

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-559

APPROVED LABELING

INFUVITE® ADULT
PHARMACY BULK PACKAGE
Multiple Vitamins for Infusion

Rx only.

For intravenous infusion after dilution only.

Pharmacy Bulk Package – Not for Direct Infusion

DESCRIPTION

INFUVITE® ADULT (PHARMACY BULK PACKAGE) is a sterile product consisting of 2 vials – 1 each of Vial 1 (50 mL) and Vial 2 (50 mL Fill in 100 mL Vial), provided as a pharmacy bulk package.

A pharmacy bulk package is a container of a sterile preparation for parenteral use that contains many single doses. The contents are intended for use in a pharmacy admixture program and are restricted to the preparation of admixtures for intravenous infusion.

Each 5 mL of Vial 1* contains:

Ascorbic acid (Vitamin C).....	200 mg
Vitamin A** (as palmitate).....	3 300 IU
Vitamin D ₃ ** (cholecalciferol).....	200 IU
Thiamine (Vitamin B ₁) (as the hydrochloride).....	6 mg
Riboflavin (Vitamin B ₂) (as riboflavin 5-phosphate sodium).....	3.6 mg
Pyridoxine HCl (Vitamin B ₆).....	6 mg
Niacinamide.....	40 mg
Dexpanthenol (as <i>d</i> -pantothenyl alcohol).....	15 mg
Vitamin E** (<i>dl</i> - α -tocopheryl acetate).....	10 IU
Vitamin K**.....	150 mcg

* with 1.4 % polysorbate 80, sodium hydroxide and/or hydrochloric acid for pH adjustment and water for injection.

** Polysorbate 80 is used to water solubilize the oil-soluble vitamins A, D, E and K.

Each 5 mL of Vial 2† contains:

Folic acid.....	600 mcg
Biotin.....	.60 mcg
Vitamin B ₁₂ (cyanocobalamin).....	5 mcg

† with 30 % propylene glycol, citric acid and/or sodium citrate for pH adjustment and water for injection.

"Aqueous" multiple vitamin preparation for intravenous infusion:

INFUVITE® ADULT (PHARMACY BULK PACKAGE) (Multiple Vitamins for Infusion) makes available a combination of important oil-soluble and water-soluble vitamins in an aqueous solution, formulated for incorporation into intravenous solutions. The liposoluble vitamins A, D, E and K have been solubilized in an aqueous medium with polysorbate 80, permitting intravenous administration of these vitamins.

INDICATIONS AND USAGE

INFUVITE® ADULT (PHARMACY BULK PACKAGE) is indicated as a daily multivitamin maintenance supplement for adults and children aged 11 and older receiving parenteral nutrition.

INFUVITE® ADULT (PHARMACY BULK PACKAGE) is also indicated in other situations where administration by the intravenous route is required. Such situations include surgery, extensive burns, fractures and other trauma, severe infectious diseases, and comatose states, which may provoke a "stress" situation with profound alterations in the body's metabolic demands and consequent tissue depletion of nutrients.

The physician should not await the development of clinical signs of vitamin deficiency before initiating vitamin therapy.

INFUVITE® ADULT (PHARMACY BULK PACKAGE) (administered in intravenous fluids under proper dilution) contributes intake of necessary vitamins toward maintaining the body's normal resistance and repair processes.

Patients with multiple vitamin deficiencies or with markedly increased requirements may be given multiples of the daily dosage for two or more days, as indicated by the clinical status.

Some patients do not maintain adequate levels of certain vitamins when a multiple vitamin preparation, such as **INFUVITE® ADULT (PHARMACY BULK PACKAGE)**, in recommended amounts, is the sole source of vitamins. Blood levels of vitamins A, C, D and folic acid may decline in patients receiving parenteral multivitamins as their sole source of vitamins for 4 to 6 months. Therefore, in patients for whom total parenteral nutrition will be continued for long periods of time blood vitamin concentrations should be monitored to ensure maintenance of adequate levels. If deficiencies appear to be developing, multiples of the formulation (1.5 to 3 times) may be needed for a period of time. When multiples of the formulation are used for more than a few weeks, vitamins A and D should be monitored occasionally to be certain that an excess accumulation of these vitamins is not occurring.

