EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee on Herbal Medicinal Products (HMPC)

Community herbal monograph on *Vitis vinifera* L., folium

Final

Discussion in Working Party on Community monographs and Community 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). Comments should be provided using this template to hmpc.secretariat@ema.europa.eu	15 April 2010
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Keywords	Herbal medicinal products; HMPC; Community herbal monographs; well-established medicinal use; traditional use; *Vitis vinifera L.;* Vitis viniferae folium; grapevine leaf

BG (bălgarski): лоза, лист	LT (lietuvių kalba): Tikrųjų vynmedžių lapai
CS (čeština): Červený list vinné révy	LV (latviešu valoda): Īstā vīnkoka lapas
DA (dansk): Vinblad	MT (malti): Werqa tad-dielja
DE (Deutsch): Rote Weinrebenblätter	NL (nederlands): Wijnstokblad
EL (elliniká): Φύλλο Αμπέλου	PL (polski): Liść winorośli właściwej
EN (English): Grapevine leaf	PT (português): Folha de videira
ES (espanol): Vid, hoja de	RO (română): Frunze de viţă-de-vie
ET (eesti keel): Viinapuu lehed	SK (slovenčina): List viniča
FI (suomi): Aitoviiniköynnös, lehti	SL (slovenščina): List vinske trte
FR (français): Feuille de vigne rouge	SV (svenska): Blad från vinranka
HU (magyar): Bortermő szőlő levél	*IS (íslenska)*: Vínviðarlauf
IT (italiano): Vite, foglia	NO (norsk): Rød vinranke, blad

[1] Correction of ATC code

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Community 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 as amended *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 as amended *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 The material complies with the Ph. Eur. monograph (ref.: 01/2008:1374).
3 The declaration of the active substance(s) for an individual finished product should be in accordance with relevant herbal quality guidance.
4 and 4 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. 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

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 required before beneficial effects are observed. Long term use is possible in consultation with a doctor.	**Posology** Indication 1) *Adults and elderly* Oral use a) Comminuted herbal substance as herbal tea 5-10 g/250 ml, 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 base (10 g contain 282 mg soft extract). Apply a thin layer on the affected area 1-3 times daily.

Method of administration Oral use.	Indication 2) and 3) *Adults and elderly* Oral use a) Comminuted herbal substance as herbal tea 5-10 g/250 ml, 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** Oral use. 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	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.

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.	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. In the absence of sufficient safety data, the use in children and adolescents below 18 years of age is not recommended.

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

Well-established use	**Traditional use**
Not known.	Not known.

4.6. Pregnancy and lactation

Well-established use	**Traditional use**
Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.	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.	Indication 1), 2) and 3) 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: Other capillary stabilizing agents ATC code: **C05CX** 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.	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**
Not known.	Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended.

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 as amended, 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

15 July 2010