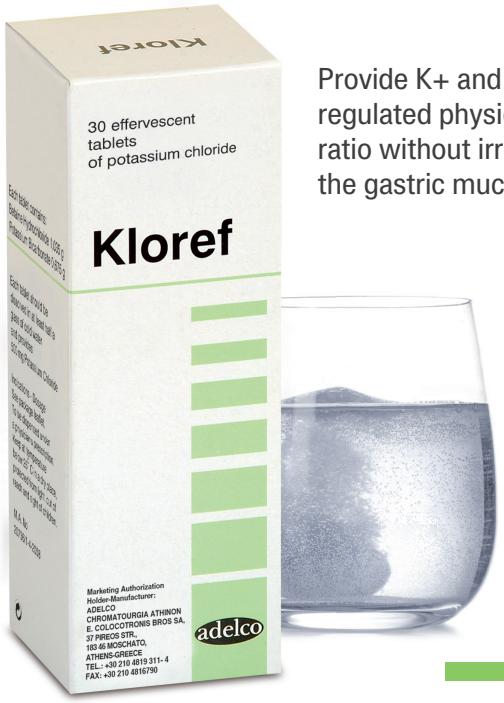
Kloref

Betaine HCl
Potassium Bicarbonate

For the prevention
and treatment of hypokalemia

Name of the medicinal product:	Kloref
Active ingredients:	Betaine Hydrochloride 1035mg/tab Potassium Bicarbonate 675mg/tab
Pharmaceutical form:	Effervescent tablets
Packaging:	Box of 30 tablets
Therapeutic indications:	For the prevention and treatment of hypokalemia and hypokalemia due to the chronic administration of agents that cause potassium loss
Method of administration:	Tablets should be taken dissolved in water, are effervescent and provide 6.7MEQ potassium and chloride per 500 mg KCl.
Posology:	Usually 1-2 tablets, three to four times daily
Marketing authorization holder & manufacturer:	ADELCO S.A.



Provide K+ and Cl- in a regulated physiological ratio without irritating the gastric mucosa.

Under prescription only medicine

For more information please refer to the Summary of Product Characteristics

Help to the safety of the products.
Fill the **«YELLOW CARD».**
REPORT:
- ALL adverse reactions for ALL drugs

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SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT: KLOREF

2. QUALITATIVE & QUANTITATIVE COMPOSITION IN ACTIVE INGREDIENTS: Each tablet contains: BETAINE HYDROCHLORIDE:1035 mg / TAB, POTASSIUM BICARBONATE: 675 mg/TAB (corresponding to K+ 263 mg/TAB). Each tablet dissolved in water corresponds to 500 mg KCl (6.7 mEq K+ and 6.7 mEq Cl-).

3. PHARMACEUTICAL FORM: White, effervescent tablets.

4. CLINICAL PARTICULARS:

4.1. Therapeutic indications: KLOREF is used for the prevention and treatment of hypokalemia, including hypokalemia owed to treatment with non potassium-sparing diuretics (such as thiazide furosemide, ethacrynic acid and chlorthalidone). It is also used when high doses of corticosteroids are administered and in cases of hypokalemia due to profuse vomiting or diarrhea.

4.2. Posology and method of administration: KLOREF effervescent tablets should be taken dissolved in water. They provide 6.7 MEQ potassium and chloride per 500 mg KCl. *Adults:* It varies depending on the severity of hypokalaemia and the underlying condition. Usually, 20 MEQ/24h are administered orally for prophylaxis. Usually, 1-2 tablets are administered three to four times daily. Higher doses are rarely required, in special urgent cases. *Elderly:* as with adults, with special attention to the contraindications and drug interactions. *Children:* The drug dose is not fixed apart from the case of hypokalaemia and it depends on patient's body weight and indications.

4.3. Contraindications: Severe renal insufficiency with oliguria or anuria and uremia, adrenal failure without substitution therapy, conditions accompanied by acute dehydration, heat stroke, hypokalaemic conditions of any etiology (e.g. diabetic ketoacidosis, extended burns or extensive soft tissue injuries, severe hemolytic crises etc)

4.4. Special warnings and precautions for use: In patients with renal failure or other condition that disturbs potassium renal excretion, intravenous or oral potassium administration poses serious risks of causing hyperkalemia and cardiac arrest.

Correction of hypokalemia in the aforementioned conditions as well as when heart disease or acidosis are present must be exercised cautiously with frequent determinations of serum potassium and electrocardiographic monitoring, always taking into account the clinical condition of the patient. Serum potassium concentrations do not necessarily reflect tissue potassium concentrations.

In patients with digitalism there is an increased risk for cardiac arrest following potassium administration (especially intravenously). Concomitant administration with potassium sparing diuretics (spironolactone, triamterene) and other aldosterone antagonists in general, as well as with sodium chloride substitutes should be avoided.

Special attention is required during potassium administration in cases of hypokalaemia with concomitant hyponatremia, hypocalcaemia or decreased blood pH, because even a small increase in its levels may have toxic effects on the myocardium and skeletal muscles. Additionally, in case of hyperchloremic metabolic acidosis with potassium depletion, potassium chloride should not be administered and other potassium salts (bicarbonate, citrate, acetate or gluconate) should be preferred. Liquid forms or effervescent tablets of potassium are the first-choice therapy, whereas tablets (simple or prolonged release) are appropriate only for patients who cannot tolerate or deny therapy with the previous forms. Tablets should not be chewed but ingested after being fully dissolved in adequate amount of water, preferably after meals. Potassium administration should be immediately discontinued if there is a suspicion for bowel obstruction, perforation or severe vomiting and abdominal pain. Rapid intravenous infusion of undiluted potassium chloride solutions involves a high risk of fatal hyperkalaemia. Prior to use, it should be diluted with a sugar solution or with sodium chloride (usually isotonic).

