EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

25 November 2010
EMA/HMPC/563270/2010
Committee on Herbal Medicinal Products (HMPC)

This document was valid from 25 November 2010 until 8 July 2020.

Overview of comments received on Community herbal monograph on *Tanacetum parthenium* (L) Schulz Bip., herba (EMA/HMPC/563270/2010)

Table 1: Organisations and/or individuals that commented on the draft Community herbal monograph on *Tanacetum parthenium* (L) Schulz Bip., herba as released for public consultation on 6 May 2010 until 15 August 2010.

	Organisations and/or individuals
1	European Scientific Cooperative on Phytotherapy (ESCOP)
2	Kooperation Phytopharmaka (KOOP PHYTO)
3	NATUREX S/A

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Table 2: Discussion of comments

GENERAL COMMENTS		
Interested party	**Comment and Rationale**	**Outcome**
ESCOP	We welcome the preparation of a Community draft monograph on Tanacetum parthenium however we propose to take into consideration the following specific comments.	.
KOOP PHYTO	Kooperation Phytopharmaka, a German scientific organisation, would like to comment on this HMPC draft assessment report on Tanacetum parthenium (L.) herba.	
NATUREX	As a general comment it has been hard to respond to this draft monograph without being able to see the draft/completed assessment report. A list of evaluated references is not sufficient without the understanding of the context of the evaluation.	

SPECIFIC COMMENTS ON TEXT			
Section number and heading	**Interested party**	**Comment and Rationale**	**Outcome**
3. Pharmaceutical Form	**Naturex**	**Comments:** "Herbal preparation in solid dosage forms for oral use. The pharmaceutical form should be described by the European Pharmacopoeia full standard term." This draft monograph makes no allowance for equivalent forms of the herb. Naturex produces a standardised dry ethanolic extract of *Tanacetum Parthenium* (L.) Schulz Bip., Herba which	Not endorsed There is no evidence that the proposed extract has been in medicinal use throughout a period of at least 30 years, including at least 15 years within the Community."

SPECIFIC COMMENTS ON TEXT			
		contains the same active ingredients and the same profile as the European Pharmacopoeia monograph. Appendix 1 to this response provides HPLC fingerprints to demonstrate this fact. Producing a standardised ethanolic extract in which the upper and lower parthenolide content are defined would maintain tighter control on the posology of the herb. **Proposed change:** to add: "Dry extract (DER 5-6:1) extraction solvent ethanol 80% v/v (Parthenolide content 0.4 – 0.7% w/w)"	The extract has to be considered a quantified extract, not a standardised one, because parthenolide is not a constituent with known therapeutic activity even though it contributes to the activity.
4.1. Therapeutic indications	ESCOP	Because both the products on the market as the literature on feverfew herb use explicitly the wording "migraine", we propose the following sentence: "Traditional herbal medicinal product used to prevent migraine headaches".	Partially endorsed. Indication has been modified and it is now similar to that proposed: "Traditional herbal medicinal product for the prophylaxis of migraine headaches."
4.2. Posology and method of aministration	ESCOP	We disagree that the duration of use is limited to two months. On the contrary according to a general paper on the treatment of migraine [1] and according to two studies on feverfew [2,3] a treatment of at least 12 weeks is recommended.	Not agreed. In the lack of sufficient data on long term use and based on the knowledge that prolonged intake can provoke rebound effects when feverfew is withdrawn, duration of use of two months has been considered suitable for a self-medication. (Johnson et al., Efficacy of feverfew as prophylactic treatment of migraine. *Brit Med J* 1985, 291:569-573).
4.2. Posology and method of	KOOP PHYTO	**Comments:** Posology Average daily dose:	Not agreed. The clinical study carried out by Johnson et al. (1985) has been conducted with patients that previously ate fresh leaves to care migraine. The controlled phase of

SPECIFIC COMMENTS ON TEXT			
administration		50 - 120 mg of powdered feverfew daily. **Proposed change (if any):** The proposed posology (100 mg daily) should be changed to the above mentioned posology. Justification: In clinical studies, daily doses of 50 – 120 mg have been tested. Ref.: Johnson ES, Kadam NP, Hylands DM, Hylands PJ. Efficacy of feverfew as prophylactic treatment of migraine. Br Med J (Clin Res Ed) 1985; 291: 569-73. Murphy JJ, Heptinstall S, Mitchell JR. Randomised double-blind placebo-controlled trial of feverfew in migraine prevention. Lancet 1988; 2: 189-92. Palevitch D, Earon G, Carasso R. Feverfew (Tanacetum parthenium) as a prophylactic treatment for migraine: a double-blind placebo-controlled study. Phytotherapy Research 1997; 11:508-11.	the study was carried out giving to patients placebo or 50 mg per day of powdered feverfew leaves. However, the number of patients actively treated in this study is very small (N=8). A chloroform extract of dried leaves, not powdered leaves, was used in the study of Murphy et al. (1988). The study of Palevitch et al. (1997) was performed on a greater number of patients (N=57) receiving 100 mg of feverfew powdered leaves. Positive results were obtained with: - a larger number of patients; - the preparation described in Ph. Eur. and proposed in the monograph. On the basis of clinical experience and traditional use and of data submitted by EU member states, the posology of 100 mg per day is considered suitable and better supported by clinical data.
4.2 Posology and method of administration	Naturex	**"Posology** Adults and elderly Average daily dose: 100 mg of powdered feverfew daily … " **Proposed change:** to add:	Not endorsed. See comment under section 3 Pharmaceutical form.

SPECIFIC COMMENTS ON TEXT			
		"Posology Adults and elderly Average daily dose: 100 mg of powdered feverfew or equivalent as dry extract daily … "	
4.4. Special warnings and precautions for use	ESCOP	We propose to add the following sentence: "Abrupt ending of a long-term treatment can provoke withdrawal symptoms, including a rebound of migraine symptoms, anxiety, insomnia and muscle and joint stiffness." [4]	Not endorsed. The warning proposed is suggested by the article of Johnson et al. (1985), Efficacy of feverfew as prophylactic treatment of migraine. *Brit Med J* 1985, 291:569-73. Clinical observations of Johnson regarded long term use (years) of feverfew, because all the patients recruited and treated for months in the study, were previously self-treating with feverfew (fresh leaves). Later, other clinical studies showed that when treatment is limited to a few months rebound symptoms are not present at the end of treatment. Anyway, in the article of Johnson the events cited in the proposed sentence are attributed to the placebo group or to patients previously self-treated with raw leaves. The article specifies "None of these symptoms were experienced by patients taking feverfew. The two patients taking feverfew who complained of stiffness in the joints had suffered this throughout their self treatment with raw leaves."