Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Phospho-soda 24.4g/10.8g Oral solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

	per 45ml dose	per 1ml
Sodium dihydrogen phosphate dihydrate	24.4 g	0.542 g
Disodium phosphate dodecahydrate	10.8 g	0.24 g

Excipient(s) with known effect: Ethanol, Sodium, Sodium benzoate (E 211).
Phospho-soda contains 29mg of ethanol per dose.
Each 45ml bottle contains 5.0 g sodium and 15 mg of sodium benzoate.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Oral solution
Clear colourless solution with a ginger-lemon odour, free from precipitation and turbidity.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

As a bowel cleanser in preparing the patient for colon surgery, or for preparing the colon for x-ray or for endoscopic examination.

Bowel cleansing agents are not to be considered as treatments for constipation.

Phospho-soda is indicated in adults.

4.2 Posology and method of administration

Posology

Two separate doses of Phospho-soda are provided to adults.

Elderly patients:

Phospho-soda should be used with caution in elderly patients. No dose adjustment is necessary in this group of patients (see section 4.4).

Patients with renal impairment:

Phospho-soda is contraindicated in patients with renal impairment (see section 4.3)

Patients with hepatic impairment:

The safety and efficacy of Phospho-soda in patients with hepatic impairment has not been established Phospho-soda is contraindicated in patients with ascites (see 4.3).

Paediatric population:

Phospho-soda is contraindicated in children below 18 years (see section 4.3).

Method of administration

The taking of Phospho-soda should be started the day before the hospital appointment.

For hospital appointments before 12 noon the dosage instructions for morning appointments should be followed and for appointments after 12 noon the dosage instructions for an afternoon appointment should be followed.

The recommended dose should not be exceeded.

Morning Appointment:

Day before appointment

7am – In place of breakfast drink at least one full glass of "clear liquid" or water, more if desired.

"Clear liquid" includes water, clear soup, strained fruit juices without pulp, black tea or black coffee, clear carbonated and non-carbonated soft drinks.

1st Dose – Straight afterwards, dilute 45ml in half a glass (120ml) cold water. Drink this solution followed by one full glass (240ml) cold water, more if desired.

Drink as much extra liquid as possible to replace the fluids lost during bowel movements.

1pm lunch – In place of lunch drink at least three full glasses (720ml) of "clear liquid" or water, more if desired.

7pm supper – In place of supper drink at least one full glass of "clear liquid" or water, more if desired.

2nd Dose – Straight afterwards, dilute 45ml in half a glass (120ml) cold water. Drink this solution followed by one full glass (240ml) cold water, more if desired.

Additional water or "clear liquid" may be taken up until midnight if necessary.

Drinking large amounts of clear liquid also helps ensure that the bowel will be clean for the procedure.

Afternoon appointment:

Day before appointment

1pm lunch – A light snack may be taken. After lunch, no more solid food must be taken until after the hospital appointment.

7pm supper – In place of supper drink at least one full glass of "clear liquid" or water, more if desired.

1st Dose – Straight afterwards, dilute 45ml in half a glass (120ml) cold water. Drink this solution followed by one full glass (240ml) cold water, more if desired.

Drink as much extra liquid as possible to replace the fluids lost during bowel movements.

During the evening, drink at least three full glasses of water or "clear liquid" before going to bed.

Day of appointment

7am breakfast – In place of breakfast drink at least one full glass of "clear liquid" or water, more if desired.

2nd Dose – Straight afterwards, dilute 45ml in half a glass (120ml) cold water. Drink this solution followed by one full glass (240ml) cold water.

Drink as much extra liquid as possible to replace the fluids lost during bowel movements. Drinking large amounts of clear liquids also helps ensure that the bowel will be clean for the procedure.

More water or "clear liquid" may be taken up until 8am.

This product normally produces a bowel movement in ½ to 6 hours.

After the procedure:
In order to replace fluid lost during the preparation for the procedure patients should be encouraged to drink plenty of fluids afterwards.

4.3 Contraindications

Do not use:

- In children under the age of 18 years.
- When nausea, vomiting or abdominal pain are present.
- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1

Do not use in patients with:

- Renal impairment;
- Primary hyperparathyroidism associated with hypercalcaemia
- Symptomatic heart failure (NYHA grade III or IV);
- Ascites;
- Known or suspected gastrointestinal obstruction;
- Megacolon (congenital or acquired);
- Gastrointestinal perforation;
- Ileus;
- Active inflammatory bowel disease.

Phospho-soda should not be used in combination with other laxative products containing sodium phosphate.

