AUSTRALIAN PRODUCT INFORMATION - PICOSALAX® (citric acid, light magnesium oxide, sodium picosulfate)

1 NAME OF THE MEDICINE

Citric acid
Light magnesium oxide
Sodium picosulfate

WARNING: Life-threatening dehydration and/or electrolyte disturbances may occur in 'at risk' groups (see 'Contraindications' and 'Precautions').

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredients: sodium picosulfate 10 mg with magnesium citrate formed in solution from light magnesium oxide 3.5 g and citric acid 12 g.

Inactive: potassium bicarbonate (equivalent to 5 mmol (195 mg) potassium), saccharin sodium, orange flavour (containing lactose monohydrate (equivalent to 4.5 mg of lactose)).

3 PHARMACEUTICAL FORM

White crystalline powder for solution.

4 CLINICAL PARTICULARS

4.1 THERAPEUTICS INDICATIONS

For clearance of the bowel prior to examination by radiography, endoscopy or surgery.

4.2 DOSE AND METHOD OF ADMINISTRATION

Instructions for timing of dose and dietary and fluid restrictions vary greatly between centres and may over-ride the recommendations given below. Clinical studies with PICOSALAX have shown the following regimens to be effective.

Adults (including the elderly) and children aged 9 years of age and older:

(if the procedure is scheduled for the afternoon, it is recommended that the Split-Dose regimen be used):

Split-Dose Regimen (evening-before and day of the procedure)
The first PICOSALAX sachet 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 evening (e.g., 5:00 to 9:00 p.m.), followed by at least five 250 mL drinks of clear liquids, 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 three 250 mL drinks of clear liquids, spread over several hours
- Clear liquids may be consumed until 2 hours before the time of the procedure.

or

Day-Before Regimen (evening-before the procedure only)
The first PICOSALAX sachet is taken in the afternoon or early evening and the second is taken approximately 6 hours later, the night before the procedure.

On the day before the procedure – 2 sachets:

- The first reconstituted sachet is taken in the afternoon or early evening (e.g., 4:00 to 6:00 p.m.), followed by at least five 250 mL drinks of clear liquids, spread over several hours
- The second reconstituted sachet is taken in the late evening (e.g., 10:00 p.m. to 12:00 a.m.), followed by at least three 250 mL drinks of clear liquids, spread over several hours
- Clear liquids may be consumed until 2 hours before the time of the procedure.

Directions for reconstitution:

Immediately before use, mix the contents of one sachet in approximately 150 mL (2/3rd of a cup) of water. Stir for 2-3 minutes, the solution should now become an off-white, cloudy liquid with a faint odour of orange. If it becomes warm wait until it cools sufficiently to drink. Drink the solution. Do not prepare the solution in advance.

Further information:

Patients should be warned to expect frequent, loose bowel movements. To avoid dehydration it is recommended to drink a sufficient amount of clear liquids whilst the effects of PICOSALAX persist. Apart from the liquid intake together with the treatment regimen (PICOSALAX + additional liquids), a normal, thirst-driven intake of clear liquids is recommended. Clear liquids may include water, clear soup, fruit juice without pulp, soft drinks, tea and/or coffee without milk (including soy and cream). Patients should be advised NOT to drink just water alone but to also drink a balanced electrolyte solution; drinking only water to replace fluid losses may lead to electrolyte imbalance, particularly hypokalemia or hyponatraemia and possibly seizures (See PRECAUTIONS). Patients should be instructed to consume only clear fluids (no solid food or milk) on the day before the procedure up until 2 hours before the time of the procedure.

4.3 CONTRAINDICATIONS

PICOSALAX is contraindicated in patients with congestive heart failure, clinically significant renal impairment, known or suspected gastrointestinal obstruction or perforation, gastric retention, gastro-intestinal ulceration, toxic colitis, toxic megacolon, ileus, those with a stoma, nausea and vomiting, acute surgical abdominal conditions such as acute appendicitis, severe dehydration, rhabdomyolysis, hypermagnesemia, active inflammatory bowel disease or hypersensitivity to any of the ingredients.

In patients with severely reduced renal function, accumulation of magnesium in plasma may occur. Another preparation should be used in such cases.

PICOSALAX should not be used in patients with undiagnosed abdominal symptoms.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Use with caution in patients with recent gastro-intestinal surgery, renal impairment, heart disease or inflammatory bowel disease. Those patients with kidney disease or impaired renal function should be monitored, as should those with pre-existing electrolyte disturbances. Diabetics may need adjustment of their medication and careful monitoring of their blood glucose.

Patients using diuretics or other medications (such as corticosteroids, lithium) that may affect water and/or electrolyte balance should also be monitored (See Section 4.5 - INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS).

In all patients, adequate fluid intake should be maintained. An insufficient or excessive oral intake of water and electrolytes could create clinically significant deficiencies, particularly in less fit patients. In this regard, patients with low bodyweight, children, the elderly, debilitated individuals and patients at risk of hypokalaemia or hyponatremia may

need particularattention. Prompt corrective action should be taken to restore fluid/electrolyte balance in patients with signs or symptoms of hypokalemia 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, PICOSALAX can cause severe or life-threatening electrolyte problems or impaired renal function in fragile or debilitated patients. Nephrocalcinosis and renal impairment may occur following use of oral sodium phosphate products in 'at risk' or inappropriate patient groups.

The period of bowel cleansing should not exceed 24 hours because longer preparation may increase the risk of water and electrolyte imbalance (See Section 4.2 – DOSE AND METHOD OF ADMINISTRATION).

PICOSALAX 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 anti-epileptics, with previously controlled epilepsy.

This medicine 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.

PICOSALAX contains lactose as a component of the flavour (4.5 mg per sachet). Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

PICOSALAX is not intended for use as a routine laxative.

