NEW ZEALAND DATA SHEET

PHOSPHO-SODA oral solution

[Monobasic sodium phosphate dihydrate and Dibasic sodium phosphate dodecahydrate]

1 PRODUCT NAME

PHOSPHO-SODA 24.4g/10.8g oral solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 45mL of PHOSPHO-SODA contains 18.8g monobasic sodium phosphate (as 24.4g monobasic sodium phosphate dihydrate) and 4.3g dibasic sodium phosphate (as 10.8g dibasic sodium phosphate dodecahydrate).

Excipient(s) with known effect:

Ethanol, Sodium, Sodium benzoate, Saccharin.

Phospho-soda contains less than 100 mg of ethanol per dose.

PHOSPHO-SODA has a sodium content of 5.0g per 45mL (11.11% w/v) and 15mg of sodium benzoate.

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Oral solution. PHOSPHO-SODA is a clear, colourless, ginger-lemon odour and flavour oral solution, free from precipitation and turbidity.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For use as part of a bowel cleansing regimen in preparing adult patients for colon surgery or for preparing the colon for x-ray or endoscopic examination.

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

4.2 Dose and method of administration

Also refer to section 4.3 and section 4.4 of this data sheet.

This product normally produces a bowel movement in half to 6 hours. Patients should be warned to expect frequent liquid stools.

PHOSPHO-SODA should not be taken by children under 18 years of age (see section 4.3).

Adults:

The recommended dosage for adults is 45mL (one bottle full) and repeated 10 to 12 hours later. The intake of "clear liquid" is an essential part of this regimen.

Please note that for:

- Early morning procedures, on the day before the procedure, the patient should only take clear liquids (see below) for breakfast, lunch and dinner and between doses.
  No solid food, milk or milk products should be taken on the day before the procedure.

Please note that the patient should not drink anything coloured red or purple.

- Mid-morning (or later) procedures, on the day before the procedure, the patient may have a light snack for lunch. After this time, patient should only take clear liquids (see below). *No solid food, milk or milk products should be taken after lunch on the day before the procedure. Please note that the patient should not drink anything coloured red or purple.*

Depending on whether the medical procedure is intended to be performed at early morning, mid-morning or later, two alternative dosage regimens are set out below:

Early Morning Procedure
The first dose is taken at 7 am on the day before the procedure. The second dose is taken at 7 pm on the evening before the procedure.

Mid-Morning (or later) Procedure
The first dose is taken at 7 pm on the evening before the procedure. The second dose is taken at 7 am (or at least 3 hours before leaving for the appointment) on the morning of the procedure.

Method of administration

First dose
To be taken as follows:
- Mix 15mL (one third of the bottle) of PHOSPHO-SODA into a full glass (approximately 250mL) of Clear Liquids (see list below) and drink.

Repeat two more times within the next 20 minutes.

Between Doses
Between the first and second doses, the patient should drink at least three more glasses (approximately 250mL each) of Clear Liquids or more if desired to prevent dehydration and to ensure that their bowel remains easily examinable for the procedure.

Second Dose
The second dose is taken as follows:
- Mix 15mL (one third of the bottle) of PHOSPHO-SODA into a full glass (approximately 250mL) of Clear Liquid (see list below) and drink.

Repeat two more times within the next 20 minutes.

After the procedure:
In order to replace fluid lost during the preparation for the procedure patients should be encouraged to drink plenty of fluid afterwards.
Important:
- PHOSPHO-SODA must be diluted with water before use (see the instructions above).

The intake of Clear Liquid is an essential part of this regimen. Please refer to Clear Liquids list below.

"Clear Liquids" list
Beverages
- Water, black tea or black coffee (no milk or non-dairy creamer). Sweeteners are acceptable,
- Clear carbonated or non-carbonated soft drinks (not coloured red or purple),
- Fruit flavoured cordials (not coloured red or purple),
- Strained fruit juices without pulp,
- Do not drink any alcoholic beverages,
- Clear soups,

- Strained low sodium chicken or beef soup without solid material.

Elderly patients:

Phosphosoda 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 sections 4.3).

4.3 Contraindications

Administration of PHOSPHO-SODA is contraindicated in:

- children under 18 years of age),
- in patients who have demonstrated hypersensitivity to the active substance or to any of the excipients listed in section 6.1,
- the event of nausea, vomiting and abdominal pain
- patients with known or suspected gastrointestinal obstruction
- patients with faecal impaction,
- ileus,
- active inflammatory bowel disease,
- hypomotility,
- congenital or acquired megacolon,
- imperforate anus,
- gastrointestinal perforation,
- symptomatic heart failure (NYHA grade III or IV)
- ascitic conditions,
- renal impairment and potentially pre-existing fluid/electrolyte disturbances,
- primary hyperparathyroidism associated with hypercalcaemia
- patients at risk of dehydration due to altered senses and/or poor fluid intake.

PHOSPHO-SODA should not be used in combination with other laxatives containing sodium phosphate.

