



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

22 May 2012
EMA/HMPC/198518/2012
Committee on Herbal Medicinal Products (HMPC)

Overview of comments received on Community herbal monograph on *Tilia cordata* Miller, *Tilia platyphyllos* Scop., *Tilia x vulgaris* Heyne or their mixtures, flos (EMA/HMPC/337066)

Table 1: Organisations and/or individuals that commented on the draft Community herbal monograph on *Tilia cordata* Miller, *Tilia platyphyllos* Scop., *Tilia x vulgaris* Heyne or their mixtures, flos as released for public consultation on 15 October 2011 until 15 February 2012.

	Organisations and/or individuals
1	European Botanical Forum (EBF)
2	Kooperation Phytopharmaka (KOOP Phyto)
3	The Association of the European Self-medication Industry (AESGP)



Table 2: Comments

General comments to draft document

Interested party	Comment and Rationale	Outcome
AESGP	AESGP in principle welcomes the development of the above-mentioned Community herbal monograph which, by providing harmonised assessment criteria for Tilia flos-containing products, should facilitate mutual recognition in Europe. However, relevant information on the dosage in children is missing and should be provided. We address this in our detailed comments	

SPECIFIC COMMENTS ON TEXT

Section number and heading	Interested party	Comment and Rationale	Outcome
4. Clinical particulars 4.1. Therapeutic indications	EBF	Indication 2) "Traditional herbal medicinal product for the relief of mild symptoms of mental stress." Is to be ammended as follows: "Traditional herbal medicinal product for the relief of psychosomatic symptoms of mental stress".	The comment cannot be endorsed. The proposed Indication 2) "Traditional herbal medicinal product for the relief of mild symptoms of mental stress." has been accepted in accordance with other approved traditional herbal medicinal products (Melissa, Avena etc) used in the same indication.
4. Clinical particulars 4.1.	EBF	The Indication 2) mentioned above is practically identical with Traditional use of COMMUNITY HERBAL MONOGRAPH ON	Cannot be endorsed, see explanation above.

Section number and heading	Interested party	Comment and Rationale	Outcome
Therapeutic indications		VALERIANA OFFICINALIS L., RADIX Traditional herbal medicinal product for relief of mild symptoms of mental stress... Doc. Ref. EMEA/HMPC/340719/2005 London, 26 October 2006 and Valerian Root is far more superior to calming efficacy of Lime Flower traditional only to psychosomatic symptoms	
4. Clinical particulars 4.1. Therapeutic indications	EBF	The Indication 2) mentioned above is furthermore also identical with Traditional use of fixed combination in Community herbal monograph on Valeriana officinalis L., radix and Humulus lupulus L., flos Indication 1) Traditional herbal medicinal product for relief of mild symptoms of mental stress. EMA/HMPC/585558/2007 Corr.1 Committee on Herbal Medicinal Products (HMPC) , London 6 June 2011 and this evidently more efficacious fixed combination should not have the identical wording with limited efficacy of Lime Flower traditional only to psychosomatic symptoms Ref . - Dr.A.Heraud:"Nouveau Dictionnaire des Plantes Médicinales" Sixième Ed. Paris, 1927 ,p. 592 - L Bézanger-Beauquesne, M Pinkas, MTorck, Les plantes dans la Thérapeutique moderne, Ed Maloine, Paris, 1986	The references proposed by EBF have not been submitted to the HMPC Secretariat, so cannot be evaluated in the assessment report.

Section number and heading	Interested party	Comment and Rationale	Outcome
4.1. Therapeutic indications	KOOP Phyto	We propose the following changes: Traditional herbal medicinal product used as a diaphoretic for the relief of symptoms of common cold.	Cannot be endorsed.
4.2 Posology and method of administration	KOOP Phyto	Traditional use: Posology Oral use We propose the following amendments: Children a) Comminuted herbal substance Daily dose: 9 months – 1 year: 0.2 – 1.0 g 1 – 4 years: 1 – 2 g 4 – 10 years: 2 – 4 g 10 – 16 years: 2 – 4 g Adolescents, Adults and elderly a) Comminuted herbal substance Single dose: Herbal tea: 1.5 g of the comminuted herbal substance in 150 ml of boiling water as a herbal infusion 2–4 times daily. Daily dose: 3 – 6 g The sentence “The use in children under 12 years of age is not recommended (see section 4.4 ‘Special warnings and	Partly endorsed. Section 4.2 is changed as follows: <i>Adolescents, Adults and Elderly</i> Indications 1) and 2) a) Comminuted herbal substance Single dose Herbal tea: 1.5 g of the comminuted herbal substance in 150 ml of boiling water as a herbal infusion 2–4 times daily. Daily dose 3-6 g <i>Children 4 – 12 years</i> Indication 1) a) Comminuted herbal substance Herbal tea: 1 g of the comminuted herbal substance in 150 ml of boiling water as a herbal infusion 2 – 4 times daily Daily dose 2-4 g The use in children below 4 years cannot be endorsed.

Section number and heading	Interested party	Comment and Rationale	Outcome
		precautions for use').” should be deleted. Herbal preparations of <i>Tiliae flos</i> (Linden flower) have a long tradition in the relief of symptoms of common cold and as a diaphoretic in all age groups in Germany, in other European countries and in the U.S.A. Despite no clinical studies exist, the long-lasting experience of physicians and other health professionals should not be ignored. The following monographs and textbooks supporting the use of Linden flower in children should be regarded: Bäumler, 2007 Bühning et al. 2008 Commission E, 1990 Dalla Libera et al. 2011 Gaby et al. 2006 Lipp, 2002 Santich and Bone, 2008 Schapowal, 2007 Both the German Commission E monograph and the American Herbal Products Association's guide on herbal safety state that Linden flower has no toxic effects. Further, Linden flower is considered as safe for use in children (Gaby et al. 2006). In our opinion, the current draft monograph is not consistent in the following point: No clinical studies have been performed for the proposed use, neither in adults nor in children. However,	Except for the reference by Bühning <i>et al.</i> 2008 (as it was submitted by AESGP), all the others proposed by Kooperation Phytopharmaka have not been submitted to the HMPC Secretariat, so cannot be evaluated in the assessment report.

Section number and heading	Interested party	Comment and Rationale	Outcome
		the draft monograph recommends the use in adolescents, adults and elderly, while it refuses the use in children due to the “lack of adequate data”. This makes no sense and documents the inconsistency of the assessment. In our opinion, preparations from Linden flower have a long tradition in the folk medicine for treatment of children and adults, supporting the long-lasting traditional use, which cannot be declined or justified on the basis of clinical studies. Traditional use means, in our opinion, the long-lasting physician’s experience of a herbal preparation in a specified indication, which is recorded in monographs and textbooks. This is true for Linden flower; see above.	
	AESGP	The dosage recommendation is described in the books of Kooperation Phytopharmaka [1] and Bühring [2]. Available evidence and experience on the use of lime flower preparations, especially the herbal tea, in children of almost all age groups can be found in various textbooks, e.g. Bühring [2] who describes the preparation of a herbal tea from lime flower as well as of two combination teas for the specific paediatric use. Similar recommendation for combination teas are given by Schilcher [3,4], e.g. a “species diaphoreticae”. A publication of Peter [5] dated 1963 mentions a clinical study of Traisman and Hardy who treated various groups of children suffering from respiratory infections with different medications and non-medicinal measures. They obtained good results using lime	For the posology for the herbal tea, please see explanation above. For the rest of the herbal preparations, no information on the daily dose for children has been provided. The suggested and submitted references from AESGP have been added to the assessment report and list of references.

