

PRESCRIBING INFORMATION

**Potassium Chloride in 0.45% Sodium Chloride Injection, USP
in Plastic Container**

VIAFLEX Container

20 mmol/L Potassium Chloride in 0.45% Sodium Chloride Injection

Solution for Infusion

Solutions Affecting the Electrolyte Balance

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**Potassium Chloride in 0.45% Sodium Chloride Injection, USP
in Plastic Container (VIAFLEX Plus Container)**

**20 mmol/L Potassium Chloride in 0.45% Sodium Chloride Injection
Electrolyte Replenisher**

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form/ Strength	Clinically Relevant Nonmedicinal Ingredients
Intravenous	Sterile Solution/ 20 mmol/L potassium chloride in 0.45% sodium chloride	Water for injection, USP

INDICATIONS AND CLINICAL USE

Potassium Chloride in 0.45% Sodium Chloride Injection, USP is indicated for:

- Fluid and electrolyte replenishment

CONTRAINDICATIONS

This product is contraindicated in patients with:

- Known hypersensitivity to the product
- Clinical conditions in which the administration of sodium, potassium, or chloride could be detrimental
- Clinically significant hyperkalemia
- Renal failure or renal impairment
- Conditions where potassium retention or sodium retention with edema occurs.

WARNINGS AND PRECAUTIONS

General

The intravenous administration of Potassium Chloride in 0.45% Sodium Chloride Injection, USP can cause fluid and/or solute overloading resulting in dilution of serum electrolyte concentrations, overhydration, congested states or pulmonary edema. 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.

In patients with diminished renal function, administration of Potassium Chloride in 0.45% Sodium Chloride Injection, USP may result in sodium or potassium retention.

Potassium salts should never be administered by IV push.

For patients receiving potassium supplement at greater than maintenance rates, frequent monitoring of serum potassium levels and serial EKGs are recommended.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies with Potassium Chloride in 0.45% Sodium Chloride Injection, USP have not been performed to evaluate carcinogenic potential, mutagenic potential or effects on fertility.

Hypersensitivity reactions

Hypersensitivity/infusion reactions, including anaphylaxis, have been reported with other products containing potassium chloride and sodium chloride. Stop the infusion immediately if signs or symptoms of hypersensitivity/infusion reactions develop. Appropriate therapeutic countermeasures must be instituted as clinically indicated (see **CONTRAINDICATIONS**).

Hyperkalemia

Potassium Chloride in 0.45% Sodium Chloride 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 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 0.45% Sodium Chloride 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 (see **DRUG INTERACTIONS**).

Hyperkalemia can cause cardiac conduction disorders (including complete heart block) and other cardiac arrhythmias at any time during infusion. Continuous ECG monitoring may be necessary to aid in the detection of cardiac arrhythmias due to hyperkalemia (see **ADVERSE REACTIONS**).

Frequently, mild or moderate hyperkalemia is asymptomatic and may be manifested only by increased serum potassium concentrations and, possibly, characteristic ECG changes. However, fatal arrhythmias can develop at any time during hyperkalemia.

Sodium retention, fluid overload, edema, and metabolic disorders

Potassium Chloride in 0.45% Sodium Chloride Injection, USP should be used with particular caution, in patients with or at risk for:

- Conditions that may cause sodium retention, fluid overload and edema (central and peripheral), such as patients with
 - Primary Hyperaldosteronism,
 - Secondary Hyperaldosteronism associated with, for example,
 - Hypertension,
 - congestive heart failure,
 - liver disease (including cirrhosis),
 - renal disease (including renal artery stenosis, nephrosclerosis),
 - Pre-eclampsia.
- Hypermnatremia,
- Hypervolemia,
- Hyperchloremia,
- Metabolic acidosis

Regarding medications that increase the risk of Hyponatremia or sodium and fluid retention, see **DRUG INTERACTIONS**.