CONTRAINDICATIONS

INFUVITE® ADULT (PHARMACY BULK PACKAGE) is contraindicated where there is a pre-existing hypervitaminosis, or a known hypersensitivity to any of the vitamins or excipients in the product.

Allergic reactions have been known to occur following intravenous administration of thiamine, and vitamin K. The formulation is contraindicated prior to blood sampling for detection of megaloblastic anemia, as the folic acid and the cyanocobalamin in the vitamin solution can mask serum deficits.

WARNINGS

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 solution, 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 $\mu\text{g}/\text{kg}/\text{day}$ accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

PRECAUTIONS

If this formulation is the only source of vitamins for long periods of time, blood concentration of each of the vitamins should be monitored, particularly vitamins A, C, D and folic acid, to determine if deficiencies are occurring. If deficiencies are developing or when long-standing vitamin deficiencies are present, it may be necessary to add therapeutic amounts of certain vitamins to supplement the maintenance vitamins provided in **INFUVITE[®] ADULT (PHARMACY BULK PACKAGE)**.

Drug – Drug/Solution Interactions:

Caution should be exercised when administering **INFUVITE[®] ADULT (PHARMACY BULK PACKAGE)** to patients on warfarin sodium-type anticoagulant therapy. In such patients, vitamin K may antagonize the hypotherbinemic response to anticoagulant drugs, such as warfarin and its congeners. Therefore, periodic monitoring of prothrombin/INR response is essential in determining the appropriate dosage of anticoagulant therapy.

INFUVITE[®] ADULT (PHARMACY BULK PACKAGE) (Multiple Vitamins for Infusion) is not physically compatible with alkaline solutions or moderately alkaline drugs such as Acetazolamide, Chlorothiazide sodium, Aminophylline or sodium bicarbonate. Tetracycline HCl and ampicillin may not be physically compatible with **INFUVITE[®] ADULT (PHARMACY BULK PACKAGE)**. Also, it has been reported that folic acid is unstable in the presence of calcium salts such as calcium gluconate. Direct addition to intravenous fat emulsions is not recommended. Consult appropriate references for listings of physical compatibility of solutions and drugs with the vitamin infusion. In such circumstances, admixture or Y-site administration with vitamin solutions should be avoided.

A number of interactions between vitamins and drugs have been reported which may affect the metabolism of either agent. The following are examples of these types of interactions.

Folic acid may lower the serum concentration of phenytoin resulting in increased seizure activity. Conversely, phenytoin may decrease serum folic acid concentrations and, therefore, should be avoided in pregnancy. Folic acid may decrease the patient's response to methotrexate therapy.

Pyridoxine may decrease the efficacy of levo-dopa by increasing its metabolism. Concomitant administration of hydralazine or isoniazid may increase pyridoxine requirements.

In patients with pernicious anemia, the hematologic response to vitamin B₁₂ therapy may be inhibited by concomitant administration of chloramphenicol.

Several vitamins have been reported to decrease the activity of certain antibiotics. Thiamine, riboflavin, pyridoxine, niacinamide and ascorbic acid have been reported to decrease the antibiotic activity of erythromycin, kanamycin, streptomycin, oxycycline and lincomycin. Bleomycin is inactivated *in vitro* by ascorbic acid and riboflavin.

Vitamin K may antagonize the hypoprothrombinemic effect of oral anticoagulants (*see bolded statement above*).

Consult appropriate references for additional specific vitamin-drug interactions.

Some of the vitamins in **INFUVITE[®] ADULT (PHARMACY BULK PACKAGE)** may react with vitamin K bisulfite or sodium bisulfite; if bisulfite solutions are necessary, patients should be monitored for vitamin A and thiamine deficiencies.

Drug-Laboratory Test Interactions:

Ascorbic acid in the urine may cause false negative urine glucose determinations.

Carcinogenesis, Mutagenesis, and Impairment of Fertility: Carcinogenicity, mutagenicity and fertility studies have not been performed with **INFUVITE[®] ADULT (PHARMACY BULK PACKAGE)**.

