Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Coloprep 1500 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 1102 mg of sodium dihydrogen phosphate monohydrate and 398 mg of disodium phosphate anhydrous

For a full list of excipients, see 6.1.

3 PHARMACEUTICAL FORM

Tablet

White to off-white oval compressed 18.7 mm x 10 mm tablets. The upper half bisected with a monogram "SLX" on the left and "102" on the right, and the lower half plain. The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

This medicine is indicated for cleansing of the bowel when required as a preparation for certain diagnostic procedures such as colonoscopy.
Coloprep is indicated in adults over 18 years of age.

4.2 Posology and method of administration

Posology

Adults (over 18 years of age):
The usual adult dosage of this medicine is 32 tablets. The total dose of phosphate is 32.79 g.

The intake of this medicine should begin the day before the colonoscopy. The day before the colonoscopy, patients may have a light, low-fibre breakfast (coffee or tea with or without sugar, toast, butter or equivalent, fruit jelly or honey). After noon, taking only "clear liquids" is permitted. "Clear liquid" may be water, light soup, diluted fruit juice without pulp, weak tea or black coffee, light soda with or without bicarbonate.

Recommended administration regimen:

The evening before the colonoscopy procedure:
· Take 4 tablets with 250 ml of water (or another clear liquid)
· Then repeat 4 times in the same conditions, every 15 minutes, for a total of 20 tablets to swallow.

The day of the colonoscopy procedure, (starting 3-5 hours before the procedure):
· Take 4 tablets with 250 ml of water (or another clear liquid)
· Then repeat 2 times in the same conditions, every 15 minutes for a total of 12 tablets to swallow.

Alternative administration regimen in case of morning colonoscopy:
For early morning colonoscopy, it is possible to adapt the dosing schedule by taking all the tablets in the evening before the procedure, and with an interval of at least 4 hours between the beginning of the intake of the first 20 tablets (to be absorbed at the rate of 4 tablets with 250ml of water or another clear liquid every 15 minutes) and the intake of the last 12 tablets (to be absorbed at the rate of 4 tablets with 250ml of water or another clear liquid every 15 minutes).

Patients should be advised of the importance of following the recommended fluid regimen and of drinking as much liquid as possible to replace lost fluids by increased intestinal peristalsis.
Drinking large amounts of clear liquid also helps ensure the cleanliness of the colon during colonoscopy. See Section 4.4 Special warnings and precautions for use.

Patients should not repeat this dosage for at least seven days. No additional laxatives are necessary when taking this medicine, particularly those agents containing sodium phosphate

Elderly:
In the elderly, the dosage is identical to that of adults. It may be useful to assess renal function before use in the elderly. This product is contraindicated in patients over 75 years of age (See section 4.3).

Paediatric population
Do not administer to children and adolescents under 18 years of age.

Method of administration

Adults (over 18 years of age):
This medicine should be administered orally according to the recommended administration regimen or to the alternative administration regimen in case of morning colonoscopy as described above.
Each intake of 4 tablets must be done with 250 ml of water or another clear liquid.
No solid food should be taken from the start of the course of treatment until after the clinical procedure.

4.3 Contraindications

· Hypersensitivity to the active substances or to any of the excipients listed in section 6.1
· Children under 18 years
· Patients over 75 years of age
· Use with other laxatives containing sodium phosphate.
· Clinically significant renal insufficiency and/or biopsy-proven acute phosphate nephropathy
· Primary hyperparathyroidism associated with hypercalcemia
· Congestive heart failure and/or uncontrolled heart failure
· Unstable angina pectoris
· Ascites
· Ileus or acute bowel obstruction or pseudo-obstruction, severe chronic constipation
· Hypomotility syndrome (such as hypothyroidism, scleroderma)
· Megacolon (congenital or acquired) or patients who have undergone gastric bypass surgery
· Bowel perforation
· Active inflammatory bowel disease (IBD).

