



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Committee on Herbal Medicinal Products (HMPC)

## European Union herbal monograph on *Rhamnus purshiana* DC., cortex

Final – Revision 1

<b>Initial assessment</b>	
Discussion in Working Party on European Union monographs and European Union list (MLWP)	January 2007 March 2007
Adopted by Committee on Herbal Medicinal Products (HMPC) for release for consultation	8 March 2007
End of consultation (deadline for comments)	15 June 2007
Re-discussion in MLWP	September 2007
Adoption by HMPC Monograph (EMA/HMPC/513579/2006) Assessment report (EMA/HMPC/513580/2006) List of references (EMA/HMPC/513578/2006) Overview of comments received during the public consultation (EMA/HMPC/369020/2007) HMPC Opinion (EMA/HMPC/405547/2007)	7 September 2007
<b>First systematic review and revision</b>	
Discussion in HMPC/MLWP	November 2016 January 2017 January 2019 July 2019 September 2019
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Keywords	Herbal medicinal products; HMPC; European Union herbal monographs; well-established use; <i>Rhamnus purshiana</i> DC.; Rhamni purshianae cortex; cascara bark
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BG (bulgarski): Американски зърнастец, кора	LT (lietuvių kalba): Amerikinių šaltekšnių žievė
CS (čeština): kůra řešetláku Purshova	LV (latviešu valoda): Amerikas krūklja miza
DA (dansk): Purshianabark	MT (Malti): qoxra tal-kaskara
DE (Deutsch): Cascararinde	NL (Nederlands): Cascarabast
EL (elliniká): κασκάρας φλοιός	PL (polski): Kora szakłaku amerykańskiego
EN (English): cascara	PT (português): cáscara sagrada
ES (español): cáscara sagrada, corteza de	RO (română): cascara sagrada
ET (eesti keel): Purshi paakspuu koor	SK (slovenčina): kôra krušiny Purshovej (kôra rešetliaka)
FI (suomi): sagrada, kuori	SL (slovenščina): skorja severnoameriške krhlike
FR (français): cascara (écorce de)	SV (svenska): sagraðabuske, bark
HR (hrvatski): kora američke krkavine	IS (íslenska):
HU (magyar): kaszkarabokor kéreg	NO (norsk): purshianabark
IT (italiano): Cascara corteccia	

# European Union herbal monograph on *Rhamnus purshiana* DC., cortex

## 1. Name of the medicinal product

To be specified for the individual finished product.

## 2. Qualitative and quantitative composition<sup>1, 2</sup>

Well-established use	Traditional use
<p>With regard to the marketing authorisation application of Article 10(a) of Directive 2001/83/EC.</p> <p><i>Rhamnus purshiana</i> DC. (<i>Frangula purshiana</i> (D.C.) A. Gray), cortex (cascara bark)</p> <p>i) Herbal substance</p> <p>Not applicable</p> <p>ii) Herbal preparations</p> <p>Comminuted herbal substance, or herbal preparations thereof, standardised</p>	<p>With regard to the registration application of Article 16d(1) of Directive 2001/83/EC.</p>

## 3. Pharmaceutical form

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

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

<sup>2</sup> The material complies with the Ph. Eur. monograph (ref .: 0105)

## 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<sup>3</sup>

Well-established use	Traditional use
<p><b>Posology</b></p> <p><i>Adolescents, adults, elderly</i></p> <p>Single dose:</p> <p>Herbal preparations equivalent to 10-30 mg hydroxyanthracene derivatives, calculated as cascarioside A, to be taken once daily at night.</p> <p>The correct individual dose is the smallest required to produce a comfortable soft-formed motion.</p> <p>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.</p> <p>The use in children under 12 years of age is contraindicated (see section 4.3 Contraindications).</p> <p>The pharmaceutical form must allow lower dosages.</p> <p><b>Duration of use</b></p> <p>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.</p> <p>If the symptoms persist during the use of the medicinal product, a doctor or a pharmacist should be consulted.</p> <p>See also section 4.4 Special warnings and precautions for use.</p>	

<sup>3</sup> 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
<b>Method of administration</b> Oral use	

### 4.3. Contraindications

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

### 4.4. Special warnings and precautions for use

Well-established use	Traditional use
<p>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. Cascara bark preparations should only be used if a therapeutic effect cannot be achieved by a change of diet or the administration of bulk forming agents.</p> <p>Patients taking cardiac glycosides, antiarrhythmic medicinal products, medicinal products inducing QT-prolongation, diuretics, adrenocorticosteroids or liquorice root, have to consult a doctor before taking cascara bark concomitantly.</p> <p>Like all laxatives, cascara bark should not be taken by patients suffering from faecal impaction and undiagnosed, acute or persistent gastrointestinal complaints, e.g. abdominal pain, nausea and vomiting, unless advised by a doctor because these symptoms can be signs of potential or existing intestinal blockage (ileus).</p> <p>When cascara bark preparations are administered</p>	

