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**OVERVIEW OF COMMENTS ON COMMUNITY HERBAL MONOGRAPH ON  
*RHAMNUS PURSHIANUS* D.C., CORTEX  
(EMEA/HMPC/513579/2006)**

*Table 1: Organisation(s) providing comments on the draft Community herbal monograph on *Rhamnus purshianus* D.C., cortex as released for consultation on 8 March 2007 until 16 June 2007.*

| Name of organisation or individual |                                                                  |
|------------------------------------|------------------------------------------------------------------|
| 1                                  | The Association of the European Self-Medication Industry (AESGP) |

**Table 2: Discussion of comments**

| <b>GENERAL COMMENTS TO DRAFT DOCUMENT</b>           |                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                            |
|-----------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| No comments                                         |                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                            |
| <b>SPECIFIC COMMENTS ON TEXT</b>                    |                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                            |
| <b>Line no or section and paragraph no</b>          | <b>Comment and rationale</b>                                                                                                                                                                                                                                                                                                                                                                   | <b>Outcome</b>                                                                                                                                                                                                                                                                                                                             |
| <b>4.2 Posology and method of administration</b>    | Instead of one administration, two administrations should be taken per day, as it is the case with bulk forming laxatives.                                                                                                                                                                                                                                                                     | One single dose daily takes into account that in general defaecation takes place after a delay of 8 - 12 hours and the patient is not disturbed in his daily activity and in his sleep. Anthranoid containing laxatives cannot be compared with bulk forming laxatives, whose effect is not as intensive as the effect of the former ones. |
|                                                     | “At bedtime” instead of “at night”.                                                                                                                                                                                                                                                                                                                                                            | We maintain “at night” like in the other anthranoid monographs. Normally it is not recommended to take a medicinal product at bedtime to avoid an insufficient internal transport of the medicinal product.                                                                                                                                |
|                                                     | The sentence “Normally it is sufficient to take this medicinal product up to two or three times a week,” should be deleted. This statement is a misinterpretation of various comments submitted earlier to other anthranoid monographs. A restriction of use to two to three times a week by self-medication up to 14 days is not justified by the data available, only for a longer term use. | We maintain this sentence, because it is sufficient that defaecation takes place every two or three days, even if the recommended duration of use is restricted.                                                                                                                                                                           |
| <b>4.4 Special warnings and precautions for use</b> | The remarks dealing with cardiac glycosides, antiarrhythmic medicinal products, medicinal products inducing QT-prolongation, diuretics, corticosteroids or liquorice root should only be mentioned under section 4.5 “Interactions with other medicinal products”.                                                                                                                             | According to the guideline on summary of product characteristics of October 2005 cross-refers are possible and sometimes recommended. The wording in this chapter describes the precaution which should be taken (consult a doctor when taking these medicinal products) and in chapter 4.5 the interaction is described.                  |

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|------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>4.6 Pregnancy and lactation</b> | <p>The wording of the ESCOP monograph is proposed: “Experimental studies, as well as many years of experience, do not indicate undesirable or damaging effects from anthranoid laxatives during pregnancy or on the foetus when used at the recommended dosage. However, in view of experimental data indicating a genotoxic risk for several anthranoids (e.g. aloe-emodin), avoid during the first trimester or take only under medical supervision.”</p>                                                                                                                                 | <p>Use is not recommended during pregnancy because the data for <i>Rhamnus purshianus</i> D.C., cortex, are insufficient and experimental data indicating a genotoxic risk for several anthranoids. There are no investigations on reproductive toxicity and in addition there are no clinical data available.</p> <p>Whereas senna and also rhubarb mainly contain dianthron-glycosides, cascara and also frangula and aloe mainly contain 10-glycosyl-anthrone, anthrachinon- and anthron-glycosides. The risk of hydrolysis in aglycones and consequently systemic absorption in the gastrointestinal tract is higher for the anthrachinon- and anthron-glycosides than for the dianthron-glycosides due to the different chemical structures. The amount of aglycones represents the possible genotoxic risk. Even for this reason cascara, frangula and aloe seem to be less appropriate for sensitive patient groups like pregnant women than senna and rhubarb.</p> <p>Only for a specified senna extract the use can be tolerated during the second and third trimester, because special investigations are available.</p> |
| <b>4.9 Overdose</b>                | <p>The sentence “Chronic ingested overdoses of anthranoid containing medicinal products may lead to toxic hepatitis,” should be deleted. There are two doubtful reports on senna preparations. For cascara itself, only one case report was believed to be associated with cholestatic hepatitis. The herbal preparation was not investigated and the medical history of the patient (paraplegia of the lower body, prior cholecystectomy for gallstones, moderate use of alcohol and co-medication of amitriptyline, cimetidine and baclofen. A causal relationship cannot be assumed.</p> | <p>We agree that concerning the cascara case report a causal relationship is unlikely according to the Roussel UCLAF causality assessment method (RUCAM Score). However, in case of the two reports on senna preparation a relationship must be assumed according to the RUCAM Score. Rhamni purshianae, cortex, is also an anthranoid containing herbal substance and therefore we also point out the possibility of toxic hepatic reactions in this chapter for cascara. We only mentioned “toxic hepatitis” in this chapter and not as undesirable effect when cascara was used as recommended. This was discussed and concluded in the MLWP.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |