# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

Manevac

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

**Each 5 g dose contains:**
2.6 g Ispaghula seed (*Plantago ovata* Forssk.);
0.11g Ispaghula husk (*Plantago ovata* Forssk);
0.34 - 0.66g Tinnevelly Senna fruit (*Cassia angustifolia* Vahl), corresponding to 15 mg hydroxyanthracene glycosides calculated as sennoside B.

**Excipients:**
Each 5g dose contains 1.04g of sucrose (See Section 4.4. 'Special warnings and precautions for use')

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Brown, sugar-coated granules.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

For short-term use
a) in cases of occasional constipation,
b) to achieve bowel regulation in bed-ridden patients,
c) in cases of haemorrhoids to achieve pain free evacuation.

### 4.2 Posology and method of administration

For oral administration.

***Method of administration:***

The patient should be sitting in an upright position prior to administration of the granules. Manevac should be placed dry on the tongue and, without chewing or crushing, swallowed with a glass of water, warm drink, milk, fruit juice or similar aqueous liquid; then maintain adequate fluid intake.
An interval of half an hour to one hour should be kept after taking another medicinal product.

***Posology:***
***Adults, the elderly and children over 12 years:***
Sachets
One sachet (5g) or two sachets (10g) to be taken once daily at night.

Granules
One (5g) or two (10g) level measuring spoons to be taken once daily at night.

The maximum daily dose of hydroxyanthracene glycosides is 30 mg. This is equivalent to two level measuring spoons or two sachets (10g of granules) of Manevac . The correct individual dose is the smallest required to produce a comfortable soft-formed motion.

Manevac 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 (see section 4.8).

**This product should not be taken immediately prior to bed-time.**

***Children***
Use in children below the age of 12 years is contraindicated (see section 4.3)

***Duration of use:***
Not to be used for more than 1 week (see section 4.4). 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 Manevac , a doctor or a pharmacist should be consulted.

## 4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- Children under 12 years of age.
- Pregnancy and lactation (see section 4.6 and 5.3).
- Patients with a sudden change in bowel habit that persists for more than 2 weeks

- Undiagnosed rectal bleeding and failure to defecate following the use of a laxative.
- possible or existing bowel obstruction (ileus)
- intestinal atony
- abnormal narrowing (stenosis) of the gastrointestinal tract
- diseases of the oesophagus and cardia
- paralysis of the intestine or megacolon
- acute inflammatory bowel disease (e.g. Crohn's disease, ulcerative colitis, appendicitis)
- severe dehydration (with loss of fluid and electrolytes)
- abdominal pain of unknown origin
- dysphagia

## 4.4 Special warnings and precautions for use

The stated dose should not be exceeded.

Manevac should always be taken with liquid.

When taken with inadequate fluid amounts, bulk forming agents can cause obstruction of the throat and oesophagus with choking and intestinal obstruction. Symptoms can be chest pain, vomiting, or difficulty in swallowing or breathing.

Like all laxatives, Manevac should not be used by patients with faecal impaction and undiagnosed, acute or persistent gastro intestinal symptoms such as abdominal pain, nausea and vomiting unless advised by a doctor because these symptoms can be signs of potential or existing intestinal blockage (ileus).

If laxatives are needed every day the cause of the constipation should be investigated. Long-term use of laxatives (more than 1 week) should be avoided. Manevac should only be used if a therapeutic effect cannot be achieved by a change of diet or the administration of pure bulk forming agents.

If the constipation does not resolve within 3 days or if abdominal pain occurs or in cases of any irregularity of faeces, the use of Manevac should be discontinued and medical advice must be sought.

The treatment of debilitated patients and / or elderly patients requires medical supervision.

In order to decrease the risk of gastrointestinal obstruction (ileus) Manevac should be used together with medicinal products known to inhibit peristaltic movement (e.g. opioids,) only under medical supervision.

Patients taking cardiac glycosides, antiarrhythmic medicinal products, medicinal products inducing QT-prolongation, diuretics, adrenocorticosteroids or liquorice root, have to consult a doctor before taking Manevac concomitantly.

