CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

18896Orig1s011

Trade Name:	**Potassium Acetate Injection**
Generic or Proper Name:	
Sponsor:	HOSPIRA INC
Approval Date:	February 16, 2001
Indication:	**Potassium Acetate Injection** is indicated as a source of potassium, for the addition to large volume intravenous fluids, to prevent or correct hypokalemia in patients with restricted or no oral intake. It is also useful as an additive for preparing specific intravenous fluid formulas when the needs of the patient cannot be met by standard electrolyte or nutrient solutions.

CENTER FOR DRUG EVALUATION AND RESEARCH

18896Orig1s011

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APPLICATION NUMBER:

18896Orig1s011

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 18-801/S-020
NDA 18-803/S-014
NDA 18-892/S-020
NDA 18-893/S-016
NDA 18-895/S-011
NDA 18-896/S-011
NDA 18-897/S-015
NDA 18-947/S-015
NDA 18-959/S-010
NDA 18-960/S-012
NDA 18-961/S-011
NDA 18-962/S-010

Abbott Laboratories
Hospital Products Division
Attention: Christine L. Henke
Specialist, Regulatory Affairs
D-389, Bldg. AP20
200 Abbott Park Road
Abbott Park, Illinois 60064-6157

Dear Ms. Henke:

Please refer to your supplemental new drug applications dated March 24, 2000, received March 27, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following drug products:

NDA 18-801/S-020	Sterile Water for Injection in Plastic Vials
NDA 18-803/S-014	0.9% Sodium Chloride Injection in Plastic Vials
NDA 18-892/S-020	Sodium Phosphates Injection in Plastic Vials
NDA 18-893/S-016	Sodium Acetate Injection in Plastic Vial
NDA 18-895/S-011	TPN Electrolytes in Plastic Vials
NDA 18-896/S-011	Potassium Acetate Injection in Plastic Vials
NDA 18-897/S-015	Sodium Chloride 50 mEq & 100 mEq in Plastic Vials
NDA 18-947/S-015	Sodium Lactate Injection in Plastic Vials
NDA 18-959/S-010	Zinc Chloride Injection
NDA 18-960/S-012	Cupric Chloride Injection
NDA 18-961/S-011	Chromic Chloride Injection
NDA 18-962/S-010	Manganese Chloride Injection

We acknowledge receipt of your submissions dated October 6, 2000. Your submission of October 6, 2000, constituted a complete response to our July 26, 2000, action letter.

These supplemental new drug applications provide for modifications to the (b) (4) Vial closure system for the above referenced (b) (4) small volume parenteral products packaged in plastic vials.

We have completed the review of these supplemental applications, and they are approved.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Steve McCort, Regulatory Project Manager, at (301) 827-6415.

Sincerely,

{See appended electronic signature page}

Duu-Gong Wu, Ph.D.
Chemistry Team Leader II, DNDC II for the
Division of Metabolic and
Endocrine Drug Products, HFD-510
DNDC II, Office of New Drug Chemistry

/s/

Duu-gong Wu
2/16/01 03:11:44 PM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

18896Orig1s011

LABELING

20 mL Single-dose

POTASSIUM ACETATE

Injection, USP

40 mEq (2 mEq/mL)

CAUTION: MUST BE DILUTED.
FOR I.V. USE.

ABBOTT LABS., N. CHICAGO, IL 60064, USA

K+

NDC 0074-8183-01

Each mL contains potassium acetate, anhyd. 196 mg. 4 mOsmol/mL (calc). pH 6.2 (5.5 to 8.0). May contain acetic acid for pH adjustment. Sterile, nonpyrogenic. Usual dose: See insert. Use only if clear and seal is intact and undamaged. Contains no bacteriostat; use promptly, discard unused portion. Contains no more than 200 mcg/L of aluminum.

℞ only

58-3832-3/R12-10/02

USE ASEPTIC TECHNIQUE

Remove cover from Fliptop vial and cleanse stopper with antiseptic.
Add to a suitable solution in an I.V. container.

Store at controlled room temperature 15° to 30°C (59° to 86°F).

257

20 mL Single-dose

POTASSIUM ACETATE Injection, USP
40 mEq (2 mEq/mL)

℞ only

ABBOTT LABORATORIES, N. CHICAGO, IL 60064, USA

CAUTION:
MUST BE DILUTED.
FOR I.V. USE.

25 Units/**NDC 0074-8183-01**

20 mL Single-dose

POTASSIUM ACETATE Injection, USP
40 mEq (2 mEq/mL)

℞ only

ABBOTT LABORATORIES, N. CHICAGO, IL 60064, USA

CAUTION:
MUST BE DILUTED.
FOR I.V. USE.