4.4 Special warnings and precautions for use

In rare cases, this medicine was associated with severe and potentially fatal electrolyte disorders, in elderly patients. The benefit / risk ratio of this medicine must be carefully assessed before use in this population at risk.
Before initiating the treatment, it is necessary to ensure the absence of known contraindications and to stress on the importance of appropriate hydration. For at risk populations, it is important to check serum electrolyte concentrations before and after treatment (see below and section 4.2 and 4.3).

This medicine should be used with caution in patients with:
— a history of renal insufficiency, history of acute phosphate nephropathy, known or suspected electrolyte disorders, arrhythmias, cardiomyopathy, in patients within three months of an acute myocardial infarction or cardiac surgery, including coronary artery bypass graft surgery, patients using diuretics, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs) or NSAIDs.
— risk factors for electrolyte disorders (e.g., dehydration, gastric retention, inability to drink sufficient quantities of liquids, hypertension or other diseases treated by medicines that can induce dehydration, see below), hypotension with clinical consequences or associated with hypovolemia, or in the elderly or weakened patients. In these patients at risk, serum electrolyte including sodium, potassium, calcium, chloride, bicarbonate, phosphate, urea and creatinine assessment should be performed before and after treatment.
— risk factors for hyponatremia, e.g. SIADH, in adequately treated hypothyroidism, adrenal insufficiency or with risk factors for development of tonic-clonic seizures, e.g. a history of seizures, use of drugs that lower the seizure threshold such as tricyclic antidepressants or withdrawal from alcohol or benzodiazepines.
— intestinal hypomotility, history of gastrointestinal surgery or who have other diseases predisposing to intestinal hypomotility. In patient with colostomy or ileostomy or being on a low salt diet, the medicine must be used with caution becausede hydration, electrolytes or acid-base imbalance may occur.
— in diabetic patients as the recommended liquid diet during the period of administration prior to the procedure may affect blood glucose levels, requiring adjustment of antidiabetic medication or insulin.

Electrolyte disorders
Serum sodium and phosphate may increase and serum calcium and potassium may decrease, therefore, hypernatraemia, hyperphosphataemia, hypocalcaemia, hypokalaemia and acidosis may occur.

Patients should be advised to drink sufficient quantities of clear liquids or water when taking this medicine. Inadequate fluid intake, as with any effective purgative, may lead to dehydration and hypovolemia, which may be exacerbated by vomiting, loss of appetite or the use of diuretics, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs) and nonsteroidal anti-inflammatory drugs (NSAIDs).

However it is recommended not to drink too much liquid in order to avoid overhydration (water intoxication). If a patient experiences one or more of any of the following symptoms, they must be advised not drink any further liquid and contact a doctor immediately. Signs and/symptoms which might indicate water intoxication in particular are nausea and vomiting, headache, blurred vision, twitching, slowed breathing, change in personality or bizarre behaviour, (hallucinations, and confusion or disorientation). If left untreated, overhydration can lead to dangerously low levels of sodium in the blood (hyponatremia). This can cause more severe symptoms, such as, muscle weakness, spasms or cramps, seizures and unconsciousness.

Renal disease and acute phosphate nephropathy
There have been very rare, but serious reports of acute phosphate nephropathy associated with transient renal failure in patients who received oral sodium phosphate products for colon cleansing prior to colonoscopy. The time of onset is typically within days; however, in some cases, the diagnosis of these events has been delayed up to several months after ingestion of these products. The majority of cases occurred in elderly women taking anti-hypertensive agents and other drugs such as diuretics or NSAIDs which can cause dehydration. Patient hydration should first be assessed by identifying those who are predisposed to dehydration or those taking drugs that may decrease the glomerular filtration rate, such as angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs), before using laxative preparations. Patients should be monitored appropriately. When prescribing this medicine, special attention must be paid to the contraindications and adequate hydration of the patient.

Prolonged QT and cardiac arrhytmia
A mild prolongation of the QT interval may rarely occur because of electrolyte imbalance such as hypocalcaemia or hypokalaemia. This medicine should be used with caution in patients who are taking medications known to prolong the QT interval. Electrolyte abnormalities such as hypernatraemia, hyperphosphataemia, hypokalaemia or hypocalcaemia should be corrected before treatment with this medicine.

