

Tablets

*Tibetan medicinal product*

**AMZV**

## **Composition**

*Active substances:* Aloes dry extract, standardised; the powder of calumba root; cascara; chebulic myrobalan fruit; condurango; elecampane; frangula bark; gentian root; ginger; heavy kaolin; long pepper; nux vomica; rhubarb; sodium hydrogen carbonate; sodium sulphate.

*Excipients:* Glucose, liquid; calcium stearate.

*PADMA LAX is also suitable for diabetics:* 1 tablet contains 0.09 g utilisable carbohydrates. PADMA LAX does not contain lactose and is gluten-free.

## **Pharmaceutical form and amount of active substances per unit**

One uncoated tablet contains: Aloes extractum siccum normatum 12.5mg (*Aloe ferox* Miller and/or *Aloe barbadensis* Miller) (DER: 1.8-2.2 : 1), standardised to 2.4-2.6 mg hydroxyanthracene derivatives (calculated as barbaloin), solvent: water; Pulvis ex Kaolinum ponderosum 25 mg; Calumbae radix 10 mg; Condurango cortex 10 mg; Helenii rhizoma 35 mg; Gentianae radix 35 mg; Myrobalani fructus 35 mg; Natrii hydrogenocarbonas 15 mg; Natrii sulfas 35 mg; Piperis longi fructus 3,5 mg; Frangulae cortex 52,5 mg; Rhamni purshianae cortex 52,5 mg; Rhei radix 70 mg; Strychni semen 1,75 mg; Zingiberis rhizoma 70 mg.

## **Indications / therapeutic use**

For the short-term treatment of acute constipation and in conditions where easy defecation is required.

## **Dosage / application**

*Adults:* 1 to 2 tablets a day.

*Children over 6 years:* 1 tablet a day.

Take the tablet(s) once daily with ample liquid, preferably in the evening. The onset of effects is delayed and begins after about 8 hours.

## **Contraindications**

Intestinal obstruction, inflammatory diseases of the gastrointestinal tract (e.g. Crohn's disease, ulcerative colitis, appendicitis), abdominal pain of unknown origin, and hypersensitivity to one of the active substances or one of the excipients according to the composition. Due to non-existent studies the use of PADMA LAX is not recommended in small children under 6 years.

### ***Warnings and precautions***

Long-term regular use of stimulant LAXatives is generally to be avoided since this can lead to habituation and increased intestinal hypomotility. The treatment should not exceed 14 days. Long-term treatment should be supervised by a doctor.

### ***Interactions***

With chronic use/abuse, the possible potassium depletion may increase the effect of cardiac glycosides. Effects on the action of Type I antiarrhythmics (pro-arrhythmic effect) and of antihistaminics such as terfenadine (arrhythmias) are also possible. The concomitant administration of diuretics or corticosteroids may aggravate the potassium depletion.

In a three-month clinical trial with PADMA LAX, no clinically relevant variations in the electrolyte balance were observed.

### ***Pregnancy / breast-feeding***

No safety studies have been carried out with PADMA LAX. For this reason the product should not be used during pregnancy, unless it is clearly necessary. Studies with products containing anthraquinones showed that traces of active metabolites of 1,8-dihydroxyanthracene derivatives can be found in breast milk. Although a LAXative effect has not been observed in breast-fed infants, the product should not be used during lactation.

### ***Effects on ability to drive and use machines***

No corresponding studies have been carried out. The active ingredients have no effect on the ability to drive motor vehicles and to operate machinery.

### ***Undesirable effects***

*Gastrointestinal symptoms:* Slight diarrhoea or abdominal cramps occur rarely. These side effects can generally be avoided by taking ample fluid or reducing the dosage.

A red discoloration of the urine which may possibly appear during the treatment is harmless. It is due to the presence of colored metabolites in the urine.

Chronic use of the product can lead to pigmentation of the colon (Pseudomelanosis coli), which is harmless and generally disappears after discontinuation of the medicine.

### ***Overdose***

In the case of severe diarrhoea, fluid and electrolytes have to be replaced; in the case of mild diarrhoea it is sufficient to reduce the dosage or to discontinue the medicine.

### ***Properties / Effects***

*ATC Code:* A06AB20

### ***Mechanism of Action***

PADMA LAX is a LAXative that is manufactured according to a proven Tibetan formulation. It contains a complex, mainly plant-based active substance mixture, which is composed of primary and secondary components according to the principles and knowledge of Tibetan Medicine: the secondary components modulate the effects of the primary components and mitigate any unwanted effects. The individual components are present in low doses and achieve the therapeutic effect in an additive, synergistic and antagonistic manner.