Long-term use of stimulant laxatives should be avoided. If stimulant laxatives are taken for longer than a brief period of treatment, this may lead to impaired function of the intestine and dependence on laxatives.

Prolonged and excessive use may lead to fluid and electrolyte imbalance and hypokalaemia. Patients with kidney disorders should be aware of possible electrolyte imbalance.

Intestinal loss of fluids may promote dehydration. Symptoms may include thirst and oliguria. In patients suffering from fluid loss where dehydration may be harmful (e.g. renal insufficiency, elderly patients) use of the product should be discontinued and only be restarted under medical supervision.

Prolonged use may precipitate the onset of an atonic, non-functioning colon.
When Manevac is administered to incontinent adults, pads should be changed more frequently to prevent extended skin contact with faeces.
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Laxatives do not help in long-term weight loss.

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

If the symptoms worsen during the use of Manevac, a doctor or a pharmacist should be consulted.

Manevac contains potent allergens. As a consequence after oral administration or contact with the skin, Manevac may cause hypersensitivity reactions (see section 4.8).

Manevac 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 (see section 4.8).

## 4.5 Interaction with other medicinal products and other forms of interaction

Enteral absorption of concomitantly administered medicines such as minerals, vitamins (B12), cardiac glycosides, coumarin derivatives, carbamazepine and lithium may be delayed. For this reason Manevac should not be taken ½ to 1 hour before or after intake of other medicinal products.

Diabetic patients should take Manevac only under medical supervision because adjustment of anti-diabetic therapy may be necessary. If Manevac is taken together with meals by insulin dependent diabetic patients it may be necessary to reduce the insulin dose.
Use of Manevac concomitantly with thyroid hormones requires medical supervision because the dose of the thyroid hormones may have to be adjusted.
Hypokalaemia (resulting from long-term laxative abuse) potentiates the action of cardiac glycosides and interacts with antiarrhythmic medicinal products, with medicinal products, which induce reversion to sinus rhythm (e.g. quinidine) and with medicinal products inducing QT-prolongation.
Concomitant use with other medicinal products inducing hypokalaemia (e.g. diuretics, adrenocorticosteroids and liquorice root) may enhance electrolyte imbalance.

## 4.6 Fertility, pregnancy and lactation

**Fertility**
Studies on fertility have not been performed.
**Pregnancy**
The use during pregnancy is contraindicated because of experimental data concerning a genotoxic risk of several anthranoids in Senna, e.g. emodin and aloe-emodin.
**Lactation**
The use during lactation is contraindicated because after administration of anthranoids, active metabolites, such as rhein, were excreted in breast milk in small amounts.

## 4.7 Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

## 4.8 Undesirable effects

Flatulence may occur with the use of Manevac, this generally disappears in the course of the treatment.

Abdominal distension and risk of intestinal or oesophageal obstruction (e.g. dysphagia) and faecal impaction may occur, particularly if swallowed with insufficient fluid. The frequency is not known.

Manevac contains potent allergens. As a consequence after oral administration or contact with the skin, Manevac may cause hypersensitivity reactions such as rhinitis, conjunctivitis, bronchospasm and in some cases anaphylaxis.. Cutaneous hypersensitivity reactions such as local or general exanthema urticaria and/or pruritus have also been reported. The frequency is not known.

Manevac 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.

Nausea and vomiting may occur. The frequency is not known.

Chronic use may lead to disorders in water equilibrium and electrolyte metabolism and may result in albuminuria and haematuria.
Furthermore, chronic use may cause pigmentation of the intestinal mucosa (pseudomelanosis coli), which usually recedes when the patient stops taking the preparation.

Yellow or red-brown (pH dependent) discolouration of urine by metabolites, which is not clinically significant, may occur during the treatment.

The frequency is not known.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme (Website: www.yellowcard.mhra.gov.uk) or search for MHRA Yellow Card in the Google Play or Apple App Store.

