

## **VI.2 Elements for a Public Summary**

### ***VI.2.1 Overview of disease epidemiology***

#### *Bowel cleanser*

Cancer of the large (lower) bowel is the third most common cancer worldwide and has a high mortality rate. Sigmoidoscopy or colonoscopy, which consist of the introduction of a tube into the colon through the anus in order to visualize the interior of lower part of the colon (sigmoidoscopy) or the whole colon (colonoscopy), are used to prevent colon cancer from

appearing, by removal of suspected lesions. Other diseases that benefit from an early diagnosis are inflammatory bowel **diseases as Crohn’s and ulcerative colitis**.

Colorectal surgery is a frequent procedure that needs oral mechanical bowel preparation. It is prescribed as well for other abdominal and pelvic surgeries, typically urologic or gynecologic procedures, even if they are not intended to involve the colon or rectum.

In order for procedures to be effective, they require that the large bowel is free from fecal residues. Bowel evacuants are used to empty the large bowel from fecal residues.

**VI.2.2 Summary of treatment benefits**

Effective performance of colonoscopy is dependant on bowel preparation. Inadequate colon cleanliness has been reported in up to 30% of patients undergoing colonoscopy<sup>18</sup>. A balance has to be made between adequate preparation and discomfort caused to patients. Colonic preparation with OSP is usually well tolerated by the patients due the low volume requered, with results in a good quality bowel cleansing.

Five reviews of published studies have compared OSP with polyethylene glycol solutions (PEG), other bowel cleanser used frecuently for the same indications. Three of the reviews concluded that excellent or good colon cleansing is significantly less frequent with PEG as compared with Oral Sodium Phosphate solution (70-77% versus 75-82%). The other two found no significant difference between PEG and OSP for overall colon cleansing. <sup>59,60,61,62,63</sup>

Several reviews of studies showed that a higher proportion of patients take the full amount of the prescribed preparation if OSP is prescribed compared with PEG; in the most recent study review, completion rate with OSP was 97% compared with 90% with large-volumen of PEG (4 litres). <sup>64</sup>

Other two reviews of studies also compared the tolerability of PEG and OSP <sup>59,60</sup>; amongst 25 studies, 14 studies reported that OSP superior tolerability, 10 reported no significant difference and only one reported that PEG was better tolerated. <sup>59</sup>

**VI.2.3 Unknowns relating to treatment benefits**

Benefits of treatment with oral Sodium Phosphate solution containing products as bowel cleanser has not been studied in the following sub-groups of patients: children under the age of 18 years, pregnancy and lactation.

**VI.2.4 Summary of safety concerns**

**IMPORTANT IDENTIFIED RISKS**

<b>Risk</b>	<b>What is known</b>	<b>Preventability</b>
<b>Kidney damage and deposits of calcium-phosphate crystal in the kidney</b>  <i>Renal failure, including</i>	Renal failure, also known as kidney failure or renal insufficiency, is a medical condition in which the kidneys fail to adequately filter waste products from the blood. The two main	Physicians should be cautious when prescribing Phospho-soda to susceptible patients. Patient’s concomitant treatment and medical history must be checked

<b>Risk</b>	<b>What is known</b>	<b>Preventability</b>
<p><i>acute phosphate nephropathy and nephrocalcinosis</i></p>	<p>forms are acute kidney injury, which is often reversible with adequate treatment, and chronic kidney disease, which is often not reversible.</p> <p>Phosphate nephropathy consists of damage to the kidneys caused by the formation of phosphate crystals within the renal tubules, damaging the nephron (basic structural and functional unit of the kidney), and can cause acute renal failure.</p> <p>Renal failure acute and chronic are rare side effect (affects 1 to 10 users in 10,000).</p> <p>Nephrocalcinosis 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. It is a very rare side effect (affects less than 1 user in 10,000).</p> <p>The product is contraindicated in patients with clinically significant impairment of renal function and primary hyperparathyroidism (inappropriate overactivity of the parathyroid glands that leads to hypercalcaemia).</p> <p>It must be use with caution in patients with an increased risk for underlying renal impairment, preexisting 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).</p>	<p>before receiving the product.</p> <p>The benefit/risk ratio of Phospho-soda needs to be carefully considered before initiating treatment in this at-risk population.</p> <p>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, the importance of also obtaining baseline and post-treatment electrolyte levels.</p>
<p><b>Changes in the amounts of salts in the body (elevated</b></p>	<p>Hyperphosphatemia is an electrolyte disturbance in which there is an abnormally elevated</p>	<p>Physicians should be cautious when prescribing Phospho-</p>

