May 2024

Updates according to SPC approved in UK on 12/2023

מקרא צבעים

מידע חדש – **XX**

1. NAME OF THE MEDICINAL PRODUCT

PICO - SALAX Orange
PICO - SALAX Cranberry

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains the following active ingredients:

Sodium picosulfate	10.0mg
Magnesium oxide, light	3.5g
Citric acid, anhydrous	12.0g

Each sachet also contains:
Potassium hydrogen carbonate 0.5g [equivalent to 5 mmol (195 mg) potassium]
Lactose (as a component of the orange flavour)

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for oral solution in sachet.
White crystalline powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

To clean the bowel prior to X-ray examination or endoscopy or surgery.

4.2 Posology and method of administration

Posology

Adults (including elderly):

The two PICO - SALAX sachets are taken dependent on the planned time of the procedure:

- The first reconstituted sachet is taken 10 to 18 hours before the procedure, followed by at least 5 x 250 ml drinks of clear liquids (not only water), spread over several hours
- The second reconstituted sachet is taken 4 to 6 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

Special populations
Limited data is available for treatment of patients with low body weight (BMI less than 18). The rehydration regimen above has not been tested in such individuals and therefore monitoring of their hydration status is required and the regimen may need to be altered appropriately (see section 4.4).

Pediatric population:
A measuring spoon is provided with the product. It is recommended that a narrow flat edge, for example the back of a knife blade, is drawn across the top of a heaped measuring spoon to obtain a flat surface of the measure. This will give ¼ of a sachet (4 g powder) per spoonful.

For the timing of dosing in children, refer to the instructions given for adults
from 1 up to 2 years: first dose is 1 spoonful, second dose is 1 spoonful
from 2 up to 4 years: first dose is 2 spoonfuls, second dose is 2 spoonfuls
from 4 up to 9 years: first dose is 1 sachet, second dose is 2 spoonfuls
9 years 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 PICO-SALAX

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 PICO-SALAX dosing whilst the effects of PICO-SALAX persist (see section 4.2, *Posology*). Apart from the liquid intake together with the treatment regimen (PICO-SALAX + 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.

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

Directions for reconstitution in children:

Reconstitute the required amount of powder in a cup containing approximately 50 ml water per spoonful. Stir for 2-3 minutes, the solution should now become an off-white, cloudy liquid with a faint odour of orange/cranberry. Drink the solution. If it becomes warm, wait until it cools sufficiently to drink.
Discard the remaining contents of the sachet.
For directions on reconstitution of the full sachet for children of 4-9 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 cardiac failure
- Gastric retention
- Gastro-intestinal ulceration
- Toxic colitis
- Toxic megacolon
- Ileus
- 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.

4.4 Special warnings and special 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 patients with low body weight, children, the elderly, debilitated individuals and patients at risk of hypokalaemia or hyponatremia may need particular attention. Prompt corrective action should be taken to restore fluid/electrolyte balance in patients with signs or symptoms of hypokalaemia or hyponatremia.
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, PICO-SALAX can cause severe or life-threatening electrolyte problems or impaired renal function in fragile or debilitated patients.

Care should also 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 4.5).
PICO-SALAX 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.

For an early time of the day procedure it may be required to take the second dose during the night and possible sleep disturbance may occur.

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.
This medicine contains lactose as a component of the orange flavour. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
This medicine contains less than 1 mmol sodium (23 mg) per sachet, that is to say essentially 'sodium-free'.

PICO-SALAX should not be used as a routine laxative.

4.5 Interaction with other medicinal products and other forms of interaction
As a purgative, PICO-SALAX increases the gastrointestinal transit rate. The absorption of other orally administered medicines (e.g. anti-epileptics, contraceptives, anti-diabetics, antibiotics) may be decreased during the treatment period (see 4.4). Medicines with the potential to chelate with magnesium (e.g tetracycline and fluoroquinolone antibiotics, iron, digoxin, chlorpromazine and penicillamine), should be taken not latter than 2 hours before and not earlier than 6 hours after administration of PICO-SALAX.
The efficacy of PICO-SALAX is lowered by bulk-forming laxatives.
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 PICO-SALAX 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
Pregnancy

For PICO-SALAX no clinical data on exposed pregnancy are available.
Studies in animals have shown reproductive toxicity (see section 5.3). As picosulfate is a stimulant laxative, for safety measure, it is preferable to avoid the use of PICO-SALAX during pregnancy.

Breastfeeding.
There is no experience with the use of PICO-SALAX in nursing mothers. However, due to the pharmacokinetic properties of the active ingredients, treatment with PICO-SALAX may be considered for females who are breastfeeding.

Fertility
There are no data on the effect of PICO-SALAX on fertility in humans. Male and female rat fertility was not affected by oral doses of sodium picosulfate up to 100 mg/kg (see section 5.3).

