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

Final

<table>
<thead>
<tr>
<th>Initial assessment</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Discussion in Working Party on European Union monographs and list (MLWP)</td>
<td>March 2009</td>
</tr>
<tr>
<td></td>
<td>July 2009</td>
</tr>
<tr>
<td></td>
<td>September 2009</td>
</tr>
<tr>
<td>Adoption by Committee on Herbal Medicinal Products (HMPC) for release for consultation</td>
<td>12 November 2009</td>
</tr>
<tr>
<td>End of consultation (deadline for comments)</td>
<td>15 April 2010</td>
</tr>
<tr>
<td>Re-discussion in MLWP</td>
<td>May 2010</td>
</tr>
<tr>
<td></td>
<td>July 2010</td>
</tr>
<tr>
<td>Adoption by HMPC</td>
<td>15 July 2010</td>
</tr>
<tr>
<td>Monograph (EMA/HMPC/16635/2009)</td>
<td></td>
</tr>
<tr>
<td>AR (EMA/HMPC/16633/2009)</td>
<td></td>
</tr>
<tr>
<td>List of references (EMA/HMPC/16634/2009)</td>
<td></td>
</tr>
<tr>
<td>List entry (EMA/HMPC/5816/2010)</td>
<td></td>
</tr>
<tr>
<td>Overview of comments received during public consultation (EMA/HMPC/276427/2010)</td>
<td></td>
</tr>
<tr>
<td>HMPC List entry Opinion (EMA/457286/2010)</td>
<td></td>
</tr>
<tr>
<td>HMPC Opinion (EMA/HMPC/457286/2010)</td>
<td></td>
</tr>
</tbody>
</table>

| 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).                           | 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’.
<table>
<thead>
<tr>
<th>Keywords</th>
<th>Herbal medicinal products; HMPC; European Union herbal monographs; well-established medicinal use; traditional use; <em>Vitis vinifera</em> L., folium; <em>Vitis viniferae</em> folium; grapevine leaf</th>
</tr>
</thead>
<tbody>
<tr>
<td>BG (bălgarski): лоза, лист</td>
<td>LT (lietuvių kalba): Tikrųjų vinmedžių lapai</td>
</tr>
<tr>
<td>CS (čeština): červený list vinné révy</td>
<td>LV (latviešu valoda): Īstā vīnkoka lapas</td>
</tr>
<tr>
<td>DA (dansk): Vinblad</td>
<td>MT (malti): werqa tad-dielja ta’ l-għeneb</td>
</tr>
<tr>
<td>DE (Deutsch): Rote Weinrebenblätter</td>
<td>NL (nederlands): wijnstok</td>
</tr>
<tr>
<td>EL (elliniká): φύλλο αμπέλου</td>
<td>PL (polski): Liść winorośli właściwej</td>
</tr>
<tr>
<td>EN (English): grapevine leaf</td>
<td>PT (português): videira, folha</td>
</tr>
<tr>
<td>ES (español): vid, hoja de</td>
<td>RO (română): frunză de vință-de-vie</td>
</tr>
<tr>
<td>ET (eesti keel): viinapuu lehed</td>
<td>SK (slovenčina): list viniča</td>
</tr>
<tr>
<td>FI (suomi): aitoviinköynnös, lehti</td>
<td>SL (slovenščina): list vinske trte</td>
</tr>
<tr>
<td>FR (français): vigne rouge (feuille de)</td>
<td>SV (svenska): vinranka, blad</td>
</tr>
<tr>
<td>HR (hrvatski): list vinove loze</td>
<td>IS (íslenska): Vínviðarlauf</td>
</tr>
<tr>
<td>HU (magyar): bortermő szőlő levél</td>
<td>NO (norsk): rød vinranke, blad</td>
</tr>
<tr>
<td>IT (italiano): Vite, foglia</td>
<td></td>
</tr>
</tbody>
</table>

European Union herbal monograph on *Vitis vinifera* L., folium
EMA/HMPC/464684/2016
European Union 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**

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td>With regard to the marketing authorisation application of Article 10(a) of Directive 2001/83/EC.</td>
<td>With regard to the registration application of Article 16d(1) of Directive 2001/83/EC.</td>
</tr>
<tr>
<td><em>Vitis vinifera</em> L., folium, (grapevine leaf)</td>
<td><em>Vitis vinifera</em> L., folium, (grapevine leaf)</td>
</tr>
<tr>
<td>i) Herbal substance</td>
<td>i) Herbal substance</td>
</tr>
<tr>
<td>Not applicable</td>
<td>Not applicable</td>
</tr>
<tr>
<td>ii) Herbal preparation</td>
<td>ii) Herbal preparation</td>
</tr>
<tr>
<td>Dry extract (DER 4-6:1); extraction solvent water</td>
<td>a) Comminuted herbal substance</td>
</tr>
</tbody>
</table>

3. **Pharmaceutical form**

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herbal preparation in solid dosage forms for oral use.</td>
<td>Comminuted herbal substance as herbal tea for oral use.</td>
</tr>
<tr>
<td></td>
<td>Herbal preparation in solid dosage forms for oral use.</td>
</tr>
<tr>
<td></td>
<td>Herbal preparation in semi-solid dosage forms for cutaneous use.</td>
</tr>
<tr>
<td></td>
<td>The pharmaceutical form should be described by the European Pharmacopoeia full standard term.</td>
</tr>
</tbody>
</table>

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

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.

