SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

PICOLAX®, Powder for oral solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains the following active ingredients:

Sodium picosulphate	10,0 mg
Magnesium oxide, light	3,5 g
Citric acid, anhydrous	12,0 g

Each sachet also contains:

Sweetener: Sodium saccharin 60 mg per sachet.

Lactose (as a component of the flavour)

For the list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for oral solution.

White crystalline powder with a faint odour of orange.

Reconstituted solution is off-white, cloudy liquid with a faint odour of orange.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

PICOLAX® is indicated for bowel emptying and cleansing by means of total gastrointestinal tract perfusion in preparation for gastrointestinal examination (such as colonoscopy, barium enema x-ray

For Internal Use - Internal

examination), prior to intravenous pyelograms (IVP), surgery or in severe constipation.

4.2 Posology and method of administration

Posology

Adults (including elderly):

The first PICOLAX® sachet (see method of Administration section below for reconstitution guidance) is taken the night before the procedure, and the second is taken the next day, in the morning prior to the procedure.

On the day before the procedure – 1 sachet:

- The first reconstituted sachet is taken in the late afternoon / evening (e.g., 5:00 to 9:00 PM), followed by at least 5 x 250 ml drinks of clear liquids (not only water), spread over several hours.

On the day of the procedure – 1 sachet:

- The second reconstituted sachet is taken in the morning (5-9 hours before the procedure), followed by at least 3 x 250 ml drinks of clear liquids (not only water), spread over several hours. Clear liquids (not only water) may be consumed until 2 hours before the time of the procedure.

Paediatric population

Children from 2 up to 9 years:

The first dose reconstituted in water as directed (see Method of Administration section below for reconstitution guidance), should be taken before 8 AM on the day before the procedure. Second dose to be taken 6 to 8 hours later.

From 2 up to 4 years: ½ sachet in the morning and ½ sachet in the afternoon.

From 4 up to 9 years: 1 sachet morning and ½ sachet in the afternoon.

Maintaining hydration in children is very important. Guidelines for treating dehydration in children should be followed to ensure adequate hydration during treatment with PICOLAX.

For Internal Use - Internal

Children from age 9 and above:

The same dose, scheduling of dose and liquid intake as for adults should be applied.

Method of administration

Route of administration: Oral

A low residue diet is recommended on the day prior to the procedure. A clear liquid diet is recommended on the day of the procedure. To avoid dehydration, it is important to follow the liquid intake recommendation as advocated together with the PICOLAX dosing whilst the effects of PICOLAX persist (see section Posology). Apart from the liquid intake together with the treatment regimen (PICOLAX + additional liquids), a normal, thirst driven intake of clear liquids is recommended.

Clear liquids should include a variety of soft drinks, clear soup, tea, coffee (without milk, soy or cream), fruit juice without pulp, and water. Liquid intake should not be restricted to only drinking water.

Directions for reconstitution in adults (including elderly):

Reconstitute a fresh sachet immediately prior to each dose. Reconstitute the contents of one sachet in a cup of cold water (approximately 150 ml). Stir for 2- 3 minutes, the solution should now become an off-white, cloudy liquid with a faint odour of orange. Drink the solution. If it has become warm, wait until it cools sufficiently to drink.

Directions for reconstitution in children:

Reconstitute a fresh sachet immediately prior to each dose. Reconstitute the required amount of powder in a cup containing approximately 100 ml cold water per ½ sachet. Stir for 2-3 minutes, the solution should now become an off-white, cloudy liquid with a faint odour of orange. Drink the solution. If it has become warm, wait until it cools sufficiently to drink. Discard the remaining contents of the sachet.

