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Committee on Herbal Medicinal Products (HMPC)

European Union herbal monograph on *Aesculus hippocastanum* L., semen

Draft – Revision 1

Initial assessment	
Discussion in Working Party on European Union monographs and European Union list (MLWP)	May 2008 July 2008 September 2008
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Adoption by HMPC Monograph (EMEA/HMPC/225319/2008) AR (EMEA/HMPC/225304/2008) List of references (EMEA/HMPC/225629/2008) Overview of comments received during the public consultation (EMEA/HMPC/262723/2009) HMPC Opinion (EMEA/HMPC/438817/2009)	16 July 2009
First systematic review	
Discussion in MLWP and HMPC	November 2016 March 2018 June 2018 September 2018 January 2019 May 2019
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Keywords	Herbal medicinal products; HMPC; European Union herbal monographs; well-established medicinal use; traditional use; *Aesculus hippocastanum* L.; Hippocastani semen; horse chestnut seed

BG (bulgarski): Див кестен, семе CS (čeština): semeno kaštanu koňského DA (dansk): Hestekastanje DE (Deutsch): Rosskastaniensamen EL (elliniká): σπέρμα ιπποκαστανέας EN (English): horse-chestnut seed ES (español): castaño de indias, semilla de ET (eesti keel): hobukastaniseeme FI (suomi): hevoskastanja, siemen FR (français): marron d'inde HR (hrvatski): sjeme divljeg kestena HU (magyar): vadgesztenyetermés IT (italiano): Ippocastano seme	LT (lietuvių kalba): Kaštonų sėklos LV (latviešu valoda): Zirgkastaņa sēklas MT (Malti): żerriegħa tal-qastan salvaġġ ta' l-indja NL (Nederlands): Paardenkastanje PL (polski): Nasienie kasztanowca PT (português): castanheiro-da-índia, semente RO (română): sămânţă de castan SK (slovenčina): semeno pagaštana SL (slovenščina): seme navadnega divjega kostanja SV (svenska): hästkastanj, frö IS (íslenska): NO (norsk): hestekastanje

European Union herbal monograph on *Aesculus hippocastanum* L., semen

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 marketing authorisation application of Article 10(a) of Directive 2001/83/EC *Aesculus hippocastanum* L., semen (horse chestnut seed) i) Herbal substance Not applicable ii) Herbal preparations Dry extracts[3] (extraction solvent ethanol 40-80% V/V) standardised to contain 6.5-10% triterpene glycosides, calculated as protoaescigenin[4] .	With regard to the registration application of Article 16d(1) of Directive 2001/83/EC *Aesculus hippocastanum* L., semen (horse chestnut seed) i) Herbal substance Not applicable ii) Herbal preparations a) Dry extract corresponding to a specified amount of triterpene glycosides, calculated as protoaescigenin[5], extraction solvent ethanol 25-50% V/V b) Liquid extract (DER 1:3.5-5) , extraction solvent ethanol 50% V/V c) Dry extract (DER 5-10:1), extraction solvent methanol 80% V/V d) Dry extract (DER 5-8:1), extraction solvent methanol 80% V/V e) Dry extract (DER 4.5-5.5:1), extraction solvent ethanol 50% V/V f) Dry extract (DER 5-7:1), extraction solvent ethanol 60% V/V g) Liquid extract (DER 1:1.5-2.5), extraction solvent ethanol 55% V/V h) Liquid extract (DER 1:2), extraction solvent

[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.: 1830)
[3] The composition of the extraction solvent and the content of triterpene glycosides must be specified in the individual extract. The herbal preparation complies with the Ph. Eur. monograph (ref.: 1829)
[4] In 2017, new lower acceptance criteria for the content of triterpene glycosides using a more specific method, i.e. LC assay, were introduced in the Ph. Eur. monographs 1830 and 1829. The previous method, i.e. absorption assay was superseded. A correlation factor of approx. 2.4 (ratio old method vs. new method) has been used in the revision.