Traditional use

<table>
<thead>
<tr>
<th>Indication 1</th>
<th>Traditional herbal medicinal product to relieve symptoms of discomfort and heaviness of legs related to minor venous circulatory disturbances.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication 2</td>
<td>Traditional herbal medicinal product for symptomatic relief of itching and burning associated with haemorrhoids after serious conditions have been excluded by a medical doctor.</td>
</tr>
<tr>
<td>Indication 3</td>
<td>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.</td>
</tr>
</tbody>
</table>

4.2. Posology and method of administration

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

---

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**

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypersensitivity to the active substance.</td>
<td>Hypersensitivity to the active substance.</td>
</tr>
</tbody>
</table>
4.4. **Special warnings and precautions for use**

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
<td><strong>Indication 1)</strong></td>
</tr>
<tr>
<td>In the event of inadequate or unsatisfactory symptomatic response within 2 weeks, a doctor should be consulted as oedema may have alternative causes.</td>
<td>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.</td>
</tr>
<tr>
<td>In the absence of sufficient safety data, the use in children and adolescents below 18 years of age is not recommended.</td>
<td>Cutaneous use: The product should not be used on broken skin, around the eyes or on mucous membranes.</td>
</tr>
<tr>
<td>If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.</td>
<td>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.</td>
</tr>
</tbody>
</table>

**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.

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 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**

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not known</td>
<td>Not known</td>
</tr>
</tbody>
</table>
4.6. Fertility pregnancy and lactation

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td>No fertility data available.</td>
<td>No fertility data available.</td>
</tr>
<tr>
<td>Safety during pregnancy and lactation has not been established. In the absence of</td>
<td>Safety during pregnancy and lactation has not been established. In the absence</td>
</tr>
<tr>
<td>sufficient data, the use during pregnancy and lactation is not recommended.</td>
<td>of sufficient data, the use during pregnancy and lactation is not recommended.</td>
</tr>
</tbody>
</table>

4.7. Effects on ability to drive and use machines

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td>No studies on the effect on the ability to drive and use machines have been</td>
<td>No studies on the effect on the ability to drive and use machines have been</td>
</tr>
<tr>
<td>performed.</td>
<td>performed.</td>
</tr>
</tbody>
</table>

4.8. Undesirable effects

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypersensitivity reactions of the skin (itching and erythema, urticaria) have</td>
<td>Contact allergy and/or hypersensitivity reactions of the skin (itching and</td>
</tr>
<tr>
<td>been reported. The frequency is not known.</td>
<td>erythema, urticaria) have been reported. The frequency is not known.</td>
</tr>
<tr>
<td>Nausea, gastrointestinal complaints and headache may occur. The frequency is not</td>
<td>Oral use: Nausea, gastrointestinal complaints and headache may occur. The</td>
</tr>
<tr>
<td>known.</td>
<td>frequency is not known.</td>
</tr>
<tr>
<td>If other adverse reactions not mentioned above occur, a doctor or a pharmacist</td>
<td>If other adverse reactions not mentioned above occur, a doctor or a qualified</td>
</tr>
<tr>
<td>should be consulted.</td>
<td>health care practitioner should be consulted.</td>
</tr>
</tbody>
</table>

4.9. Overdose

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td>No cases of overdose have been reported.</td>
<td>No case of overdose has been reported.</td>
</tr>
</tbody>
</table>

5. Pharmacological properties

5.1. Pharmacodynamic properties

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

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not known</td>
<td>Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC.</td>
</tr>
</tbody>
</table>

5.3. Preclinical safety data

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td>No signs of acute toxicity in rats or mice after oral administration of 10,000 mg/kg body weight.</td>
<td>Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC, unless necessary for the safe use of the product.</td>
</tr>
<tr>
<td>No sub-acute toxicity in rats, in doses up to 250 mg/kg body weight daily for 90 days.</td>
<td>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).</td>
</tr>
<tr>
<td>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.</td>
<td>Tests on genotoxicity, carcinogenicity and reproductive toxicity have not been performed for comminuted and powdered preparations.</td>
</tr>
<tr>
<td>The teratogenicity study in rabbits (treatment from 6th-18th day of pregnancy) did not reveal any toxic effects in doses up to 3,000 mg/kg body weight.</td>
<td></td>
</tr>
<tr>
<td>Tests on genotoxicity and reproductive toxicity do not give any reason for concern.</td>
<td></td>
</tr>
<tr>
<td>Tests on carcinogenicity have not been performed.</td>
<td></td>
</tr>
</tbody>
</table>

6. Pharmaceutical particulars

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not applicable</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

7. Date of compilation/last revision

30 May 2017