Risk	What is known	Preventability
<p><b>level of phosphate and lowered level of calcium in the blood)</b></p> <p><i>Electrolyte abnormalities, (hyperphosphataemia and hypocalcaemia)</i></p>	<p>level of phosphate in the blood. Often, calcium levels are lowered (hypocalcemia) due to precipitation of phosphate with the calcium in tissues. These alterations may have consequences in the kidneys and in the heart.</p> <p>Phospho-soda has been rarely associated with severe and potentially fatal cases of electrolyte disorders in elderly patients.</p> <p>They are a very rare side effects: (affects less than 1 user in 10,000)</p> <p>The product is contraindicated in patients with primary hyperparathyroidism (inappropriate overactivity of the parathyroid glands, that leads to hypercalcaemia).</p> <p>It must be use with caution in patients with an increased risk for underlying renal impairment, preexisting 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).</p>	<p>soda to susceptible patients. Patient’s concomitant treatment and medical history must be checked before receiving the product.</p> <p>The benefit/risk ratio of Phospho-soda needs to be carefully considered before initiating treatment in this at-risk population.</p> <p>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, the importance of also obtaining baseline and post-treatment electrolyte levels.</p>
<p><b>Cardiac effects (heart attack, delayed repolarization of the heart following a heartbeat, abnormal heart rhythm)</b></p> <p><i>Cardiac effects (myocardial infarction, QT prolongation,</i></p>	<p>Cardiac disorders such as heart attack, delayed repolarization of the heart following a heartbeat, abnormal heart rhythm are very rare side effects (affects less than 1 user in 10,000).</p> <p>The product is contraindicated in patients with congestive heart failure.</p> <p>It must be use with caution in</p>	<p>Physicians should be cautious when prescribing Phospho-soda to susceptible patients. Patient’s concomitant treatment and medical history must be checked before receiving the product.</p> <p>The benefit/risk ratio of Phospho-soda needs to be carefully considered before initiating treatment in this at-</p>

Risk	What is known	Preventability
<i>arrhythmias)</i>	patients with an increased risk for underlying heart disease and in patients with an increased risk for preexisting 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).	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, the importance of also obtaining baseline and post-treatment electrolyte levels.

**IMPORTANT POTENTIAL RISKS**

Risk	What is known (Including reason why it is considered a potential risk)
<b>Medication errors, including overdose.</b>	<p>A medication error is considered to be any unintended failure in the medication process, including the prescribing, dispensing or administration of a medicinal product while in the control of the healthcare professional (HCP), patient or consumer, which leads to, or has the potential to lead to, harm to the patient. Examples of common medication errors include giving a medication to the wrong patient, the wrong dose of a medication being given to a patient or forgetting to give a patient a medication that had been prescribed for them.</p> <p>There have been fatal cases when Phospho-soda has been used in excessive doses, given to patient of inadequate age or to patients with contraindicated diseases.</p> <p>Patients experiencing overdose have presented heart, muscular, respiratory, anxiety, and pain. Overdoses can lead to alterate levels of the body salts and leads to renal injury.</p> <p>Recovery from the toxic effect of excess ingestion can normally be achieved by rehydration, though the intravenous administration of fluids.</p>

**MISSING INFORMATION**

<b>Risk</b>	<b>What is known</b>
<b>Use in pregnancy</b>	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.
<b>Use in lactation</b>	It is not known whether Phospho-soda is eliminated 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.

**VI.2.5 Summary of risk minimisation measures by safety concern**

All medicines have a SmPC which provides physicians, pharmacists, and other healthcare professionals with details on how to use the medicine, the risks and recommendations for minimizing them. An abbreviated version of this in lay language is provided in the form of the package information leaflet (PIL). The measures in this documents as well as the prescription-only status are known as routine risk minimization measures which are considered sufficient for this medicinal product.

No additional risk minimization measures are proposed.

**VI.2.6 Planned post authorisation development plan**

Not applicable. No additional post-authorisation development plan is proposed.

**VI.2.7 Summary of changes to the Risk Management Plan over time**

Not applicable.