25 Units/**NDC 0074-8183-01**

(01) 1 030074 818301 8

Each mL contains potassium acetate, 196 mg.
May contain acetic acid for pH adjustment.
4 mOsmol/mL (calc). pH 6.2 (5.5 to 8.0).
Usual dose: See insert.
Sterile, nonpyrogenic.

Aseptically add to a suitable I.V. solution. Contains no bacteriostat; use promptly; discard unused portion. Use only if clear and seal is intact and undamaged.

98-4482.3/R7-10/98

Printed in USA

POTASSIUM ACETATE
Injection, USP
40 mEq in 20 mL
(2 mEq K^+ and 2 mEq CH_3COO^-/mL)
FOR ADDITIVE USE ONLY AFTER DILUTION IN I.V. FLUIDS
Plastic Vial ℞ only

DESCRIPTION
Potassium Acetate Injection, USP, 40 mEq (2 mEq/mL) is a sterile, nonpyrogenic, *concentrated solution* of potassium acetate in water for injection. The solution is administered after dilution by the intravenous route as an electrolyte replenisher. *It must not be administered undiluted.*

58- 6820 -R13-Rev. April, 2002

Each 20 mL vial contains 3.93 g of potassium acetate which provides 40 mEq each of potassium (K^+) and acetate (CH_3COO^-). It contains no bacteriostat, antimicrobial agent or added buffer. May contain acetic acid for pH adjustment. pH 6.2 (5.5 to 8.0). The osmolar concentration is 4 mOsmol/mL (calc.).

The solution is intended as an alternative to potassium chloride to provide potassium ion (K^+) for addition to large volume infusion fluids for intravenous use.

Potassium acetate, USP is chemically designated CH_3COOK, colorless crystals or white crystalline powder very soluble in water.

The semi-rigid vial is fabricated from a specially formulated polyolefin. It is a copolymer of ethylene and propylene. The safety of the plastic has been confirmed by tests in animals according to USP biological standards for plastic containers. The container requires no vapor barrier to maintain the proper drug concentration.

CLINICAL PHARMACOLOGY

As the principal cation of the intracellular fluid, potassium plays an important role in fluid and electrolyte balance. The normal potassium concentration in the intracellular fluid compartment is about 160 mEq/liter. The normal serum potassium range is 3.5 to

5.0 mEq/liter. The kidney normally regulates potassium balance but does not conserve potassium as well or as promptly as it conserves sodium. The daily turnover of potassium in the normal adult averages 50 to 150 mEq (milliequivalents) and represents 1.5 to 5% of the total potassium content of the body.

Acetate (CH_3COO^-), a source of hydrogen ion acceptors, is an alternate source of bicarbonate (HCO_3^-) by metabolic conversion in the liver. This has been shown to proceed readily, even in the presence of severe liver disease.

INDICATIONS AND USAGE

Potassium Acetate Injection, USP, 40 mEq is indicated as a source of potassium, for the addition to large volume intravenous fluids, to prevent or correct hypokalemia in patients with restricted or no oral intake. It is also useful as an additive for preparing specific intravenous fluid formulas when the needs of the patient cannot be met by standard electrolyte or nutrient solutions.

CONTRAINDICATIONS

Potassium administration is contraindicated in patients with severe renal insufficiency or adrenal insufficiency and in diseases where high potassium levels may be encountered.

WARNINGS

Potassium Acetate Injection, USP, 40 mEq must be diluted before use.

To avoid potassium intoxication, infuse potassium-containing solutions slowly. Potassium replacement therapy should be monitored whenever possible by continuous or serial electrocardiography (ECG). Serum potassium levels are not necessarily dependable indicators of tissue potassium levels.

Solutions which contain potassium ions 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.

In patients with diminished renal function, administration of solutions containing potassium ions may result in potassium retention.

Solutions containing acetate ions should be used with great care in patients with metabolic or respiratory alkalosis. Acetate should be administered with great care in those conditions in which there is an increased level or an impaired utilization of this ion, such as severe hepatic insufficiency.

WARNING: This product contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature

neonates are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which contain aluminum.

Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than 4 to 5 mcg/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

PRECAUTIONS

Do not administer unless solution is clear and seal is intact. Discard unused portion.

Potassium replacement therapy should be guided primarily by ECG monitoring and secondarily by the serum potassium level.

High plasma concentrations of potassium may cause death by cardiac depression, arrhythmias or arrest.

Use with caution in the presence of cardiac disease, particularly in digitalized patients or in the presence of renal disease.

Solutions containing acetate ion should be used with caution as excess administration may result in metabolic alkalosis.

