6 May 2020
EMA/HMPC/113700/2019
Committee on Herbal Medicinal Products (HMPC)

European Union herbal monograph on *Rheum palmatum* L. and *Rheum officinale* Baillon, radix

Final – Revision 1

Initial assessment	
Discussion in Working Party on European Union monographs and European Union list (MLWP)	May 2007 July 2007
Adopted by Committee on Herbal Medicinal Products (HMPC) for release for consultation	05 July 2007
End of consultation (deadline for comments).	15 October 2007
Re-discussion in MLWP	October 2007
Adoption by HMPC Monograph (EMEA/HMPC/189624/2007) AR (EMEA/HMPC/189626/2007) List of references (EMEA/HMPC/189625/2007) Overview of comments received during the public consultation (EMEA/HMPC/494207/2007) HMPC Opinion (EMEA/HMPC/494334/2007)	31 October 2007
First systematic review and revision	
Discussion in HMPC/MLWP	November 2016 January 2017 July 2019 September 2019
Adopted by HMPC for release for consultation	25 September 2019
End of consultation (deadline for comments)	15 January 2020
Re-discussion in HMPC	March 2020 May 2020
Adoption by HMPC	06 May 2020

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Keywords	Herbal medicinal products; HMPC; European Union herbal monographs; well-established use; *Rheum palmatum* L. and *Rheum officinale* Baillon, Rhei radix; Rhubarb root

BG (bulgarski): Ревен, корен CS (čeština): reveňový kořen DA (dansk): Rabarberrod DE (Deutsch): Rhabarberwurzel EL (elliniká): ρήου ριζα EN (English): Rhubarb root ES (español): ruibarbo, raíz de ET (eesti keel): rabarberijuur FI (suomi): raparperi, juuri FR (français): rhubarbe (racine de) HR (hrvatski): rabarbarin korijen HU (magyar): rebarbara-gyökértörzs IT (italiano): Rabarbaro radice	LT (lietuvių kalba): Rabarbarų šaknys LV (latviešu valoda): Rabarberu saknes MT (Malti): għerq tar-rubarbru NL (Nederlands): Chinese Rabarber, Getande Rabarber PL (polski): Korzeń rzewienia PT (português): ruibarbo RO (română): revent SK (slovenčina): koreň rebarbory SL (slovenščina): korenina kitajske rabarbare SV (svenska): rabarber, rot IS (íslenska): NO (norsk): rabarbrarot

European Union herbal monograph on *Rheum palmatum* L. and *Rheum officinale* Baillon, radix

1. Name of the medicinal product

To be specified for the individual finished product.

2. Qualitative and quantitative composition[1, 2]

Well-established use	Traditional use
With regard to the marketing authorisation application of Article 10(a) of Directive 2001/83/EC. *Rheum palmatum* L. or *Rheum officinale* Baillon or their hybrids or a mixture of these two species and/or their hybrids, radix (rhubarb root) i) Herbal substance Not applicable ii) Herbal preparations Comminuted herbal substance, or herbal preparations thereof, standardised.	With regard to the registration application of Article 16d(1) of Directive 2001/83/EC.

3. Pharmaceutical form

Well-established use	Traditional use
Standardised comminuted herbal substance as herbal tea for oral use. Standardised herbal preparations in liquid or solid dosage forms for oral use. The pharmaceutical form should be described by the European Pharmacopoeia full standard term.	

[1] The declaration of the active substance(s) for an individual finished product should be in accordance with relevant herbal quality guidance.

[2] The material complies with the Ph. Eur. monograph (ref.: 0291)

4. Clinical particulars

4.1. Therapeutic indications

Well-established use	Traditional use
Herbal medicinal product for short-term use in cases of occasional constipation.	

