Potassium Chloride Extended-release Tablets, USP®

DESCRIPTION

Potassium Chloride Extended-release Tablets, USP® (Klor-Con®) are a solid oral dosage form of potassium chloride. Each tablet contains 65 mg or 75 mg of potassium chloride equivalent to 8 mg or 10 mg of potassium in a wax matrix tablet. This formulation is intended to provide an extended-release of potassium from the matrix to minimize the likelihood of producing high, localized concentrations of potassium within the gastrointestinal tract. Klor-Con® Extended-release Tablets are an electrolyte replacer. The chemical name is potassium chloride, and the structural formula is KCl. Potassium chloride, USP® is a white, granular powder or colorless crystals. It is odorless and has a salty taste. Its solutions are neutral to litmus. It is freely soluble in water and insoluble in alcohol.

Inactive ingredients: Hydrogenated vegetable oil, magnesium stearate, polyethylene glycol, polysynthetic alcohol, silicon dioxide, talc and titanium dioxide. Yellow tablets also contain D&C Yellow No. 10 aluminum lake and FD&C Yellow No. 2 aluminum lake. Blue tablets also contain FD&C Blue No. 1 aluminum lake and FD&C Blue No. 2 aluminum lake.

CLINICAL PHARMACOLOGY

The potassium ion is the principal intracellular cation of most body tissues. Potassium ions participate in a number of essential physiological processes including the maintenance of intracellular toxicity, the transmission of nerve impulses, the contraction of cardiac, skeletal and smooth muscle and the maintenance of normal renal function.

The intracellular concentration of potassium is approximately 150 to 160 mEq per liter. The normal adult plasma concentration is 3.5 to 5 mEq per liter. An active ion transport system maintains this gradient across the plasma membrane.

Potassium is a normal dietary constituent and under steady state conditions the amount of potassium absorbed from the gastrointestinal tract is equal to the amount excreted in the urine. The usual dietary intake of potassium is 50 to 100 mEq per day.

Potassium depletion will occur whenever the rate of potassium loss through renal excretion and/or loss from the gastrointestinal tract exceeds the rate of potassium intake. Such depletion usually develops slowly as a consequence of prolonged therapy with oral diuretics, primary or secondary hyperaldosteronism, diabetic ketoacidosis, severe diarrhea, or inadequate replacement of potassium in patients on prolonged parenteral nutrition. Depletion can develop rapidly with severe diarrhea, especially if associated with vomiting. Potassium depletion due to these causes is usually accompanied by a concomitant loss of chloride and is manifested by hypokalemia and metabolic alkalosis. Potassium depletion may produce weakness, fatigue, disturbances of cardiac rhythm (primarily ectopic beats), prominent U-waves in the electrocardiogram, and, in advanced cases, fixed paralysis and/or impaired ability to concentrate urine.

If potassium depletion associated with metabolic alkalosis cannot be managed by correcting the fundamental cause of the deficiency, e.g., where the patient requires long term diuretic therapy, supplemental potassium in the form of high potassium food or potassium chloride may be able to restore normal potassium levels. In rare circumstances (e.g., patients with renal tubular acidosis) potassium depletion may be associated with metabolic acidosis and hyperchloremia. In such patients potassium replacement should be accomplished with potassium salts other than the chloride, such as potassium bicarbonate, potassium citrate, potassium acetate or potassium gluconate.

The potassium chloride in Klor-Con® Extended-release Tablets is completely absorbed before it leaves the small intestine. The wax matrix is not absorbed and is excreted in the feces, usually within 24 hours. The potassium is slowly released from the matrix due to the finding that a significant increase in time is required for renal excretion of the first 50% of the Klor-Con® Extended-release Tablets as compared to the solution.

