EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

11 March 2010
EMA/HMPC/7084/2010
Committee on Herbal Medicinal Products (HMPC)

This document was valid from 11 March 2010 until 30 May 2017.

Overview of comments received on Community herbal monograph on *Echinacea purpurea* (L.) Moench, radix (EMA/HMPC/577784/2008)

Table 1: Organisations and/or individuals that commented on the draft Community herbal monograph on *Echinacea purpurea* (L.) Moench, radix as released for public consultation on 16 July 2009 until 15 December 2009.

	Organisations and/or individuals
1	Association of the European Self-Medication Industry (AESGP)
2	Naturex S/A, France
3	Dr Václav Bažata, Industrial Pharmacist
4	European botanical forum (EBF)

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Table 2: Discussion of comments

General comments to draft document

Interested party	Comment and Rationale	Outcome
AESGP	AESGP welcomes the preparation of the above-mentioned Community herbal monograph which may facilitate mutual recognition in Europe by providing harmonised assessment criteria for herbal medicinal products.	Agreed.
EBF	The wording of Therapeutic indications in Community Herbal Monographs is generally too soft in case of Traditional use to distinguish it from herbal non-medicinal products.	Herbal medicinal products are distinguished by word "treatment", which could not be used for herbal non-medicinal products.
Dr Bažata	Policy of precautionary principle to exclude all children bellow age of 12 years of age in Posology without any justification or only "lack of data" substantiation is dubious and may be harmful to SME businesses.	Traditional use in children is not documented. Herbal medicinal products currently on the market are not recommended to children.

SPECIFIC COMMENTS ON TEXT

Section number and heading	Interested party	Comment and Rationale	Outcome
2. Qualitative and quantitative composition	AESGP	Comments: The powdered herbal substance is a preparation found in the French (Arkogélules Echinacée), Spanish (Arcocapsulas Echinacea) and UK (Phytocold) markets as encapsulated preparation. Encapsulated powdered purple coneflower root was first marketed in 1985 in France. Marketing authorisations have been granted by the Spanish and UK authorities in September 1995 and December 1995, respectively. In Germany, the Commission E monograph for Echinacea purpurea root describes the use of an infusion with boiled water. In the USP monograph the production of an Echinacea extract is described as follows: Powdered Echinacea extract is prepared from dried root by extraction with a hydroalcoholic mixture or other suitable solvents. The ratio of the starting crude plant material to powdered extract is between 2:1 and 8:1. Therefore we suggest widening the extraction solvent range to 30-60 % ethanol, and the DER to (2-8:1). Proposed change: i) Herbal substance Dried cut root ii) Herbal preparations Powdered herbal substance	Not endorsed: - The period of medicinal use of the herbal substance and products containing the powdered herbal substance is below 30 years in the Community according to Directive 2004/24/EC. - Extracts other than the dry extract (6.5:1), extraction solvent ethanol 45% (v/v), have not been used for 30 years in the Community or the use is not documented according to Directive 2004/24/EC.

Section number and heading	Interested party	Comment and Rationale	Outcome
		Dry extract (2-8:1), extraction solvent ethanol 30-60% (v/v)	
3. Pharmaceutical form	AESGP	Comments According to the changes proposed above the wording of this section should be modified as follows: Proposed change: Traditional use: Herbal substance or herbal preparations in solid or liquid dosage forms for oral and oromucosal use or as herbal tea for oral use.	Not endorsed: The use of herbal substance for herbal tea and of the powdered herbal substance are not endorsed (see above); therefore the change of wording for the pharmaceutical form section is not applicable.
4.2 Posology and method of administration	AESGP	Comments All encapsulated powdered purple coneflower root preparations (Arkogélules Echinacée, Arcocapsulas Echinacea, Phytocold) correspond to a single dose of 250 mg. Recommended daily doses according to the marketing authorisations are: Arcocapsulas Echinacea: 500 mg 2 to 3 times daily (1000-1500 mg per day) Phytocold: 250-500 mg 3 times daily (750-1500 mg per day). We suggest modifying the daily dose for all herbal preparations to the equivalent of the daily dose for the herbal substance, i.e.; Proposed change:	Not endorsed (same reason as above).