Use in the elderly
As described in this SECTION 4.4 – SPECIAL WARNINGS AND PRECAUTIONS FOR USE.

Use in children
PICOSALAX should not be used in children under 9 years of age.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

As a purgative, PICOSALAX increases 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.

Broad spectrum antibiotics may decrease the effect of PICOSALAX by interfering with the colonic bacteria needed to break down sodium picosulfate to form its active substance.

Medicines with the potential to chelate with magnesium (e.g. tetracyclines and fluoroquinolone antibiotics, iron, digoxin, chlorpromazine and penicillamine) should be taken at least 2 hours before and not less than 6 hours after administration of PICOSALAX.

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

Caution is also advised when PICOSALAX is used in patients on NSAIDs or drugs known to induce SIADH (Syndrome of Inappropriate Antidiuretic Hormone secretion) e.g. tricyclic antidepressants, selective serotonin re-uptake inhibitors, antipsychotic drugs and carbamazepine as these drugs may increase the risk of water retention and/or electrolyte imbalance.

The efficacy of PICOSALAX is lowered by bulk-forming laxatives.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effect on fertility

Studies with PICOSALAX in animals have shown no impairment of fertility or embryo-fetal toxicity. In studies with sodium picosulfate alone, embryofetal toxicity has been observed in rats and rabbits at very high doses.

Use in pregnancy

Whilst animal reproduction studies with sodium picosulfate have revealed no evidence of a harmful action on the fetus, clinical experience of the use of PICOSALAX during pregnancy is limited and caution should be observed, particularly during the first trimester.

Use in lactation

Neither sodium picosulfate nor magnesium citrate has been shown to be excreted in breast milk. As there is no experience with the use of PICOSALAX in nursing mothers, the product should only be used if clearly indicated.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Not relevant.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The most common adverse reactions are vomiting, nausea, abdominal pain and headache. Hyponatraemia is rare but is the most commonly reported serious adverse reaction. Adverse reactions from spontaneous reports are presented by frequency category based on incidence in clinical trials when known. Frequency from spontaneous reports for adverse reactions never observed in clinical trials is based on an algorithm as recommended in the European Commission SmPC guideline, 2009, rev 2.

MedDRA Organ Class	**Common (≥1/100 to ≤1/10)**	**Uncommon (≥1/1000 to <1/100)**	**Rare (≥1/10.000 to <1/1.000)**
Immune system disorders		Anaphylactic reaction, hypersensitivity	
Metabolism and nutrition disorders		Hyponatraemia and hypokalaemia	
Psychiatric disorders		Confusional state Including Disorientation	
Nervous system disorders	Headache	Epilepsy, Generalised tonic-clonic seizure[a], Seizure[b], Loss of or depressed level of consciousness Syncope Dizziness	Presyncope

Gastrointestinal disorders	Vomiting, Nausea, Proctalgia, Abdominal pain	Diarrhoea[c], iIleal ulcers*[d]	Anal incontinence[e]
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.

Diarrhoea and faecal incontinence are the primary clinical effect of PICOSALAX.

Hyponatraemia has been reported with or without associated convulsions.

Reporting suspected adverse reactions after registration 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 at http://www.tga.gov.au/reporting-problems.

4.9 OVERDOSE
Overdosage would lead to profuse diarrhoea with dehydration and fluid/electrolyte imbalance. Treatment is by general supportive measures and correction of fluid and electrolyte imbalance.

For information on the management of overdose, contact the Poison Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES
5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of Action
The active components of PICOSALAX are sodium picosulfate, which stimulates bowel movements following metabolism by colonic bacteria, and magnesium citrate which acts as an osmotic laxative by increasing intestinal osmotic pressure thereby promoting retention of fluid within the bowel. The combined action of these components results in evacuation of the bowel contents.

Sodium picosulfate itself is pharmacologically inactive but is metabolised to an active metabolite, desacetylbisacodyl (bis(*p-hydroxyphenyl*)pyridyl-2-methane), which influences the chemoreceptors in the mucosa to increase intestinal motility. Desacetylbisacodyl is the same active metabolite formed following ingestion of bisacodyl, is insoluble in water and is minimally absorbed from the gastro-intestinal tract.

Clinical trials
No data available.

5.2 PHARMACOKINETIC PROPERTIES
No data available.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity
No data available.

Carcinogenicity
No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Refer to Section 2 – QUALITATIVE AND QUANTITATIVE COMPOSITION.

6.2 INCOMPATIBLES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

3 years. The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30^0C.

6.5 NATURE AND CONTENTS OF CONTAINER

Picosalax sachets contain a white crystalline powder. It is supplied in boxes containing 2 sachets.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSIOCHEMICAL PROPERTIES

Sodium picosulfate. Molecular formula: $C_{18}H_{13}NNa_2O_8S_2$, MW: 481.4, CAS: 10040-45-6
Light magnesium oxide. Molecular formula: MgO, MW: 40.3, CAS: 1309-48-4
Citric acid. Molecular formula: $C_6H_8O_7$, MW: 192.1, CAS: 77-92-9

7 MEDICINES SCHEDULE (POISONS STANDARD)

S3 (Pharmacist Only Medicine)

8 SPONSOR

Ferring Pharmaceuticals Pty Ltd
Suite 2, Level 1, Building 1
20 Bridge Street
Pymble NSW 2073
Australia

9 DATE OF FIRST APPROVAL

15 May 2007

10 DATE OF REVISION

23 August 2019

For the most current approved PI, please refer to https://www.ebs.tga.gov.au/ or http://www.ferring.com.au/

PICOSALAX is a registered trademark of Ferring B.V.

Summary table of changes

Section Changed	Summary of new information
ALL	PI reformatted to align with TGA's *Form for providing Product Information,* March 2018 version.