Serum electrolytes and water imbalance

Depending on the volume and rate of infusion and depending on a patient's underlying clinical condition, intravenous administration of Potassium Chloride in 0.45% Sodium Chloride Injection, USP can cause:

- Electrolyte disturbances such as
 - Hypermnatremia,
 - Hyponatremia (see Hyponatremia).
- Acid–base imbalance.
- Overhydration/Hypervolemia and, for example, congested states, including central (e.g., pulmonary congestion) and peripheral edema.

Clinical evaluation and periodic laboratory determinations may be necessary to monitor changes in fluid balance, electrolyte concentrations, and acid–base balance during prolonged parenteral therapy or whenever the condition of the patient or dosage and rate of administration warrants such evaluation.

Hyponatremia

Monitoring of serum sodium is particularly important for hypotonic fluids. Potassium Chloride in 0.45% Sodium Chloride Injection, USP has an osmolality of 194 mOsmol/L.

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 Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH)), due to the risk of hospital-acquired hyponatremia.

Potassium Chloride in 0.45% Sodium Chloride Injection, USP should be used with particular caution, in patients with or at risk for hyponatremia, 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.

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.

Severe renal impairment

Potassium Chloride in 0.45% Sodium Chloride 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 0.45% Sodium Chloride Injection, USP may result in sodium retention, fluid overload, and/or may predispose to hyperkalemia.

Air embolism

Do not connect flexible plastic containers in series in order to avoid air embolism due to possible residual air contained in the primary container.

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.

SPECIAL POPULATIONS

Pregnancy and Lactation

Pregnancy Category C. Animal reproduction studies have not been conducted with Potassium Chloride in 0.45% Sodium Chloride Injection, USP. It is also not known whether Potassium Chloride in 0.45% Sodium Chloride Injection, USP can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity.

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Potassium Chloride in 0.45% Sodium Chloride Injection, USP is administered to a nursing mother.

There are no adequate data from the use of Potassium Chloride in 0.45% Sodium Chloride Injection, USP in pregnant or lactating women. Healthcare providers should carefully consider the potential risks and benefits for each specific patient before administering Potassium Chloride in 0.45% Sodium Chloride Injection, USP.

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 a physician experienced in pediatric intravenous fluid therapy. Safety and effectiveness of Potassium Chloride in 0.45% Sodium Chloride Injection, USP in pediatric patients have not been established by adequate and well-controlled studies. However, the use of potassium chloride injection in pediatric patients to treat potassium deficiency states when oral replacement therapy is not feasible is referenced in the medical literature.

Pediatric Hyponatremia-related issues

Children (including neonates and older children) are at increased risk of developing hyponatremia as well as for developing hyponatremic encephalopathy. The infusion of Potassium Chloride in 0.45% Sodium Chloride Injection, USP together with the non-osmotic secretion of ADH (antidiuretic hormone) may result in hyponatremia. Plasma electrolyte concentrations should be closely monitored in the pediatric population.

Geriatric use

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 and/or concomitant drug therapy.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

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.

Symptoms may result from an ion excess or deficit, therefore frequent monitoring of electrolyte levels is essential.

Reactions reported with the use of potassium-containing solutions include nausea, vomiting, abdominal pain, and diarrhea.

Signs and symptoms of potassium intoxication include paresthesias of the extremities, areflexia, muscular or respiratory paralysis, mental confusion, weakness, hypotension, cardiac arrhythmias, heart block, and cardiac arrest.

Potassium-containing solutions are irritating to tissues, therefore extreme care should be taken to avoid perivascular infiltration.

Post-Marketing Adverse Reactions

Other (Class) Reactions

IMMUNE SYSTEM DISORDERS: Hypersensitivity

METABOLISM AND NUTRITIONAL DISORDERS: Hyperkalemia, Hyponatremia, Hypermnatremia, Acidosis hyperchloremic, Fluid overload

CARDIAC DISORDERS: Cardiac arrest as a manifestation of rapid intravenous administration and/or of hyperkalemia.