4.2. Posology and method of administration[3]

Well-established use	Traditional use
Posology *Adolescents, adults, elderly* Single dose: Herbal preparation equivalent to 20-30 mg hydroxyanthracene derivatives, calculated as rhein, to be taken once daily at night. The correct individual dose is the smallest required to produce a comfortable soft-formed motion. Herbal tea: amount of comminuted herbal substance (equivalent to not more than 30 mg hydroxyanthracene derivatives) in 150 ml of boiling water as herbal infusion. The use in children under 12 years of age is contraindicated (see section 4.3 Contraindications). The pharmaceutical form must allow lower dosages. **Duration of use** Not to be used for more than 1 week. Usually it is sufficient to take this medicinal product up to two to three times during that week. If the symptoms persist during the use of the medicinal product, a doctor or a pharmacist should be consulted. See also section 4.4 Special warnings and	

[3] For guidance on herbal substance/herbal preparation administered as herbal tea or as infusion/decoction/macerate preparation, please refer to the HMPC 'Glossary on herbal teas' (EMA/HMPC/5829/2010 Rev.1).

Well-established use	Traditional use
precautions for use. **Method of administration** Oral use	

4.3. Contraindications

Well-established use	Traditional use
Hypersensitivity to the active substance. Cases of intestinal obstructions and stenosis, atony, appendicitis, inflammatory colon diseases (e.g. Crohn's disease, ulcerative colitis), abdominal pain of unknown origin, severe dehydration state with water and electrolyte depletion. Pregnancy and lactation (see section 4.6 and 5.3). Children under 12 years of age.	

4.4. Special warnings and precautions for use

Well-established use	Traditional use
Long-term use of stimulant laxatives should be avoided, as use for more than a brief period of treatment may lead to impaired function of the intestine and dependence on laxatives. If laxatives are needed every day the cause of the constipation should be investigated. Rhubarb preparations should only be used if a therapeutic effect cannot be achieved by a change of diet or the administration of bulk forming agents. Patients taking cardiac glycosides, antiarrhythmic medicinal products, medicinal products inducing QT-prolongation, diuretics, adrenocorticosteroids or liquorice root, have to consult a doctor before taking rhubarb root concomitantly. Like all laxatives, rhubarb root preparations should not be taken by patients suffering from faecal impaction and undiagnosed, acute or persistent gastro-intestinal complaints, e.g. abdominal pain, nausea and vomiting unless advised by a doctor because these symptoms can	

Well-established use	Traditional use
be signs of potential or existing intestinal blockage (ileus). When rhubarb root preparations are administered to incontinent adults, pads should be changed more frequently to prevent extended skin contact with faeces. Patients with kidney disorders should be aware of possible electrolyte imbalance. If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted. For liquid dosage forms containing ethanol the appropriate labelling for ethanol, taken from the 'Guideline on excipients in the label and package leaflet of medicinal products for human use', must be included.	

4.5. Interactions with other medicinal products and other forms of interaction

Well-established use	Traditional use
Hypokalaemia (resulting from long-term laxative abuse) potentiates the action of cardiac glycosides and interacts with antiarrhythmic medicinal products. Concomitant use with diuretics, adrenocorticosteroids and liquorice root may enhance loss of potassium.	

4.6. Fertility, pregnancy and lactation

Well-established use	Traditional use
Pregnancy The use during pregnancy is contraindicated due to experimental data concerning a genotoxic risk of several anthranoids, e.g. emodin and aloe-emodin. **Lactation** The use during lactation is contraindicated because after administration of anthranoids,	

Well-established use	Traditional use
active metabolites, such as rhein, were excreted in breast milk in small amounts. **Fertility** No fertility data are available (see section 5.3 preclinical safety data).	

4.7. Effects on ability to drive and use machines

Well-established use	Traditional use
No studies on the effect on the ability to drive and use machines have been performed.	