For Internal Use - Internal

For directions on reconstitution of the full sachet for children from 4 up to 9 years, refer to the instructions given for adults.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1
- Congestive heart failure
- Gastric retention
- Gastrointestinal ulceration
- Toxic colitis
- Toxic megacolon
- Ileus
- Nausea and vomiting
- Acute surgical abdominal conditions such as acute appendicitis
- Known or suspected gastrointestinal obstruction or perforation.
- Severe dehydration
- Rhabdomyolysis
- Hypermagnesemia
- Active inflammatory bowel disease
- Patients with a stoma
- Undiagnosed rectal bleeding
- Diabetes mellitus
- Hypertension
- Renal impairment
- Hypersensitivity to oral saline laxatives and dehydration.

For Internal Use - Internal

4.4 Special warnings and precautions for use

PICOLAX® should not be used if there is a sudden change in bowel habits that persists for a period greater than 2 weeks, rectal bleeding or failure to have a bowel movement after use of a laxative. This may indicate a serious condition.

Because a clinically relevant benefit of bowel cleansing prior to elective, open colorectal surgery could not be proven, bowel cleansers should only be administered before bowel surgery if clearly needed. The risks of the treatment should be carefully weighed against possible benefits and needs depending on surgical procedures performed.

PICOLAX® should not be given to children younger than 2 years.

PICOLAX® should not be used in the presence of hypertension, a low salt diet and kidney disease except under the supervision of a doctor.

PICOLAX® should not be used in the presence of abdominal pain, nausea, vomiting or recent gastrointestinal surgery.

Frequent or prolonged use of PICOLAX® may result in loss of normal bowel function and dependence on laxatives.
The period of bowel cleansing should not exceed 24 hours because longer preparation may increase the risk of water and electrolyte imbalance.

It is important that the patient follow the recommended dosing schedule and take adequate fluids (at least 6 to 8 glasses of liquids each day when using PICOLAX®).

For Internal Use - Internal

Adequate fluid intake or replacement should be ensured as PICOLAX® is likely to cause transient hypovolaemia (see section 4.2).

An insufficient or excessive oral intake of water and electrolytes could create clinically significant abnormalities, particularly in less fit patients. In this regard patients with low body weight, children, the elderly, debilitated individuals and patients at risk of hypokalaemia or hyponatraemia may need particular attention. Prompt corrective action should be taken to restore fluid/electrolyte balance in patients with signs or symptoms of hypokalaemia or hyponatraemia.

Drinking only water to replace the fluid losses may lead to electrolyte imbalance, which may in severe cases lead to complications such as seizures and coma. In rare cases, PICOLAX® can cause severe or life-threatening electrolyte problems or impaired renal function in fragile or debilitated patients.

Patients with pre-existing electrolyte disturbances should be closely monitored.

Care should also be taken in patients with heart disease or inflammatory bowel disease.

Use with caution in patients on medicine that might affect water and/or electrolyte balance e.g. diuretics, corticosteroids, lithium (see section 4.5).

PICOLAX® may modify the absorption of regularly prescribed oral medication and should be used with caution e.g., there have been isolated reports of seizures in patients on antiepileptics, with previously controlled epilepsy (see sections 4.5 and 4.8).

Patients, who are unconscious or semi-unconscious; with impaired gag reflex; who are prone to regurgitation or aspiration should be carefully observed during the administration of PICOLAX®.

PICOLAX® contains 5 mmol (or 195 mg) potassium per sachet. This should be taken into consideration by patients with reduced kidney function or patients on a controlled potassium diet.

PICOLAX® contains lactose as a component of the flavour. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take PICOLAX®.

For Internal Use - Internal

4.5 Interaction with other medicines and other forms of interaction

As a purgative, PICOLAX® increases the gastrointestinal transit rate. The absorption of other orally administered medicines (e.g., anti-epileptics, contraceptives, anti-diabetics, antibiotics) may therefore be modified during the treatment period (see section 4.4).

Caution is also advised when PICOLAX® is used in patients on non-steroidal anti-inflammatory drugs (NSAIDs) or medicines known to induce syndrome of inappropriate antidiuretic hormone secretion (SIADH) e.g., tricyclic antidepressants, selective serotonin re-uptake inhibitors, antipsychotic medicines and carbamazepine as these medicines may increase the risk of water retention and/or electrolyte imbalance.

