AUSTRALIAN PRODUCT INFORMATION - PHOSPHO®-SODA (monobasic sodium phosphate AND dibasic sodium phosphate)

WARNING:

Life threatening dehydration and/or electrolyte disturbances may occur in 'at risk' groups – see Section 4.3 CONTRAINDICATIONS and Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE.

1 NAME OF THE MEDICINE

PHOSPHO®-SODA (monobasic sodium phosphate and dibasic sodium phosphate)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Ingredients: 18.8 g monobasic sodium phosphate (as 24.4 g monobasic sodium phosphate dihydrate) and 4.3 g dibasic sodium phosphate (as 10.8 g dibasic sodium phosphate dodecahydrate) per 45 mL bottle.

Excipients with known effect: Each 45 mL of bottle contains saccharin, benzoates and 5.0 g sodium.

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

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.

4.2 DOSE AND METHOD OF ADMINISTRATION:

Refer to Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE and Section 4.3 CONTRAINDICATIONS.

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

This product normally produces a bowel movement within ½ 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 CONTRAINDICATIONS).

Adults:
The recommended dosage for adults is 45 mL (one full bottle) and repeated 10 to 12 hours later. The intake of clear liquids 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 a.m. on the day before the procedure. The second dose is taken at 7 p.m. on the evening before the procedure.

Mid-morning (or later) procedure:
The first dose is taken at 7 p.m. on the evening before the procedure. The second dose is taken at 7a.m. (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 15 mL (one third of the bottle) of PHOSPHO-SODA into a full glass (approximately 250 mL) 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 250 mL 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 15 mL (one third of the bottle) of PHOSPHO-SODA into a full glass (approximately 250 mL) 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

PHOSPHO-SODA should be used with caution in elderly patients. No dose adjustment is necessary in this group of patients (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

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 substances or to any of the excipients listed in Section 6.1 LIST OF EXCIPIENTS, patients with faecal impaction, ileus, known or suspected gastrointestinal obstruction, when nausea, vomiting or abdominal pain are present, active inflammatory bowel disease, hypomotility, gastrointestinal perforation, Hirschsprung's disease (congenital megacolon), megacolon (acquired), imperforate anus, primary hyperparathyroidism associated with hypercalcaemia, symptomatic heart failure (NYHA grade III or IV), ascitic conditions, renal impairment and potentially pre-existing fluid/electrolyte disturbances, and patients at risk of dehydration due to altered senses and/or poor fluid intake.

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 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 DOSE AND METHOD OF ADMINISTRATION and 4.3 CONTRAINDICATIONS), the importance of also obtaining baseline and post-treatment electrolyte levels.

Identified precautions

At risk patients

PHOSPHO-SODA, which contains 4.82 mEq sodium and 12.45 mEq phosphate per mL, should be used with **extreme caution**, in the elderly, the frail or debilitated, patients with colostomy and patients on a low salt diet, as they are particularly at risk. These patients should receive additional fluids by mouth, both prior to, and after administration of PHOSPHO-SODA, to ensure that dehydration does not occur. Close attention should be paid to their hydration status and their electrolyte levels (particularly potassium, calcium and phosphorus) should be monitored. Patients undergoing major bowel procedures, who are on nil by mouth for significant periods of time, should have their electrolytes monitored and receive intravenous fluids containing potassium and calcium, prior to surgery.

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, such as diuretics, angiotensin converting enzyme inhibitors (ACE-Is), angiotensin receptor blockers (ARBs), or non-steroidal anti-inflammatory drugs (NSAIDs) 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.

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.

Use in diabetics
Adjustments of a diabetic patient's insulin or oral anti-diabetic medication may be necessary 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 patient's glucose blood levels.

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.

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.

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.

Sodium, benzoates and ethanol content
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.

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 Section 4.3 CONTRAINDICATIONS).

