European Medicines Agency
Evaluation of Medicines for Human Use

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OVERVIEW OF COMMENTS RECEIVED ON 'COMMUNITY HERBAL MONOGRAPH ON *HAMAMELIS VIRGINIANA* L., FOLIUM' (EMEA/HMPC/114586/2008)

Table 1: Organisations and/or individuals that commented on the draft 'Community herbal monograph on *Hamamelis virginiana* L., folium' as released for public consultation on 6 November 2008 until 15 March 2009.

	Organisations and/or individuals
1	European Scientific Cooperative on Phytotherapy (ESCOP)
2	The Association of the European Self-Medication Industry (AESGP)

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Table 2: Discussion of comments

GENERAL COMMENTS		
Interested party	**Comment and Rationale**	**Outcome**
ESCOP	The draft text relates only to cutaneous, oromucosal and rectal uses of hamamelis leaf preparations. Oral use is also well-documented, particularly in the treatment of venous circulatory disturbances, and should be taken into account. • The ESCOP monograph (2003) [1] supports the oral use of hamamelis leaf for the "Symptomatic treatment of complaints related to varicose veins, such as painful and heavy legs, and of haemorrhoids", citing general textbooks [2,3] and several reviews. • The French regulatory guideline, Spécialités pharmaceutiques á base de plantes: avis aux fabricants concernant les demandes d'autorisation de mire sur le marché (Bulletin Officiel N° 86/20 bis, August 1986 and subsequent editions), recognizes the oral use of hamamelis preparations in subjective manifestations of venous insufficiency such as heavy legs and for the symptoms of haemorrhoids. • The oral use of various hamamelis leaf preparations in cases of venous insufficiency (varicose veins, haemorrhoids, heavy legs) was documented in the 9th edition of the *Pharmacopée Francaise* under *Fiches de documentation de pratique officinale* (July 1978) [4]. • Severa] hamamelis leaf preparations for oral use were specified in the *British Herbal Pharmacopoeia* (1979) [5] and the subsequent 1983 edition. • The German Standardzulassung (1986) for hamamelis leaf recommended oral use of an infusion for the treatment of diarrhoea [6]. Herbal preparations and posology described in the above publications include: • Comminuted herbal substance for preparation of an infusion: 4-6 g daily [1,4-6]. • Liquid extract from dried leaf (1:1, extraction solvent: ethanol 45% V/V): 4-12 ml daily [1,4,5]. **Note:** This liquid extract is described in the British Pharmaceutical Codex 1973 (Hamamelis Liquid Extract) [7] and the Pharmacopée Frangaise VIII 1965 (Extrait Fluide d'Hamamélis) [8].	Not agreed. Although the oral use of hamamelis leaf for certain indications is documented in different handbooks as well as in the French regulatory guideline, there is not sufficient evidence of the oral use of such products which fulfil their plausibility as established in the Directive 2004/24/EC, so the proposal is not accepted.

Interested party	Comment and Rationale	Outcome
	• Powdered herbal substance: 0.5-2 g daily [4]. **Note*:*** The powdered herbal substance is authorized in France and Spain as a traditional herbal medicinal product to reduce sensations of heavy legs or the discomfort of haemorrhoids in single oral doses (in capsules) of *290* and 220 mg respectively, and corresponding daily doses of 870-1740 mg or 660-1980 mg. The herbal preparations listed in Section 2, as well as semi-solid preparations and suppositories described in Section 4.2, have been precisely and rigidly defined in the draft. However, there is no scientifc evidence to justify those preparations to the exclusion of various other comparable, long-established and well-documented preparations - some examples of which are proposed below for addition to the text. In the absence of controlled studies, a more flexible approach (within limits) to the preparations to be used would be helpful towards harmonization across the 25 EU member states.	

