PRESCRIBING INFORMATION

Potassium Chloride in 5% Dextrose Injection, USP
In VIAFLEX Plastic Container

IV Fluid and Nutrient Replenisher

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Date of Revision:
March 11, 2021

Submission Control No: 249296

Potassium Chloride in 5% Dextrose Injection, USP
In VIAFLEX Plastic Container

SUMMARY PRODUCT INFORMATION

Potassium Chloride in 5% Dextrose Injection, USP is a sterile, nonpyrogenic solution for fluid and electrolyte replenishment and caloric supply in a single dose container for intravenous administration. It contains no antimicrobial agents. Composition, osmolarity, pH, ionic concentration and caloric content are shown in **Table 1.**

Table 1.

	Size	Composition (g/l)		Osmolarity		Ionic Concentration		How Supplied	
Potassium Chloride in 5% Dextrose Injection, USP	mL	Dextrose Hydrous, USP*	Potassium Chloride, USP (KCl)	mOsmol/L	pH	Potassium	Chloride	Caloric Conct. (kcal/L)	
20 mmol/L	1000	50	1.5	292	4.0	20	20	170	
40 mmol/L	1000	50	3	332	4.0	40	40	170	

*The dextrose is purified from corn and may contain fructose.

The VIAFLEX plastic container is fabricated from a specially formulated polyvinyl chloride (PL 146 Plastic).

Water in a solution in the container can permeate through the plastic wall, but in an insufficient amount to significantly affect the solution. Before the product expires, a very small amounts of chemical components of the plastic can be leached into the solution in the container, such as up to 5 parts per million for DEHP. No safety issues of the plastic material were identified in USP biological tests in animals as well as by tissue culture toxicity studies.

ACTIONS

Potassium Chloride in 5% Dextrose Injection, USP has value as a source of water, electrolytes and calories. It is capable of inducing diuresis depending on the clinical condition of the patient.

INDICATIONS AND CLINICAL USE

Potassium Chloride in 5% Dextrose Injection, USP is indicated as a source of water, electrolytes and calories. Dextrose-containing solutions may also be indicated in clinical conditions where enteral nutritional supply is or is expected to be insufficient or impossible.

CONTRAINDICATIONS

Potassium Chloride in 5% Dextrose Injection, USP is contraindicated in the following conditions:

- Patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container. For a complete listing, see the SUMMARY PRODUCT INFORMATION section of the Prescribing Information.
- Known allergy to corn or corn products since dextrose in the products is purified from corn.
- Clinically significant hyperglycemia
- Clinically significant hyperkalemia

WARNINGS AND PRECAUTIONS

WARNINGS

Hypersensitivity Reactions

Hypersensitivity/infusion reactions, including anaphylaxis, have been reported with other potassium chloride and dextrose products. The infusion must be stopped immediately if signs or symptoms of suspected hypersensitivity/infusion reactions develop. Appropriate therapeutic countermeasures must be instituted as clinically indicated. Since dextrose in Potassium Chloride in 5% Dextrose Injection, USP is derived from corn, the product should not be used in patients with known allergy to corn or corn products (see CONTRAINDICATIONS section).

Hyperkalemia

Potassium Chloride in 5% Dextrose Injection, USP should be administered with caution, to patients with conditions predisposing to hyperkalemia and/or associated with increased sensitivity to potassium, such as patients with:

- severe renal impairment,
- acute dehydration,
- extensive tissue injury or burns,
- certain cardiac disorders such as congestive heart failure or atrioventricular (AV) block (especially if they receive digitalis),
- potassium-aggravated skeletal muscle channelopathies (e.g., hyperkalemic periodic paralysis, paramyotonia congenita, and potassium-aggravated myotonia/paramyotonia).
- Potassium Chloride in 5% Dextrose Injection, USP should be administered with caution to patients who are at risk of experiencing hyperosmolality, acidosis, or undergoing correction of alkalosis (conditions associated with a shift of potassium from intracellular to extracellular space) and patients treated concurrently or recently with agents or products that can cause hyperkalemia or increase the risk of hyperkalemia (see Drug Interactions).
- Other groups of patients in whom Potassium Chloride in 5% Dextrose Injection, USP should be used with caution include patients with cardiac arrhythmia. Arrhythmias can develop at any time during hyperkalemia. Frequently, mild or moderate hyperkalemia is

asymptomatic and may be manifested only by increased serum potassium concentrations and, possibly, characteristic ECG changes.

