

Summary of product characteristics

1. NAME OF THE MEDICINAL PRODUCT

Herbion[®] plantain syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of syrup (1 measuring spoon) contains:

- 2,5 g liquid aqueous extract of *Plantago lanceolata* L.s.l., leaves narrowleaf (ribwort) plantain and *Malva sylvestris* L., common mallow flower, equivalent to 0,25 g narrowleaf (ribwort) plantain and 0,25 g mallow flower. Extraction solvent: Water
- 65,00 mg of ascorbic acid (vitamin C) in the form 73,12 mg sodium ascorbate.

Excipient(s) with known effect: sucrose and methyl parahydroxybenzoate (E218)

Each 5 ml of syrup (1 measuring spoon) contains 4 g of sucrose and 9.24 mg of methyl parahydroxybenzoate.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Syrup.

The syrup is brown to reddish-brown with specific odour and taste. Slight sediment typical of natural substances can be noticed.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Herbion plantain syrup is a medicine of herbal origin that is recommended in the complex therapy of inflammatory disease of the upper respiratory tract, accompanied by dry cough. The use in the indications above is based exclusively on long-term experience.

4.2 Posology and method of administration

Adults and children over 14 years of age should take 2 measuring spoonfuls of syrup 3 to 5 times daily. Children from 7 to 14 years of age should be given 1 to 2 measuring spoonfuls of syrup 3 times daily and children from 4 to 7 years of age, 1 measuring spoonful of syrup 3 times daily.

Method of administration

Oral use.

The patient should not eat or drink anything immediately after taking the medicine because food and drink could accelerate the removal of the medicine from the mucous membranes of the mouth and throat.

Shake the bottle before use.

4.3 Contraindications

Hypersensitivity to the active substances or any of the excipients.

Pregnancy and lactation.

Children under 4 years of age.

Due to the content of ascorbic acid, the product should not be used in patients with thrombosis,

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tendency to thrombosis, thrombophlebitis, increased blood clotting, diabetes mellitus, renal insufficiency, nephrolithiasis, glucose-6-phosphate dehydrogenase deficiency or hyperoxaluria.

With caution

Caution is required when the medicinal product is prescribed to patients with kidney disease, sideroblastic anaemia, sickle cell anaemia, thalassemia, hemochromatosis, polycythemia, progressive malignant disease.

4.4 Special warnings and precautions for use

If the symptoms do not resolve within a week or if they get worse during treatment, a doctor or pharmacist should be consulted.

If dyspnoea, fever or bloody sputum occur, a doctor or pharmacist should be consulted.

It is recommended that the patient should drink plenty of tea and other warm beverages while taking the syrup, but not immediately after taking the syrup.

Herbion plantain syrup contains sucrose and is therefore not recommended for diabetics.

Important information about some of the ingredients of Herbion plantain syrup

Herbion plantain syrup contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Methyl parahydroxybenzoate (E218) can cause allergic reactions (possibly delayed).

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use of medicines that suppress cough (antitussives) and reduce sputum production is not recommended without medical advice.

No interactions with food have been reported.

4.6 Pregnancy and lactation

Since the safety data during pregnancy and breast-feeding are limited, the syrup should not be used during pregnancy and breast-feeding.

4.7 Effects on ability to drive and use machines

The medicine is not known to affect the ability to drive and use machines.

4.8 Undesirable effects

Undesirable effects that may occur during the use of Herbion plantain syrup are classified into the following groups in order of frequency:

- very common ($\geq 1/10$),
- common ($\geq 1/100$ to $< 1/10$),
- uncommon ($\geq 1/1,000$ to $< 1/100$),
- rare ($\geq 1/10,000$ to $< 1/1,000$),
- very rare ($< 1/10,000$), not known (cannot be estimated from the available data).

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Frequency of undesirable effects listed by individual organ systems:

Immune system disorders

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- rare: hypersensitivity to drug ingredients.

If severe undesirable effects occur, treatment should be discontinued.

4.9 Overdose

No cases of overdose have been reported.