NERVOUS SYSTEM DISORDERS: Hyponatremic encephalopathy

DRUG INTERACTIONS

Drug-Drug Interactions

No studies have been conducted by Baxter Healthcare Corporation. Caution is advised in patients treated with lithium. Renal sodium and lithium clearance may be increased during administration

of Potassium Chloride in 0.45% Sodium Chloride Injection, USP and this can result in decreased lithium levels.

Potassium Chloride in 0.45% Sodium Chloride 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, ACE inhibitors, angiotensin II receptor antagonists, or the immunosuppressants cyclosporine and tacrolimus.

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 0.45% Sodium Chloride 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, antipsychotics, opioids.

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

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

Potassium Chloride in 0.45% Sodium Chloride Injection, USP should be used with particular caution in patients on concomitant medications that may increase the risk of sodium and fluid retention, such as corticosteroids or corticotrophin.

Potassium Chloride in 0.45% Sodium Chloride Injection, USP should be administered with caution in patients treated on concomitant medications that increase the risk of hyponatremia such as diuretics, and certain antiepileptic and psychotropic medications.

DOSAGE AND ADMINISTRATION

Recommended Dose and Dosage Adjustment

The choice of the specific potassium chloride and sodium chloride formulation, dosage, volume, rate and duration of administration depend on the age, weight and clinical condition of the patient and concomitant therapy. Administration should be determined by a physician experienced in intravenous fluid therapy monitored by laboratory determination.

Frequent laboratory determinations and clinical evaluations are essential to monitor changes in blood glucose, electrolyte concentrations, and fluid and electrolyte balance during prolonged parenteral therapy.

Fluid administration should be based on calculated maintenance of replacement fluid requirements for each patient. In the average adult, daily requirements of sodium, chloride, potassium and fluids can generally be met by the infusion of two litres of 0.45% sodium chloride solution with 20 mmol of potassium chloride.

Administration

To avoid potassium intoxication, do not infuse solutions rapidly.

Infusion rates for the administration of potassium-containing solutions generally should not exceed 10 mmol per hour or 120 mmol per day. The maximum rate of infusion should not exceed 20 mmol per hour in the absence of cardiac monitoring.

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

Potassium Chloride in 0.45% Sodium Chloride Injection, USP in VIAFLEX plastic containers should be infused intravenously using sterile equipment.

The osmolarity of a final admixed infusion solution must be taken into account when peripheral administration is considered. Hyperosmolar solutions may cause venous irritation and phlebitis. Thus, clinically significant Hyperosmolar solutions are recommended to be administered through a large central vein, for rapid dilution of the Hyperosmolar solution. For osmolarity and pH of Potassium Chloride in 0.45% Sodium Chloride Injection, USP please refer to the **Table 1**.

Rapid correction of hyponatremia and hypernatremia is potentially dangerous (risk of serious neurologic complications).

INSTRUCTIONS FOR USE AND HANDLING AND DISPOSAL

Additives may be incompatible. Complete information is not available. Those additives known to be incompatible should not be used. Before adding a substance or medication, verify that it is soluble and stable in Potassium Chloride in 0.45% Sodium Chloride Injection, USP, and that the pH range of Potassium Chloride in 0.45% Sodium Chloride Injection, USP is appropriate. Additional electrolyte supplementation may be indicated according to the clinical needs of the patient. When introducing additives to Potassium Chloride in 0.45% Sodium Chloride Injection, USP, the instructions for use of the medication to be added and other relevant literature must be consulted. Consult with pharmacist, if available. If, in the informed judgment of the physician, it is

deemed advisable to introduce additives, use aseptic technique. After addition, if there is a discoloration 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. Discard any unused portion. For single use only.

DIRECTIONS FOR USE OF VIAFLEX PLUS PLASTIC CONTAINER

Warning: Do not use 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.

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. In the case of damage, the container should be discarded. 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 port 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.

OVERDOSE

Treatment of Overdosage

In the event of a fluid or solute overload during parenteral therapy, re-evaluate the patient's conditions and institute appropriate corrective treatment.

In the event of an overdose with potassium-containing solutions, discontinue the infusion immediately and institute corrective therapy to reduce serum potassium levels as necessary.