WARNING: Life threatening dehydration and/or electrolyte disturbances may occur in 'at risk' groups - see section 4.4.

4.4 Special warnings and precautions for use

PHOSPHO-SODA can only be used at the prescribed dosage and following instructions for use.

Severe and life-threatening disorders in elderly patients

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

Special attention should be taken when prescribing Phospho-soda 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 is effective in the bowel from half an hour to 6 hours after intake. If no effect is seen in the bowel during the 6 hours following intake of PHOSPHO-SODA, administration should be discontinued immediately and a physician should be consulted, because there is a risk of dehydration.

Patients should be informed that stools will be more frequent and liquid.

Patients should be encouraged to drink as much liquid as possible to prevent dehydration. When too little liquid is drank when using a laxative, there is a risk of dehydration and hypovolaemia.

Dehydration and hypovolaemia resulting from use of a laxative may worsen if no adequate liquid is taken, if nausea or vomiting occur, when appetite is reduced, and when diuretics, antihypertensive drugs (e.g. angiotensin converting enzyme inhibitors (ACE-Is), angiotensin receptor blockers (ARBS), calcium channel blockers), and non-steroidal anti-inflammatory drugs (NSAIDs) are used, and may be associated with acute renal failure. Some rare cases of acute renal failure have been reported with laxatives such as sodium phosphate 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.

Nephrocalcinosis secondary to acute phosphate nephropathy

Nephrocalcinosis 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; Nephrocalcinosis 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.

Potential risk factors for acute phosphate-induced nephropathy include advanced age, inadequate hydration during use of laxatives, treatment with an ACE inhibitor, sartans, diuretics, or NSAIDs, and presence of hypertension or atherosclerosis.

Care should be taken to prescribe Phospho-soda per recommendations with a particular attention to known contraindications and 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 increased sodium and phosphate levels and decreased potassium and calcium levels and, thus, of hyperphosphataemia, hypernatraemia, hypocalcaemia, hypokalaemia, and acidosis.

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

A slightly prolonged QT interval resulting from an electrolyte imbalance, such as hypocalcaemia and hypokalaemia, is seen in some cases. These changes are not clinically significant.

Hypomotility

Use with caution in patients with intestinal hypomotility, undergoing gastrointestinal surgery, or with other conditions that may cause hypomotility problems. In patients who have undergone colostomy or ileostomy or on a low salt diet, the preparation should be used with caution, because electrolyte balance disorders, dehydration, or an acid-base balance disorder may occur.

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.

Use in Diabetic Patients:

As the liquid diet during the period of administration and prior to bowel surgery, x-ray of the colon or colonoscopy may affect the diabetic patients' glucose blood levels, adjustment of their insulin or oral anti-diabetic medication may be necessary.

4.5 Interaction with other medicines and other forms of interaction

Caution should be taken when patients are taking antihypertensives, (e.g calcium channel blockers, angiotensin converting enzyme inhibitors (ACE-Is), angiotensin receptor blockers (ARBS)), diuretics, lithium, or other drugs that may impair electrolyte balance, because they may cause hypokalaemia, hypocalcaemia, hyperphosphataemia, hypernatraemia, and acidosis.

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

During the intake of Phospho-soda 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.

Concomitant administration with other sodium phosphate preparations is contraindicated.

Concurrent administration of polyethylene glycol bowel cleansing preparations and PHOSPHO-SODA may be dangerous and is not recommended (see section 4.8).

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no clinical data on use of PHOSPHO-SODA in pregnant women, nor animal studies on the effect on pregnancy, embryofoetal development, delivery, and postnatal development. The potential risk for humans is not known. PHOSPHO-SODA should not be used during pregnancy unless strictly necessary.

Breastfeeding

Because of potential harm to the infant from phosphate excreted in breast milk, the use of this product is not recommended in nursing mothers unless the probable clinical benefit outweighs the possible risk.

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

Within each frequency group, undesirable effects are classified by decreasing severity: Very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1000, <1/100); rare (≥1/10,000, <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data).

MeDRA System Organ Class (SOC)	**Very common (≥ 1/10)**	**Common (≥ 1/100 to < 1/10)**	**Uncommon (≥ 1/1000 to < 1/100)**	**Rare (≥ 1/10,000 to < 1/1,000)**	**Very rare (≤ 1/10,000)**	**Not known**
Immune system disorders					Hypersensitivity	

Metabolism and nutrition disorders			Dehydration		Hyperphosphataemia, Hypocalcaemia, Hypokalaemia, Hypernatraemia, Metabolic acidosis, Tetany	Hyponatraemia complicated by neurological disorders, such as confusion, coma or convulsions
Nervous system disorders	Dizziness	Headache			Loss of consciousness, Paraesthesia	
Cardiac disorders					Myocardial infarction, Arrhythmia, Slight QT interval prolongation	
Vascular disorders					Hypotension	
Gastrointestinal disorders	Diarrhoea, Abdominal pain, Abdominal distension, Nausea	Vomiting, Colonoscopia abnormal*				
Skin and subcutaneous tissue disorders					Allergic dermatitis	
Musculoskeletal and connective tissue disorders:					Muscle cramp	
Renal and urinary disorders				Nephrocalcinosis secondary to acute phosphate nephropathy	Acute renal failure, Chronic renal failure	
General disorders and administration site conditions	Chills, Asthenia	Chest pain				

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

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

There have been fatal cases of hyperphosphataemia with concomitant hypocalcaemia, hypernatraemia and acidosis when PHOSPHO-SODA has been used in excessive doses, given to children or to obstructed patients.

