SUMMARY OF PRODUCT CHARACTERISTICS
1. **NAAM VAN HET GENEESMIDDEL**

Pikopil tabletten 5 mg  
Pikopil tabletten 7.5 mg

2. **QUALITATIVE AND QUANTITATIVE COMPOSITION**

**[Pikopil 5 mg tablets]**
Each tablet contains sodium picosulfate monohydrate equivalent to 5 mg sodium picosulfate anhydrous.  
Excipient with known effect: 1 tablet contains 97.0 mg lactose

**[Pikopil 7.5 mg tablets]**
Each tablet contains sodium picosulfate monohydrate equivalent to 7.5 mg sodium picosulfate anhydrous.  
Excipient with known effect: 1 tablet contains 145.5 mg lactose

For the full list of excipients, see section 6.1.

3. **PHARMACEUTICAL FORM**

Tablet  
**[Pikopil 5 mg tablets]**  
White to off-white, round, flat bevelled-edge tablets with a score line, diameter 7 mm, height 2.4 mm.  
The tablet can be divided into equal doses.  
**[Pikopil 7.5 mg tablets]**  
White to off-white, round, flat bevelled-edge tablets with a score line, diameter 8 mm, height 2.4 mm.  
The tablet can be divided into equal doses.

4. **CLINICAL PARTICULARS**

4.1 **Therapeutic indications**

Short term relief of chronic or habitual constipation.  
Pikopil is indicated in adults and in children aged from 4 years.

4.2 **Posology and method of administration**

**Posology**

It is recommended to start with the lowest dose. The dose may be adjusted up to the maximum recommended dose to produce regular stools.  
The maximum recommended daily dose should not be exceeded.  
**Adults**  
5 – 7.5 mg (corresponding to 1 – 1.5 Pikopil 5 mg tablets or 1 Pikopil 7.5 mg tablet) swallowed at bedtime.  
Dosage can be titrated individually. Once regularity has re-started dosage should be reduced and can usually be stopped.

**Paediatric population**  
*Children from 10 years of age*
5 – 7.5 mg (corresponding to 1 – 1.5 Pikopil 5 mg tablets or 1 Pikopil 7.5 mg tablet) swallowed at bedtime.

Children from 4 to less than 10 years of age
2.5 – 5 mg (corresponding to ½ – 1 Pikopil 5 mg tablet) swallowed at bedtime.

Pikopil tablets 5 mg should not be used in children below 4 years of age. Pikopil tablets 7.5 mg should not be used in children below 10 years of age.

The safety and efficacy of Pikopil tablets in children below 4 years of age have not been established. No data are available.

Method of administration

The tablet should be swallowed with adequate fluid.

As for all intestinal irritants, Pikopil should basically not be taken longer than three subsequent days.

The maintenance of an adequate fluid intake during treatment is essential, especially for younger patients and the elderly who are more susceptible to the effects of dehydration.

4.3 Contraindications

- Hypersensitivity to the active substance, other triarylmethanes or to any of the excipients listed in section 6.1.
- Interference with the passage of food through the intestine (eg, ileus).
- Acute inflammatory bowel diseases
- Severe painful and/or feverish acute abdominal conditions (e.g. appendicitis) potentially associated with nausea and vomiting
- Severe dehydration

4.4 Special warnings and precautions for use

Prolonged or excessive use can lead to fluid and electrolyte imbalance and hypokalemia, dehydration or diarrhea.

Dizziness and / or syncope have been reported in patients using sodium picosulfate. The available data in these cases indicate defecation syncope (or syncope straining at stool) or vasovagal response to abdominal pain related to constipation and not necessarily a response to the administration of sodium picosulfate itself.

The indicated doses should not be exceeded.

Like all laxatives, Pikopil must not be used daily for a long period of time without examination of the cause of constipation.

Pikopil may be used by children only after consultation with a doctor.

The use may not be continued if no bowel movement follows.

Excipient Lactose

Patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
4.5 Interaction with other medicinal products and other forms of interaction

The concomitant use of diuretics or adreno-corticosteroids may increase the risk of electrolyte imbalance if excessive doses of Pikopil are taken.

Electrolyte imbalance may lead to increased sensitivity to cardiac glycosides.

Concurrent administration of broad-spectrum antibiotics may reduce the laxative action of Pikopil.

4.6 Fertility, pregnancy and lactation

Pregnancy

For sodium picosulfate no clinical data on exposed pregnancies are available.

Reproduction studies with sodium picosulfate performed in animals have revealed no evidence of teratogenic potential. However, embryofetal toxicity has been observed in rats and rabbits at high doses (see section 5.3). Therefore, Pikopil should not be taken during pregnancy unless the expected benefit is thought to outweigh any possible risk and only on medical advice.

Breastfeeding

Clinical data show that neither the active moiety of sodium picosulfate (BHPM or bis-(p-hydroxyphenyl)-pyridyl-2-methane) nor its glucuronides are excreted into the milk. Nevertheless, as with all medicines, Pikopil should not be taken during breast feeding unless the expected benefit is thought to outweigh any possible risk and only on medical advice.

Fertility

There are no studies available on the effect on fertility in humans. Animal studies showed no effect on fertility.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, patients should be advised that side effects such as dizziness and / or syncope (see sections 4.4 and 4.8) may occur.

If dizziness and / or syncope occur (e.g. due to stomach spasms), patients should avoid potentially hazardous tasks such as driving or using machines.

4.8 Undesirable effects

The frequency of adverse reactions is based on the following convention: very common (≥ 1/10), common (≥ 1/100 to <1/10), uncommon (≥ 1/1.000 to <1/100), rare (≥ 1/10.000 to <1/1.000), very rare (<1/10.000), not known (can not be estimated from the available data).