## 4.9 Overdose

Overdose may cause abdominal discomfort, flatulence and possibly intestinal obstruction due to the content of ispaghula. Adequate fluid intake should be maintained and management should be symptomatic.
The major symptoms of overdose/abuse are griping pain and severe diarrhoea with consequent losses of fluid and electrolytes, which should be replaced. Diarrhoea may especially cause potassium depletion, which may lead to cardiac disorders and muscular asthenia, particularly where cardiac glycosides, diuretics, adrenocorticosteroids or liquorice root are being taken at the same time.
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

Pharmacotherapeutic group: Laxatives
ATC-code: A 06 AB

The active ingredient ispaghula husk consists of the episperm and collapsed adjacent layers removed from the seeds of Plantago ovata Forssk (Plantago ispaghula Roxb.). Ispaghula husk is particularly rich in alimentary fibres and mucilages, its mucilage content being higher than that of other Plantago species. Ispaghula husk is capable of absorbing up to 40 times its own weight in water. Ispaghula husk consists of 85% water-soluble fibre; it is partly fermentable (in vitro 72% unfermentable residue) and acts by hydration in the bowel. Gut motility and transit rate can be modified by ispaghula through mechanical stimulation of the gut wall as a result of the increase in intestinal bulk by water and the decrease in viscosity of the luminal contents or by contact with rough fibre particles. When taken with a sufficient amount of liquid (at least 30 ml per 1 g Manevac) ispaghula produces an increased volume of intestinal contents due to its highly bulking properties and hence a stretch stimulus, which triggers defaecation; at the same time the swollen mass of mucilage forms a lubricating layer, which makes the transit of intestinal contents easier.
The other active substance, senna pods contain 1,8-dihydroxyanthracene derivatives which possess a laxative effect. The β-O-linked glycosides (sennosides) are not absorbed in the upper gut; they are converted by bacteria of the large intestine into the active metabolite (rhein anthrone).
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 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

**Absorption**
The active substance ispaghula seed / husk hydrates and swells to form a mucilage because it is only partially solubilised. Polysaccharides, such as those which dietary fibres are made of, must be hydrolysed to monosaccharides before intestinal uptake can occur. Less than 10 % of the mucilage gets hydrolysed in the stomach, with formation of free arabinose.
Intestinal absorption of the free arabinose is approximately 85 % to 93 %. Aglyca are absorbed in the upper gut. Animal experiments with radio-labeled rhein anthrone administered directly into the caecum demonstrated absorption < 10%.

**Biotransformation**
The sugar residues of the xylan backbone and the side chains of psyllium are joined by ß-linkages, which cannot be broken by human digestive enzymes. To varying degrees, dietary fibre is fermented by bacteria in the colon, resulting in production of carbon dioxide, hydrogen, methane, water, and short-chain fatty acids, which are absorbed and brought into the hepatic circulation. In humans, psyllium reaches the large bowel in a highly polymerised form that is fermented to a limited extent, resulting in increased faecal concentration and excretion of short-chain fatty acids. The β-O-linked glycosides (sennosides) of the active substance senna pods are neither absorbed in the upper gut nor split by human digestive enzymes. They are converted by the bacteria of the large intestine into the active metabolite (rhein anthrone). In contact with oxygen, rhein anthrone is oxidised into rhein and sennidins.

**Distribution**
Rhein and sennidins can be found in the blood, mainly in the form of glucuronides and sulphates. In human pharmacokinetic studies with senna pods powder (20 mg sennosides), administered orally for 7 days, a maximum concentration of 100 ng rhein/ml was found in the blood. An accumulation of rhein was not observed. Active metabolites, e.g. rhein, pass in small amounts into breast milk. Animal experiments demonstrated that placental passage of rhein is low.

**Excretion**
After oral administration of sennosides, 3 - 6% of the metabolites are excreted in urine; some are excreted in bile. Most of the sennosides (ca. 90%) are excreted in faeces as polymers (polyquinones) together with 2 - 6% of unchanged sennosides, sennidins, rhein anthrone and rhein.

## 5.3 Preclinical safety data

**Ispaghula husk**

There are only data for ispaghula husk and psyllium without defining the exact test preparation available.