No toxic effects associated with overdose are known.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotheapeutic group: Cough suppressants, excluding combinations with expectorants; ATC code: R05D.

The effect has not been proven in clinical studies but is based on pharmacological studies and many years of empirical experiences (level of evidence of efficacy: IV).

Herbion plantain syrup contains an aqueous extract of two herbal drugs, the ribwort plantain (*Plantago lanceolata L.*) leaves and the common mallow (*Malva sylvestris L.*) flowers, and vitamin C. Due to its mucilage content, the syrup protects the mucous membrane of the respiratory tract and soothes dry cough in colds and respiratory tract inflammations. Mucilage forms a thin film over a mucous membrane and protects it mechanically from cough-inducing irritants.

The active substances of the ribwort plantain leaves are mucilages and iridoid glycosides (aucubin). Due to its aucubin content, the aqueous extract of the ribwort plantain leaves has a bacteriostatic effect and reduces upper respiratory tract inflammations. The antibacterial effect is attributed to the aglycone - aucubigenin, which is liberated from aucubin after the activity of plant beta-glucosidases. Due to the mucilage content of the extracts, it acts as a mucilaginosum in dry, irritating cough associated with upper respiratory inflammations.

Common mallow flowers also contain mucilage, tannin and the anthocyanin glycoside malvin. The extract acts as a mucilaginosum locally on the mucous membrane of the upper respiratory tract. The mucilages form a thin mechanical protective coating over the mucous membrane and thus reduce the cough reflex. In this way they relieve cough caused by the irritation of the respiratory tract mucosa in inflammatory processes or by different irritant environmental factors.

Vitamin C takes part in many metabolic processes in the body. It is involved in the redox systems and takes part in collagen synthesis, the formation of haemoglobin and in numerous other processes. It increases the immune response of the body and promotes cell regeneration.

5.2 Pharmacokinetic properties

There are no pharmacokinetic studies with the syrup or the extract but some studies have been performed with certain isolated active substances.

The mucilaginous polysaccharides of both drugs are not absorbed and metabolized after ingestion but they act locally on the mucous membrane as a protective layer.

No pharmacokinetic studies with aucubin have been performed in humans. In rabbits fed ribwort plantain, aucubigenin was recovered in the urine.

The absorption of ascorbic acid (vitamin C) starts in the mucous membrane of the mouth and continues in the duodenum and the small intestine. It is distributed throughout the tissues and cells. Ascorbic acid reaches higher concentrations in the leukocytes and platelets than in the erythrocytes and plasma. About 25% of vitamin C is bound to plasma proteins and a healthy human body contains about 1.5 grams of vitamin C.

In the human body, ascorbic acid is reversibly oxidized to dehydroascorbic acid; it is partly metabolized into oxalic acid and ascorbate-2-sulphate, which are excreted in the urine. The excess ascorbic acid, which is not needed by the body, is excreted unchanged in the urine.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction.

There are no preclinical data on the toxicity of the syrup and separate drugs but there are toxicity studies of isolated active substances.

The main active substances of both drugs are mucilages, which are not absorbed and are not toxic.

To date, there have been no reports of intoxication due to the use of the drug *Plantaginis lanceolatae folium*, which contains relatively small quantities of aucubin (0.3-2.5%).

Acute toxicity of aucubin in animals: no deaths occurred in mice after intraperitoneal use, even at doses up to 900 mg/kg body weight.

Antispermatic activity of the isolated active substance malvidine chloride was observed in monkeys receiving the active substance at a dose of 50 mg/kg body weight for 60 days.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose

Methyl parahydroxybenzoate (E218)

Orange oil flavour

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

The syrup should be used within 3 months after opening the bottle.

6.4 Special precautions for storage

Before opening the bottle:

Do not store above 30 °C.

After opening the bottle:

Do not store above 25 °C.

6.5 Nature and contents of container

Bottle (type III, in accordance with the Ph. Eur.), plastic closure, measuring spoon: 150 ml of syrup, in a box.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia

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8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT