SUMMARY OF PRODUCT CHARASTERISTICS

1. Name of the medicinal product

Sodium Picosulfate, Magnesium Oxide and Anhydrous Citric Acid for Oral Solution 10mg/3.5g/12g per packet
Heterolaxa

2. Qualitative and quantitative composition

Each Packet contains 10mg Sodium Picosulfate USP, 3.5g Magnesium Oxide and 12g anhydrous citric acid USP.
For the full list of excipients, see section 6.1.

3. Pharmaceutical form

White crystalline powder for oral solution

4. Clinical particulars

4.1 Therapeutic indications

For Evacuation of the bowel prior to radiological, endoscopic or surgical procedures.

4.2 Posology and 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 Sodium Picosulfate, Magnesium oxide and Anhydrous citric acid for Oral solution 10mg/3.5g/12g per packet dosing while the effects of Sodium Picosulfate, Magnesium oxide and Anhydrous citric acid for Oral solution 10mg/3.5g/12g per packet persist (see section 4.2, Posology). Apart from the liquid intake together with the treatment regimen (Sodium Picosulfate, Magnesium oxide and Anhydrous citric acid for Oral solution 10mg/3.5g/12g per packet + additional liquids), a normal, thirst driven intake of clear liquids is recommended. Clear liquids should include a variety of fruit juice without pulp, soft drinks, clear soup, tea, coffee (without milk, soy, or cream) and water. Liquid intake should not be restricted to only drinking water.

Posology

Directions for reconstitution:
Reconstitute the contents of one sachet in a cup of water (approximately 150ml). Stir for 2-3 minutes. Thesolution should now become an off-white, cloudy liquid with a faint odour of orange. Drink the solution.If it becomes warm wait until it cools sufficiently to drink.

Adults (including elderly):

The first Sodium Picosulfate, Magnesium oxide and Anhydrous citric acid for Oral solution 10mg/3.5g/12g per packet sachet is taken before 8 am the day before the procedure and the second istaken 6 to 8 hours later.

On the day before the procedure – 2 sachets:

- The first reconstituted sachet is taken before 8 am, followed by at least 5x 250 ml drinks of clear liquids (not only water), spread over several hours.

- The second reconstituted sachet is taken 6 to 8 hours later, followed by at least 3x 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.

Children:

The first dose reconstituted in water as directed, taken before 8 am on the day before the procedure. Second dose 6 to 8 hours later.
From 1 up to 2 years: ¼ sachet morning, ¼ sachet afternoon
From 2 up to 4 years: ½ sachet morning, ½ sachet afternoon
From 4 up to 9 years: 1 sachet morning, ½ sachet afternoon

9 and above: adult dose

Maintaining hydration in children is very important. Guidelines for treating dehydration in children should be followed to ensure adequate hydration during treatment with Sodium Picosulfate, Magnesium oxide and Anhydrous citric acid for Oral solution 10mg/3.5g/12g per packet.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1
- Congestive cardiac failure
- Gastric retention
- Gastro-intestinal ulceration
- Toxic colitis
- Toxic megacolon
- Ileus
- Severe nausea and vomiting
- Acute surgical abdominal conditions such as acute appendicitis
- Known or suspected gastro-intestinal obstruction or perforation
- Severe dehydration
- Rhabdomyolysis
- Hypermagnesemia
- Active inflammatory bowel disease
- In patients with severely reduced renal function, accumulation of magnesium in plasma may occur. Another preparation should be used in such cases.

Not to be administered to unconscious patients or those with impaired consciousness, general weakness and patients with a tendency to aspiration or regurgitation or impaired swallowing reflex.

4.4 Special warnings and precautions for use

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.

An insufficient or excessive oral intake of water and electrolytes could create clinically significant abnormalities, particularly in less fit patients. In this regard, children, the elderly, debilitated individuals and patients at risk of hypokalemia 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, Sodium Picosulfate, Magnesium oxide and Anhydrous citric acid for Oral solution 10mg/3.5g/12g per packet can cause severe or life-threatening electrolyte problems or impaired renal function in fragile or debilitated patients. Care should be taken in patients with recent gastro-intestinal surgery, renal impairment, heart disease or inflammatory bowel disease.
Use with caution in patients on drugs that might affect water and/or electrolyte balance e.g. diuretics, corticosteroids, lithium (see section 4.5).
Sodium Picosulfate, Magnesium oxide and Anhydrous citric acid for Oral solution 10mg/3.5g/12g per packet 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 4.5 and 4.8).
The period of bowel cleansing should not exceed 24 hours because longer preparation may increase the risk of water and electrolyte imbalance.
Excipients
Lactose
This medicine contains lactose as a component of the flavour. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
Pottasium
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.
Sodium Picosulfate, Magnesium oxide and Anhydrous citric acid for Oral solution 10mg/3.5g/12g per packet should not be used as a routine laxative.

4.5 Interaction with other medicinal products and other forms of interaction
As a purgative, Sodium Picosulfate, Magnesium oxide and Anhydrous citric acid for Oral solution 10mg/3.5g/12g per packet 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 (see section 4.4).
Medicines with the potential to chelate with magnesium (e.g. tetracycline and fluroquinolone antibiotics, iron, digoxin, chlorpromazine and penicillamine) should be taken not later than 2 hours before and not earlier than 6 hours after administration of Sodium Picosulfate, Magnesium oxide and Anhydrous citric acid for Oral solution 10mg/3.5g/12g per packet.
The efficacy of Sodium Picosulfate, Magnesium oxide and Anhydrous citric acid for Oral solution 10mg/3.5g/12g per packet is lowered by bulk-forming laxatives.
Care should be taken with patients already receiving drugs which may be associated with hypokalemia (such as diuretics or corticosteroids, or drugs where hypokalemia is a particular risk i.e. cardiac glycosides). Caution is also advised when Sodium Picosulfate, Magnesium oxide and Anhydrous citric acid for Oral solution 10mg/3.5g/12g per packet is used in patients on NSAIDS or drugs known to induce SIADH 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.

4.6 Fertility, pregnancy and lactation

For Sodium Picosulfate, Magnesium oxide and anhydrous citric acid for Oral solution 10mg/3.5g/12g per packet no clinical data on exposed pregnancy are available. Studies with Sodium Picosulfate, Magnesium oxide and anhydrous citric acid for Oral solution 10mg/3.5g/12g per packet 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 (see section 5.3). Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

There is no experience with the use of Sodium Picosulfate, Magnesium oxide and Anhydrous citric acid for Oral solution 10mg/3.5g/12g per packet in nursing mothers, so the drug should only be used in nursing mothers if clearly needed

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

The most common adverse reactions are vomiting, nausea, abdominal pain and headache. Hyponatremia 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 (≥1/10000 to ≤1/1000)**
Immune system disorders		Anaphylactic reaction, hypersensitivity	
Metabolism and nutrition disorders*		Hypokalemia	Hyponatraemia
Psychiatric disorders		Confusional state including disorientation	
Nervous system disorders	Headache	Epilepsy, Generalised tonic-clonic seizures, Seizure, Loss of or depressed level of consciousness, Syncope, Dizziness	Presyncope
Gastrointestinal disorders	Vomiting, nausea, abdominal pain	Diarrhoea[b]	Ileal ulcer, anal incontinence, proctalgia

Skin and subcutaneous tissue disorders		Rash (including erythematous rash, maculo-papular rash, urticaria, purpura)	

a In epileptic patients, there have been isolated reports of seizure/grand mal convulsion without associated hyponatraemia.
b Isolated cases of severe diarrhoea have been reported post-marketing.
c Isolated cases of mild reversible aphthoid ileal ulcers have been reported.

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 e-PV desktop applications (https://drive.google.com/file/d/16hwTz0587ZWtSWadbBAMwQPOD_KSExZP/view) or search for e-PV Mobile applications on the Google Play or Apple App Store.

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

5. Pharmacological properties
5.1 Pharmacodynamic properties
Pharmacological Classification: 16.5.2 Stimulant Laxatives

The active components of Sodium Picosulfate, Magnesium oxide and Anhydrous citric acid for Oral solution 10mg/3.5g/12g per packet are sodium picosulfate and magnesium citrate. Sodium Picosulfate is a locally acting stimulant cathartic, which after bacterial cleavage in the colon forms the active laxative compound, bis-(p-hydroxyphenyl)-pyridyl-2-methane (BHPM), which has a dual-action with stimulation of the mucosa of both the large intestine and of the rectum.
Magnesium citrate acts as an osmotic laxative by retaining moisture in the colon. The combined action of the two substances is of a 'washing out' effect combined with peristaltic stimulation to clear the bowel. The product is not intended for use as a routine laxative.

5.2 Pharmacokinetic properties
Sodium picosulfate and magnesium citrate, the two components of Sodium Picosulfate, Magnesium oxide and anhydrous citric acid for Oral solution 10mg/3.5g/12g per packet , are locally active with minimal systemic exposure.
After administration of Sodium Picosulfate, Magnesium oxide and Anhydrous citric acid for Oral solution 10mg/3.5g/12g per packet (2 sachets separated by 6 hours), picosulfate reached mean levels of 2.3 and 3.2 ng/mL (Cmax) at a median of 2 and 8 hours (Tmax) after the first and second sachet, respectively. The corresponding values for magnesium were 0.90 and 0.95 mmol/L at 4 and 10 hours, respectively. The baseline value was 0.75 mmol/L.
The mean terminal half-life of picosulfate was 7.4 hours. The fraction of the sodium picosulfate dose excreted unchanged in urine was 0.11%. Plasma levels of BHPM were consistently low or undetectable and urinary samples showed that the majority of excreted BHPM was the

glucuronide-conjugated form. Clinical studies in bowel cleansing before colonoscopy have shown an increase from baseline to colonoscopy visit in serum magnesium of approximately 0.11 mmol/L (from 0.86 to 0.97 mmol/L). All changes in serum magnesium were transient and within normal limits, including in patients with mild to moderate renal impairment.

5.3 Preclinical safety data
Non-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity and genotoxicity.
Due to the very short treatment duration no long-term studies in animals have been performed. Reproductive studies have shown no potential for impairment of fertility or harm to the foetus for sodium picosulfate and Sodium Picosulfate, Magnesium oxide and Anhydrous citric acid for Oral solution 10mg/3.5g/12g per packet.
In a study on pre- and postnatal development, the NOAEL of Sodium Picosulfate, Magnesium oxide and Anhydrous citric acid for Oral solution 10mg/3.5g/12g per packet was the mid dose of 750 mg/kg BID. The adverse effect that occurred in the 2000 mg/kg BID group (approximately 8 times the recommended human dose), was pup mortality, between lactation days 2 to 4 due to maternal toxicity. Effects in reproductive and developmental toxicity studies with sodium picosulfate alone were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.

6. Pharmaceutical particulars
6.1 List of excipients
Glyceryl Behenate
Potassium bicarbonate
Saccharin Sodium
Orange flavor 501071 AP0551
Citric Acid Anhydrous
Magnesium Oxide

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
24 months

6.4 Special precautions for storage
Store below 30°C

6.5 Nature and contents of container
4 ply laminated film with Aluminium foil.

6.6 Special precautions for disposal and other handling
No Special requirements.

7. Applicant
Hetero Labs Limited

7-2-A2, Hetero Corporate
Industrial Estates
Sanath Nagar, Hyderabad-500 018
Telangana
India

8. Manufacturer
M/s. Annora Pharma Private Limited
Survey No.261, Annaram village
Gummadidala Mandal
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India

9. Registration details
Zimbabwe registration number: 2023/16.5.2/6401
Zimbabwe Category of distribution: Prescription Preparations (P.P.)

10. Date of revision of the text
21 April 2023