



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 18-008/ S-066
NDA 18-037/ S-066
NDA 19-308/ S-023

Baxter Healthcare Corporation
Attention: Amy Giertych, Senior Director,
Global Regulatory Affairs
1620 Waukegan Road, MPGR-AL
McGaw Park, IL 60085

Dear Ms. Giertych:

Please refer to your supplemental new drug applications dated October 20, 2006, received October 25, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for 5% Dextrose, 0.45% Sodium Chloride and Potassium Chloride Injections in Plastic Container (PL 146[®]), 5% Dextrose, 0.2% Sodium Chloride and Potassium Chloride Injections in Plastic Container (PL 146[®]), and Potassium Chloride in 5% Dextrose and 0.9% Sodium Chloride Injections in Plastic Container (PL 146[®]).

These "Changes Being Effected" supplemental new drug applications provide for minor revisions to the package insert.

We completed our review of these applications, as amended. These applications are approved, effective on the date of this letter, for use as recommended in the enclosed final printed labeling (FPL) submitted on October 20, 2006.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Ryan Barraco, Regulatory Project Manager, at (301) 796-0846.

Sincerely,

{See appended electronic signature page}

Brian E. Harvey, M.D., Ph.D.
Director
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure

Baxter

Potassium Chloride in 5% Dextrose and Sodium Chloride Injection, USP in AVIVA Plastic Container

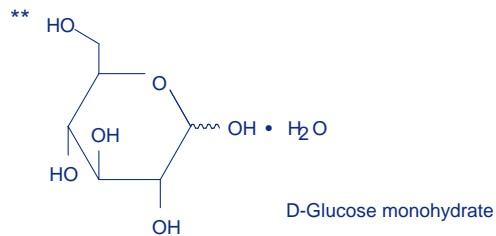
Description

Potassium Chloride in 5% Dextrose and Sodium Chloride 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 (mL)	Composition (g/L)			*Osmolarity (mOsmol/L) (calc.)	pH	Ionic Concentration (mEq/L)			Caloric Content (kcal/L)
		**Dextrose Hydrous, USP	Sodium Chloride, USP (NaCl)	Potassium Chloride, USP (KCl)			Sodium	Potassium	Chloride	
Potassium Chloride in 5% Dextrose and 0.2% Sodium Chloride Injection, USP										
mEq Potassium										
10 mEq	1000	50	2	0.75	341	4.5 (3.5 to 6.5)	34	10	44	170
20 mEq	1000	50	2	1.5	361	4.5 (3.5 to 6.5)	34	20	54	170
10 mEq	500									
30 mEq	1000	50	2	2.24	381	4.5 (3.5 to 6.5)	34	30	64	170
40 mEq	1000	50	2	3	401	4.5 (3.5 to 6.5)	34	40	74	170
Potassium Chloride in 5% Dextrose and 0.33% Sodium Chloride Injection, USP										
mEq Potassium										
20 mEq	1000	50	3.3	1.5	405	4.5 (3.5 to 6.5)	56	20	76	170
10 mEq	500									
30 mEq	1000	50	3.3	2.24	425	4.5 (3.5 to 6.5)	56	30	86	170
40 mEq	1000	50	3.3	3	446	4.5 (3.5 to 6.5)	56	40	96	170
Potassium Chloride in 5% Dextrose and 0.45% Sodium Chloride Injection, USP										
mEq Potassium										
10 mEq	1000	50	4.5	0.75	426	4.5 (3.5 to 6.5)	77	10	87	170
20 mEq	1000	50	4.5	1.5	447	4.5 (3.5 to 6.5)	77	20	97	170
10 mEq	500									
30 mEq	1000	50	4.5	2.24	466	4.5 (3.5 to 6.5)	77	30	107	170
40 mEq	1000	50	4.5	3	487	4.5 (3.5 to 6.5)	77	40	117	170
Potassium Chloride in 5% Dextrose and 0.9% Sodium Chloride Injection, USP										
mEq Potassium										
20 mEq	1000	50	9	1.5	601	4.5 (3.5 to 6.5)	154	20	174	170
40 mEq	1000	50	9	3	641	4.5 (3.5 to 6.5)	154	40	194	170