Seizures
There have been rare reports of generalised tonic-clonic seizures and/or loss of consciousness associated with use of sodium phosphate products in patients with no prior history of seizures. The seizure cases were associated with electrolyte

abnormalities (e.g., hyponatremia, hypokaliemia, hypocalcemia, and hypomagnesemia) and low serum osmolality. The neurologic abnormalities resolved with correction of fluid and electrolyte abnormalities.

Colon aphtous ulcerations
Single or multiple aphthous ulcerations, located in the sigmoid or rectum were observed by endoscopy. They consist in either lymphoid follicle or discrete inflammatory in filtrates or epithelial abnormalities observed following the use of the bowel preparation. These anomalies have no clinical relevance and disappear spontaneously. These findings should be considered in patients with known or suspected inflammatory bowel disease.

Risk of ischaemic colitis
Severe cases of ischaemic colitis requiring hospitalisation have been reported. Therefore, this diagnosis should be considered in the event of severe and/or persistent abdominal pain with or without rectal bleeding after the administration of this medicine.

This medicinal product contains 10 016 mg of sodium per course of treatment, equivalent to 500% of the WHO recommended maximum daily intake of 2 g sodium for an adult. A course of treatment consists of 32 tablets of Coloprep. This should be taken into consideration by patients on a controlled sodium diet.

Patients should be advised that they will have frequent and watery stools. This medicine usually acts ½ hour to 6 hours after dosing. Undigested or partially digested medicine may be seen in the watery stool or during colonoscopy. Undigested tablets of other medications may also be seen. When there is no bowel movement increase within 6 hours after taking this medicine, the patient should be aware of the necessity to discontinue the drug and contact a doctor immediately because there is a risk of dehydration.

This medicine should not be used as a treatment for constipation.

4.5 Interaction with other medicinal products and other forms of interactions

No drug interaction studies have been conducted for this medicine.

As with other purgatives the absorption of other orally administered medicines (e.g. oral contraceptives, antibiotics, antidiabetics, antiepileptic drugs) may be delayed or completely prevented.

Phosphate absorption is reduced by concomitant aluminium, calcium or magnesium salts. Phosphate absorption is increased by concomitant administration of vitamin D.

Care should be taken with patients taking calcium channel blockers, diuretics, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), drugs known to prolong the QT interval, NSAIDs, drugs containing parathyroid hormone, lithium treatment or other medications that might affect electrolyte levels as hyperphosphataemia, hypocalcaemia, hypokalaemia, hypernatraemic dehydration or acidosis may occur.

This medicine must not be used with other laxatives containing sodium phosphate.

4.6 Fertility, pregnancy and lactation

No clinical data on exposed pregnancies are available or even data from animal studies on the embryonic / fetal development, childbirth and postnatal development. The potential risk for humans is unknown. This medicine should not be used during pregnancy unless clearly necessary.

Not knowing if this medicine is excreted in breast milk and also if the sodium phosphate may pass into breast milk, it is advisable to draw the milk and not to use as soon after the first intake of this medicine up to 24 hours after taking the second dose. Therefore, women should not breastfeed their babies within 24 hours after taking the second dose of this medicine.

4.7 Effects on ability to drive and use machines

This medicine may cause dizziness, probably due to dehydration, and this may have a minor or moderate influence on the ability to drive and use machines.

4.8 Undesirable effects

The side effects listed below have been reported at 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). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Cardiac disturbances
Very rare: myocardial infarction, arrhythmias
Rare: mild prolonged QT interval

Gastrointestinal disorders
Very common: abdominal bloating, abdominal pain and nausea
Common: vomiting, abnormalities in colonoscopy (single or multiple aphthous like ulcerations located in the sigmoid and rectum without clinical relevance and disappearing spontaneously without treatment), abnormalities in gastroscopy (erythematous gastritis like lesions and/or superficial gastric ulcerations with necrotizing base, most often asymptomatic and spontaneously regressive).