SPECIFIC COMMENTS ON TEXT			
Section number and heading	**Interested party**	**Comment and Rationale**	**Outcome**
2. Qualitative and quantitative composition	ESCOP	ii) Herbal preparations **We recommend addition of the following to the list of herbal preparations:** Powdered herbal substance Dry extract from dried leaf (extraction solvent: ethanol 45% *V/V), as described in the British Pharmaceutical Codex 1973 [9]*. Liquid extract from dried leaf (1:1, extraction solvent: ethanol 45% *V/V), as described in the British Pharmaceutical Codex 1973 [7]*	Partially agreed. The liquid extract (1:1; 45% ethanol V/V) is already included for the external use. The oral use is not accepted in the monograph.
3. Pharma-ceutical form	ESCOP	**We propose additions to the text of the first two sentences, to read:** Comminuted herbal substance as herbal tea for **oral,** oromucosal or cutaneous use. Herbal preparations in **solid,** semisolid or liquid dosage forms for **oral,** cutaneous or oromucosal use.	Not agreed. See above.
4.1.Therapeutic indications	ESCOP	**We propose a further indication:** **d)** for the relief of symptoms of discomfort and heaviness of legs related to minor venous circulatory disturbances.	Not agreed. The indication has already been discussed at HMPC. The information of products on the market together with the available data are not sufficient to accept such indication.

Section number and heading	Interested party	Comment and Rationale	Outcome
4.2. Posology and method of administration	ESCOP	***Posology*** **We propose the following additions to the text:** **Under Indication a)** For cutaneous use: *(in addition to the preparations already described)* Liquid extract from dried leaf (1:1, extraction solvent: ethanol 45% V/V) in a strength corresponding to 10% as a semi-solid preparation. *As described in the British Pharmaceutical Codex 1973 [10].* **Under Indication b)** For cutaneous use: *(in addition to the preparations already described)* Liquid extract from dried leaf (1:1, extraction solvent: ethanol 45% V/V) in a strength corresponding to 10% as a semi-solid preparation. *As described in the British Pharmaceutical Codex 1973 [101.* For rectal use: *(in addition to the suppository already described)* Suppository containing 200 mg of dry extract from dried leaf (extraction solvent: ethanol 45% V/V). *As described in the British Pharmaceutical Codex 1973 [11].* For oral use: Comminuted herbal substance to be taken as a herbal tea: 4-6 g daily Powdered herbal substance: 0.5 to 2 g daily Liquid extract from dried leaf (1:1, extraction solvent ethanol 45%): 4-12 ml daily.	Already included. There are no products with this dry extract on the UK market. Not agreed.

Section number and heading	Interested party	Comment and Rationale	Outcome
		Under Indication d) *Adults and elderly* <u>For oral use</u>: Comminuted herbal substance to be used as a herbal tea: 4-6 g daily Powdered herbal substance: 0.5 to 2 g daily Liquid extract (1:1) extraction solvent ethanol 45%: 4-12 ml daily.	Not agreed.
		Duration of treatment **Indication b)** Haemorrhoids are generally a long-term condition and we consider that the recommended duration of use of 4 days would be far too short in many cases. **We propose amendment to:** If symptoms persist or do not improve within one month a doctor or qualified health-care practitioner should be consulted.	Not agreed.
		For Indication d) we propose: If symptoms persist or do not improve within 2 weeks a doctor or qualified health-care practitioner should be consulted. This would be consistent with the duration of oral use recommended in similar indications in two Community monographs already adopted: *Melitotus officinalis (L.)* Lam., herba and *Ruscus aculeatus* L., rhizoma.	Indication d) is not accepted.
		Method of administration **We propose an addition to the text, to read:** For **oral** or rectal administration, and cutaneous or oromucosal application.	Oral use not accepted.

Section number and heading	Interested party	Comment and Rationale	Outcome
2. Qualitative and quantitative composition	AESGP	The following preparation should be added under **ii) Herbal preparations, traditional use:** - **Tincture prepared from dried leaves (1:10), extraction solvent ethanol 55% (V/V).** The tincture (1:10; ethanol 55% V/V) is marketed in France since 1965 and hence fulfils the 30 years criteria; we would like to have it added to the traditionally used preparations.	Not agreed. Available data on the preparation are insufficient to establish safe use in specified conditions over a period of 30 years.
3. Pharma-ceutical form	AESGP	The oral route of administration should be added as follows: "*Herbal preparations in semi-solid or liquid dosage forms for cutaneous, oromucosal or **oral** use*". This corresponds to the product mentioned above.	Not agreed.
4.2. Posology and method of administration	AESGP	***Posology*** The following posology (corresponding to the product mentioned above) should be added: **Indication b)** ***Adults and elderly*** **For oral use:** **50-150 drops of tincture in ethanol 55% V/V (1:10) up to 3-4 times daily, as a single dose.** ***Method of administration*** The oral use should be reflected as follows: ***"**For rectal administration, cutaneous, or mucosal application and **oral use**".***	Inclusion of preparation was not agreed (see above).