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



The flexible container is made with non-latex plastic materials specially designed for a wide range of parenteral drugs including those requiring delivery in containers made of polyolefins or polypropylene. For example, the AVIVA container system is compatible with and appropriate for use in the admixture and administration of paclitaxel. In addition, the AVIVA container system is compatible with and appropriate for use in the admixture and administration of all drugs deemed compatible with existing polyvinyl chloride container systems. The solution contact materials do not contain PVC, DEHP, or other plasticizers.

The suitability of the container materials has been established through biological evaluations, which have shown the container passes Class VI U.S. Pharmacopeia (USP) testing for plastic containers. These tests confirm the biological safety of the container system.

The flexible container is a closed system, and air is prefilled in the container to facilitate drainage. The container does not require entry of external air during administration.

The container has two ports: one is the administration outlet port for attachment of an intravenous administration set and the other port has a medication site for addition of supplemental medication (See Directions for Use). The primary function of the overwrap is to protect the container from the physical environment.

Clinical Pharmacology

Potassium Chloride in 5% Dextrose and Sodium Chloride 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 Usage

Potassium Chloride in 5% Dextrose and Sodium Chloride Injection, USP is indicated as a source of water, electrolytes and calories.

Contraindications

Solutions containing dextrose may be contraindicated in patients with known allergy to corn or corn products.

Warnings

Potassium Chloride in 5% Dextrose and Sodium Chloride Injection, USP should be used with great care, if at all, in patients with congestive heart failure, severe renal insufficiency, and in clinical states in which there exists edema with sodium retention.

Potassium Chloride in 5% Dextrose and Sodium Chloride Injection, USP should be used with great care, if at all, in patients with hyperkalemia, severe renal failure, and in conditions in which potassium retention is present.

Injections containing carbohydrates with low electrolyte concentration should not be administered simultaneously with blood through the same administration set because of the possibility of pseudoagglutination or hemolysis. The container label for these injections bears the statement: Do not administer simultaneously with blood.

The intravenous administration of Potassium Chloride in 5% Dextrose and 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 5% Dextrose and Sodium Chloride Injection, USP may result in sodium or potassium retention.

In very low birth weight infants, excessive or rapid administration of dextrose injection may result in increased serum osmolality and possible intracerebral hemorrhage.

Potassium salts should never be administered by IV push.

Precautions

General

Do not connect flexible plastic containers of intravenous solutions in series connections. Such use could result in air embolism due to residual air being drawn from one container before administration of the fluid from a 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.

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

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

Laboratory Tests

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

Drug Interactions

Caution must be exercised in the administration of Potassium Chloride in 5% Dextrose and Sodium Chloride Injection, USP to patients receiving corticosteroids or corticotropin.

Studies have not been conducted to evaluate additional drug/drug or drug/food interactions with Potassium Chloride in 5% Dextrose and Sodium Chloride Injection, USP.

Carcinogenesis, mutagenesis, impairment of fertility

Studies with Potassium Chloride in 5% Dextrose and Sodium Chloride Injection, USP have not been performed to evaluate carcinogenic potential, mutagenic potential or effects on fertility.

Pregnancy: Teratogenic Effects

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

Labor and Delivery

Studies have not been conducted to evaluate the effects of Potassium Chloride in 5% Dextrose and Sodium Chloride Injection, USP on labor and delivery. Caution should be exercised when administering this drug during labor and delivery.

Nursing Mothers

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 5% Dextrose and Sodium Chloride Injection, USP is administered to a nursing mother.

Pediatric Use

Safety and effectiveness of Potassium Chloride in 5% Dextrose and 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.