General disorders and administration site conditions
Very common: chills, asthenia
Common: chest pain

Immune system disorders
Rare: hypersensitivity reactions such as rash, pruritus, urticaria, throat tightness, bronchospasm, dyspnea, pharyngeal oedema, dysphagia, paresthesia and swelling of the lips and tongue and facial swelling, anaphylaxis
Very rare: allergic dermatitis

Metabolism and nutrition disorders
Uncommon: dehydration
Rare: hypomagnesaemia
Very rare: dysnatraemia, hypocalcaemia, hypokalaemia, hyperphosphataemia, metabolic acidosis, tetany

Musculoskeletal and connective tissue disorders
Very rare: muscle cramps

Nervous system disorders
Common: headache and dizziness;
Very rare: generalised tonic-clonic seizures and/or loss of consciousness, paresthesia

Renal and urinary disorders
Very rare: Increased blood urea nitrogen (BUN), increased creatinine, acute renal failure, chronic renal failure, nephrocalcinosis, acute phosphate nephropathy and renal tubular necrosis.

Vascular disorders
Very rare: hypotension

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

In case of overdose, patients may experience the following symptoms: dehydration, hypovolaemia, hypotension, cardiac arrhythmias, tachypnea, cardiac arrest, shock, respiratory failure, dyspnea, convulsions, paralytic ileus, anxiety, pain. Overdoses can lead to high sodium and phosphate serum concentrations and to a decrease in calcium and potassium concentrations. In such cases, hypernatraemia, hyperphosphataemia, hypocalcaemia, hypokalaemia and acidosis may occur.

When taking excessive doses of this medicine, fatal cases of hyperphosphataemia with concomitant hypocalcaemia, hypernatraemia and acidosis have been reported in children or patients with bowel obstruction.

Cases of complete recovery after overdose have also been documented both in children after accidental ingestion of this medicine and in patients with bowel obstruction, one having taken six times the recommended dose.

Treatment of overdose usually consists in rehydration; the administration of intravenous 10% calcium gluconate may be needed.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: OSMOTICALLY ACTING LAXATIVE
ATC code: A06AD

This medicine is a saline laxative that acts by an osmotic process by increasing fluid retentionin the lumen of the small intestine. The fluid accumulation in ileum produces distention and thus facilitates peristalsis and bowel evacuation.

5.2 Pharmacokinetic properties

Approximately 60-65% of ingested dietary phosphate is absorbed from the gastro-intestinal tract via an active energy-dependent process.

Phosphate distributes into plasma and extracellular fluid, cell membranes and intracellular fluids.
More than 90% of plasma phosphate is filtered and 80% of the filtered phosphate is actively reabsorbed in the steady state. The ionised, inorganic form of phosphate in the circulating plasma is excreted almost entirely by the kidneys. This medicine is not expected to be metabolised in the liver.

Clinical studies with a higher dose of a previous formulation of this medicine have demonstrated that maximum peak plasma concentrations of serum inorganic phosphorous are achieved at approximately three hours after the administration of the first 30 g dose of this medicine, where serum inorganic phosphorous levels are increased by a mean of 1.21 ± 0.53 mmol/L. Following a second 30 g dose of this medicine a maximum peak plasma concentration of serum inorganic phosphorous is obtained at approximately four hours and the serum inorganic phosphorous levels are increased by a mean of 1.42 ± 0.60 mmol/L. The dosing instructions for this medicine recommend a first dose of 30 g and a second dose of 18 g.

5.3 Preclinical safety data

Limited non-clinical data reveal no special hazard for humans.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Macrogol 8000
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Keep the bottle tightly closed in order to protect from moisture.

6.5 Nature and contents of container

High-density polyethylene (HDPE) bottles with sealing pad and child-resistant cap, containing 2 silica gel desiccants.

There are 32 tablets in each bottle.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

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78401 CHATOU Cedex
France

8 MARKETING AUTHORISATION NUMBER

PA1993/003/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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