Excess administration of Potassium Chloride in 0.45% Sodium Chloride Injection, USP can cause:

- Hyponatremia (which can lead to CNS manifestations including seizures, coma, cerebral edema and death).
- Hypermnatremia, especially in patients with severe renal impairment.
- Hyperkalemia, manifestations of Hyperkalemia may include:
 - disturbances in cardiac conduction and arrhythmias, including bradycardia, heart block, asystole, ventricular tachycardia, ventricular fibrillation,
 - Hypotension,
 - muscle weakness up to and including muscular and respiratory paralysis, paresthesia of extremities,
 - gastrointestinal symptoms (ileus, nausea, vomiting, abdominal pain).
- Fluid overload (which can lead to central and/or peripheral edema).
- See also **WARNINGS AND PRECAUTIONS**; and **ADVERSE REACTIONS**.

Treatment of hyperkalemia includes the following:

1. Elimination of potassium-rich foods, medications, and IV medications containing potassium or medication that can induce hyperkalemia.
2. Dextrose Injection, USP, 10% or 25% containing 10 units of crystalline insulin per 20 grams of dextrose administered intravenously, 300 to 500 mL per hour.
3. Absorption and exchange of potassium using sodium or ammonium cycle cation exchange resin, orally and as retention enema.
4. Use of hemodialysis or peritoneal dialysis.

In treating hyperkalemia in digitalized patients, too rapid a lowering of plasma potassium concentration can cause digitalis toxicity.

When assessing an overdose, any additives in the solution must also be considered. The effects of an overdose may require immediate medical attention and treatment. Interventions include discontinuation of Potassium Chloride in 0.45% Sodium Chloride Injection, USP administration, dose reduction, and other measures as indicated for the specific clinical constellation.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Potassium Chloride in 0.45% Sodium Chloride Injection, USP has value as a source of water and electrolytes. It is capable of inducing diuresis depending on the clinical condition of the patient.

STORAGE AND STABILITY

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. It is recommended that the product be stored at room temperature (15°C-30°C); brief exposure up to 40°C (104°F) does not adversely affect the product.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Description

Potassium Chloride in 0.45% Sodium Chloride Injection, USP is a sterile, nonpyrogenic, solution for fluid and electrolyte replenishment in a single dose container for intravenous administration. It contains no antimicrobial agents. Composition, osmolarity, pH and ionic concentration are shown in **Table 1**.

Table 1

	Size (mL)	Composition (g/L)		*Osmolarity (mOsmol/L) (Calc.)	pH	Ionic Concentration (mmol/L)		
		Sodium Chloride, USP (NaCl)	Potassium Chloride, USP (KCl)			Sodium	Potassium	Chloride
20 mmol/L Potassium Chloride in 0.45% Sodium Chloride	1000	4.5	1.5	194	5.5 (3.5 to 6.5)	77	20	97

* Normal physiologic osmolarity range is approximately 280 to 310 mOsmol/L. Administration of substantially hypertonic solutions (>600 mOsmol/L) may cause vein damage.

Potassium Chloride in 0.45% Sodium Chloride Injection, USP in VIAFLEX Plus Plastic Container is available as follows:

Code	Size (mL)	Product Name
JB1357	1000	20 mmol/L Potassium Chloride in 0.45% Sodium

		Chloride Injection
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The VIAFLEX Plus plastic container is fabricated from a specially formulated polyvinyl chloride (PL 146 Plastic). VIAFLEX Plus on the container indicates the presence of a drug additive in a drug vehicle. The VIAFLEX Plus plastic container system utilizes the same container as the VIAFLEX plastic container system. The amount of water that can permeate from inside the container into the overwrap is insufficient to affect the solution significantly. Solutions in contact with the plastic container can leach out certain of its chemical components in very small amounts within the expiration period, e.g., di-2-ethylhexyl phthalate (DEHP), up to 5 parts per million. However, the safety of the plastic has been confirmed in tests in animals according to USP biological tests for plastic containers as well as by tissue culture toxicity studies.

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For Product Information

1-800-933-0303