Dextrose is safe and effective for the stated indications in pediatric patients (see **Indications and Usage**). As reported in the literature, the dosage selection and constant infusion rate of intravenous dextrose must be selected with caution in pediatric patients, particularly neonates and low birth weight infants, because of the increased risk of hyperglycemia/hypoglycemia. Frequent monitoring of serum glucose concentrations is required when dextrose is prescribed to pediatric patients, particularly neonates and low birth weight infants.

Geriatric Use

Clinical studies of Potassium Chloride in 5% Dextrose and Sodium Chloride Injection, USP 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 the responses between 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 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

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.

Dosage and Administration

As directed by a physician. Dosage is dependent upon the age, weight and clinical condition of the patient as well as laboratory determinations.

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 a final filter is recommended during administration of all parenteral solutions, where possible.

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

Additives may be incompatible. Complete information is not available. Those additives known to be incompatible should not be used. Consult with pharmacist, if available. If, in the informed judgment of the physician, it is deemed advisable to introduce additives, use aseptic technique. Mix thoroughly when additives have been introduced. Do not store solutions containing additives.

How Supplied

Potassium Chloride in 5% Dextrose and Sodium Chloride Injection, USP in AVIVA plastic container is available as follows:

Code	Size (mL)	NDC	Product Name
6E1604	1000	0338-6334-04	10 mEq/L Potassium Chloride in 5% Dextrose and 0.2% Sodium Chloride Injection, USP
6E1614	1000	0338-6335-04	20 mEq/L Potassium Chloride in 5% Dextrose and 0.2% Sodium Chloride Injection, USP
6E1613	500	0338-6335-03	
6E1624	1000	0338-6336-04	30 mEq/L Potassium Chloride in 5% Dextrose and 0.2% Sodium Chloride Injection, USP
6E1634	1000	0338-6337-04	40 mEq/L Potassium Chloride in 5% Dextrose and 0.2% Sodium Chloride Injection, USP
6E1474	1000	0338-6348-04	20 mEq/L Potassium Chloride in 5% Dextrose and 0.33% Sodium Chloride Injection, USP
6E1473	500	0338-6348-03	

6E1484	1000	0338-6349-04	30 mEq/L Potassium Chloride in 5% Dextrose and 0.33% Sodium Chloride Injection, USP
6E1494	1000	0338-6350-04	40 mEq/L Potassium Chloride in 5% Dextrose and 0.33% Sodium Chloride Injection, USP
6E1644	1000	0338-6329-04	10 mEq/L Potassium Chloride in 5% Dextrose and 0.45% Sodium Chloride Injection, USP
6E1654	1000	0338-6330-04	20 mEq/L Potassium Chloride in 5% Dextrose and 0.45% Sodium Chloride Injection, USP
6E1653	500	0338-6330-03	
6E1664	1000	0338-6331-04	30 mEq/L Potassium Chloride in 5% Dextrose and 0.45% Sodium Chloride Injection, USP
6E1674	1000	0338-6332-04	40 mEq/L Potassium Chloride in 5% Dextrose and 0.45% Sodium Chloride Injection, USP
6E2434	1000	0338-6342-04	20 mEq/L Potassium Chloride in 5% Dextrose and 0.9% Sodium Chloride Injection, USP
6E2454	1000	0338-6343-04	40 mEq/L Potassium Chloride in 5% Dextrose and 0.9% Sodium Chloride Injection, USP

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. It is recommended the product be stored at room temperature (25°C); brief exposure up to 40°C does not adversely affect the product.

Directions for Use of AVIVA Plastic Container

To Open

Tear overwrap down side at slit and remove solution container. Moisture and 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

Caution: Do not use plastic containers in series connections.

Caution: Use only with a non-vented set or a vented set with the vent closed.

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

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.

Baxter Healthcare Corporation

Deerfield, IL 60015 USA

07-19-50-548

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/s/

Brian Harvey
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