	July 2016 September 2016
Adoption by Committee on Herbal Medicinal Products (HMPC) for release for consultation	22 November 2016
End of consultation (deadline for comments[1]).	15 March 2017
Re-discussion in MLWP	March 2017
Adoption by HMPC	30 May 2017

[1] No comments were received during the period of public consultation. Therefore the final monograph is published together with the final assessment report and list of references, without an 'Overview of comments received during the public consultation'

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Keywords	Herbal medicinal products; HMPC; European Union herbal monographs; well-established medicinal use; traditional use; *Vitis vinifera* L., folium; Vitis viniferae folium; grapevine leaf

BG (bălgarski): лоза, лист CS (čeština): červený list vinné révy DA (dansk): Vinblad DE (Deutsch): Rote Weinrebenblätter EL (elliniká): φύλλο αμπέλου EN (English): grapevine leaf ES (espanol): vid, hoja de ET (eesti keel): viinapuu lehed FI (suomi): aitoviiniköynnös, lehti FR (français): vigne rouge (feuille de) HR (hrvatski): list vinove loze HU (magyar): bortermő szőlő levél IT (italiano): Vite, foglia	LT (lietuvių kalba): Tikrųjų vynmedžių lapai LV (latviešu valoda): Īstā vīnkoka lapas MT (malti): werqa tad-dielja ta' l-għeneb NL (nederlands): wijnstok PL (polski): Liść winorośli właściwej PT (português): videira, folha RO (română): frunză de viţă-de-vie SK (slovenčina): list viniča SL (slovenščina): list vinske trte SV (svenska): vinranka, blad IS (íslenska): Vínviðarlauf NO (norsk): rød vinranke, blad

European Union herbal monograph on V*itis vinifera* L., folium

1. Name of the medicinal product

To be specified for the individual finished product.

2. Qualitative and quantitative composition[2,3]

Well-established use	**Traditional use**
With regard to the marketing authorisation application of Article 10(a) of Directive 2001/83/EC. *Vitis vinifera* L., folium, (grapevine leaf) [4] i) Herbal substance Not applicable ii) Herbal preparation Dry extract (DER 4-6:1); extraction solvent water	With regard to the registration application of Article 16d(1) of Directive 2001/83/EC. *Vitis vinifera* L., folium, (grapevine leaf) [5] i) Herbal substance Not applicable ii) Herbal preparation a) Comminuted herbal substance b) Powdered herbal substance c) Soft extract (DER 2.5-4:1); extraction solvent water

3. Pharmaceutical form

Well-established use	**Traditional use**
Herbal preparation in solid dosage forms for oral use.	Comminuted herbal substance as herbal tea for oral use. Herbal preparation in solid dosage forms for oral use. Herbal preparation in semi-solid dosage forms for cutaneous use. The pharmaceutical form should be described by the European Pharmacopoeia full standard term.

2 Detailed specifications for the herbal substance shall be given by references to bibliographic sources in absence of a monograph in the European Pharmacopoeia, a national pharmacopoeia or national codex currently used officially in a Member State.
3 The declaration of the active substance(s) for an individual finished product should be in accordance with relevant herbal quality guidance.
4 and 5 The material complies with the monograph of the Pharmacopée Française X., 1996

4. Clinical particulars

4.1. Therapeutic indications

Well-established use	Traditional use
Herbal medicinal product for treatment of chronic venous insufficiency, which is characterised by swollen legs, varicose veins, a feeling of heaviness, pain, tiredness, itching, tension and cramps in the calves.	Indication 1) Traditional herbal medicinal product to relieve symptoms of discomfort and heaviness of legs related to minor venous circulatory disturbances. Indication 2) Traditional herbal medicinal product for symptomatic relief of itching and burning associated with haemorrhoids after serious conditions have been excluded by a medical doctor. Indication 3) Traditional herbal medicinal product for symptomatic treatment of cutaneous capillary fragility. The product is a traditional herbal medicinal product for use in specified indications exclusively based upon long-standing use.

4.2. Posology and method of administration[6]

Well-established use	Traditional use
Posology *Adults and elderly* Dry extract (DER 4-6:1; water) Single dose: 360-720 mg Daily dose: 360-720 mg *Use in children and adolescents* The use in children and adolescents under 18 years of age is not recommended (see section 4.4 'Special warnings and precautions for use'). **Duration of use** The recommended duration of use is 12 weeks. Two to three weeks of treatment may be	**Posology** Indication 1) *Adults and elderly* Oral use a) Comminuted herbal substance as herbal tea Herbal tea: 5-10 g of dried leaves in 250 ml of boiling water as herbal infusion, 2 times daily. b) Powdered herbal substance 270-350 mg, 3-5 times daily Cutaneous use c) Soft extract (DER 2.5-4:1; water) in a cream

[6] 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).