**Immune system disorders**

Uncommon: Hypersensitivity *

**Nervous system disorders**

Uncommon: Dizziness*, syncope*#

**Gastrointestinal disorders**

Very common: Diarrhoea,

Common: Abdominal cramps, abdominal pain, abdominal discomfort
Uncommon: Vomiting, nausea.

**Skin and subcutaneous tissue disorders**
Uncommon: Skin reactions* such as angioedema*, drug eruption*, rash*, pruritus*.

# The occurrence of dizziness and syncope after ingestion of sodium picosulfate leads to the conclusion that it is a vasovagal reaction (eg abdominal spasms, defecation) (see section 4.4).

* This undesirable effect has not been reported in clinical trials of sodium picosulfate. The frequency 'uncommon' is calculated based on the total number of patients treated in accordance with the EU SmPC guideline (3/1020 = 0.00294, which corresponds to 'uncommon').

**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 national reporting system listed in Appendix V*.

### 4.9 Overdose

**Symptoms:**
When high doses are taken watery stools (diarrhea), abdominal cramps and a clinically significant loss of fluid, potassium and other electrolytes can occur.

Furthermore, cases of colonic mucosal ischemia have been reported in association with doses of sodium picosulfate considerably higher than those recommended for the routine management of constipation.

Laxatives when taken in chronic overdosage may cause chronic diarrhea, abdominal pain, hypokalemia, secondary hyperaldosteronism and renal calculi. Renal tubular damage, metabolic alkalosis and muscle weakness secondary to hypokalemia have also been described in association with chronic laxative abuse.

**Therapy:**
Within a short time of ingestion, absorption can be reduced or prevented by inducing vomiting or by gastric lavage. Replacement of fluids and correction of electrolyte imbalance may be required. This is especially important in the elderly and young children.

Administration of antispasmodics may be of some value.

### 5. PHARMACOLOGICAL PROPERTIES

#### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Contact laxatives
ATC code: A06AB08

Sodium picosulfate, the active ingredient of Pikopil, is a locally acting laxative from the triarylmethane group which after bacterial cleavage in the colon has a dual-action with stimulation of the mucosa of both the large intestine and the rectum. Stimulation of the mucosa of the large intestine results in colonic peristalsis, with promotion of accumulation of water and consequently electrolytes in the colonic lumen. This results in a stimulation of defecation, reduction of transit time and softening of the stool.
As a laxative that acts on the large intestine, sodium picosulfate specifically stimulates the natural process of defecation in the lower region of the gastro-intestinal tract. Therefore, sodium picosulfate is ineffective in changing the digestion and absorption of calories and essential nutrients in the small intestine.

5.2 Pharmacokinetic properties

Absorption and Distribution
After oral ingestion, sodium picosulfate reaches the colon without any appreciable absorption. Therefore, enterohepatic circulation is avoided.

Biotransformation
The active laxative compound, bis-(p-hydroxyphenyl)-pyridyl-2-methane (BHPM), is formed by bacterial cleavage in the distal segment of the intestine.

Elimination
Following conversion, only small amounts of BHPM are absorbed and are almost completely conjugated in the intestinal wall and the liver to form the inactive BHPM glucuronide. After oral administration of 10 mg sodium picosulfate 10.4% of the total dose was excreted as BHPM glucuronide in urine after 48 hours. In general, urinary excretion decreases when higher doses of sodium picosulfate are being administered.

Pharmacokinetic / Pharmacodynamic relationship(s)
Considering the pharmacokinetic and pharmacodynamic properties of this formulation, the effect occurs between 6 and 12 hours after dosing. This is determined by the release of the active substance (BHPM). There is no direct or indirect relationship between the laxative effect and plasma levels of the active substance.

5.3 Preclinical safety data

Published animal data suggest no special hazards for humans with regard to unwanted pharmacological effects, and toxicity following repeat doses. In vitro and in vivo studies indicated no genotoxic potential. No animal carcinogenicity studies have been performed.

Reproductive toxicity studies in rats and rabbits did not reveal any teratogenic potential after oral dosing of sodium picosulfate up to 10000 and 1000 mg/kg/day, respectively. Embryo-fetal toxicity was apparent in rats and rabbits at 1000 mg/kg/day, manifested as lower fetal weight and an increase in resorptions in rabbits. In rats, daily doses of 10 mg/kg and 100 mg/kg during late gestation (fetal development) and lactation reduced body weight gain of the offspring. At 100 mg/kg there was also an increased number of dead pups at birth. Male and female rat fertility was not affected by oral doses of sodium picosulfate up to 100 mg/kg.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Lactose monohydrate; maize starch; starch, pregelatinised maize; silica, colloidal anhydrous; magnesium stearate (E572).

6.2 Incompatibilities
Not applicable.
6.3  Shelf life
24 months

6.4  Special precautions for storage
This medicinal product does not require any special storage conditions.

6.5  Nature and contents of container
Packed in colorless PVC/Aluminium foil blister
Pack sizes: 10 and 30 tablets
Not all pack sizes may be marketed.

6.6  Special precautions for disposal
No special requirements.

7. Houder van de vergunning voor het in de handel brengen
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Vital Pharma GmbH
Frankfurter Landstrasse 8
D-61352 Bad Homburg v.d.H
Duitsland

8. Nummers van de vergunning voor het in de handel brengen
Pikopil tabletten 5 mg  RVG 115880
Pikopil tabletten 7,5 mg  RVG 115881

9. Datum van eerste verlening van de vergunning / hernieuwing van de vergunning
Datum van eerste verlening van de vergunning: 2 februari 2016

10. Datum van herziening van de tekst
Laatste gedeeltelijke wijziging betreft rubriek 6.3: 21 december 2017