4.5. Interactions with other medicinal products and other forms of interaction: Concomitant administration with potassium sparing diuretics (spironolactone, triamterene) and, in general, aldosterone antagonists and sodium chloride substitutes, is contraindicated if cardiac glycosides are administered concurrently(Special warnings and precautions for use).

4.6. Pregnancy and lactation: Drug administration during pregnancy and lactation should be based on the evaluation of the drug necessity and usefulness compared to the drug effect on the fetus and the breastfeeding infant.

4.7. Effects on ability to drive and use machines: None reported.

4.8. Undesirable effects: The most frequent side effects are: Nausea, vomiting, diarrhea and abdominal discomfort or pain particularly following oral administration. Skin rashes are rarely reported.

When parenterally administered, local irritation and tissue necrosis may occur in case of extravasation, whereas phlebitis (chemical) and venous spasm have been reported. Ulceration, stenosis and hemorrhage from the esophagus as well as from the rest of the gastrointestinal tract resulting even in death, have been reported following potassium chloride tablet administration (simple, enteric-coated or extended-release). The most serious risk of potassium administration, particularly following parenteral and to a lesser extent oral administration, is hyperkalaemia with dangerous and sometimes fatal results. Hyperkalaemia may be latent and symptomatic or may be accompanied by clinical symptoms such as paraesthesia of the extremities, flaccid paralysis, confusion, weakness and heaviness of the lower extremities, blood pressure decrease, cardiac or respiratory suppression, swallowing difficulty, cardiac arrhythmias or/and cardiac arrest. Characteristic ECG changes are observed.

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 the Greek National Organization for Medicines: 284 Mesogeion Av., GR-15562 Xolargos, Athens, Greece. Tel: +30 21 32040380/337, Fax: +30 21 06549585, Website: http://www.eof.gr

4.9. Overdose: In individuals with normal potassium secretory mechanisms, the oral administration of potassium salts rarely causes severe hypokalaemia. Hyperkalaemia may be observed only in individuals with impaired secretory function and may be treated as follows: 1. Intravenous administration of 300-500 ml/h of 10% dextrose solution containing 1-20 units of crystalline insulin per liter. 2. Acidosis correction, if present, with intravenous administration of sodium bicarbonate. Use of ion-exchanging resins, hemodialysis or peritoneal dialysis.

5. PHARMACOLOGICAL PROPERTIES:

5.1. Pharmacodynamic properties: KLOREF is an effervescent tablet which is administered orally, and replaces potassium loss which observed in cases of hypokalaemia due to treatment with diuretics, high doses of corticosteroids and gastroenteritis. Potassium constitutes the main intracellular cation. Oral or parenteral administration is used for: a) potassium salt depletion due to diarrhea, polyuria etc b) chronic administration of agents that cause potassium loss (corticosteroids, diuretics) c) secondary hyperaldosteronism syndrome (nephrosis, liver cirrhosis etc) and d) patients under prophylactic treatment with digoxin or antiarrhythmics because hypokalaemia may deteriorate arrhythmias. Potassium bicarbonate may be administered in hyperchloremic acidosis orally or intravenously if there is also potassium depletion (renal tubular disorders, gastrointestinal disturbances).

5.2. Pharmacokinetic properties: α. General characteristics: It is rapidly absorbed by stomach. It is well tolerated by gastric mucosa and does not cause irritation. β. Characteristics in patients:

Special caution should be exercised during potassium chloride administration in patients with renal disease and hyperkalaemia conditions due to acute conditions such as diabetic acidosis, hemolytic crises or extensive burns.

5.3. Preclinical safety data: In patients with normal secretory mechanisms, the recommended dose of potassium chloride does not cause hyperkalaemia. Acute toxicity: Hyperkalaemia, arrhythmias, paraesthesias, blood pressure decrease or fatal complication. Gastrointestinal lesions, especially ulcerations are observed with the administration of simple, enteric-coated or extended-release tablets. Chronic toxicity: The administration of tablets that are soluble in stomach may cause gastrointestinal tract ulceration and hemorrhage from the esophagus and the rest of the gastrointestinal tract. Mutagenic activity-oncogenesis: Not reported. Reproduction toxicity: Not reported.

6. PHARMACEUTICAL DATA:

6.1. List of excipients: Saccharin, Sodium Lauryl Sulfate, Acacia, Docusate Sodium, Polyvidone, Citric Acid, Magnesium Stearate, Ethanol 96%, Lemon Flavour, Lime Flavour

6.2. Incompatibilities: Concomitant administration with potassium sparing diuretics, such as triamterene, spironolactone.

6.3. Shelf life: 24 months.

6.4. Special storage precautions: Keep at temperature below 25ºC in a dry place, protected from light, out of reach and sight of children.

6.5. Nature and contents of container: Plastic vial containing 30 tablets. The vial is packaged in a box containing the patient information leaflet.

6.6. Instructions for use/handling: Not required.

7. MARKETING AUTHORIZATION HOLDER: ADELCO CHROMATOURGIA ATHINON, E. COLOCOTRONIS BROS. S.A., TEL. +30 210 4819 311-4, FAX : +30 210 4816 790

8. MARKETING AUTHORIZATION NUMBER: 20736/1-4-2008

9. DATE OF FIRST AUTHORIZATION IN GREECE: 26-10-1972

10. DATE OF REVISION OF THE TEXT: 07/2014