4.4 Special warnings and precautions for use

Phospho-soda 24.4g/10.8g Oral solution has been rarely associated with severe and potentially fatal cases of electrolyte disorders in elderly patients. **The benefit/risk ratio of** Phospho-soda 24.4g/10.8g Oral solution **needs to be carefully considered before initiating treatment in this at-risk population.**

Special attention should be taken when prescribing Phospho-soda 24.4g/10.8g Oral solution to any patient with regard to known contraindications and the importance of adequate hydration and, in at-risk populations (see below and sections 4.2 and 4.3.), the importance of also obtaining baseline and post-treatment electrolyte levels.

At risk patients

Use with caution in patients with an increased risk for underlying renal impairment, pre-existing electrolyte disturbances, increased risk for electrolyte disturbances (e.g. dehydration, gastric retention, colitis, inability to take adequate oral fluid, hypertension or other conditions in which the patients are taking products that may result in dehydration, see below), hypotension with clinical impact or associated with hypovolaemia, heart disease, acute myocardial infarction, unstable angina,

or with debilitated or elderly patients. In these at-risk patients, baseline and post-treatment sodium, potassium, calcium, chloride, bicarbonate, phosphate, blood urea nitrogen and creatinine values should be obtained if clinically indicated.

Dehydration

This product usually works within ½ to 6 hours. If there has been no bowel movement within 6 hours of taking Phospho-soda, instruct the patient to stop use and contact a doctor immediately as dehydration could occur.

Patients should be warned to expect frequent, liquid stools. Patients should be encouraged to drink as much liquid as possible to help prevent dehydration. Inadequate fluid intake when using any effective purgative may lead to excessive fluid loss possibly producing dehydration and hypovolemia. Dehydration and hypovolemia from purgation may be exacerbated by inadequate oral fluid intake, nausea, vomiting, loss of appetite, or use of antihypertensive drugs (e.g. angiotensin converting enzyme inhibitors (ACE-Is), angiotensin receptor blockers (ARBS), calcium channel blockers), diuretics, and non-steroidal anti-inflammatory drugs (NSAIDs) and may be associated with acute renal failure. There have been rare reports of acute renal failure with purgatives, including sodium phosphates and PEG-3350.

Patients with conditions that may predispose to dehydration or those taking medications which may decrease glomerular filtration rate**,** should be assessed for hydration status prior to use of purgative preparations and managed appropriately.

Nephrocalcinos is secondary to acute phosphate nephropathy

Nephrocalcinos is associated with acute renal failure and deposits of calcium-phosphate crystals in the renal tubules has been rarely reported in patients using sodium phosphates for bowel cleansing; Nephrocalcinos is is a serious adverse event that may result in permanent renal function impairment and the requirement of long-term dialysis. The majority of these reports occurred in elderly female patients taking drugs to treat hypertension or other drug products, such as diuretics or NSAIDs, that may result in dehydration.

Care should be taken to prescribe Phospho-soda per recommendations with a particular attention to known contraindications, adequate hydration prior to, during the preparation and after the procedure and adherence to recommended spacing of doses.

Electrolyte disorders

There is a risk of elevated serum levels of sodium and phosphate and decreased levels of calcium and potassium; consequently hypernatraemia, hyperphosphataemia, hypocalcaemia, hypokalaemia, and acidosis may occur.

Hyponatraemia possibly complicated by neurological disorders, such as confusion, coma or convulsions, may occur.

Slight QT interval prolongation may rarely occur as a result of electrolyte imbalances such as hypocalcaemia or hypokalaemia. These changes are clinically insignificant.

Hypomotility

Use with caution in patients with hypomotility disorders or who have had gastro-intestinal surgery or have other medical conditions predisposing them to hypomotility disorders. If the patient has had a colostomy or ileostomy, or must keep to a salt-free diet, the preparation must be used with caution, since a disturbance of electrolyte balance, dehydration or a disturbance of acid balance may arise.

Lesions

Single or multiple aphthoid-like punctiform lesions located in the rectosigmoid region have been observed by endoscopy. These were either lymphoid follicles or discrete inflammatory infiltrates or epithelial congestions/changes revealed by the colonic preparation. These abnormalities are not clinically significant and disappear spontaneously without any treatment.

This medicinal product contains 5000 mg sodium per 45 ml dose, equivalent to 250% of the WHO recommended maximum daily intake of 2 g sodium for an adult. Consideration should therefore be given to the potential harm to patients requiring a low-sodium diet.

This medicinal product contains 15 mg sodium benzoate (E 211) in each 45 ml dose.

This medicinal product contains small amounts of ethanol (alcohol), less than 100 mg per 45 ml.

This medicine contains 29 mg of alcohol (ethanol) in each 45 ml dose. The amount in 45 ml of this medicine is equivalent to less than 0.73 ml beer or 0.29 ml wine. The small amount of alcohol in this medicine will not have any noticeable effects.

