POTASSIUM CHLORIDE - potassium chloride capsule, extended release
Amneal Pharmaceuticals

POTASSIUM CHLORIDE EXTENDED-RELEASE CAPSULES, USP, 10 mEq

R_x Only

DESCRIPTION

Potassium Chloride Extended-Release Capsules, USP, 10 mEq are oral dosage forms of microencapsulated potassium chloride containing 750 mg of potassium chloride USP equivalent to 10 mEq of potassium.

Dispersibility of potassium chloride (KCl) is accomplished by microencapsulation and a dispersing agent. The resultant flow characteristics of the KCl microcapsules and the controlled-release of K^+ ions by the microcapsular membrane are intended to avoid the possibility that excessive amounts of KCl can be localized at any point on the mucosa of the gastrointestinal tract.

Each crystal of KCl is microencapsulated by a process with an insoluble polymeric coating which functions as a semi-permeable membrane; it allows for the controlled-release of potassium and chloride ions over an eight-to-ten-hour period. Fluids pass through the membrane and gradually dissolve the potassium chloride within the micro-capsules. The resulting potassium chloride solution slowly diffuses outward through the membrane. Potassium Chloride Extended-Release Capsules, USP, 10 mEq are electrolyte replenishers. The chemical name of the active ingredient is potassium chloride and the structural formula is KCl. Potassium chloride USP occurs as a white, granular powder or as colorless crystals. It is odorless and has a saline taste. Its solutions are neutral to litmus. It is freely soluble in water and insoluble in alcohol.

The inactive ingredients are ethylcellulose, gelatin, sodium lauryl sulfate and triethyl citrate.

CLINICAL PHARMACOLOGY

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 tonicity, 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 therapy with diuretics, primary or secondary hyperaldosteronisms, diabetic ketoacidosis, 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, flaccid 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.

INDICATIONS AND USAGE

BECAUSE OF REPORTS OF INTESTINAL AND GASTRIC ULCERATION AND BLEEDING WITH CONTROLLED-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 treatment of patients with hypokalemia with or without metabolic alkalosis, in digitalis intoxications, 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., digitalized patients or patients with significant cardiac arrhythmias, hepatic cirrhosis with ascites, states of aldosterone excess with normal renal function, potassium-losing nephropathy, and certain diarrheal states.

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 diuretic 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, amiloride) (see **OVERDOSAGE**).

Controlled-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 capsule passage through the gastrointestinal tract.

WARNINGS

Hyperkalemia (see **OVERDOSAGE**)

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 adjustments.

Interaction with Potassium-Sparing Diuretics

Hypokalemia should 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 by inhibiting aldosterone production. Potassium supplements should be given to patients receiving ACE inhibitors only with close monitoring.

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 to 50 per 100,000 patient years) compared to sustained-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. Potassium Chloride Extended-Release Capsules, USP, 10 mEq are microencapsulated capsules formulated to provide a controlled rate of release of microencapsulated 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 controlled-release formulation under conditions which did not resemble usual or recommended clinical practice (i.e., 96 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 accompanied by evidence of bleeding (hemoccult testing). The relevance of these findings to the usual conditions (i.e., non-fasting, no anticholinergic agent, smaller doses) under which controlled-release potassium chloride products are used is uncertain; epidemiologic studies have not identified an elevated risk, compared to microencapsulated products, for upper gastrointestinal lesions in patients receiving wax matrix formulations. Potassium Chloride Extended-Release Capsules, USP, 10 mEq should be discontinued immediately and the possibility of ulceration, obstruction or perforation considered if severe vomiting, abdominal pain, distention, or gastrointestinal bleeding occur.

Metabolic Acidosis

Hypokalemia in patients with metabolic acidosis should be treated with an alkalinizing potassium salt such as potassium bicarbonate, potassium citrate, potassium acetate, or potassium gluconate.

PRECAUTIONS

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 bear in mind 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 suitable liquid. To take each dose without crushing, chewing, or sucking the capsules. 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 digitalis preparations. To check with the physician if there is trouble swallowing capsules or if the capsules seem to stick in the throat.

To check with the physician at once if tarry stools or other evidence of gastrointestinal bleeding is noticed.

Laboratory Tests Regular serum potassium determinations are recommended, especially in patients with renal insufficiency or diabetic nephropathy. 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.

Pregnancy: Teratogenic Effects: Category C Animal reproduction studies have not been conducted with Potassium Chloride Extended-Release Capsules, USP, 10 mEq. 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. 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 pediatric patients have not been established.

Geriatric Use Clinical studies of Potassium Chloride Extended-Release Capsules did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

ADVERSE REACTIONS

One of the most severe adverse effects is hyperkalemia (see **CONTRAINDICATIONS, WARNINGS, AND OVERDOSAGE**). Gastrointestinal bleeding and ulceration have been reported in

patients treated with Potassium Chloride Extended-Release Capsules, USP, 10 mEq (see **CONTRAINDICATIONS** and **WARNINGS**). In addition to gastrointestinal bleeding and ulceration, perforation and obstruction have been reported in patients treated with other solid KCl dosage forms, and may occur with Potassium Chloride Extended-Release Capsules, USP, 10 mEq. The most common adverse reactions to the oral potassium salts are nausea, vomiting, flatulence, abdominal discomfort, and diarrhea. These symptoms are due to irritation of the gastrointestinal tract and are best managed by taking the dose with meals, or reducing the amount taken at one time. Skin rash has been reported rarely with potassium preparations.

