



European Medicines Agency  
Evaluation of Medicines for Human Use

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**OVERVIEW OF COMMENTS RECEIVED ON  
COMMUNITY HERBAL MONOGRAPH ON *CURCUMA LONGA* L., RHIZOMA  
(EMA/HMPC/456845/2008)**

Table 1: Organisations and/or individuals that commented on the draft 'Community herbal monograph on *Curcuma longa* L., rhizoma' as released for public consultation on 15 December 2008 until 15 March 2009.

Organisations and/or individuals	
1	Kooperation Phytopharmaka GbR, Germany
2	Sabinsa Europe GmbH, Germany
3	Federal Institute for Drugs and Medicinal Products (BfArM), Germany
4	Association of the European Self-Medication Industry (AESGP)

Table 2: Discussion of comments

GENERAL COMMENTS		
Interested party	Comment and Rationale	Outcome
	One interested party welcomes, in principle, the development of the above-mentioned Community herbal monograph which, by providing harmonised assessment criteria for <i>Curcuma long</i> -containing products, should facilitate mutual recognition in Europe.	Endorsed
	<p>One interested party, in principle welcomes the preparation of the above-mentioned Community herbal monograph. However, some modifications should be inserted from their point of view, in particular a commonly used dry extract has not been taken into consideration.</p> <p>It is assumed that according to the HMPC's overview on their assessment work as of November 2008, a separate monograph will be established for <i>Curcumae xanthorrhizae rhizoma</i>. This is important from their point of view because there are some preparations in the German market containing <i>Curcumae xanthorrhizae rhizoma</i> which should be included in an HMPC monograph.</p>	<i>Curcuma xanthorrhiza</i> is already included in the work program.

SPECIFIC COMMENTS ON TEXT		
Section number and heading	Comment and Rationale	Outcome
2. Qualitative and quantitative composition	<p>We suggest to add under ii) Herbal preparations:</p> <p>Dry extract (13-25:1), extraction solvent: ethanol 96 % (V/V )</p> <p>This preparation is marketed in Germany as "Curcu-Truw, Hartkapseln" with the mentioned extract since 1991.</p> <p>We enclose two studies (1,2) and would appreciate consideration about attaching this preparation to the category of "well-established use".</p>	<p>Addition of dry extract (13-25:1) ethanol 96% (V/V) can be accepted.</p> <p>The submitted studies are not sufficient to support a “Well established use” indication</p>
2. Qualitative and quantitative composition	<p>We suggest adding under ii) Herbal preparations:</p> <p><b>“Dry extract (13-25:1), extraction solvent: ethanol 96 % (V/V)”</b></p> <p>This preparation is marketed in Germany as "Curcu-Truw, Hartkapseln" with the mentioned extract since 1991.</p>	Addition of dry extract (13-25:1) ethanol 96% (V/V) can be accepted.
2. Qualitative and quantitative composition	<p>2.ii</p> <p>Please add additional bullet point</p> <p><b>D) extracts.</b></p> <p>The extract of the curcuma longa root has also to be taken in consideration, because this is the widely used form.</p>	Endorsed.
2. Qualitative and quantitative composition	<p>We propose to add the following herbal preparation in the monograph:</p> <p><b>‘dry extract (13-25:1), extraction solvent: ethanol 96% (V/V)’</b></p> <p>because this preparation has a marketing authorisation at least since 1976 in Germany (see German answer to request for information concerning Cucumae longae rhizome and assessment report). The bibliographic data for this preparation cannot support a well-established use.</p>	Endorsed.

4.1 Therapeutic indication	<p>Please add:</p> <p><b>”This product is an antioxidant. The product has anti-inflammatory action.”</b></p> <p>The antioxidant and anti-inflammatory use is extensively studied and proven. Literature reference please see attached list.</p>	Not endorsed, this is not a therapeutic indication.
4.1 Therapeutic indication	<p>We propose to reword the traditional indication as follows:</p> <p><b>‘Traditional herbal medicinal product used for the symptomatic treatment of mild gastrointestinal complaints, especially linked to mild functional biliary disorders’</b></p> <p>The main pharmacological property of Curcuma longa should be clarified by adding ‘especially linked to mild functional biliary disorders’ to differentiate between the different herbal substances for treatment of mild gastrointestinal complaints. Furthermore the term ‘dyspepsia’ is defined by ROME III Criteria and can only be used after diagnosis by exclusion.</p>	Not endorsed because "biliary disorders" require medical diagnosis.
4.1 Therapeutic indication	<p>In accordance with the above-mentioned preparation and two studies (1,2) we suggest the following wording:</p> <p><b><i>“Dyspeptic complaints, especially in case of functional disorders of the bile duct/ (or) ... in case of biliary dysfunction.”</i></b></p> <p>We believe that the studies (1,2) justify the well-established use of Curcuma long in the above referred indication.</p> <p>In case a well-established use is not accepted, we think that the use in biliary disorders can be proven by the textbook of Madaus (1979) (included in the HMPC reference list) as well as by the textbook of Hager (1973) (3)</p>	<p>Not endorsed because "biliary dysfunction" requires medical diagnosis.</p> <p>The submitted studies are not sufficient to support a “Well established use” indication</p>