Well-established use	Traditional use
<p>to incontinent adults, pads should be changed more frequently to prevent extended skin contact with faeces.</p> <p>Patients with kidney disorders should be aware of possible electrolyte imbalance.</p> <p>If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.</p> <p>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.</p>	

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

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

#### ***4.6. Fertility, pregnancy and lactation***

Well-established use	Traditional use
<p><b>Pregnancy</b></p> <p>The use during pregnancy is contraindicated because of experimental data concerning a genotoxic risk of several anthranoids, e.g. emodin and aloe-emodin.</p> <p><b>Lactation</b></p> <p>The use during lactation is contraindicated because after administration of anthranoids, active metabolites, such as rhein, were excreted in breast milk in small amounts.</p> <p><b>Fertility</b></p> <p>No fertility data are available (see section 5.3</p>	

Well-established use	Traditional use
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
<p>Hypersensitivity:</p> <p>Hypersensitivity reactions (pruritus, urticaria, local or generalised exanthema) may occur.</p> <p>Gastrointestinal disorders:</p> <p>Cascara bark 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 a consequence of individual overdosage. In such cases dose reduction is necessary.</p> <p>Furthermore, chronic use may cause pigmentation of the intestinal mucosa (pseudomelanosis coli), which usually recedes when the patient stops taking the preparation.</p> <p>Kidney and urinary tract symptoms:</p> <p>Long term use may lead to water and electrolyte imbalance and may result in albuminuria and haematuria.</p> <p>Yellow or red-brown (pH dependent) discolouration of urine by metabolites, which is not clinically significant, may occur during the treatment.</p> <p>The frequency is not known.</p> <p>If other adverse reactions not mentioned above occur, a doctor or a pharmacist should be consulted.</p>	

## 4.9. Overdose

Well-established use	Traditional use
<p>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.</p> <p>Chronic ingested overdoses of anthranoid containing medicinal products may lead to toxic hepatitis.</p>	

## 5. Pharmacological properties

### 5.1. Pharmacodynamic properties

Well-established use	Traditional use
<p>Pharmaco-therapeutic group: contact laxatives</p> <p>ATC-code: A06AB07</p> <p>1,8-dihydroxyanthracene derivatives possess a laxative effect.</p> <p>Cascarosides A and B are mixed anthrone-C- and O-glycosides, Cascarosides C, D, E and F are 8-O-<math>\beta</math>-D-glucosides, which are largely not split by human digestive enzymes in the upper gut and therefore not absorbed to a large extent. They are converted by the bacteria of the large intestine into the active metabolites (mainly emodin-9-anthrone).</p> <p>There are two different mechanisms of action:</p> <ol style="list-style-type: none"><li>1. Stimulation of the motility of the large intestine resulting in accelerated colonic transit.</li><li>2. Influence on secretion processes by two concomitant mechanisms <i>viz.</i> inhibition of absorption of water and electrolytes (<math>\text{Na}^+</math>, <math>\text{Cl}^-</math>) 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 concentrations of fluid and electrolytes in the lumen of the colon.</li></ol>	

Well-established use	Traditional use
<p>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.</p>	

### 5.2. Pharmacokinetic properties

Well-established use	Traditional use
<p>The <math>\beta</math>-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). The absorbed anthraquinone aglycones are transformed into their corresponding glucuronides and sulphate derivatives.</p> <p>It is not known to what extent emodin-9-anthrone is absorbed. However, in the case of senna, animal experiments with radio-labeled rhein-anthrone administered directly into the caecum show that only a very small proportion (less than 10%) of rhein-anthrone is absorbed.</p> <p>Active metabolites, such as rhein, pass in small amounts into breast milk. Animal experiments demonstrated that placental-passage of rhein is low.</p>	

### 5.3. Preclinical safety data

Well-established use	Traditional use
<p>There are limited preclinical data on cascara bark preparations but details are lacking.</p> <p>Cascara bark (140 and 420 mg/kg: no further details provided) did not induce the development of colonic aberrant crypti foci (ACF, considered a consistent predictor of tumour outcome) and tumours and did not modify the number of azoxymethane-induced ACF and tumours in both doses in rats treated for 13 weeks (alone or in combination). Dietary exposure of rats (0.05% and 0.1% of the diet) of the anthraquinone glycosides of cascara for 56 successive days did not cause appearance of ACF: However, the higher dosage increased the incidence of ACF</p>	

Well-established use	Traditional use
<p>induced by 1,2-dimethyl-hydrazine in rats.</p> <p>Studies with emodin (a constituent of cascara bark preparations) revealed effects on oestrus cycle length and nephropathy in mice.</p> <p>Furthermore, several hydroxyl anthracene derivatives were mutagenic and genotoxic in several <i>in vitro</i> test systems, however this was not proven in <i>in vivo</i> systems.</p> <p>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.</p>	

## 6. Pharmaceutical particulars

Well-established use	Traditional use
Not applicable	

## 7. Date of compilation/last revision

6 May 2020