4.8. Undesirable effects

Well-established use	Traditional use
Hypersensitivity: Hypersensitivity reactions (pruritus, urticaria, local or generalised exanthema) may occur. Gastrointestinal disorders: Rhubarb root may produce abdominal pain and spasm and passage of liquid stools, in particular in patients with irritable colon. However, these symptoms may also occur generally as consequence of individual overdosage. In such cases dose reduction is necessary. Furthermore, chronic use may cause pigmentation of the intestinal mucosa (pseudomelanosis coli), which usually recedes when the patient stops taking the preparation. Kidney and urinary tract symptoms: Long-term use may lead to water and electrolyte imbalance and may result in albuminuria and haematuria. Yellow or red-brown (pH dependent) discolouration of urine by metabolites, which is not clinically significant, may occur during treatment. The frequency is not known. If other adverse reactions not mentioned above	

Well-established use	Traditional use
occur, a doctor or a pharmacist should be consulted.	

4.9. Overdose

Well-established use	Traditional use
The major symptoms of overdose/abuse are griping pain and severe diarrhoea with consequent losses of fluid and electrolytes. Treatment should be supportive with generous amounts of fluid. Electrolytes, especially potassium, should be monitored. This is especially important in the elderly. Chronic ingested overdoses of anthranoid containing medicinal products may lead to toxic hepatitis.	

5. Pharmacological properties

5.1. Pharmacodynamic properties

Well-established use	Traditional use
Pharmaco-therapeutic group: contact laxatives ATC-code: A06AB 1,8-dihydroxyanthracene derivatives possess a laxative effect. The *β*-O-linked glycosides e.g. sennosides are not absorbed in the upper gut; they are converted by bacteria of the large intestine into the active metabolites, the anthrones. There are two different mechanisms of action: 1. Stimulation of the motility of the large intestine resulting in accelerated colonic transit. 2. Influence on secretion processes by two concomitant mechanisms *viz*. inhibition of absorption of water and electrolytes (Na^+, Cl^-) into the colonic epithelial cells (antiabsorptive effect) and increase of the leakiness of the tight junctions and stimulation of secretion of water and electrolytes into the lumen of the colon (secretagogue effect) resulting in enhanced	

Well-established use	Traditional use
concentrations of fluid and electrolytes in the lumen of the colon. Defaecation takes place after a delay of 8-12 hours due to the time taken for transport to the colon and metabolisation into the active compound.	

5.2. Pharmacokinetic properties

Well-established use	Traditional use
The *β*-O-linked glycosides are not split by human digestive enzymes and therefore not absorbed in the upper gut to a large extent. They are converted by the bacteria of the large intestine into the active metabolite (emodin-9-anthrone). Mainly anthraquinone aglycones are absorbed and transformed into their corresponding glucuronides and sulphate derivatives. After oral administration of rhubarb root preparations, rhein, emodin and traces of chrysophanol are found in human urine. After administration of other anthranoids, active metabolites, such as rhein, pass in small amounts into breast milk. Animal experiments demonstrated that placental-passage of rhein is low.	

5.3. Preclinical safety data

Well-established use	Traditional use
Total rhubarb (from *Rheum palmatum* L.) anthraquinones were orally administered for 13 weeks to Sprague Dawley rats at a dose of 0, 140, 794, 4500 mg/kg bw. In the highest dose group, nephrotoxicity was discernible at 13 weeks. In the *Salmonella*/microsome assay an ethanolic root extract of *Rheum officinale* Baillon was weakly mutagenic in strain TA 1537 with and without metabolic activation. No further toxicological data are available for rhubarb root itself or preparations thereof. Studies with emodin (a constituent of rhubarb root preparations) revealed effects on oestrus	

Well-established use	Traditional use
cycle length and nephropathy in mice. Furthermore, several hydroxyl anthracene derivatives were mutagenic and genotoxic in several *in vitro* test systems, however this was not proven in *in vivo* systems. In long term carcinogenicity studies effects on kidneys and colon/caecum were reported. Reproductive toxicity seen was connected to maternal toxicity due to diarrhoeal effects.	

6. Pharmaceutical particulars

Well-established use	Traditional use
Not applicable	

7. Date of compilation/last revision

6 May 2020