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		Oral and oromucosal use: 1 chewable tablet containing 40 mg extract (6.5:1) and corresponding to 260 mg of herbal substance, every second hour (maximum 9 tablets a day). Powdered herbal substance: 250 mg 3 to 6 times daily. Cut or powdered herbal substance for tea and other preparations: 0.25-2.34 g (daily dose) The use in children under 12 years of age is contraindicated (see section 4.3 'Contraindications'). See comments below	
4.3 Contraindications	AESGP	Comments: We propose to delete the sentence concerning the children under twelve (see above). The contraindication concerning the autoimmune diseases is based on theory and not on practice. We propose to take over the wording as accepted for the community herbal monograph on Echinacea purpurea herb. Proposed change: Hypersensitivity to the active substance or to plants of the Asteraceae (Compositae) family. Because of its immunostimulating activity, Echinacea must not be used in cases of progressive systemic disorders, autoimmune disorders, immunodeficiencies, immunosuppression and diseases	The warning that Echinacea should not be used in cases of progressive systemic disorders, autoimmune disorders, immunodeficiencies, immunosuppression and diseases of the white blood cell system has been moved from section 4.3 to section 4.4 because of insufficient scientific data according to the 'Guideline on Summary of Product Characteristics' (version September 2009).

Section number and heading	Interested party	Comment and Rationale	Outcome
		of the white blood cell system	
4.4 Special warnings and precautions for use	AESGP	Comments: The risk of possible allergic reactions ìs already mentioned under contraindication, therefore there is no need to repeat it once more. We propose to delete the second paragraph. The use in children below the age of 12 should be mentioned here instead of under section 4.3 . We propose the following wording: Proposed change: The use in children below 12 year of age is not recommended because a safe use has not been sufficiently documented.	The comment regarding the use in children below 12 years of age is endorsed: The statement 'The use in children under 12 years of age has not been established due to lack of adequate data.' now appears in section 4.4 (the use in that population is no longer a contraindication in section 4.3), according to the 'Guideline on Summary of Product Characteristics' (version September 2009). The comment regarding the risk of allergic reactions is not endorsed because it refers to possible allergic reactions other than those to the active substance(s) or to plants of the Asteraceae (Compositae) family which is mentioned under 4.3.
2 Well-established use, Part (ii) Herbal preparations	Naturex SA	Comments: The proposed ratio of dry root:extract of 6.5:1 and extraction solvent of 45% (v/v) ethanol is too limiting and does not take into account the efficiency of the extraction process and number of extractions Proposed change (if any): To amend this ratio to "6-8:1", with extraction solvent of 45-75% is proposed to allow a yield of between 16.5 and 12.5%, in order to obtain an extract with the right phenol content. We note that the European Pharmacopoeia monograph (01-2008) (Attachment 1 to this response) does not apply to extracts of Echinacea purpurea, although the HPLC Figure 1823-1 identifies	Not endorsed. Traditional use of presented extracts is not documented. Since active compounds of purple coneflower root extracts are not known, the comparison of HPLC chromatograms of phenolic compounds is irrelevant.

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		the key peaks for active phenols caftaric acid, chlorgenic acid and cichoric acid. There is however a US Pharmacopoeia monograph for powdered Echinacea purpurea hydroalcoholic extract (USP32–NF27 Page 1001) (Attachment 2 to this response) which allows an extraction ratio of between 2:1 to 8:1 with a content of not less than 4% of total phenols. We present as Attachment 3 to this response: A comparison of the HPLC profiles an extract prepared with an extraction solvent of 75% ethanol achieving a 7:1 yield compared to one prepared in accordance with the USP monograph. A comparison of HPLC profiles an extract prepared with an extraction solvent of 75% ethanol achieving a 8:1 yield compared to an extract prepared with 45% ethanol and a 6.5:1 yield. In both cases it can clearly be seen that the identify and purity of the extract remains true to the original EMEA and USP monographs and the currently proposed Community Herbal Monograph.	
4.1. Therapeutic indications	Dr. Bažata EBF	Comments: Indication is not reflecting the totality of evidence, f.i. ESCOP Monograph in Second Edition Suppl.2009 ECHINACEAE	Not endorsed. The proposed indication is not supported with documentation on 30 years of use in the Community

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		PURPUREAE RADIX, where is given at heading Therapeutic indications: Adjuvant therapy and prophylaxis of recurrent infections of the upper respiratory tract (common colds) and also of the urogenital tract . (EMEA draft of Herbal Monograph is mentioning only „Traditional herbal medicinal product for supportive treatment of common cold." , despite in Inventory of herbal substances for assessment – Aphabetical order , Doc.Ref.EMEA/HMPC/494079/2007 are ESCOP herbal monograph on Echinaceae purpureae radix 1824/5 listed on page 6) Proposed change (if any): To include " Adjuvant therapy and prophylaxis of recurrent infections of the upper respiratory tract (common colds) and also of the urogenital tract " instead of too plain„ for supportive treatment of common cold. ", , with deleting the words "Traditional herbal medicinal product" as redundant (given in disclaimer of each THMP label)	according to Directive 2004/24/EC.