Hyperkalemia may result even with low dosage. Please refer to OVERDOSAGE for Hyperkalemia symptoms and treatments.

Use in Patients with or at risk of Severe Renal Impairment
Potassium Chloride in 5% Dextrose Injection, USP should be administered with particular caution, to patients with or at risk of severe renal impairment. In such patients, administration of Potassium Chloride in 5% Dextrose Injection, USP may result in or predispose to hyperkalemia and/or fluid overload.

Risk of Hypo and Hyperosmolality, Serum Electrolytes, and Water Imbalance
Depending on the volume and rate of infusion and depending on a patient's underlying clinical condition and capability to metabolize dextrose, intravenous administration of dextrose can cause:

- Hyperosmolality, osmotic diuresis and dehydration
- Hypoosmolality
- Electrolyte disturbances such as
    - Hyponatremia,
    - Hypokalemia (Potassium Chloride without Dextrose or Potassium Chloride with a higher concentration is recommended for correcting hypokalemia)
    - Hypophosphatemia,
    - Hypomagnesemia,
- Acid-base imbalance
- Overhydration/Hypervolemia and, for example, congested states, including central (eg., pulmonary congestion) and peripheral edema. Particular caution should be taken in patients with conditions that may cause sodium retention, fluid overload, and edema (central and peripheral).
- Hyponatremia and a decrease in extracellular sodium concentrations related to hyperglycemia causing a transcellular shift of water.
- Infusion of Potassium Chloride in 5% Dextrose Injection, USP corresponds to the increasing body's load of free water, possibly leading to hypoosmotic hyponatremia.

The risk of dilutional states is inversely proportional to the electrolyte concentrations of the injection. The risk of solute overload causing congested states with peripheral and pulmonary edema is directly proportional to the electrolyte concentrations of the injection.

Particular caution is advised in patients at increased risk of and from water and electrolyte disturbances that could be aggravated by increased free water load, hyperglycemia or possibly required insulin administration (See Hyperglycemia).

Hyponatremia
Glucose 5% preparations are isotonic solutions. In the body, however, glucose containing fluids can become extremely physiologically hypotonic due to rapid glucose metabolization.

Monitoring of serum sodium is particularly important for hypotonic fluids. Potassium Chloride in 5% Dextrose Injection, USP has an osmolarity of 292-332 mOsmol/L. Please refer to **Table 1** of SUMMARY PRODUCT INFORMATION for exact osmolarity values.

Depending on the tonicity of the solution, the volume and rate of infusion, and depending on a patient's underlying clinical condition and capability to metabolize glucose, intravenous administration of glucose can cause electrolyte disturbances, most importantly hypo- or hyperosmotic hyponatremia.

High volume infusion must be used under specific monitoring in patients with cardiac or pulmonary failure, and in patients with non-osmotic vasopressin release (including SIADH), due to the risk of hospital-acquired hyponatremia.

Acute hyponatremia can lead to acute hyponatremic encephalopathy (brain edema) characterized by headache, nausea, seizures, lethargy and vomiting. Patients with brain edema are at particular risk of severe, irreversible and life-threatening brain injury.

The risk for developing hyponatremia is increased, for example,

- in children
- in elderly patients
- in women
- postoperatively
- in persons with psychogenic polydipsia
- in patients treated with medications that increase the risk of hyponatremia (see DRUG INTERACTIONS).

The risk for developing hyponatremic encephalopathy is increased, for example,

- in pediatric patients (≤16 years of age)
- in women (in particular, premenopausal women)
- in patients with hypoxemia
- in patients with underlying central nervous system disease

Rapid correction of hyponatremia may cause serious neurologic complications, in particular in pediatric patients (see SPECIAL POPULATIONS/Pediatric Hyponatremia-related Issues).