<b>4.2. Posology and method of administration</b>	<p>81 mg dry extract (13-25:1), extraction solvent: ethanol 96 % (V/V ), twice daily.</p> <p>This dosage recommendation corresponds to the preparation "Curcu-Truw, Hartkapseln". The German expert information is enclosed (3).</p> <p>Furthermore we recommend to replace "children and adolescents under 18 years of age" by "children under 12 years of age", because there are no safety issues that might require a restriction.</p>	<p>Endorsed.</p> <p>Not endorsed, there are no published safety data available to justify safe use in children and adolescents under 18 years of age.</p>
<b>4.2. Posology and method of administration</b>	<p>We propose to add:  <i><b>“81 mg dry extract (13-25:1), extraction solvent: ethanol 96 % (V/V), twice daily.”</b></i></p> <p>This dosage recommendation corresponds to the above mentioned preparation "Curcu-Truw, Hartkapseln". The German expert information is enclosed (3).</p>	<p>Endorsed</p>
<b>4.2. Posology and method of administration</b>	<p>Please add under Posology:  <b>“D) Extracts 250 mg to 8 g per day”.</b></p> <p>This is based on various studies conducted by us. Literature reference please see attached list.</p>	<p>Not endorsed because the extracts have not been specified.</p>
<b>4.2. Posology and method of administration</b>	<p>The corresponding posology (rapporteur: to dry extract (13-25:1), extraction solvent: ethanol 96% (V/V)) is:  <b>‘80-160 mg daily corresponding to 1,5 - 3 g dried herbal substances, divided in 2 - 5 partial doses daily’</b></p>	<p>Endorsed.</p>
<b>4.3. Contraindications</b>	<p>We propose to reword as follows:  <b>‘Hypersensitivity to the active substance.  Liverdisease, gallstones, obstruction of bile conduct, cholecystitis, colic-like abdominal pain.’</b></p> <p>The wording ‘any other biliary disorders that require medical supervision and advice’ is not adequate for patients’ information. How does the patient know, which biliary disorders require medical supervision? Therefore we propose to add ‘cholecystitis, colic-like abdominal pain’.</p>	<p>Not endorsed because the patient cannot diagnose cholecystitis.</p>

<b>4.4 Special warnings and precautions for use</b>	In accordance with our explanation under 4.3. we recommend to delete "and adolescents"	Not endorsed. There are no available published safety data to justify safe use in children and adolescents under 18 years of age.
<b>4.5 Interactions with other medicinal products and other forms of interaction</b>	To our knowledge, there are no reports available about clinically relevant interactions with warfarin. Only some in vitro experiments showed potential interactions. This is confirmed by the assessment made in the attached Periodic Safety Update Report which has been prepared in a joint project in Germany and which covers a period from 1 August 2002 until 1 August 2008. Hence, we suggest deleting the sentence. Alternatively, if this is not seen as acceptable, it should be replaced by the following wording: "There is no report showing clinically relevant interactions with warfarin. Only results from <i>in vivo</i> experiments have shown potential interactions with warfarin".	Endorsed. The interaction is deleted. The (possible) interaction with warfarin is discussed in the assessment report.
<b>4.5 Interactions with other medicinal products and other forms of interaction</b>	Interactions with warfarin: According to the available literature, interactions have only been observed in in vitro experiments. There are no reports available about any clinical relevance. For this reason we suggest the following wording: "Data from in vitro experiments have shown potential interactions with warfarin".	Partly endorsedThe interaction is deleted. The (possible) interaction with warfarin is discussed in the assessment report.
References	<p><b>Literature not included so far:</b></p> <p>[1] Häringer E. Wirkungen bei funktioneller Dyspepsie und Effekte auf Lipidwerte: Curcuma longa-Extrakt. Naturheilpraxis 2004(1):106-111.</p> <p>[2] Kammerer E, Fintelmann V. Curcuma-Wurzelstock bei dyspeptischen Beschwerden - Ergebnisse einer Anwendungsbeobachtung an 440 Patienten. Natura Med 2001;16 (8):1-8.</p> <p>[3] Hagers Handbuch der Pharmazeutischen Praxis. 4. Band. Chemikalien und Drogen C1-G. Berlin-Heidelberg: Springer Verlag, 1973:384-387.</p> <p>[4] Fachinformation (Expert information) Curcu-Truw, August 2008.</p>	<p>Endorsed (included as reference 113)</p> <p>Endorsed (included as reference 114)</p> <p>Not endorsed: this reference deals with <i>Curcuma xanthorrhiza</i></p> <p>Not endorsed: this reference does not specifically mention <i>Curcuma longa</i>, only curcuma root</p>