Increased urinary potassium excretion is first observed 1 hour after administration of Klor-Con® Extended-release Tablets, and reaches a peak at approximately 4 hours, and extends up to 8 hours. Mean daily steady-state plasma levels of potassium following daily administration of Klor-Con® Extended-release Tablets cannot be distinguished from those following administration of potassium chloride solution or from control plasma levels of potassium ion.

INDICATIONS AND USAGE

BECAUSE OF REPORTS OF INTESTINAL AND GASTRIC ULCERATION AND BLEEDING WITH EXTENDED-RELEASE POTASSIUM CHLORIDE PREPARATIONS, THESE DRUGS SHOULD BE RESERVED FOR THOSE PATIENTS WHO CANNOT TOLERATE OR REFUSE TO TAKE LIQUID OR EFFERVESCENT POTASSIUM PREPARATIONS OR FOR PATIENTS IN WHOM THERE IS A PROBLEM OF COMPLIANCE WITH THESE PREPARATIONS.

1. For the therapeutic use of patients with hypokalemia, with or without metabolic alkalosis; in digitalis intoxication; and in patients with hypokalemic familial periodic paralysis. If hypokalemia is the result of diuretic therapy, consideration should be given to the use of a lower dose of diuretic, which may be sufficient without leading to hypokalemia.

2. For the prevention of hypokalemia in patients who would be at particular risk if hypokalemia were to develop, e.g., digitized patients or patients with significant cardiac arrhythmias. The use of potassium salts in patients receiving diuretics for uncomplicated essential hypertension is often unnecessary when such patients have a normal dietary pattern and when low doses of the diuretic are used. Serum potassium should be checked periodically, however, and if hypokalemia occurs, dietary supplementation with potassium-containing foods may be adequate to control milder cases. In more severe cases, and if dose adjustment of the diuretics is ineffective or unwarranted, supplementation with potassium salts may be indicated.

CONTRAINDICATIONS

Potassium supplements are contraindicated in patients with hyperkalemia since a further increase in serum potassium concentration in such patients can produce cardiac arrest. Hyperkalemia may complicate any of the following conditions: chronic renal failure, systemic acidosis such as diabetic acidosis, acute dehydration, extensive tissue breakdown as in severe burns, adrenal insufficiency or the administration of a potassium-sparing diuretic (e.g., spironolactone, triamterene or amiloride) (see OVERDOSE).

Extended-release formulations of potassium chloride have produced esophageal ulceration in certain cardiac patients with esophageal compression due to an enlarged left atrium. Potassium supplementation, when indicated in such patients, should be given as a liquid preparation.

All solid oral dosage forms of potassium chloride are contraindicated in any patient in whom there is structural, pathological (e.g., diabetic gastroparesis) or pharmacologic (use of anticholinergic agents or other agents with anticholinergic properties at sufficient doses to exert anticholinergic effects) cause for arrest or delay in tablet passage through the gastrointestinal tract.

WARNINGS

Hyperkalemia (see OVERDOSE): In patients with impaired mechanisms for excreting potassium, the administration of potassium salts can produce hyperkalemia and cardiac arrest. This occurs most commonly in patients given potassium by the intravenous route but may also occur in patients given potassium orally. Potentially fatal hyperkalemia can develop rapidly and be asymptomatic.

The use of potassium salts in patients with chronic renal disease, or any other condition which impairs potassium excretion, requires particularly careful monitoring of the serum potassium concentration and appropriate dosage adjustment.

Interaction with Potassium-sparing Diuretics: Hyperkalemia would not be treated by the concomitant administration of potassium salts and a potassium-sparing diuretic (e.g., spironolactone, triamterene or amiloride), since the simultaneous administration of these agents can produce severe hyperkalemia.

Interaction with Angiotensin Converting Enzyme Inhibitors: Angiotensin converting enzyme (ACE) inhibitors (e.g., captopril, enalapril) will produce some potassium retention and/or impaired ability to concentrate urine, which impairs potassium excretion, requires particularly careful monitoring of the serum potassium concentration and appropriate dosage adjustment.