Preventive and corrective measures must be instituted as clinically indicated.

Hyperglycemia

Rapid administration of dextrose solutions may produce substantial hyperglycemia which may result in or contribute to electrolyte losses, dehydration and hypovolemia due to osmotic diuresis and a hyperosmolar syndrome. At certain clinical conditions it also may increase the risk of hypoosmotic hyponatremia by shifting of intracellular water to extracellular space.

Use with caution in critically ill patients in whom hyperglycemia commonly occurs due to diabetes, impaired glucose tolerance, impaired fasting glucose, or is stress-induced.

Hyperglycemia may increase the risk of cardiac complications, infection, systemic sepsis, acute renal failure and even death in certain clinical conditions, especially in acute stress conditions.

In order to avoid hyperglycemia the infusion rate should not exceed the patient's ability to utilize glucose.

To reduce the risk of hyperglycemia-associated complications, the infusion rate must be adjusted to the level suitable to the patient's ability to utilize glucose and/or insulin administered if blood glucose levels exceed levels considered acceptable for the individual patient.

Potassium Chloride in 5% Dextrose and Injection, USP should be administered with caution in patients with, for example:

- impaired glucose tolerance (such as in diabetes mellitus, renal impairment, or in the presence of sepsis, trauma, or shock),
- severe malnutrition (risk of precipitating a refeeding syndrome),
- thiamine deficiency, e.g., in patients with chronic alcoholism (risk of severe lactic acidosis due to impaired oxidative metabolization of pyruvate),
- water and electrolyte disturbances that could be aggravated by increased glucose and/or free water load (see Risk of Hypo and Hyperosmolality, Serum Electrolytes, and Water Imbalance)

Other groups of patients in whom Potassium Chloride in 5% Dextrose and Injection, USP should be used with caution include:

- Patients with ischemic stroke. Hyperglycemia has been implicated in increasing cerebral ischemic brain damage and impairing recovery after acute ischemic strokes.
- Patients with severe traumatic brain injury (in particular during the first 24 hours following the trauma). Early hyperglycemia has been associated with poor outcomes in patients with severe traumatic brain injury.
- Newborns (see Special Populations/Pediatrics)

Prolonged intravenous administration of dextrose and associated hyperglycemia may result in decreased rates of glucose-stimulated insulin secretion.

Potassium Chloride in 5% Dextrose Injection, USP should be used with caution in patients with overt or subclinical diabetes mellitus.

Hypokalemia

The infusion of solutions with Potassium Chloride in 5% Dextrose Injection, USP may result in Hypokalemia. Hypokalemia can lead to arrhythmias, muscle weakness, paralysis, heart block, and rhabdomyolysis. Potassium Chloride in 5% Dextrose Injection, USP should be used with particular caution, warranting close clinical monitoring, for example:

- in persons with metabolic alkalosis,
- in persons with thyrotoxic or hypokalemic periodic paralysis,
- in persons with increased gastrointestinal losses (e.g., diarrhea, vomiting),
- in persons on prolonged low potassium diet (e.g., undernourished or cachectic patients),
- in persons with primary hyperaldosteronism,

- in patients treated with medications that increase the risk of hypokalemia (e.g. hydrochlorothiazide, loop diuretics, beta-2 agonists, or insulin).

Fructose
This product may contain fructose as an impurity in the dextrose material. Exercise caution when this product is used in patients with hereditary fructose intolerance. In these patients, fructose may result in hypoglycemia, metabolic acidosis, liver toxicity which manifests as vomiting, nausea, sweating, jaundice, hemorrhage, seizures or coma or even death. The severity of the reactions is dependent on the amount and duration of fructose intake.

Refeeding Syndrome
Refeeding severely undernourished patients may result in the refeeding syndrome that is characterized by the shift of potassium, phosphorus, and magnesium intracellularly as the patient becomes anabolic. Thiamine deficiency and fluid retention may also develop. Careful monitoring and slowly increasing nutrient intakes while avoiding overfeeding can prevent these complications.

PRECAUTIONS

Blood
Potassium Chloride in 5% Dextrose Injection, USP should not be administered simultaneously with blood through the same administration set with citrate anticoagulated/preserved blood because of the possibility of pseudoagglutination or hemolysis.