The following is a brief characterisation of the components:

*Herbal drugs containing 1,8-dihydroxyanthracene derivatives* (Aloes extractum, Frangulae cortex, Rhamni purshianae cortex und Rhei radix): various constituents of these drugs have a LAXative effect. Two mechanisms of action are responsible for this effect. On the one hand they influence the motility of the muscles of the large intestine, on the other hand they stimulate the active secretion of chloride ions into the lumen of the large intestine, which results in increased water secretion. Together, these effects lead to a shorter colonic transit time and a softer stool.

*Herbal drugs containing bitter principles* (Calumbae radix, Condurango cortex, Gentianae radix, Helenii rhizoma, Strychni semen): The bitter compounds stimulate gastric secretion and support the digestive processes in the stomach and the small intestine.

In toxic doses, strychnine acts as a centrally-active convulsant poison (the lethal dose in adults starts at about 1 mg/kg body weight). Convulsions have been observed in isolated cases in humans, already with doses of 1.5 mg of strychnine. When taken in a dosage of 2 tablets a day (corresponds to 3.5 mg strychni semen, i.e. 90 µg strychnine), the herbal drug acts as a toxicologically harmless bitter drug.

*Herbal drugs containing essential oils* (Zingiberis rhizoma, Piperis longi fructus): These have spasmolytic and carminative effects.

*Herbal drugs containing tannins* (Myrobalani fructus, Rhei radix): These protect the mucosa from irritation and have a local antiinflammatory effect.

*Kaolin*: Acts as adsorbent for many substances.

*Natrii hydrogenocarbonas*: It is widely used as an acid binding salt, especially in antacids.

*Natrii sulfas*: Acts as a saline LAXative.

#### *Clinical efficacy*

In a double-blinded, randomised pilot study with 61 adult patients suffering from constipation predominant irritable bowel syndrome, a significant increase in the frequency of defecation and a significant improvement in the quality of the stools were observed in comparison with patients receiving placebo. The inhibition of the patient's daily activities by abdominal pain was significantly reduced. In particular, the prevalence of moderate to severe pain was reduced. The concomitant symptom flatulence and the incomplete bowel evacuation also improved significantly.

#### **Pharmacokinetics**

Anthracene derivatives are present in the herbal drugs mainly in the form of glycosides. In the upper gastrointestinal tract these glycosides are neither hydrolysed nor absorbed. Only in the large intestine they are broken down by bacterial enzymes into the corresponding anthrone and anthranole compounds, which represent the LAXative principle.

Active metabolites are likely to be expected in the upper gastrointestinal tract only in very small quantities (aloe-emodin anthrone, Rhine), even with an intake of 2 tablets, However, no studies have been conducted in this respect.

#### **Preclinical data**

No preclinical studies have been carried out with PADMA LAX itself.

*Anthranoid-containing drugs*:

*Acute and repeated dose toxicity:* The available preclinical data with aloe extracts and aloin A showed no or only slight toxicity.

*Toxicity to reproduction:* Data from studies with aloe extracts or aloin A showed no embryolethal, fetotoxic or teratogenic effects.

*Genotoxicity:* *In vitro* and *in vivo* genotoxicity studies with *Aloe capensis* showed no genotoxic risk.

*In vitro* genotoxicity studies with extracts from *Rhei radix* and *Frangulae cortex* showed positive results. However, studies with *frangula* extracts on mammalian cells proved to be negative.

The mutagenicity that was found in *in vitro* studies with anthraquinones (aloe-emodin, emodin, physcion, chrysophanol) could not be confirmed in the *in vivo* genotoxicity studies.

The sennosides A and B and rhein showed negative results both *in vitro* and *in vivo*.

*Carcinogenic potential:* A standardised senna-glycoside extract with an aloe-emodin content similar to what would be expected in aloe was not carcinogenic. Likewise long-term *in vivo* studies with aloin and with emodin showed no carcinogenic effect.

### ***Additional information***

#### *Incompatibilities*

Not applicable.

#### *Effect on diagnostic measures*

None known

#### *Shelf life*

The medicinal product may only be used up to the date indicated with “EXP” on the package.

#### *Special storage instructions*

Store PADMA LAX tablets protected from light and in the original package at room temperature (15 - 25°C).

Store out of the reach of children.

#### *Instructions for handling*

Not applicable.

### ***Marketing authorisation number***

35872 (Swissmedic).

### ***Packages***

Tablets: 20 [D], 60 (not available at the moment) [B].

### ***Marketing authorisation holder***

PADMA AG, Haldenstrasse 30, CH-8620 Wetzikon, Switzerland

***Manufacturer***

PADMA AG, Haldenstrasse 30, CH-8620 Wetzikon, Switzerland

***Date of revision of the text***

September 2004.