required before beneficial effects are observed. Long term use is possible in consultation with a doctor. **Method of administration** Oral use	base (10 g contain 282 mg soft extract). Apply a thin layer on the affected area 1-3 times daily. Indication 2) and 3) *Adults and elderly* Oral use a) Comminuted herbal substance as herbal tea Herbal tea: 5-10 g of dried leaves in 250 ml of boiling water as herbal infusion, 2 times daily. b) Powdered herbal substance 270-350 mg, 3-5 times daily **Duration of use** Indication 1) The recommended duration of use is 4 weeks. If the symptoms persist for more than 2 weeks during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted. Indications 2) and 3) If the symptoms persist for more than 1 week during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted. The use in children and adolescents under 18 years of age is not recommended (see section 4.4 'Special warnings and precautions for use'). **Method of administration** Indication 1), 2) and 3) Oral use Indication 1) Cutaneous use.

4.3. Contraindications

Well-established use	**Traditional use**
Hypersensitivity to the active substance.	Hypersensitivity to the active substance.

4.4. Special warnings and precautions for use

Well-established use	Traditional use
If there is inflammation of the skin, thrombophlebitis or subcutaneous induration, severe pain, ulcers, sudden swelling of one or both legs, cardiac or renal insufficiency, a doctor should be consulted. In the event of inadequate or unsatisfactory symptomatic response within 2 weeks, a doctor should be consulted as oedema may have alternative causes. In the absence of sufficient safety data, the use in children and adolescents below 18 years of age is not recommended. If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.	Indication 1) If there is inflammation of the skin, thrombophlebitis or subcutaneous induration, severe pain, ulcers, sudden swelling of one or both legs, cardiac or renal insufficiency, a doctor should be consulted. Cutaneous use: The product should not be used on broken skin, around the eyes or on mucous membranes. Oral use: In the event of inadequate or unsatisfactory symptomatic response within 2 weeks, a doctor should be consulted as oedema may have alternative causes. Indication 2) If rectal bleeding occurs during the treatment of haemorrhoids a doctor or a qualified health care practitioner should be consulted. In the event of inadequate or unsatisfactory symptomatic response within 1 week, a doctor should be consulted. Indication 3) In the event of inadequate or unsatisfactory symptomatic response within 1 week, a doctor should be consulted as oedema may have alternative causes. Indication 1), 2) and 3) In the absence of sufficient safety data, the use in children and adolescents below 18 years of age is not recommended. If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

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

Well-established use	Traditional use
Not known	Not known

4.6. Fertility pregnancy and lactation

Well-established use	Traditional use
No fertility data available. Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.	No fertility data available. Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and 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.	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
Hypersensitivity reactions of the skin (itching and erythema, urticaria) have been reported. The frequency is not known. Nausea, gastrointestinal complaints and headache may occur. The frequency is not known. If other adverse reactions not mentioned above occur, a doctor or a pharmacist should be consulted.	Contact allergy and/or hypersensitivity reactions of the skin (itching and erythema, urticaria) have been reported. The frequency is not known. Oral use: Nausea, gastrointestinal complaints and headache may occur. 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 cases of overdose have been reported.	No case of overdose has been reported.

5. Pharmacological properties

5.1. Pharmacodynamic properties

Well-established use	Traditional use
Pharmacotherapeutic group: Herbal medicinal product for venous diseases. ATC code: C05CX	Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC.

The efficacy of orally administered dry extract of red vine leaves (4-6:1) in reducing oedema has been studied in patients suffering from chronic venous insufficiency (CVI, grade I or II). Grapevine leaf extract improves the microvascular blood flow in CVI patients.	

5.2. Pharmacokinetic properties

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

5.3. Preclinical safety data

Well-established use	**Traditional use**
No signs of acute toxicity in rats or mice after oral administration of 10,000 mg/kg body weight. No sub-acute toxicity in rats, in doses up to 250 mg/kg body weight daily for 90 days. In the micronucleus test, the gene mutation test in V79 cells of Chinese hamsters and the Ames Salmonella/microsome plate incorporation test the extract of grapevine leaf proved not to be mutagenic. The teratogenicity study in rabbits (treatment from 6^{th}-18^{th} day of pregnancy) did not reveal any toxic effects in doses up to 3.000 mg/kg body weight. Tests on genotoxicity and reproductive toxicity do not give any reason for concern. Tests on carcinogenicity have not been performed.	Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC, unless necessary for the safe use of the product. Tests on genotoxicity and reproductive toxicity do not give any reason for concern for the cutaneous use of the soft extract (2.5-4:1; water). Tests on genotoxicity, carcinogenicity and reproductive toxicity have not been performed for comminuted and powdered preparations.

6. Pharmaceutical particulars

Well-established use	**Traditional use**
Not applicable	Not applicable

7. Date of compilation / last revision

30 May 2017