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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 *VITIS VINIFERA* L. VAR. *TINCTORIA*, FOLIUM

DISCUSSION IN WORKING PARTY ON COMMUNITY MONOGRAPHS AND COMMUNITY LIST (MLWP)	March 2009 July 2009 September 2009
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ADOPTION BY HMPC	

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KEYWORDS	Herbal medicinal products; HMPC; Community herbal monographs; well-established medicinal use; traditional use; *Vitis vinifera* L. var. *tinctoria*; Vitis viniferae folium; red vine leaf

BG (bălgarski):
CS (čeština):
DA (dansk):
DE (Deutsch): Rebe Blatter
EL (elliniká): Φύλλο Αμπέλου
EN (English):
ES (espanol): Hojas de vid roja
ET (eesti keel):
FI (suomi):
FR (français): Feuilles de vigne
HU (magyar):
IT (italiano): Fogli della vite
LT (lietuvių kalba):
LV (latviešu valoda):
MT (malti):
NL (nederlands): Wijnstok bladeren
PL (polski): liść winorośli właściwej
PT (português): Folhas da videira
RO (română):
SK (slovenčina):
SL (slovenščina):
SV (svenska):
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COMMUNITY HERBAL MONOGRAPH ON *VITIS VINIFERA* L., FOLIUM

1. NAME OF THE MEDICINAL PRODUCT

To be specified for the individual finished product.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION [1]

Well-established use	Traditional use
With regard to the marketing authorisation application of Article 10(a) of Directive 2001/83/EC as amended	With regard to the registration application of Article 16d(1) of Directive 2001/83/EC as amended
Vitis vinifera L. var. *tinctoria*, folium (red vine leaf)	*Vitis vinifera* L. var. *tinctoria*, folium (red vine leaf)
i) Herbal substance Not applicable	i) Herbal substance Not applicable
ii) Herbal preparation Dry extract of red vine leaves (4-6:1; extraction solvent water) quantified to flavonoids content 3-7%	ii) Herbal preparation • Comminuted herbal substance • Powdered herbal substance • Dry extract (3:1; extraction solvent water) • Soft extract (4-6:1; 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 or liquid dosage forms for oral use. Herbal preparation in semi-solid dosage forms for cutaneous use. Herbal preparation in liquid dosage forms (eye drops) [2] for ocular use. The pharmaceutical form should be described by the European Pharmacopoeia full standard term.

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

[2] The medicinal product complies with the Ph. Eur. monograph on eye preparations (01/2008:1163)

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.	a) Traditional herbal medicinal product to relieve symptoms of discomfort and heaviness of legs related to minor venous circulatory disturbances. b) Traditional herbal medicinal product for symptomatic relief of itching and burning associated with haemorrhoids. c) Traditional herbal medicinal product for symptomatic treatment of cutaneous capillary fragility. d) Traditional herbal medicinal product to be used for the temporary relief of discomfort due to dryness of the eye or to exposure to wind or sun. The product is a traditional herbal medicinal product for use in the 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 (4-6:1; water) Single dose: 360 mg Daily dose: 360 mg to 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 6 weeks. At least 4 weeks of treatment may be required before any beneficial effect is observed. Long term use is possible in consultation with a doctor. **Method of administration** Oral use.	**Posology** Indication a) *Adults and elderly* Oral use • Comminuted dried leaves as herbal tea 5-10 g/250 ml, 2 times a day • Powdered dried leaf, capsules Single dose: 270-350 mg Daily dose: 1 capsule 3 times a day (5 capsules a day if necessary) • Dry extract (3:1; water): 169 mg, up to 3 times a day Cutaneous use • Soft extract (4-6:1; water) in a cream base (10 g contain 282 mg soft extract). Apply a thin layer on the affected area 1-3 times / day

	Indication b) and c) *Adults and elderly* Oral use • Comminuted dried leaves as herbal tea 5-10 g/250 ml, 2 times a day • Powdered dried leaf, capsules Single dose: 270-350 mg Daily dose: 1 capsule 3 times a day (5 capsules a day if necessary) • Dry extract (3:1; water): 169 mg, up to 3 times a day Indication d) *Adults and elderly* • Soft extract (4-6:1; extraction solvent water) Eye drops (1 g of extract / 100 ml): 1 drop/each eye, 2-8 times a day **Duration of use** Indication a) 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. Indication b) and c) 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. Indication d) The recommended duration of use is 4 days. If the symptoms persist for more than 2 days 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. Ocular 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, varicosis or subcutaneous induration 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.	Indication a) 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. 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 b) 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 as oedema may have alternative causes. Indication c) In the event of inadequate or unsatisfactory symptomatic response within 1 week, a doctor should be consulted as oedema may have alternative causes. Indication d) Stop use and consult a doctor if you experience eye pain, changes in vision, continued redness or irritation of the eye, or if the condition worsens or persists for more than 48 hours.

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, headache and vertigo, may occur. The frequency is not known. If other adverse reactions, not mentioned above, occur, a doctor or a pharmacist should be consulted.	Indication a), b), c) and d) Contact allergy and/or hypersensitivity reactions of the skin (itching and erythema, urticaria) have been reported. The frequency is not known. Indication a), b) and c) Oral use Nausea, gastrointestinal complaints, headache and vertigo, 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: **C05 CP02** Red vine leaf extract contains flavonoids of the flavonol type (quercetin-3-O-β-D-glucuronide, isoquercitrin [quercetin-3-O-β-glucoside], and kaempferol-3-glucoside), that have shown to exert anti-inflammatory and antioedematous effects *in vitro* and *in vivo*. 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).	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 red vine 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 (4-6:1; water). Tests on carcinogenicity have not been performed.

6. PHARMACEUTICAL PARTICULARS

Well-established use	Traditional use
Not applicable.	Not applicable.

7. DATE OF COMPILATION/LAST REVISION

13 January 2010