OVERDOSAGE

The administration of oral potassium salts to persons with normal excretory mechanisms for potassium rarely causes serious hyperkalemia. However, if excretory 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 to 8.0 mEq/L) and characteristic electrocardiographic changes (peaking of T-waves, loss of P-waves, depression of ST segment, and prolongation of the QT interval). Late manifestations include muscle paralysis and cardiovascular collapse from cardiac arrest (9 to 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 to 20 units of crystalline insulin per 1,000 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 digitalis, 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 dietary intake of potassium by the average adult is 50 to 100 mEq per day. Potassium depletion sufficient to cause hypokalemia usually requires the loss of 200 or more mEq 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 to 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. Because of the potential for gastric irritation (see **WARNINGS**), Potassium Chloride Extended-Release Capsules, USP, 10 mEq should be taken with meals and with a full glass of water or other liquid.

Patients who have difficulty swallowing capsules may sprinkle the contents of the capsule onto a spoonful of soft food. The soft food, such as applesauce or pudding, should be swallowed immediately without chewing and followed with a glass of cool water or juice to ensure complete swallowing of the microcapsules. The food used should not be hot and should be soft enough to be swallowed without chewing. Any microcapsule/food mixture should be used immediately and not stored for future use.

HOW SUPPLIED

Potassium Chloride Extended-Release Capsules, USP, **10 mEq** are clear transparent elongated hard gelatin capsule filled with white to off-white coated pellets and imprinting ‘AMNEAL’ on the cap and ‘542’ on the body, each containing 750 mg microencapsulated potassium chloride (equivalent to 10 mEq K).

They are available as follows:

Bottles of 100: 65162-542-10

Bottles of 500: 65162-542-50

Bottles of 1000: 65162-542-11

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature].

Dispense in tight container.

Manufactured by:

Amneal Pharmaceuticals Co. (I) Pvt. Ltd.

Ahmedabad, INDIA 382220

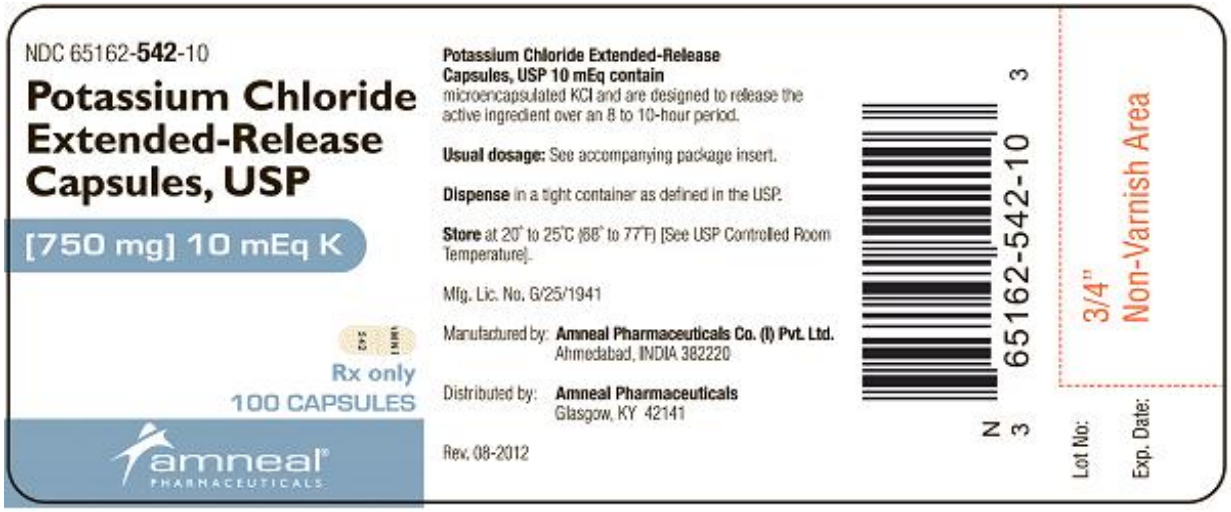
Distributed by:

Amneal Pharmaceuticals

Glasgow, KY 42141, USA

Rev. 02-2011

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL



POTASSIUM CHLORIDE

potassium chloride capsule, extended release

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG LABEL	**Item Code (Source)**	NDC:65162-542
Route of Administration	ORAL	**DEA Schedule**	

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
POTASSIUM CHLORIDE (POTASSIUM CATION)	POTASSIUM CHLORIDE	750 mg

Inactive Ingredients

Ingredient Name	Strength
ETHYLCELLULOSES	
GELATIN	
SODIUM LAURYL SULFATE	
TRIETHYL CITRATE	

Product Characteristics

Color	WHITE (transparent)	**Score**	no score
Shape	CAPSULE	**Size**	26mm
Flavor		**Imprint Code**	AMNEAL;542
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:65162-542-10	100 in 1 BOTTLE		
2	NDC:65162-542-50	500 in 1 BOTTLE		
3	NDC:65162-542-11	1000 in 1 BOTTLE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA202128	02/22/2013	

Labeler - Amneal Pharmaceuticals (123797875)

Registrant - Amneal Pharmaceuticals (123797875)

Establishment

Name	Address	ID/FEI	Business Operations
Amneal Pharmaceuticals Co. (I) Pvt. Ltd.		915076126	ANALYSIS(65162-542), LABEL(65162-542), MANUFACTURE(65162-542), PACK(65162-542)

Establishment

Name	Address	ID/FEI	Business Operations
Amneal Pharmaceuticals		963900878	ANALYSIS(65162-542)