4.7 Effects on ability to drive and use machines
Not relevant.

4.8 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 disorder		Anaphylactic reaction, hypersensitivity	
Metabolism and nutrition disorders		~~hypokalaemia~~Hypokalaemia	Hyponatraemia

Nervous system disorders	Headache	Epilepsy, generalised tonic-clonic seizure[a] , seizure, ~~Loss~~ loss of or depressed level of consciousness, syncope, dizziness. ~~Confusional~~ confusional state including disorientation	Presyncope
Gastrointestinal disorders	Vomiting, nausea, abdominal pain	* Diarrhoea[b]	Ileal ulcer[c], anal incontinence, proctalgia
Skin and subcutaneous tissue disorders		Rash (including erythematous rash and maculo-papular rash, urticaria, purpura)	

[a] In epileptic patients, there have been isolated reports of seizure/generalised tonic-clonic seizure 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 authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il/

4.9 Overdose

Overdos~~ag~~e 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

Pharmacotherapeutic group: Contact Laxatives
ATC code: A06A B58

The active components of PICO-SALAX 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.

Clinical efficacy and safety
The dosing regimen as described in section 4.2 Posology, and herein further referred to as the tailored dosing regimen, was investigated and evaluated in trial 000121 (OPTIMA) The efficacy, safety and tolerability of PICO-SALAX administered according to the tailored dosing regimen was compared with the fixed schedule of dosing (i.e. first dose is taken before 8am and second dose is taken 6-8 hours later on the day before procedure), called Day- before dosing regimen (204 patients were randomized, 131 received tailored dosing, 73 received day before dosing).
Superiority of the tailored dosing regimen was demonstrated compared to the day before dosing regimen in overall colon cleansing and responder status for ascending colon cleansing. For overall colon cleansing (primary endpoint), the tailored dosing regimen was compared to the Day -before dosing regimen, based on the treatment difference in mean total Ottawa Scale score (4.26 versus 8.19 in mean total Ottawa scale score for tailored dosing regimen and Day- before dosing regimen respectively, with a corresponding p-value <0.0001, for the Intend to Treat (ITT) analysis set). For the responder status of the ascending colon (key secondary endpoint), the proportion of patients with an Ottawa Scale score of either 0 (excellent) or 1 (good), was compared between the tailored dosing regimen and the Day- before dosing regimen. Patients randomized to the tailored dosing regimen were observed to have a 4.05 times greater chance of being a responder with respect to ascending colon cleansing compared to patients randomized to the Day -before dosing regimen.

Endpoint	Study Population (n=204)	PICO-SALAX day before dosing regimen Estimate (n=73)	PICO-SALAX tailored dosing regimen Estimate (95%CI) (n=131)
Mean Total Ottawa Scale Score (Adjusted estimate)	ITT	8.19	4.26 -3.93(-4.99,-2.87) p-value < 0.0001
Proportion of patients with an Ottawa Scale score of either 0(excellent) or 1 (good) for Ascending Colon Cleansing (Crude estimate)	ITT	15.1%	61.1% RD* 0.46 (0.34; 0.58) RR** 4.05 (2.31; 7.11)

* Absolute Risk Difference (Crude)
** Relative Risk (Crude)

5.2 Pharmacokinetic properties
Both active components are locally active in the colon, and neither are absorbed in any detectable amounts.

5.3 Preclinical safety data
Prenatal developmental studies in rats and rabbits did not reveal any teratogenic potential after oral dosing of sodium picosulfate, but embryotoxicity has been observed in rats at 1000 and 10000 mg/kg/day and in rabbits at 1000 mg/kg/day. The corresponding safety margins were 3000 to 30000 times the anticipated human dose. In rats, daily doses of 10 mg/kg during late gestation (foetal development) and lactation reduced body weights and survival of the offspring. 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:

PICO-SALAX Orange:
Potassium hydrogen carbonate, ~~granular Sodium saccharin~~ Saccharin sodium,

Natural spray dried orange flavour which contains ~~acacia gum (Gum~~ gum ~~Arabic~~ ~~arabic~~~~E414~~), lactose ~~(Lactose Foodstuffs)~~, ascorbic acid ~~E300~~, butylated hydroxyanisole ~~E320~~.

PICO-SALAX Cranberry:
Potassium hydrogen carbonate
Sodium saccharin
Cranberry flavour S/D

6.2 Incompatibilities
None known

6.3 Shelf life
The expiry date of the product is indicated on the packaging materials

Once the sachet has been opened, use immediately in order to protect from moisture and discard any unused powder or solution.

6.4 Special precautions for storage
Do not store above 25°C. Store in the original package.

4.5 Nature and contents of container
Sachet:
4 layers: paper-low density polyethylene-aluminium-thermofusible resin
Each pack contains a pair of sachets that can be separated by tearing apart the perforated strip.
In addition each pack contains measuring spoon. A full measuring spoon contains 4gr powder.
Weight of sachet contents: 16.1g

6.6 Instructions for use, handling and disposal
None

7. MANUFACTURER
Ferring GmbH, Germany

8. LICENSE HOLDER
Ferring Pharmaceuticals Ltd

8, Hashita Street, Industrial Park Caesarea 3088900
ISRAEL

9. Marketing authorization number: PICO-SALAX Orange: 144-04-32928-
PICO-SALAX Cranberry: 157-91-35155-

This leaflet was revised in ~~April~~ May ~~2021~~2024 ~~according to MOH guidelines~~.