Gastrointestinal Lesions: Solid oral dosage forms of potassium chloride can produce ulcerative and/or stenotic lesions of the gastrointestinal tract. Based on spontaneous adverse reaction reports, enteric-coated preparations of potassium chloride are associated with an increased frequency of small bowel lesions (40-50 per 100,000 patient years) compared to extended-release wax matrix formulations (less than one per 100,000 patient years). Because of the lack of extensive marketing experience with microencapsulated products, a comparison between such products and wax matrix or enteric-coated products is not available. Klor-Con® (Potassium Chloride Extended-release Tablets, USP) are wax matrix tablets formulated to provide an extended release of potassium chloride and thus to minimize the possibility of high local concentration of potassium near the gastrointestinal wall.

Prospective trials have been conducted in normal human volunteers in which the upper gastrointestinal tract was evaluated by endoscopic inspection before and after one week of solid oral potassium chloride therapy. The ability of this model to predict events occurring in usual clinical practice is unknown. Trials which approximated usual clinical practice did not reveal any clear differences between the wax matrix and microencapsulated dosage forms. In contrast, there was a higher incidence of gastric and duodenal lesions in subjects receiving a high dose of a wax matrix extended-release formulation under conditions which did not resemble usual or recommended clinical practice (i.e., 56 mEq per day in divided doses of potassium chloride administered to fasted patients, in the presence of an anticholinergic drug to delay gastric emptying). The upper gastrointestinal lesions observed by endoscopy were asymptomatic and were not
Pediatric Use: Since oral potassium becomes part of the body potassium pool, so long as body potassium does not lead to hyperkalemia would have an adverse effect on the fetus or would affect reproductive capacity. Nursing Mothers: The normal potassium ion content of human milk is about 13 mEq per liter. It is not known if Klor-Con Extended-release Tablets have an effect on this. Since oral potassium becomes part of the body potassium pool, so long as body potassium is not excessive, the contribution of potassium chloride supplementation should have little or no effect on the level in human milk. PREGNANCY: Pregnancy Category C. Animal reproduction studies have not been conducted with Klor-Con Extended-release Tablets. It is unlikely that potassium supplementation that does not lead to hyperkalemia would have an adverse effect on the fetus or would affect reproductive capacity. Nursing Mothers: The normal potassium ion content of human milk is about 13 mEq per liter. It is not known if Klor-Con Extended-release Tablets have an effect on this. Since oral potassium becomes part of the body potassium pool, so long as body potassium is not excessive, the contribution of potassium chloride supplementation should have little or no effect on the level in human milk. Pediatric Use: Safety and effectiveness in the pediatric population have not been established. General: The diagnosis of potassium depletion is ordinarily made by demonstrating hypokalemia in a patient with a clinical history suggesting some cause for potassium depletion. In interpreting the serum potassium level, the physician should be aware that acute alkalosis per se can produce hypokalemia in the absence of a deficit in total body potassium while acute acidosis per se can increase the serum potassium concentration into the normal range even in the presence of a reduced total body potassium. The treatment of potassium depletion, particularly in the presence of cardiac disease, renal disease or acidosis requires careful attention to acid-base balance and appropriate monitoring of serum electrolytes, the electrocardiogram and the clinical status of the patient. Information for Patients: Physicians should consider reminding the patient of the following: To take each dose with meals and with a full glass of water or other liquid. To take this medicine following the frequency and amount prescribed by the physician. This is especially important if the patient is also taking diuretics and/or diabetics preparations. To check with the physician if there is trouble swallowing the tablets or if the tablets seem to stick in the throat. To check with the physician at once if tarry stools or other evidence of gastrointestinal bleeding is noticed. To take each dose without chewing, crushing or sucking the tablets. Laboratory Tests: When blood is drawn for analysis of plasma potassium it is important to recognize that artifactual elevations can occur after improper venipuncture technique or as a result of in vitro hemolysis of the sample. Drug interactions: Potassium-sparing diuretics, angiotensin converting enzyme inhibitors (see WARNINGS). Carcinogenesis, Mutagenesis, Impairment of Fertility: Carcinogenicity, mutagenicity and fertility studies in animals have not been performed. Potassium is a normal dietary constituent. OVERDOSAGE: The administration of oral potassium salts to persons with normal excretory mechanisms for potassium rarely causes serious hyperkalemia. However, if excretion mechanisms are impaired, or if potassium is administered too rapidly intravenously, potentially fatal hyperkalemia can result (see CONTRAINDICATIONS and WARNINGS). It is important to recognize that hyperkalemia is usually asymptomatic and may be manifested only by an increased serum potassium concentration (6.5-8.0 mEq/L) and characteristic electrocardiographic changes (peaking of T-waves, loss of P-wave, depression of S-T segment and prolongation of the QT interval). Late manifestations include muscle paralysis and cardiovascular collapse from cardiac arrest (9-12 mEq/L). Treatment measures for hyperkalemia include the following: 1. Elimination of foods and medications containing potassium and of any agents with potassium-sparing properties. 2. Intravenous administration of 300 to 500 mL/hr of 10% dextrose solution containing 10-20 units of crystalline insulin per 1.0 mL. 3. Correction of acidosis, if present, with intravenous sodium bicarbonate. 4. Use of exchange resins, hemodialysis or peritoneal dialysis. In treating hyperkalemia, it should be recalled that in patients who have been stabilized on digitals, too rapid a lowering of the serum potassium concentration can produce digitalis toxicity. The extended release feature means that absorption and toxic effects may be delayed for hours. Consider standard measures to remove any unabsorbed drug. DOSAGE AND ADMINISTRATION: The usual daily potassium intake by the average adult is 50 to 100 mEq per day. Potassium depletion sufficient to cause hypokalemia usually requires the loss of 200 mEq or more of potassium from the total body store. Dosage must be adjusted to the individual needs of each patient. The dose for the prevention of hypokalemia is typically in the range of 20 mEq per day. Doses of 40–100 mEq per day or more are used for the treatment of potassium depletion. Dosage should be divided if more than 20 mEq per day is given such that no more than 20 mEq is given in a single dose. Each Klor-Con Extended-release Tablet provides 8 mEq or 10 mEq of potassium chloride. Klor-Con Extended-release Tablets (Potassium Chloride Extended-release Tablets, USP) should be taken with meals and with a glass of water or other liquid. This product should not be taken on an empty stomach because of its potential for gastric irritation (see WARNINGS). NOTE: Klor-Con Extended-release Tablets must be swallowed whole and never crushed, chewed or sucked. How supplied: Film-coated Klor-Con 8 (light blue, debossed with “KC 8”), Klor-Con 10 (yellow, debossed with “KC 10”), round tablets containing: 600 mg potassium chloride (equivalent to 8 mEq) in bottles of 100 (NDC 0245-0040-11), bottles of 500 (NDC 0245-0040-15), unit dose packages of 100 (NDC 0245-0040-01), bulk packs of 5,000 for repack only (NDC 0245-0040-55), and bulk packs of 10,000 for repack only (NDC 0245-0040-99); 750 mg potassium chloride (equivalent to 10 mEq) in bottles of 100 (NDC 0245-0041-11), bottles of 500 (NDC 0245-0041-15), unit dose packages of 100 (NDC 0245-0041-01), bulk packs of 5,000 for repack only (NDC 0245-0041-55), and bulk packs of 10,000 for repack only (NDC 0245-0041-99). Store at controlled room temperature, 15-30°C (59-86°F). Protect from light and moisture. Dispose in a light container with child-resistant closure. Manufactured by UPSHER-SMITH LABORATORIES, INC. Minneapolis, MN 55447 102978-00 Revisted 1008