Risk of Air Embolism
Do not use flexible plastic containers in series connections. Such use could result in air embolism due to residual air being drawn from the primary container before administration of the fluid from the secondary container is completed.

Pressurizing intravenous solutions contained in flexible plastic containers to increase flow rates can result in air embolism if the residual air in the container is not fully evacuated prior to administration.

Use of a vented intravenous administration set with the vent in the open position could result in air embolism. Vented intravenous administration sets with the vent in the open position should not be used with flexible plastic containers.

MONITORING AND LABORATORY TESTS

Clinical evaluation and periodic laboratory determinations are necessary to monitor changes in fluid balance, electrolyte concentrations (especially potassium), and acid base balance during prolonged parenteral therapy or whenever the condition of the patient or the rate of administration warrants such evaluation.

SPECIAL POPULATIONS

Pregnancy and Lactation

Pregnancy Category C. Animal reproduction studies have not been conducted with Potassium Chloride in 5% Dextrose and Injection, USP. It is also not known whether Potassium Chloride in 5% Dextrose Injection, USP can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Potassium Chloride in 5% Dextrose Injection, USP should be given to a pregnant woman only if clearly needed.

Intrapartum maternal intravenous dextrose infusion may result in fetal hyperglycemia and metabolic acidosis as well as rebound neonatal hypoglycemia due to fetal insulin production (See Pediatric Glycemia-related Issues).

Healthcare practitioners should carefully consider the potential risks and benefits for each specific patient before administering.

Pediatrics

The infusion rate and volume depends on the age, weight, clinical and metabolic conditions of the patient, concomitant therapy and should be determined by the consulting physician experienced in pediatric intravenous fluid therapy.

Pediatric Glycemia-related Issues

Newborns, especially those born premature and with low birth weight, are at increased risk of developing hypo- or hyperglycemia and therefore need close monitoring during treatment with intravenous dextrose solutions to ensure adequate glycemic control, in order to avoid potential long term adverse effects (See Pregnancy and Lactation).

Hypoglycemia in the newborn can cause:

- prolonged seizures,
- coma, and
- cerebral injury

Hyperglycemia can be fatal in extremely low birth weight neonates and has been associated with:

- cerebral injury, including intraventricular hemorrhage,
- late onset bacterial and fungal infection,
- retinopathy of prematurity,
- necrotizing enterocolitis,
- bronchopulmonary dysplasia
- increased oxygen requirements,
- prolonged length of hospital stay, and
- death

Pediatric Hyponatremia-related Issues

Children (including neonates and older children) are at increased risk of developing hypoosmotic hyponatremia as well as for developing hyponatremic encephalopathy.

The infusion of hypotonic fluids together with the non-osmotic secretion of ADH may result in hyponatremia.

Acute hyponatremia can lead to acute hyponatremic encephalopathy (brain edema) characterized by headache, nausea, seizures, lethargy and vomiting. Patients with brain edema are at particular risk of severe, irreversible and life-threatening brain injury.
Plasma electrolyte concentrations should be closely monitored in the pediatric population.

Rapid correction of hyponatremia is potentially dangerous (risk of serious neurologic complications). Dosage, rate, and duration of administration should be determined by a physician experienced in pediatric intravenous fluid therapy.

Geriatrics
When selecting the type of infusion solution and the volume/rate of infusion for a geriatric patient, consider that geriatric patients are generally more likely to have cardiac, renal, hepatic and other diseases or concomitant drug therapy.

ADVERSE REACTIONS

Post-marketing Adverse Reactions
The following adverse reactions have been reported in the post-marketing experience, listed by MedDRA System Organ Class (SOC), then by Preferred Term in order of severity, where feasible.

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS: Infusion site rash, Infusion site pain.