Pregnancy Category C.
Animal reproduction studies have not been conducted with potassium acetate. It is also not known whether potassium acetate can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Potassium acetate should be given to a pregnant woman only if clearly needed.

Pediatric Use: The safety and effectiveness of potassium acetate have been established in pediatric patients.

Geriatric Use: An evaluation of current literature revealed no clinical experience identifying differences in response 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 other drug therapy.

Potassium ions are known to be substantially excreted by the kidney, and the risk of toxic reactions 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

Adverse reactions involve the possibility of potassium intoxication. The signs and symptoms of potassium intoxication include paresthesias of the extremities, flaccid paralysis, listlessness, mental confusion, weakness and heaviness of the legs, hypotension, cardiac arrhythmias, heart block, electrocardiographic abnormalities such as disappearance of P waves, spreading and slurring of the QRS complex with development of a biphasic curve and cardiac arrest. See WARNINGS and PRECAUTIONS.

OVERDOSAGE

In the event of overdosage, discontinue infusion containing potassium acetate immediately and institute corrective therapy as indicated to reduce elevated serum potassium levels and restore acid-base balance if necessary. See WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.

DOSAGE AND ADMINISTRATION

Potassium Acetate Injection, USP, 40 mEq is administered intravenously *only after dilution in a larger volume of fluid.* The dose and rate of administration are dependent upon the individual needs of the patient. ECG and serum potassium should be monitored as a guide to dosage. Using aseptic technique, all or part of the contents of one or more vials may be added to other intravenous fluids to provide any desired number of milliequivalents (mEq) of potassium (K^+) with an equal number of milliequivalents of acetate (CH_3COO^-).

Maximum infusion rate: The infusion rate should not exceed 1 mEq/kg/hr.

Normal daily requirements:

Newborn:	2-6 mEq/kg/24 hr.
Children:	2-3 mEq/kg/24 hr.
Adult:	40-80 mEq/24 hr.

Intraosseous infusion can be an alternate route for drug administration when intravenous access is not readily available.

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

HOW SUPPLIED

Potassium Acetate Injection, USP, 40 mEq (2 mEq/mL) of K^+ is supplied in a 20 mL partial-fill single-dose fliptop vial (List 8183).

Each container is partially filled to provide air space for complete vacuum withdrawal of the contents into the I.V. container.

Store at controlled room temperature 15° to 30°C (59° to 86°F) (see USP).

Printed in USA

ABBOTT LABORATORIES, NORTH CHICAGO, IL 60064, USA

POTASSIUM ACETATE
Injection, USP
40 mEq in 20 mL
(2 mEq K^+ and 2 mEq CH_3COO^-/mL)
FOR ADDITIVE USE ONLY AFTER DILUTION IN I.V. FLUIDS
Plastic Vial

℞ only

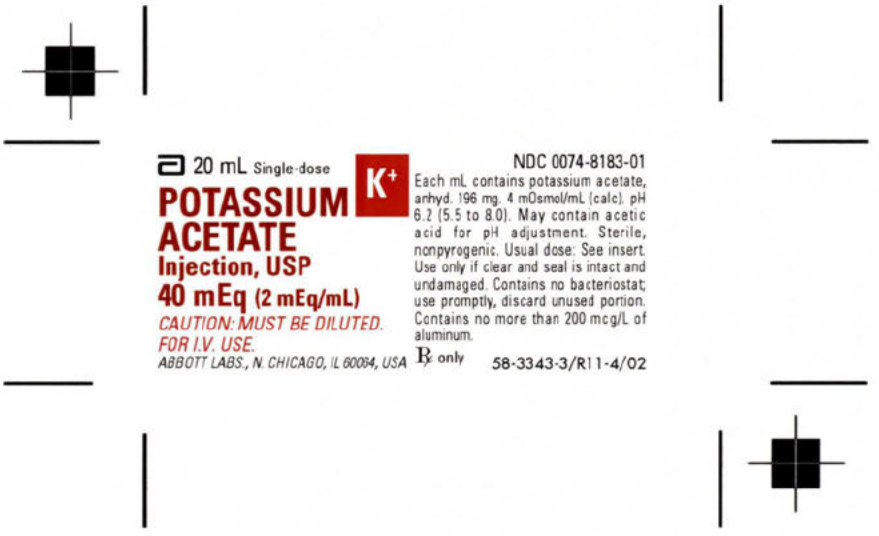
DESCRIPTION

Potassium Acetate Injection, USP, 40 mEq (2 mEq/mL) is a sterile, nonpyrogenic, *concentrated solution* of potassium acetate in water for injection. The solution is administered after dilution by the intravenous route as an electrolyte replenisher. *It must not be administered undiluted.*

58- 6820 -R13-Rev. April, 2002

APPROVED

DEC 24 2002



20 mL Single-dose

POTASSIUM ACETATE
Injection, USP
40 mEq (2 mEq/mL)

CAUTION: MUST BE DILUTED.
FOR I.V. USE.