Ispaghula husk was fed to rats at levels up to 10% of the diet (in three 28-day studies and one 13-week study). Consumption ranged from 3,876 to 11,809 mg/kg/day (3 to 16 times of the human dosage calculated for a 60 kg human). Treatment induced lower serum total protein, albumin, globulin, total iron-binding capacity, calcium, potassium, and cholesterol; and higher aspartate transaminase and alanine transaminase activities relative to control. The absence of any increases in urinary protein and any differences in growth or feed efficiency in ispaghula husk fed rats may give evidence that there are no adverse effects on protein metabolism. Because absorption of ispaghula husk is very limited, histopathological evaluations were limited to the gastrointestinal tract, liver, kidneys and gross lesions without observing any treatment-related effect. In a study on fertility, embryo-foetal development and pre- and postnatal development (multigeneration study) ispaghula husk (0, 1, 2.5, or 5% (w/w) of the diet) was administered continuously through two generations to rats. For fertility and foetal development and teratogenesis the NOAEL was 5% of the diet, while for offspring growth and development the NOAEL was given with 1% of the diet based on reductions in pup weights. The study on embryo-foetal development in rabbits (ispaghula husk as 0, 2.5, 5 or 10% (w/w) of diet) has to be considered as preliminary. Conclusions cannot be drawn.

**Genotoxicity and carcinogenicity**
Tests on genotoxicity and carcinogenicity have not been performed.

**Senna fruit (pods)**
There are only few preclinical studies available for senna pods or preparations thereof. In a 90-day rat study, senna pods were administered at dose levels from 100 mg/kg up to 1500 mg/kg (human equivalence dose of 16 to 242 mg/kg). In all groups minor epithelial hyperplasia of the large intestine was observed and was reversible within the 8-week recovery period. The hyperplastic lesions of the forestomach epithelium were reversible as well. Dose dependent tubular basophilia and epithelial hypertrophy of the kidneys were seen at a dose of, or greater than 300 mg/kg per day without affecting function. These changes were also reversible. Storage of a brown tubular pigment led to a dark discoloration of the renal surface which remained to a lesser degree after the recovery period. No change was seen in the colonic nervous plexus. A no-observable-effect level (NOEL) could not be obtained in this study.

Senna pods, extracts thereof and several hydroxyl anthracene derivatives (except sennosides, rhein and sennidins) were mutagenic and genotoxic in several in vitro test systems. However, for senna and aloe-emodin this was not proven in in vivo systems.

In long term carcinogenicity studies with senna pods effects on kidneys and colon/caecum were reported.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Caraway oil
Spanish Sage oil
Peppermint oil
Acacia
Talc
Iron oxides E 172
Hard paraffin
Liquid paraffin
Sucrose

## 6.2 Incompatibilities

None known.

## 6.3 Shelf life

60 months (sachets)

36 months (250g composite container and 400g composite container)

## 6.4 Special precautions for storage

Do not store above 30°C. (sachets)
Do not store above 25°C. (400g composite container and 250g composite container)

## 6.5 Nature and contents of container

Sachet:

The sachet consists of 3 layers made of (from outside to inside): Paper, aluminium foil, polyethylene (PE).

Pack size: 6, 14 or 20 sachets with 5g of granules each.

Composite container with screw cap:

The composite container, cylindrical in shape with an inner lid and a screw cap both made of polypropylene (PP). The container consists of paper, aluminium foil and inner lacquer of PET with a base consisting of a tin plate.

Pack size: 250g

Composite container with aluminium tear-off membrane:

Composite container (see above) with upper closure system: aluminium membrane with pull-tab and plastic lid (plugged in) of polypropylene (PP).

Pack size: 400g

A 7ml measuring spoon (5g of granules) of polypropylene (PP) is added to all multi-dose containers.

Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal

None stated.

## 7 MARKETING AUTHORISATION HOLDER

Cooper Consumer Health B.V.,
Verrijn Stuartweg 60, 1112 AX Diemen,
The Netherlands

## 8 MARKETING AUTHORISATION NUMBER(S)

PL 60682/0019

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

13/05/2025

## 10 DATE OF REVISION OF THE TEXT

11/08/2025