



European Medicines Agency  
Evaluation of Medicines for Human Use

**This document was valid from September 2007 until September 2012.**

London, 7 September 2007  
Doc. Ref. EMA/HMPC/373075/2007

**OVERVIEW OF COMMENTS RECEIVED ON  
'COMMUNITY HERBAL MONOGRAPH ON  
PRIMULA VERIS L., PRIMULA ELATIOR (L.) HILL, FLOS'  
(EMA/HMPC/64684/2007)**

Table 1: Organisations providing comments on the draft 'Community herbal monograph on *Primula veris* L. and *Primula eliator* (L.) Hill, flos' as released for consultation in March 2007 until 15 June 2007

	Organisation
1.	Bundesinstitut für Arzneimittel und Medizinprodukte - Germany (BfArM)

General comments	Comment and rationale		Rapporteur's comments
List of references	The literature list should be amended and evaluated:	BfArM	
	1) de Corres LF, Corrales JL, Munoz D, Leanizbarrutia I (1984): Dermatitis alergicas de contacto por plantas. <i>Allergol et Immunopathol</i> 12/4: 313-319		The authors investigated <i>Primula obconica</i> not <i>P. veris</i> or <i>P. elatior</i> . Reference therefore not included.
	2) Ernst E, Sieder C, März R (1995): Adverse drug reactions to herbal and synthetic expectorants. <i>Internat J Risk safety Med</i> 7/3: 219-225		The authors studied not <i>Primula</i> flower alone but the combination product "Sinupret". The contribution of <i>P.</i> flower to the adverse effects cannot be estimated. Reference therefore not included.
	3) Ernst E (1995): Nebenwirkungen pflanzlicher und synthetischer Expektorantien. <i>Z Phytother Abstractband 6. Phytotherapiekongress 5.-7.10.1995, Berlin</i>		The reference is an abstract of a congress contribution. The content is identical with the reference cited above. Reference therefore not included.
	4) Fregert S, Hjorth N (1977) The <i>Primula</i> allergen primin. <i>Contact Dermatitis</i> 3: 172-174		The authors did not find primin in a sample of <i>P. elatior</i> . Unfortunately the plant part is not mentioned. Therefore the reference is of minor relevance, since other authors found primin in the aerial parts of <i>P. elatior</i> (see AR reference Hausen BM (1978)). Reference included in the AR.
	5) Grecu L, Cucu V (1975): Saponine aus <i>Primula officinalis</i> und <i>Primula elatior</i> . <i>Planta Med</i> 27: 247-253		Analytical methods out of date. Reference therefore not included.
	6) Grujic-Vasic J, Kovac EE, Rimpapa Z (1983): Noxious effects of <i>Primula veris</i> , <i>Cyclamen europaeum</i> and <i>Saponaria officinalis</i> saponins on fish. <i>Folia Med Fac Med Univ Saraviniensis</i> 18: 127-32		Fish-toxicity is a general property of saponins, no connection to safety or efficacy of <i>Primula</i> flower. Reference therefore not included.
	7) Hjorth N (1966): <i>Primula</i> dermatitis <i>Trans St. John's Hospital Dermatol Soc</i> 52: 207-219		The authors investigated <i>Primula obconica</i> not <i>P. veris</i> or <i>P. elatior</i> . Reference therefore not included.
	8) Lepoittevin JP, Benezra C (1991): Allergic contact dermatitis caused by naturally occurring quinones. <i>Pharm Weekblad Scient</i> 13/3: 119-122		The authors investigated <i>Primula obconica</i> not <i>P. veris</i> or <i>P. elatior</i> . Reference therefore not included.
	9) Logan RA, White IR (1988): <i>Primula</i> dermatitis: prevalence, detection and outcome. <i>Contact Dermatitis</i> 9/1: 68-69		The authors investigated <i>Primula obconica</i> not <i>P. veris</i> or <i>P. elatior</i> . Reference therefore not included.
	10) Merfort I (2002) Heil- und Nutzpflanzen mit Haut-Tücken. <i>Pharm. Ztg</i> 147/3: 10-15		No additional information. Secondary literature. Reference therefore not included.
	11) Nakamura T. <i>Primula</i> dermatitis in Japan. <i>Contact Dermatitis</i> 328-329		The authors investigated <i>Primula obconica</i> not <i>P. veris</i> or <i>P. elatior</i> . Reference therefore not included.