Other Reactions
Other adverse reactions reported with other similar products include:

IMMUNE SYSTEM DISORDERS: Anaphylactic reaction/Hypersensitivity

METABOLISM AND NUTRITION DISORDERS: Hyperkalemia, Hypokalemia, Hyponatremia

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS: Infusion site reactions, including Infusion site vesicles, Infusion site pruritus, Infusion site phlebitis, Chills, Pyrexia

NERVOUS SYSTEM DISORDERS: Hyponatremic encephalopathy

CARDIAC DISORDERS: Cardiac arrest (as a manifestation of hyperkalemia)

Reactions which may occur because of the solution or the technique of administration include febrile response, infection at the site of injection, venous thrombosis or phlebitis extending from the site of injection, extravasation, and hypervolemia.

If an adverse reaction does occur, discontinue the infusion, evaluate the patient, institute appropriate therapeutic countermeasures, and save the remainder of the fluid for examination if deemed necessary.

DRUG INTERACTIONS

Both the glycemic effects of Potassium Chloride in 5% Dextrose Injection, USP and its effects on water and electrolyte balance should be taken into account when using Potassium Chloride in 5% Dextrose Injection, USP in patients treated with other substances that affect glycemic control, or fluid and/or electrolyte balance.

Potassium Chloride in 5% Dextrose Injection, USP should be used with caution in patients treated concurrently or recently with agents or products that can cause hyperkalemia or increase the risk of hyperkalemia, such as potassium-sparing diuretics (e.g., amiloride, spironolactone, triamterene), corticosteroids, ACE inhibitors, ciclosporin, tacrolimus and drugs that contain potassium. Administration of potassium in patients treated with such agents is associated with an increased risk of severe and potentially fatal hyperkalemia, in particular in the presence of other risk factors for hyperkalemia.

Caution is advised when administering Potassium Chloride in 5% Dextrose Injection, USP to patients treated with drugs leading to an increased vasopressin effect. The below listed drugs increase the vasopressin effect, leading to reduced renal electrolyte free water excretion and may increase the risk of hyponatremia following treatment with i.v. fluids. (see WARNINGS AND PRECAUTIONS and ADVERSE REACTIONS).

Drugs stimulating vasopressin release such as chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors (SSRIs), 3.4-methylenedioxy-N-methamphetamine, ifosfamide, antipsycotics, opioids.

Drugs potentiating vasopressin action such as chlorpropamide, non steroidal anti inflammatories (NSAIDS), cyclophosphamide.

Vasopressin analogues such as desmopressin, oxytocin, vasopressin, terlipressin.

Caution is advised when administering Potassium Chloride in 5% Dextrose Injection, USP to patients treated with drugs that may increase the risk of hyponatremia, such as diuretics and antiepileptics (e.g., oxcarbazepine).

Medications that may increase the risk of sodium and fluid retention, such as corticosteroids or corticotropin.

DOSAGE AND ADMINISTRATION

For intravenous infusion.

The choice of specific potassium chloride and dextrose concentrations, dosage, volume, rate and duration of administration depends on the age, weight, and clinical condition of the patient, concomitant therapy, and administration should be determined by a physician. For patients with electrolyte and glucose abnormalities and for pediatric patients, consult a physician experienced in intravenous fluid therapy.

For 40 mmol Potassium Chloride in 5% Dextrose Injection, USP, hyperosmolar solutions may cause venous irritation and phlebitis. Thus, any hyperosmolar solutions are recommended to be administered through a large central vein, for thorough and rapid dilution of the hyperosmolar solution. See Table 1 for information on the products' osmolarity.

For patients with serum potassium concentration greater than 2.5mmol/L, the recommended infusion rate should not exceed 10mmol/Hour and the recommended daily dose should not exceed 200mmol/d. Higher infusion rates or daily dose limits should be applied with extreme caution.

A gradual increase of flow rate should be considered when starting administration of dextrose-containing products.

Electrolyte supplementation may be indicated according to the clinical needs of the patient.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

Do not administer unless solution is clear and seal is intact.

All injections in VIAFLEX plastic containers are intended for intravenous administration using sterile equipment.

Use of an in-line filter is recommended during administration of all parenteral solutions, where possible.

Additives may be incompatible. Complete information is not available. When introducing additives to Potassium Chloride in 5% Dextrose Injection, USP, the instructions for use of the medication to be added and other relevant literature must be consulted.