4.5 Interaction with other medicinal products and other forms of interactions

Use with caution in patients taking antihypertensives (e.g calcium channel blockers, angiotensin converting enzyme inhibitors (ACE-Is), angiotensin receptor blockers (ARBS)), diuretics, lithium treatment or other medications that might affect electrolyte levels as hyperphosphataemia, hypocalcaemia, hypokalaemia, hypernatraemic dehydration and acidosis may occur.

During the intake of Phospho-soda 24.4g/10.8g Oral solution the absorption of drugs from the gastrointestinal tract may be delayed or even completely prevented. The efficacy of regularly taken oral drugs (e.g. oral contraceptives, antiepileptic drugs, antidiabetics, antibiotics) may be reduced or completely absent. Caution is also advised when taking medicines known to prolong the QT interval.

Use with caution in patients who are taking parathyroid hormone medications.

4.6 Fertility, pregnancy and lactation

Pregnancy
For Phospho-soda, no clinical data on exposed pregnancies and no data from animal studies with respect to effects on pregnancy, embryonal/fetal development, parturition and postnatal development are available. The potential risk for humans is unknown. Phospho-soda should not be used during pregnancy unless clearly necessary.

Breastfeeding
It is not known whether Phospho-soda is excreted in human milk. As sodium phosphate may pass into the breast milk, it is advised that breast milk is expressed and discarded from the first dose to 24 hours after the second dose of the bowel cleansing solution. Women should not breast-feed their infants until 24 hours after receiving the second dose of Phospho-soda.

Fertility
No data is available on the effect of Phospho-soda on male and female fertility .

4.7 Effects on ability to drive and use machines

Phospho-Soda may cause dizziness, probably as a result of dehydration.
Phospho-Soda has minor to moderate influence on the ability to drive and use machines.

4.8 Undesirable effects

The following adverse reactions were reported with frequencies corresponding to: 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 (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

IMMUNE SYSTEM DISORDERS
Very rare
Hypersensitivity

METABOLISM AND NUTRITION DISORDERS
Uncommon
Dehydration

Very rare
Hyperphosphataemia
Hypocalcaemia
Hypokalaemia
Hypernatraemia
Metabolic acidosis
Tetany

Not known
Hyponatraemia complicated by neurological disorders, such as confusion, coma or convulsions

NERVOUS SYSTEM DISORDERS
Very common
Dizziness

Common
Headache

Very rare
Loss of consciousness
Paraesthesia

CARDIAC DISORDERS
Very rare
Myocardial infarction
Arrhythmia

VASCULAR DISORDERS
Very rare
Hypotension

GASTROINTESTINAL DISORDERS
Very common
Diarrhoea
Abdominal pain
Abdominal distension
Nausea

Common
Vomiting
Colonoscopia abnormal (Single or multiple aphthoid-like punctiform lesions located in the rectosigmoid region that are not clinically significant and disappear spontaneously without any treatment)

SKIN AND SUBCUTANEOUS TISSUE DISORDERS
Very rare
Dermatitis allergic

MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS
Very rare
Muscle cramp

RENAL AND URINARY DISORDERS
Rare

Nephrocalcinos is secondary to acute phosphate nephropathy

Very rare
Renal failure acute
Renal failure chronic

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS
Very common
Chills
Asthenia

Common
Chest pain

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 HPRA Pharmacovigilance, Website: www.hpra.ie

4.9 Overdose

There have been fatal cases of hyperphosphataemia with concomitant hypocalcaemia, hypernatraemia and acidosis when Phospho-soda 24.4g/10.8g Oral solution has been used in excessive doses, given to children or to obstructed patients.

Patients experiencing overdose have presented the following symptoms: dehydration, hypotension, tachycardia, bradycardia, tachypnoea, cardiac arrest, shock, respiratory failure, dyspnoea, convulsions, ileus paralytic, anxiety, pain. Overdoses can lead to elevated serum levels of sodium and phosphate and decreased levels of calcium and potassium. In those cases, hypernatremia, hyperphosphatemia, hypocalcemia, hypokalemia, and acidosis may occur.

There are also documented cases of complete recovery from overdoses in both children accidentally given Phospho-soda 24.4g/10.8g Oral solution, and also in patients with obstruction, one of whom received a six-fold overdose.

Recovery from the toxic effect of excess ingestion can normally be achieved by rehydration, though the intravenous administration of 10% calcium gluconate may be necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Osmotically acting laxative, ATC code: A06AD

Phospho-soda is a saline laxative that acts by osmotic processes to increase fluid retention in the lumen of the small intestine. Fluid accumulation in the ileum produces distension and, in turn, promotes peristalsis and bowel evacuation.