Well-established use	Traditional use
	ethanol 19% m/m i) Dry extract (DER 3-6:1), extraction solvent water

3. Pharmaceutical form

Well-established use	Traditional use
Herbal preparations in modified or immediate release dosage forms for oral use. The pharmaceutical form should be described by the European Pharmacopoeia full standard term.	Herbal preparations in semi-solid dosage forms for cutaneous use. Herbal preparations in solid or liquid dosage forms 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
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 relief of signs of bruises, such as local oedema and haematoma. 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* Standardised dry extract corresponding to a content of 20 mg triterpene glycosides calculated	**Posology** Indication 1) Herbal preparations a)-f)

Well-established use	Traditional use
as protoaescigenin[5] 2 times daily. There is no relevant indication in children and adolescents under 18 years of age. **Duration of use** 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	*Adults and elderly* a) In semi-solid dosage forms: herbal preparation in an amount equivalent to 0.4% triterpene glycosides, calculated as protoaescigenin[6] b) In semi-solid dosage forms: amount equivalent to 20% herbal preparation c) In semi-solid dosage forms: amount equivalent to 3.2% herbal preparation d) In semi-solid dosage forms: amount equivalent to 0.85% herbal preparation e) In semi-solid dosage forms: amount equivalent to 3.8% herbal preparation f) In semi-solid dosage forms: amount equivalent to 1.6% herbal preparation For all preparations a)-f): Single dose: Apply a thin layer on the affected area Daily dose: 1-3 times. Herbal preparations g)-i) *Adults and elderly* g) Single dose: 300 mg liquid extract 2 times daily Daily dose: 600 mg h) Single dose: 154 mg 3-4 times daily Daily dose: 462-616 mg daily i) Single dose: 99 mg dry extract 2 times daily Daily dose: 198 mg For all preparations a)-i): There is no relevant use in children and adolescents under 18 years of age. Indication 2) Herbal preparation a)-b)

[5] In 2017, new lower acceptance criteria for the content of triterpene glycosides using a more specific method, i.e. LC assay, were introduced in the Ph. Eur. monographs 1830 and 1829. The previous method, i.e. absorption assay was superseded. A correlation factor of approx. 2.4 (ratio old method vs. new method) has been used in the revision.

Well-established use	Traditional use
	Adolescents, adults and elderly a) In semi-solid dosage forms: herbal preparation in an amount equivalent to approx. 0.4% triterpene glycosides, calculated as protoaescigenin[6] b) In semi-solid dosage forms: amount equivalent to 20% herbal preparation For preparation a)-b) Single dose: Apply a thin layer on the affected area Daily dose: 1-3 times The use in children under 12 years of age is not recommended (see section 4.4 'Special warnings and precautions for use'). **Duration of use** Indication 1) If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted. Indication 2) If the symptoms persist longer than 5 days during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted. **Method of administration** Herbal preparation a)-f): Cutaneous use Herbal preparation g)-i): Oral use

4.3. Contraindications

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

[6] In 2017, new lower acceptance criteria for the content of triterpene glycosides using a more specific method, i.e. LC assay, were introduced in the Ph. Eur. monographs 1830 and 1829. The previous method, i.e. absorption assay was superseded. A correlation factor of approx. 2.4 (ratio old method:new method) has been used in the revision.

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. If the symptoms worsen or signs of skin infections occur during the use of the medicinal product, a doctor or a pharmacist should be consulted.	If symptoms worsen or signs of skin infections occur during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted. Cutaneous use: The product should not be used on broken skin, around the eyes or on mucous membranes. 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. Indication 2) In the absence of sufficient safety data, the use in children below 12 years of age is not recommended.

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

Well-established use	Traditional use
None reported	None reported

4.6. Fertility, 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. 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.

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
Gastrointestinal complaints, headache, vertigo, itching and allergic reactions have been reported. The frequency is not known. If other adverse reactions not mentioned above occur, a doctor or a pharmacist should be consulted.	Cutaneous use: Hypersensitivity reactions of the skin (itching and erythema) have been reported. The frequency is not known. Oral use: Gastrointestinal complaints, headache, vertigo, itching and allergic reactions have been reported. The frequency is not known. Cutaneous and oral use: 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.	No case of overdose has been reported.

5. Pharmacological properties

5.1. Pharmacodynamic properties

Well-established use	Traditional use
Pharmacotherapeutic group: Vasoprotectives Proposed ATC code: C05CX03 The exact mechanism of action is not known, but preclinical and clinical pharmacological studies indicate that an effect on venous tone and capillary filtration rate is involved. Based on a systematic review (meta-analysis) of 17 clinical trials, it can be concluded that horse chestnut seed extract significantly reduces symptoms of chronic venous insufficiency, such as oedema, pain and itching compared to placebo.	Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC.

5.2. Pharmacokinetic properties

Well-established use	Traditional use
No relevant data available.	Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC.

5.3. Preclinical safety data

Well-established use	Traditional use
Available preclinical data indicate low toxicity following oral administration of the herbal preparation. Adequate tests on reproductive toxicity, genotoxicity and 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. Adequate tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed.

6. Pharmaceutical particulars

Well-established use	Traditional use
Not applicable	Not applicable

7. Date of compilation / last revision

15 May 2019