Those additives known to be incompatible should not be used. When introducing additives, aseptic technique must be used.

Before adding a substance or medication, verify that it is soluble in and/or stable in Potassium Chloride in 5% Dextrose Injection, USP and that the pH range of Potassium Chloride in 5% Dextrose Injection, USP is appropriate.

After addition, if there is color change and/or the appearance of precipitates, insoluble complexes or crystals, do not use.

Mix thoroughly when additives have been introduced. Do not store solutions containing additives.

For single use only.

Discard any unused portion.

OVERDOSAGE

Excess administration of Potassium Chloride in 5% Dextrose Injection, USP can cause:

- Hyperkalemia. (See Warnings and Precautions) If hyperkalemia is present or suspected, discontinue the infusion immediately and institute close ECG, laboratory and other monitoring and, as necessary, corrective therapy to reduce serum potassium levels. Manifestations of hyperkalemia may include:
    - disturbances in cardiac conduction and arrhythmias, including bradycardia, heart block, asystole, ventricular tachycardia, ventricular fibrillation, and ECG changes (peaking of T waves, loss of P waves, and QRS widening). However, the correlation between potassium levels and ECG changes is not precise, and whether or at which potassium level certain ECG signs develop depends on factors such as patient sensitivity, the presence of other electrolyte disorders and the rapidity of the development of hyperkalemia.
    - hypotension,
    - muscle weakness up to and including muscular and respiratory paralysis, paresthesia of extremities,
    - gastrointestinal symptoms (ileus, nausea, vomiting, abdominal pain).
- Hyperglycemia, adverse effects on water and electrolyte balance, and corresponding complications. For example, severe hyperglycemia, severe dilutional hyponatremia, hyponatremia (which can lead to CNS manifestations including seizures, coma, and cerebral edema) and their complications, can be fatal (See Warnings and Precautions).
- Fluid overload (which can lead to central and/or peripheral edema) (See Warnings and Precautions).

When assessing an overdose, any additives in the solution must also be considered.

Clinically significant overdose of Potassium Chloride in 5% Dextrose Injection, USP may, therefore, constitute a medical emergency.

Interventions include discontinuation of Potassium Chloride in 5% Dextrose Injection, USP administration, dose reduction, calcium chloride, administration of insulin and other measures such as hemodialysis as indicated for the specific clinic constellation.

DOSAGE FORMS, COMPOSITION AND PACKAGING

How Supplied

Potassium Chloride in 5% Dextrose Injection, USP in VIAFLEX plastic container is available as shown in **Table 1.**

Directions for Use of Viaflex Plastic Container
For Information on Risk of Air Embolism – see WARNINGS AND PRECAUTIONS.

To Open
Tear overwrap down side at slit and remove solution container. Visually inspect the container. If the outlet port protector is damaged, detached, or not present, discard container as solution path sterility may be impaired. Some opacity of the plastic due to moisture absorption during the sterilization process may be observed. This is normal and does not affect the solution quality or safety. The opacity will diminish gradually. Check for minute leaks by squeezing inner bag firmly. If leaks are found, discard solution as sterility may be impaired. If supplemental medication is desired, follow directions below.

Preparation for Administration
1. Suspend container from eyelet support.
2. Remove protector from outlet port at bottom of container.
3. Attach administration set. Refer to complete directions accompanying set.

To Add Medication

Warning: Additives may be incompatible.

To add medication before solution administration
1. Prepare medication site.
2. Using syringe with 19 to 22 gauge needle, puncture resealable medication port and inject.
3. Mix solution and medication thoroughly. For high density medication such as potassium chloride, squeeze ports while ports are upright and mix thoroughly.

To add medication during solution administration
1. Close clamp on the set.
2. Prepare medication site.
3. Using syringe with 19 to 22 gauge needle, puncture resealable medication port and inject.
4. Remove container from IV pole and/or turn to an upright position.
5. Evacuate both ports by squeezing them while container is in the upright position.
6. Mix solution and medication thoroughly.
7. Return container to in use position and continue administration.

Storage
Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. Store at 15°C to 25°C.

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Last revised: March 11, 2021