	12) Oberst R (1986) Akute Tracheobronchitis. Kassenarzt 26:45-46		The article describes an open study with Phytobronchin, a product containing several herbal ingredients as well as ephedrine hydrochloride and guaifenesin. The product does not contain Primulae flos. Reference therefore not included.
	13) Primorac M, Sekulovic D, Antonic S (1985): In vitro determination of the spermicidal activity of plant saponins. Pharmazie 40/8: 585		Spermicidal activity is a general property of saponins, no connection to safety or efficacy of Primula flower. Reference therefore not included.
	14) Schubert HJ, Prater E, Sell M: Patch testing with primin in white petrolatum. Contact dermatitis 286		Article discusses the best way for preparation of test material of primin for patch tests. No relevance for the monograph. Reference therefore not included.
	15) Steinegger E, Hänsel R (1972): Primula-Geruchsstoffe In: Lehrbuch der Pharmakognosie und Phytopharmazie. Springer Verlag Berlin Heidelberg 3. Auflage 119-120; 210		The reference is already considered in the most recent edition (Hänsel R et al (2007)).
	16) Sterner W, Chibanguza G, März R (1983): Experimentelle Überprüfung der sekretolytischen Eigenschaften eines Phytopharmakons (Sinupret) und seiner Einzelkomponenten. Postervortrag 54. Jahresversammlung Deutsche Gesellschaft HNO-Heilkunde, Kopf- und Hals-Chirurgie Travemünde 15.-19.1983 101		Only abstract of a congress contribution. Original data later published (see AR reference Chibanguza et al (1984)).
	17) Wagner H (1993). Neues über die Therapie von Bronchitis und Sinusitis. Z. Phytother 14: 73-74		Evaluation of the activity of Sinupret, a combination of 5 herbal substances. The monograph refers primarily to Primula flos as the only active ingredient. Reference therefore not included.

Line no or section and paragraph no	Comment and rationale		Rapporteur's comments
<b>2. Qualitative and quantitative composition</b>	Concerning herbal preparations, the declaration of the mentioned preparations must be brought in line with the mentioned Procedure Paper (EMA/HMPC/182320/2005 Rev. 2), already existing monographs and currently developing guidance (Draft "Guideline on Declaration..." EMA/HMPC/CHMP/287539/2005). Therefore, the DER and the extraction solvent should be given according the following example: -liquid extract (1:1), extraction solvent: ethanol 25% (V/V)	BfArM	Endorsed.
<b>4.2 Posology and method of administration</b>	We propose to put the text in line with the text of posology of the valerian root monograph. In the AR the dosage is calculated towards x g drug. The sentence "The daily dosage is equivalent/correspond to ... g of the herbal substance." should be added also in the monograph. The texts of different monographs should be consistent.	BfArM	The dosage of the liquid extract is not calculated on the basis of equivalents of the herbal substance. It is taken from the British Herbal Pharmacopoeia and this is a traditional dosage. Therefore the proposed sentence should not be added.
<b>4.4 - Special warnings and precautions for use</b>	"The use in children under 12 year is not recommended, because no data <u>on safety</u> are available ....."	BfArM	Endorsed.
<b>4.5 Interactions</b>	The following text should be introduced: No studies on interactions with other medications have been performed. Interactions are not reported.	BfArM	Not endorsed. The proposed wording 'none reported' has been chosen for other monographs too.
<b>5. Pharmacological properties</b>	A short summary of results of in-vitro and in-vivo studies with preparations of Primula flos should be added.	BfArM	Since data on pharmacological properties are not required, the MLWP agreed to present these details in the assessment report only.