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EMA/HMPC/625788/2015  
Committee on Herbal Medicinal Products (HMPC)

## European Union herbal monograph on *Aloe barbadensis* Mill. and on *Aloe* (various species, mainly *Aloe ferox* Mill. and its hybrids), folii succus siccatus

Final

<b>Initial assessment</b>	
Discussion in Working Party on European Union monographs and European Union list (MLWP)	January 2006 March 2006
Adoption by Committee on Herbal Medicinal Products (HMPC) for release for consultation	3 March 2006
End of consultation (deadline for comments)	30 June 2006
Re-discussion in MLWP	September 2006
Adoption by HMPC	7 September 2006
<b>First systematic review</b>	
Discussion in Working Party on European Union monographs and list (MLWP)	September 2015 November 2015 February 2016 April 2016 May/June 2016 September 2016
Adoption by HMPC	22 November 2016

Keywords	Herbal medicinal products; HMPC; European Union herbal monographs; well-established medicinal use; barbados aloes; <i>Aloe barbadensis</i> Mill.; cape aloes; <i>Aloe</i> (mainly <i>Aloe ferox</i> Mill. and its hybrids) Aloes folii succus siccatus, dried juice of leaves
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<p>BG (bulgarski): (Алое, барбадоско /Алое, капско)</p> <p>CS (čeština): aloe, usušená šťáva z listů (aloe kapská, aloe barbadoská)</p> <p>DA (dansk): Aloe (Barbados-Aloe, Kapitaloe)</p> <p>DE (Deutsch): (Curacao-Aloe, Kap-Aloe)</p> <p>EL (elliniká): (Αλόες- αλόη των Barbados, αλόη του Ακρωτηρίου)</p> <p>EN (English): aloes</p> <p>ES (español): aloe, zumo desecado de hoja de (Aloe de Barbado y Aloe del Cabo)</p> <p>ET (eesti keel): aaloe</p> <p>FI (suomi): aloe (barbadosin aloe, kapin aloe)</p> <p>FR (français): (aloès des Barbades, aloès du Cap)</p> <p>HR (hrvatski): suhi sok alojevog lista (barbadoški aloj)</p> <p>HU (magyar): (barbadoszi aloe, tövises aloé)</p> <p>IT (italiano): Aloe, foglia succo essiccato (Aloe delle Barbados, Aloe del Capo)</p>	<p>LT (lietuvių kalba): Alavijai</p> <p>LV (latviešu valoda): Alvejas lapu sula, izžāvēta (Aloje)</p> <p>MT (Malti): il-meraq niexef tal-weraq tas-sabbara (Sabbara)</p> <p>NL (Nederlands): Aloë</p> <p>PL (polski): (Alona barbadoska, Alona przylądkowa)</p> <p>PT (português): (Aloés de Barbados, Aloés do Cabo)</p> <p>RO (română): aloe</p> <p>SK (slovenčina): aloe, suchá šťava z listu (Aloa barbadoská, Aloa kapská)</p> <p>SL (slovenščina): posušen sok lista aloje (barbadoška aloja, kapska aloja)</p> <p>SV (svenska): aloe, blad, torkad växtsaft (Barbadosaloe, Kapitaloe)</p> <p>IS (islenska):</p> <p>NO (norsk): (Barbados-aloe, kap-aloe)</p>
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# European Union herbal monograph on *Aloe barbadensis* Mill. and on *Aloe* (various species, mainly *Aloe ferox* Mill. and its hybrids), folii succus siccatus

## 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>Aloe barbadensis</i> Mill., folii succus siccatus (barbados aloes)</p> <p><i>Aloe</i> (various species, mainly <i>Aloe ferox</i> Mill. and its hybrids), folii succus siccatus (cape aloes)</p> <p>i) Herbal substance</p> <p>Not applicable</p> <p>ii) Herbal preparations</p> <p>a) Dry extract (DER 1-3:1), extraction solvent water, standardised to contain 28.6 - 36.6% hydroxyanthracene derivatives, calculated as aloin (photometric method)</p>	

## 3. Pharmaceutical form

Well-established use	Traditional use
<p>Standardised herbal preparations in liquid or solid 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.: 0257 and/or 0258)

## 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

Well-established use	Traditional use
<p><b>Posology</b></p> <p><i>Adolescents over 12 years of age, adults, elderly</i></p> <p>Single dose:</p> <p>Herbal preparation equivalent to 10 – 30 mg hydroxyanthracene derivatives, calculated as aloin, to be taken once daily at night. The correct individual dose is the smallest required to produce a comfortable soft-formed motion.</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> <p><b>Method of administration</b></p> <p>Oral use</p>	

### 4.3. Contraindications

Well-established use	Traditional use
Hypersensitivity to the active substance.	

Well-established use	Traditional use
<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. Aloe 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 aloes concomitantly.</p> <p>Like all laxatives, aloes 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 be signs of potential or existing intestinal blockage (ileus).</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</p>	

Well-established use	Traditional use
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, adrenal corticosteroids and liquorice root may enhance loss of potassium.	

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

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

#### **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><i>Hypersensitivity</i></p> <p>Hypersensitivity reactions may occur.</p> <p>The frequency is not known.</p> <p><i>Gastrointestinal disorders</i></p> <p>Aloes may produce abdominal pain and spasm</p>	

Well-established use	Traditional use
<p>and passage of liquid stools, in particular in patients with irritable colon. However, these symptoms may also occur generally as a consequence of individual over dosage. 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>The frequencies are not known.</p> <p><i>Kidney and Urinary tract symptoms</i></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 frequencies are 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>Pharmacotherapeutic group: contact laxatives</p> <p>Proposed ATC code: A 06 AB</p> <p>1,8-dihydroxyanthracene derivatives possess a laxative effect.</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 (Na<sup>+</sup>, Cl<sup>-</sup>) 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> <p>Defaecation takes place after a delay of 6 - 12 hours due to the time taken for transport to the colon and metabolism into the active compound.</p>	

### 5.2. Pharmacokinetic properties

Well-established use	Traditional use
<p>Aloinosides, aloins and hydroxyaloins pass directly into the large intestine where they are metabolised by bacterial enzymes (<i>viz.</i> <i>Eubacterium</i> sp. strain BAR) into the active anthrone compounds, mainly aloe-emodin-9-anthrone. It is not known to what extent aloe-emodin-9-anthrone is absorbed. However, in the case of senna, animal experiments with radio-labelled rhein-anthrone administered directly into the caecum show that only a very small proportion (less than 10%) of rhein-anthrone is absorbed.</p>	

Well-established use	Traditional use
<p>Systemic metabolism of free anthranoids depends on their ring constituents. In the case of aloe-emodin, it has been shown in animal experiments that at least 20-25% of an oral dose is absorbed. The bioavailability of aloe-emodin is much lower than the absorption, because it is quickly oxidised to rhein and unknown metabolites, or conjugated.</p> <p>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.</p>	

### 5.3. Preclinical safety data

Well-established use	Traditional use
<p>There are no preclinical tests available for aqueous extracts from aloe or similar preparations.</p> <p>Studies with emodin (a major constituent of <i>Aloes folii succus siccatus</i>) revealed effects on oestrous cycle length in rats and nephropathy in mice. 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. In long term carcinogenicity studies effects on kidneys and colon/caecum were reported. Reproductive toxicity seen was connected to maternal toxicity due to diarrhoeal affects.</p>	

## 6. Pharmaceutical particulars

Well-established use	Traditional use
Not applicable	

## 7. Date of compilation/last revision

22 November 2016