Section number and heading	Interested party	Comment and Rationale	Outcome
		flower tea without any other medication. We suggest adding the following posology for children: 9 months up to 1 year of age: 0.2 – 1 g daily 1 to 4 years of age: 1 – 2 g daily 4 to 12 years of age: 2 – 4 g daily and, as a consequence deleting the statement that the use is not recommended in children under 12 years of age.	
4.4. Special warnings and precautions for use	KOOP Phyto	Traditional use The sentence “The use in children under 12 years of age has not been established due to lack of adequate data.” should be deleted. Linden flower is considered as safe for use in children (Gaby et al. 2006).	Partly endorsed for children over 4 years of age, see explanation above.
	AESGP	There is much evidence and experience available, particularly in the German market, on the use of lime flower preparations, especially the herbal tea, in children of almost all age groups, as stated under 4.2. with the respective references [1-5]. As explained under 4.2., the sentence “The use in children under 12 years of age has not been established due to the lack of adequate data.” should be deleted.	Partly endorsed for children over 4 years of age, see explanation above.

Section number and heading	Interested party	Comment and Rationale	Outcome
4.6. Fertility, pregnancy and lactation	KOOP Phyto	Traditional use The sentences “In the absence of sufficient data, the use during pregnancy and lactation is not recommended. No fertility data available.” should be deleted. No reasons are known to avoid Linden flower during pregnancy and breast-feeding (Gaby et al. 2006). Further, it should be remembered that Linden flower has been listed as GRAS (Generally Recognised As Safe) (Barnes et al. 2007).	Not endorsed. No data on the use during pregnancy and lactation are available. Because of the absence of sufficient data the use during pregnancy and lactation cannot be recommended.
	AESGP	[1] Kooperation Phytopharmaka, editor. Kinderdosierungen von Phytopharmaka. 3rd ed. Bonn, 2002:140. [2] Bühring U, Ell-Beiser H, Girsch M. Heilpflanzen in der Kinderheilkunde. Stuttgart: Sonntag Verlag, 2008: 97, 196, 218,240. [3] Schilcher H. Phytotherapie in der Kinderheilkunde. 2nd ed. Stuttgart: Wissenschaftliche Verlagsgesellschaft, 1992:40-41. [4] Schilcher H, Dorsch W. Phytotherapie in der Kinderheilkunde. 4th ed. Stuttgart: Wissenschaftliche Verlagsgesellschaft, 2006:44-45. [5] Peter H. Zur Pharmakologie wichtiger Arzneipflanzen. Physikalisch-diätetische Therapie in Klinik und Praxis 1963;4(11): 211-215.	The proposed and submitted references by AESGP have been added to the assessment report and list of references.

Literature cited:

Barnes J, Anderson LA, Phillipson JD. Herbal Medicines. 2th ed. Pharmaceutical Press, London, 2007, 409-410.

Bäumler S. HEILPFLANZEN PRAXIS HEUTE. Porträts Rezepturen Anwendung. URBAN & FISCHER, München • Jena, 2007

Bühning U, Ell-Beiser H, Girsch M (2008). Heilpflanzen in der Kinderheilkunde. Das Praxis-Lehrbuch. Sonntag-Verlag, Stuttgart, 2008.

Commission E (1990). Monographie BGA/BfArM (Kommission E). *Tiliae flos*. Lindenblüten. Bundesanzeiger 990, 164.

Dalla Libera D, Colombo B, Pavan G, De Feo D, Comi G. Prescription of complementary and alternative medicine in paediatric headache patients P947. Twenty-first Meeting of the European Neurological Society 28–31 May, 2011 Lisbon, Portugal J Neurol (2011) 258 (Suppl 1):1–295

Gaby AR *et al*. The Natural Pharmacy. REVISED AND UPDATED 3RD EDITION. Schuyler W Lininger, Jr., Healthnotes Publisher. 2006

Lipp FJ. Kräuterheilkunde. Taschen GmbH. Köln, 2002

Santich R, Bone K. PHYTOTHERAPY ESSENTIALS: Healthy Children. Optimising Children's Health with Herbs. PHYTOTHERAPY PRESS, Warwick, Queensland, 2008

Schapowal S: Phytopharmaka bei Atemwegsinfekten in der Pädiatrie Zeitschrift für Phytotherapie 2007; 28: 174-180.