Patients with renal impairment
PHOSPHO-SODA is contraindicated in patients with renal impairment (see Section 4.3 CONTRAINDICATIONS)

Use in the elderly
PHOSPHO-SODA should be used with caution in elderly patients. No dose adjustment is necessary in this group of patients (see Section 4.2 DOSE AND METHOD OF ADMINISTRATION).

Paediatric use
PHOSPHO-SODA is contraindicated in children below 18 years (see Section 4.3 CONTRAINDICATIONS).

Effects on laboratory tests
No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES 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 and lithium preparations or other medication that might affect electrolyte levels, as hyperphosphataemia, hypocalcaemia, hypernatraemic dehydration and acidosis may occur.

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.

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

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility
No animal studies on reproduction toxicity have been conducted with PHOSPHO-SODA. No data is available on the effect of PHOSPHO-SODA on male and female fertility.

Use in pregnancy
For PHOSPHO-SODA, no clinical data on exposed pregnancies and no data from animal studies with respect to effects on pregnancy, embryonal/foetal development, parturition and postnatal development are available. The potential risk for humans is unknown.

Because of potential harm to the foetus from phosphate absorbed across the placenta, the use of this product is not recommended in pregnant women unless clearly necessary and the probable clinical benefit outweighs the possible risk.

Use in lactation
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.

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 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Oral sodium phosphate products can cause dehydration (between 1 and 4 L fluid loss), hyperphosphataemia, hypocalcaemia, other electrolyte abnormalities and associated complications.

Severe adverse reactions (serious serum electrolyte disturbances and hypokalaemia) and fatalities have been reported in patients who belonged to the ‘at risk’ groups (the elderly, the frail, those with renal impairment and cardiac failure), patients with known contraindications (including children under 18 years) and concurrent administration with polyethylene glycol bowel cleansing preparation.

Transient hyperphosphataemia, some degree of hypovolaemia and significant differences in serum electrolyte levels have been noted in clinical trials. In healthy and fit patients these have returned to initial pre-treatment levels within 24 hours.

In addition, there have been occasional reports of nausea, vomiting, abdominal pain, bloating, fatigue, anal irritation, allergic reactions with or without rash, hunger and sleep loss.

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).

Table 1: Tabulated list of adverse reactions

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		Hyperphospha-taemia, 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	
Vascular disorders					Hypotension	
Gastrointestinal disorders	Diarrhoea, Abdominal pain, Abdominal distension, Nausea	Vomiting, Colonoscopia abnormal*				
Skin and subcutaneous disorders					Dermatitis allergic	
Musculoskeletal and connective tissue disorders					Muscle cramp	
Renal and urinary disorders				Nephrocalci-nosis secondary to acute phosphate nephropathy	Renal failure acute, Renal failure chronic	
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 effects

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 www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia) or 0800 764 766 (New Zealand).

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.

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

There are also documented cases of complete recovery from overdoses in both children accidentally given PHOSPHO-SODA, and also in patients with obstruction, one of whom received a six-fold overdose.

Recovery from the toxic effects of accidental excess ingestion can normally be achieved by rehydration, although the intravenous administration of 10% calcium gluconate may be necessary if there is significant hypocalcaemia or tetany has occurred.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Pharmacotherapeutic group: Osmotically acting laxative, ATC code: A06AD17.
PHOSPHO-SODA is a saline mixture which acts by osmotic processes to increase fluid retention in the lumen of the small intestine. Fluid retention in the ileum produces distension, in turn promoting peristalsis and evacuation. It has a purgative effect. Individual responses vary. It usually acts shortly after 30 minutes but may take as long as 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.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