Care should be taken with patients already receiving medicines which may be associated with hypokalaemia (such as diuretics or corticosteroids, lithium or medicines where hypokalaemia is a particular risk i.e., cardiac glycosides).

PICOLAX® may reduce the effectiveness of anticoagulants, digoxin and phenothiazines (especially chlorpromazine).

Concurrent use of PICOLAX® and ciprofloxacin and etidronate is not recommended since it decreases the absorption of these medicines.

Medicines with the potential to chelate with magnesium (e.g., tetracycline and fluoroquinolone antibiotics, iron, digoxin, chlorpromazine and penicillamine) should be taken not later than 2 hours before and not earlier than 6 hours after administration of PICOLAX®.

The efficacy of PICOLAX® is lowered by bulk-forming laxatives.

For Internal Use - Internal

Co-administration of sodium polystyrene sulfonate and PICOLAX® should be avoided as it may lead to severe systemic alkalosis.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety during pregnancy has not been established.

Breastfeeding

The safety during breastfeeding has not been established.

Fertility

There are no data on the effect of PICOLAX® on fertility in humans.

4.7 Effects on ability to drive and use machines

Adverse events have been reported where PICOLAX® may less frequently cause dizziness, light-headedness or confusion. Patients should be advised that their physical and/or mental abilities required for operating machinery or driving vehicles may be impaired, if these effects are experienced.

4.8 Undesirable effects

The most frequent adverse reactions are vomiting, nausea, abdominal pain and headache. Hyponatraemia is rare but is the most frequently reported serious adverse reaction.

MedDRA Organ Class	**Common (≥1/100 to ≤1/10)**	**Uncommon (≥1/1000 to ≤1/100)**	**Rare (≥1/10 000 to <1/1 000)**

For Internal Use - Internal

Immune system disorder		Anaphylactic reaction, hypersensitivity	
Metabolism and nutrition disorders		Hypokalaemia	Hyponatraemia
Psychiatric disorders		Confusional state including disorientation	
Nervous system disordes	Headache	Epilepsy Generalised tonic-clonic seizure[a] Seizure[b] Loss of or depressed level of consciousness Syncope Dizziness	Presyncope
Gastrointestinal disorders	Vomiting, Nausea and abdominal pain	Diarrhoea[c]	Ileal ulcers[d] Anal incontinence[e], Proctalgia
Skin and subcutaneous tissue disorders		Rash (including erythematous and maculo-papular rash, urticaria, purpura)	

[a] Defined as grand mal convulsion in previous MedDRA versions. In epileptic patients, there have been isolated reports of seizure/grand mal convulsion without associated hyponatraemia.

[b] Defined as convulsions in previous MedDRA versions.

[c] Isolated cases of severe diarrhoea have been reported post-marketing.

[d] Isolated cases of mild reversible aphthoid ileal ulcers have been reported.

[e] Defined as faecal incontinence in previous MedDRA versions.

For Internal Use - Internal

The frequencies of the side effects are based on post-marketing experience.

Diarrhoea and faecal incontinence are the primary clinical effect of PICOLAX®.

Hyponatraemia has been reported with or without associated convulsions. In epileptic patients, there have been isolated reports of seizure/grand mal convulsion without associated hyponatraemia. There have been isolated reports of anaphylactoid reaction.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

Overdose would lead to profuse diarrhoea. Treatment is by general supportive measures and correction of fluid and electrolyte balance.

The symptoms of an overdosage are those of the electrolyte imbalance that occurs such as confusion, irregular heartbeat, muscle cramps, unusual tiredness or weakness. In the event of overdosage the most important treatment would be rehydration of the patient. The electrolyte levels should be carefully monitored, and immediate corrective action should be taken to restore electrolyte balance with appropriate fluid replacements.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A. 11.5 Laxatives

For Internal Use - Internal

Pharmacotherapeutic group: Contact Laxatives

ATC code: A06A B58

The active components of PICOLAX® are sodium picosulphate and magnesium citrate. Sodium picosulphate is hydrolysed by colonic bacteria to form an active metabolite bis (ρ-hydroxyphenyl) pyridyl-2-methane, BHPM, which acts directly on the colonic and rectal mucosa to stimulate colonic and rectal peristalsis.