In the event of overdose or accidental intake, severe adverse reactions may occur, including dehydration, hypotension, tachycardia, bradycardia, tachypnoea, cardiac arrest, shock, respiratory failure, dyspnoea, seizures, paralytic ileus, anxiety, and abdominal pain. An overdose may cause increased serum sodium and phosphate levels and decreased levels of calcium and potassium. In these cases, hypokalaemia, hypocalcaemia, hyperphosphataemia, hypernatraemia, and acidosis may occur.

Cases of complete recovery after an overdose have been reported both in children accidentally given PHOSPHO-SODA and in patients with obstruction, including one with a six-fold overdose.

Recovery from toxicity due to overdose may normally be achieved with rehydration, although intravenous administration of 10% calcium gluconate is required in some cases

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: osmotically acting laxatives

ATC code: A06AD17

PHOSPHO-SODA is a saline laxative that works by osmotic processes to increase fluid retention in small bowel lumen. The resultant fluid accumulation in the ileum causes distention and induces in turn bowel movement and evacuation. The start of these peristaltic movements depends on the patient and occurs 1 to 2 hours after administration.

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 group. 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.

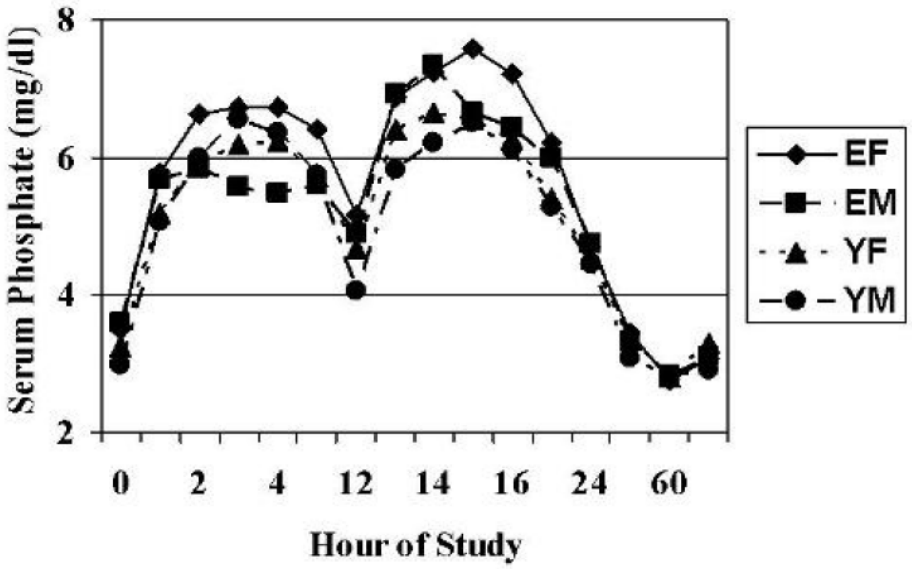
Results showed an increase in serum concentrations of sodium and phosphate but a decrease of potassium and calcium after each dose.

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

Figure 1: Time-course of mean phosphate concentration for age-gender groups



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 Phospho-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 studies related to reproductive toxicity in animals have been conducted with PHOSPHO-SODA.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

PHOSPHO-SODA contains the following excipients:

Glycerol
Saccharin sodium
Sodium benzoate

Purified water

Ginger Lemon Extract 5741–5G containing Oleoresin Ginger, Ethanol (Alcohol), Oil Lemon, Partially Deterpinated Oil Lemon, Citric Acid and Purified Water.

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 in each 45 ml dose.

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

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and contents of container

PHOSPHO-SODA is available in 45mL bottles.

6.6 Special precautions for disposal and other handling

This product must be diluted with water before use.

7 MEDICINE SCHEDULE

Pharmacist Only Medicine.

8 SPONSOR

Pharmaco (NZ) Ltd
4 Fisher Crescent
Mt Wellington
Auckland 1060
Telephone: 09 377 3336

9 DATE OF FIRST APPROVAL

29/07/1993

10 DATE OF REVISION OF THE TEXT

24 August 2021 CCDS vs 2, dated May 2019

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
2, 3	Update to wording to align with CCDS v2, May 2019
4.1, 4.2	Update to restrict patient population to adults only
4.3, 4.4, 4.5, 4.8	Safety update and rewording to align with CCDS v2, update to adverse event table.
5.2	Update to Pharmacokinetic section to align with CCDS v2
6.1	Update to wording of the excipients