ABBOTT LABS., N. CHICAGO, IL 60064, USA

K^+

NDC 0074-8183-01

Each mL contains potassium acetate, anhyd. 196 mg, 4 mOsmol/mL (calc), pH 6.2 (5.5 to 8.0). May contain acetic acid for pH adjustment. Sterile, nonpyrogenic. Usual dose: See insert. Use only if clear and seal is intact and undamaged. Contains no bacteriostat; use promptly, discard unused portion. Contains no more than 200 mcg/L of aluminum.

℞ only

58-3343-3/R11-4/02

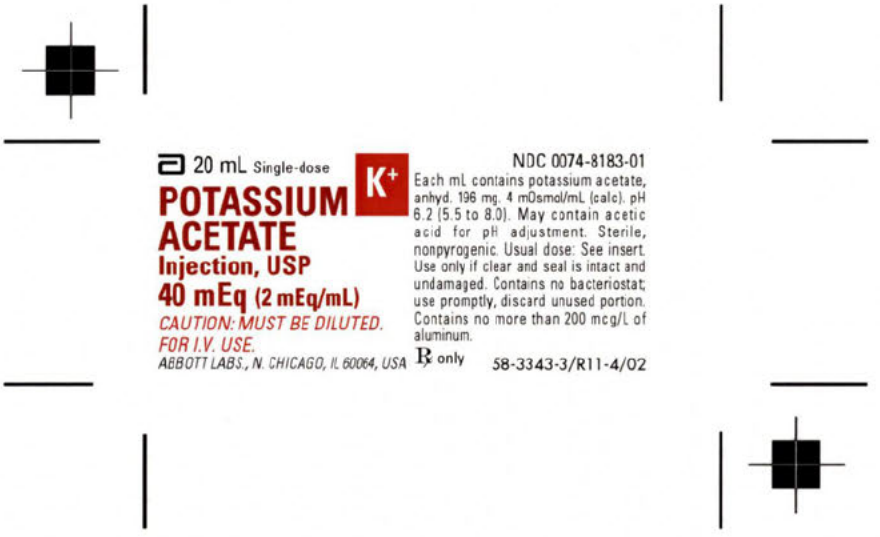
Labeling: SCS-012 BL

NDA No 18896 Rec'd 8-16-02

Reviewed by: [signature] 1/28/03

APPROVED

DEC 2 4 2002



20 mL Single-dose

POTASSIUM ACETATE
Injection, USP
40 mEq (2 mEq/mL)

K+

CAUTION: MUST BE DILUTED. FOR I.V. USE.

ABBOTT LABS., N. CHICAGO, IL 60064, USA

NDC 0074-8183-01

Each mL contains potassium acetate, anhyd. 196 mg. 4 mOsmol/mL (calc). pH 6.2 (5.5 to 8.0). May contain acetic acid for pH adjustment. Sterile, nonpyrogenic. Usual dose: See insert. Use only if clear and seal is intact and undamaged. Contains no bacteriostat; use promptly, discard unused portion. Contains no more than 200 mcg/L of aluminum.

℞ only

58-3343-3/R11-4/02

Labeling: SES→12 BL

NDA No 18996 Rec'd 8.16→2

Reviewed by: VDa

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

18896Orig1s011

CLINICAL MICROBIOLOGY/VIROLOGY REVIEW(S)

CONSULTATIVE REVIEW FOR HFD-510
MICROBIOLOGIST'S REVIEW #2 OF NDA 18-801/S-020
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY REVIEW STAFFDecember
December 27, 2000

A. 1. NDAs:

18-801/S-020	**18-897/S-015**
18-803/S-014	**18-947/S-015**
18-892/S-020	**18-959/S-010**
18-893/S-016	**18-960/S-012**
18-895/S-011	**18-961/S-011**
18-896/S-011	**18-962/S-010**

NAME AND ADDRESS OF APPLICANT:
Abbott Laboratories
Hospital Products Division
200 Abbott Park, Illinois 60064-3537