Magnesium oxide and citric acid react to create magnesium citrate in solution, which is an osmotic agent that causes retention of water within the gastrointestinal tract. The combined action of the two substances is of a 'washing out' effect combined with peristaltic stimulation to clear the bowel.

5.2 Pharmacokinetic properties

Sodium picosulfate and magnesium citrate, the two components of PICOLAX®, are locally active, with minimal systemic exposure.

Absorption

After administration of the first packet of PICOLAX® in 16 healthy subjects, mean maximum concentration (C_{max}) for picosulfate of 2,3 ± 1,4 ng/mL was reached at 2 hours. After administration of 2 packets of PICOLAX® separated by 6 hours, picosulfate reached the mean C_{max} of 3,2 ± 2,6 ng/mL at approximately 7 hours (T_{max}). In the same study, baseline uncorrected magnesium reached a C_{max} of approximately 1,9 mEq/L, which occurred at 10 hours post first packet administration (T_{max}). This represents an approximately 20 % increase from the baseline.

Distribution

The apparent volume of distribution (V/F) for picosulfate was 4 199 liters in healthy adults.

Metabolism and Elimination

For Internal Use - Internal

Sodium picosulfate, which is a prodrug, is converted to its active metabolite, BHPM, by colonic bacteria. Plasma concentration of the free BHPM were low, and below the lower limit of quantification (0,1 ng/mL) in 13 out of 16 subjects studied. The fraction of the sodium picosulfate dose excreted unchanged in urine was 0,2 %. In urine, the majority of excreted BHPM was in the glucuronide conjugated form. The terminal half-life of sodium picosulfate was 7,4 hours. The apparent clearance (CL/F) of picosulfate was 629 L/h.

Pharmacokinetics in Paediatric patients

Pharmacokinetics of picosulfate was studied in paediatric patients aged from 9 to 16 years old.

For picosulfate, the apparent clearance is from 316 to 409 L/h. The corresponding estimates for apparent volume of distribution are from 2 457 to 3 935 liters. The derived half-life using these model estimates would be 7 hours. The picosulfate reached the mean C_{max} of 3,5 ± 2,1 ng/mL at approximately 6 to 7 hours (T_{max}).

The baseline uncorrected mean serum magnesium concentration was 2,02 mEq/L at 10 hours after the first dose of PICOLAX® and ranged from 1,7 to 2,46 mEq/L in paediatric patients from 9 to 16 years of age.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Potassium hydrogen carbonate (5 mmol [or 195 mg] potassium per sachet).

Sodium saccharin (60 mg per sachet).

Natural, spray dried orange flavour which contains acacia gum, lactose, ascorbic acid, butylated hydroxyanisole.

6.2 Incompatibilities

Not applicable.

For Internal Use - Internal

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at or below 25 °C. Protect from light.

Store in the original package.

The reconstituted solution must be used immediately after chilling in the refrigerator.

6.5 Nature of contents of the container

PICOLAX® powder for oral solution is supplied in white unit dose sachets. Double sachets divided by tear-off perforation are packed in cartons of 2 x 25 sachets or an original patient pack containing 2 sachets. The sachet is made from a four layer foil of paper-polyethylene aluminium-thermofusible resin (Surlyn).

Certain presentations described here, may not all be available on the market.

6.6 Special precautions for disposal and other handling

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Ferring (Pty) Ltd.

Route 21 Corporate Offices

6 Regency Drive

Irene Ext. 30

8. REGISTRATION NUMBER

A39/11.5/0058

For Internal Use - Internal

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

02 March 2012

10. DATE OF REVISION OF TEXT

20 May 2022

Namibia NS2
Reg. No/Nr:13/11.5/0194
Botswana S3
Reg. No/Nr: BOT1402674B

For Internal Use - Internal