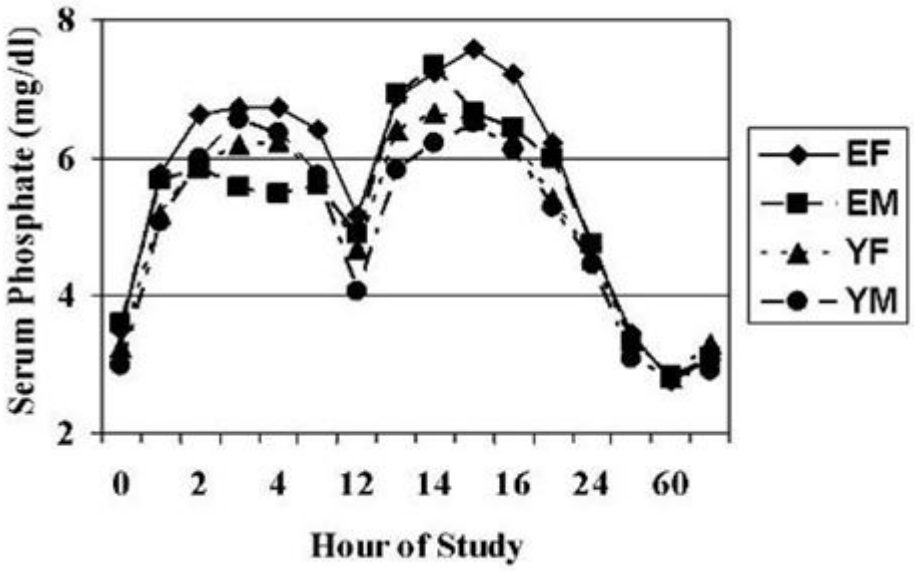
5.2 Pharmacokinetic properties

Administration of oral sodium phosphates solution caused transient serum electrolyte shifts in healthy volunteers. An open-label study was performed with twenty-four healthy adult volunteers who received oral sodium phosphates solution to evaluate the time course and degree of electrolyte shifts in two age and two gender groups. The study was designed to mimic the bowel preparation regimen commonly used prior to colonoscopy, including a clear liquid diet, timing of sodium phosphate doses and proper hydration. The followed regimen of 2 x 45 ml of oral sodium phosphate and additional clear liquids was in line with the approved dosing regimen of the product. The study population was balanced for gender and age. One-half of the study participants were aged 65 years or older.

Results showed an increase in serum concentrations of sodium and phosphate but a decrease of potassium and calcium after each dose.

The mean serum phosphate concentration for all subjects was 3.33 mg/dL at baseline, then it peaked at 6.26 mg/dL at hour 3, decreased to 4.70 mg/dL just prior to the second dose (hour 12), and peaked again at 6.86 mg/dL at hour 14. By hour 36, all serum phosphate concentrations had returned to normal.

Figure shows the time-course of mean serum phosphate concentration for each age-gender subgroup, Elderly females suffered the most altered values.



Mean serum sodium concentration fluctuated within the normal range (134-147 mmol/L), however 4 subjects had sodium values above the upper limit of normal.

The fall in serum potassium and calcium concentrations fluctuated within the normal individual range and then returned to baseline values by 12 hours after administration of the second dose. 29% of subjects reported serum calcium values below the normal lower limit (8.5 mg/dL) for up to 36 hours after the administration of the first dose. Nevertheless, no clinical cases of hypocalcaemia were noted.

In conclusion, the serum electrolyte concentration shifts in healthy adults volunteers associated with the administration of 2 x 45 mL of NaP were clinically insignificant, were transient and resolved within 12 to 24 hours after completing the bowel preparation regimen.

The effect on the pharmacokinetic of Phosphos-Soda for patients with renal impairment has not been studied. Extrapolation of these data from healthy volunteers to at risk patients (e.g. renal patients) is not possible (See sections 4.3, 4.4).

5.3 Preclinical safety data

No animal studies on reproduction toxicity have been conducted with Phospho-soda 24.4g/10.8g Oral solution.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycerol
Saccharin Sodium
Sodium Benzoate (E211)
Ginger Lemon Flavour*
Purified Water

*Ginger Lemon Flavour:
Oleoresin Ginger

Alcohol
Oil Lemon
Partially Deterpenated Oil Lemon
Citric Acid
Water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

Once opened use immediately. Discard any unused portion.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Phospho-soda 24.4g/10.8g Oral solution is supplied in cartons containing 2 x 45ml or 100 x 45ml (hospital pack) polyethylene bottles with polypropylene, aluminium foil-lined screw caps.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

This product must be diluted with water before use.

7 MARKETING AUTHORISATION HOLDER

Casen-Recordati S.L.
Autovia De Logrono, km. 13,300
50180 Utebo (Zaragoza)
Spain

8 MARKETING AUTHORISATION NUMBER

PA2028/004/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 30 April 2010

10 DATE OF REVISION OF THE TEXT

June 2022