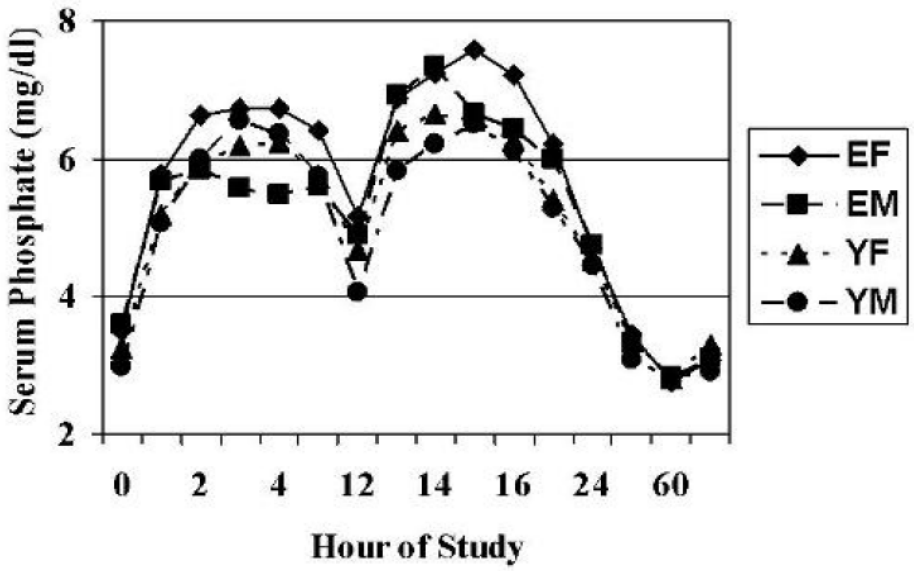
Administration of oral sodium phosphates solution caused transient serum electrolyte shifts in healthy volunteers. An open-label study was performed with twenty-four healthy adult volunteers who received oral sodium phosphates solution to evaluate the time course and degree of electrolyte shifts in two 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 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.

The figure below 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 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 Section 4.3 CONTRAINDICATIONS and Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

5.3 PRECLINICAL SAFETY DATA

Genotoxicity
No data available.

Carcinogenicity
No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF 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.

6.2 INCOMPATIBILITIES

Refer to Section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS.

6.3 SHELF LIFE

36 months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30°C.
Once opened, use immediately. Discard any unused portion.

6.5 NATURE AND CONTENTS OF CONTAINER

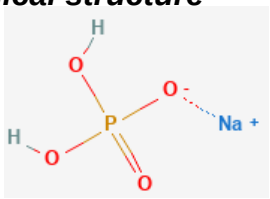
PHOSPHO-SODA is available in a carton containing 1x45 mL polyethylene bottle. Each bottle (45 mL) contains 18.8 g monobasic sodium phosphate (as 24.4 g monobasic sodium phosphate dihydrate) and 4.3 g dibasic sodium phosphate (as 10.8 g dibasic sodium phosphate dodecahydrate).

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

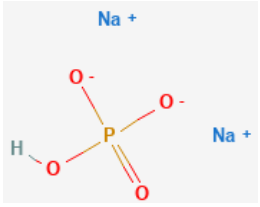
In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure



monobasic sodium phosphate



dibasic sodium phosphate

CAS number

Monobasic sodium phosphate dihydrate:
Molecular formula NaH_2PO_4, $2H_2O$, MW 156.0, CAS: 13472-35-0

Dibasic sodium phosphate dodecahydrate:
Molecular formula Na_2HPO_4,$12H_2O$, MW 358.1, CAS: 10039-32-4

7 MEDICINE SCHEDULE (POISONS STANDARD)

Pharmacist Only Medicine (S3)

8 SPONSOR

Chiesi Australia Pty Ltd
Suite 3, 22 Gillman Street
Hawthorn East VIC 3123
E: medicalaffairs.au@chiesi.com

9 DATE OF FIRST APPROVAL

13 December 2016

10 DATE OF REVISION

08 June 2021

Summary table of changes

Section changed	Summary of new information
8	Change of sponsor and contact details

PHOSPHO®-SODA is a registered trademark of Casen Recordati, S.L.