2. NAME OF DRUG:

NDA 18-801 Sterile Water for Injection in Plastic Vials
NDA 18-803 0.9% Sodium Chloride Injection in Plastic Vials
NDA 18-892 Sodium Phosphates Injection in Plastic Vials
NDA 18-893 Sodium Acetate Injection in Plastic vials
NDA 18-895 TPN Electrolytes in Plastic Vials
` **NDA 18-896 Potassium Acetate Injection in Plastic Vials**
NDA 18-897 Sodium Chloride 50 mEq & 100 mEq in Plastic Vials
NDA 18-947 Sodium Lactate Injection in Plastic Vials
NDA 18-959 Zinc Chloride Injection
NDA 18-960 Cupric Chloride Injection
NDA 18-961 Chromic Chloride Injection
NDA 18-962 Manganese Chloride Injection

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: Sterile small volume parenterals for intravenous administration, supplied in 10 mL, 15 mL/20 mL and 20 mL plastic (b) (4) **Vials. Rx**

4. METHOD OF STERILIZATION: (b) (4)

5. PHARMACOLOGICAL CATEGORY AND/OR PRINCIPAL INDICATION:
Small volume parenterals to be used as a drug diluent, source of sodium, or supplement for total parenteral nutrition (TPN).

6. DRUG PRIORITY CLASSIFICATION: N/A

B. 1. DATE OF INITIAL SUBMISSION: March 24, 2000 (Review #1)

2. AMENDMENTS:

(1) May 23, 2000 (Review #1)

(2). October 6, 2000 (Review #2)
ASSIGNED FOR REVIEW: October 31, 2000
(3) December 14, 2000 (Review #2)
(4) December 20, 2000 (Review #2)

3. SUPPORTING DOCUMENTS: (b) (4) (b) (4)

C. REMARKS:

The subject supplements provide for "minor" modifications to the closure system of (b) (4) **plastic vials used for the small volume parenteral drug products listed above.**

The amendment of October 6, 2000 responds to the Agency's letter of July 26, 2000 in which requests were made for additional information and data in support of sterility assurance.

The amendments of December 14 and 20, 2000 respond to requests made in a telephone conversation held on December 8, 2000 between V. Greenman (HFD-805) and Christine Hanke, Jill Sackett and Tom May of Abbott Laboratories.

D. CONCLUSIONS AND RECOMMENDATIONS

Recommend approval of the supplements for sterility assurance of the plastic (b) (4) **vials with the modified closure system. See Review Notes.**

_____
Vivian Greenman

cc:
Original NDA 18-801
HFD-160/Consult File
HFD-510/CSO/Steve McCort
Chemist/David Lewis
HFD-805/V. Greenman
Drafted by: V. Greenman
R/D initialed by: P. Cooney
Filename, C:\NDA18801.S20R2

(b) (4) **and all positive and negative controls were satisfactory. The study performed** (b) (4) (b) (4) (b) (4) **This study supports container/closure integrity** (b) (4) (b) (4)

SATISFACTORY

APPEARS THIS WAY ON ORIGINAL

/s/

Vivian Greenman
1/9/01 03:06:25 PM
MICROBIOLOGIST

Peter Cooney
1/9/01 04:28:17 PM
MICROBIOLOGIST

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

18896Orig1s011

ADMINISTRATIVE AND CORRESPONDENCE DOCUMENTS

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: February 5th, 2001

FROM: David B. Lewis, Ph.D., reviewer, DNDCII, ONDC

SUBJECT: Microbiology Review # 2, dated January 10th, 2001

TO: **NDA 18-801/S-020 Division File.**

CC the following HFD-510 Division Files:

- **NDA 18-803/S-014**
- **NDA 18-803/S-020**
- **NDA 18-892/S-020**
- **NDA 18-893/S-016**
- **NDA 18-896/S-011**
- **NDA 18-897/S-015**
- **NDA 18-947/S-015**
- **NDA 18-959/S-010**
- **NDA 18-960/S-012**
- **NDA 18-961/S-011**
- **NDA 18-962/S-010**

CC the following HFD-110 Division File:

- **NDA 19-030/S-012**

The firm responded to a list of deficiencies/information requests from V. Greenman (Microbiology Reviewer). These responses were covered in Microbiology Review # 2, dated 1-10-01. The application is now approvable, from the standpoint of sterility assurance, and is now approvable, regarding chemistry, manufacturing and controls information. An approval letter may be issued.

<u>Conclusion</u>: The bundled application is now approvable, regarding chemistry, manufacturing and controls.

/s/

David Lewis
2/9/01 03:14:00 PM
CHEMIST
CMC information is now adequate. An approval letter may now be issued . Summary in attached memorandum.
Here is the memo, regarding the microbiology approval for the (b) (4)-modification bundle [Abbott]. All eleven other bundle members are included for this memo. Need your electronic concurrence.

Duu-gong Wu
2/9/01 03:20:34 PM
CHEMIST