Pregnancy: **Pregnancy Category C:** Animal reproduction studies have not been conducted with **INFUVITE[®] ADULT (PHARMACY BULK PACKAGE)** (Multiple Vitamins for Infusion). **INFUVITE[®] ADULT (PHARMACY BULK PACKAGE)** should be given to a pregnant woman only if clearly needed. Pregnant women should follow the U.S. Recommended Daily Allowances for their condition, because their vitamin requirements may exceed those of nonpregnant women. The use of **INFUVITE[®] ADULT** has not been studied in human pregnancy.

Nursing Mothers: Lactating women should follow the U.S. Recommended Daily Allowances for their condition, because their vitamin requirement may exceed those of nonlactating women. 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 **INFUVITE® ADULT (PHARMACY BULK PACKAGE)** is administered to a nursing mother.

Pediatric Use: Safety and effectiveness in children below the age of 11 years have not been established.

ADVERSE REACTIONS

There have been rare reports of anaphylactoid reactions following parenteral multivitamin administration. Rare reports of anaphylactoid reactions have also been reported following large intravenous doses of thiamine. However, the risk is negligible if thiamine is co-administered with other vitamins of the B group.

There have been rare reports of the following types of reactions:

Dermatologic - rash, erythema, pruritis

CNS - headache, dizziness, agitation, anxiety

Ophthalmic - diplopia

Allergic - urticaria, shortness of breath, wheezing and angioedema.

OVERDOSAGE

The fat-soluble vitamins A, D and E can accumulate to harmful levels. The possibility of hypervitaminosis A or D should be borne in mind. Clinical manifestations of hypervitaminosis A have been reported in patients with renal failure receiving 1.5 mg/day retinol. Therefore, vitamin A supplementation of renal failure patients should be undertaken with caution.

Water-soluble vitamins are readily excreted in the urine. Treatment of vitamin overdosage usually consists of withdrawal of the vitamin.

DOSAGE AND ADMINISTRATION

INFUVITE® ADULT (PHARMACY BULK PACKAGE) is ready for immediate use in adults and children aged 11 years and older when added to intravenous infusion fluids.

INFUVITE® ADULT (PHARMACY BULK PACKAGE) should not be given as a direct, undiluted intravenous injection as it may give rise to dizziness, faintness and possible tissue irritation.

Preparation of **INFUVITE® ADULT (PHARMACY BULK PACKAGE)** for intravenous feeding should be done by transferring the contents of Vial 1 into the contents of Vial 2 to provide ten 10 mL single doses. One daily 10 mL dose should be added directly to not less than 500 mL, and preferably 1 000 mL, of intravenous dextrose, saline or similar infusion solutions. Discard any unused portion.

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

After **INFUVITE® ADULT (PHARMACY BULK PACKAGE)** is diluted in an intravenous infusion, the resulting solution should be refrigerated unless it is to be used immediately. The solution should be used within 24 hours after dilution. Some of the vitamins in this product, particularly A, D and riboflavin, are light sensitive; therefore, exposure to light should be minimized.

Once closure system has been compromised, withdrawal of container contents should be completed within 4 hours.

INFUVITE® ADULT (PHARMACY BULK PACKAGE) IS A PHARMACY BULK PACKAGE. IT IS NOT INTENDED FOR DIRECT INFUSION. DISCARD UNUSED PORTION.

DIRECTIONS FOR DISPENSING FROM PHARMACY BULK VIAL

The Pharmacy Bulk Vial is intended for single puncture, multiple dispensing and for intravenous use only. The contents are intended for use in a pharmacy admixture program and are restricted to the preparation of admixtures for infusion. The Pharmacy bulk package is to be used only in a suitable work area such as a laminar flow hood (or an equivalent clean air compounding area). Dispensing from Pharmacy Bulk Vial should be completed as soon as possible after initial entry.

HOW SUPPLIED

INFUVITE® ADULT (PHARMACY BULK PACKAGE) – NDC 54643 5649 2, is available in boxes containing 2 vials – 1 each of Vial 1 (50 mL) and Vial 2 (50 mL Fill in 100 mL Vial). Mix contents of Vial 1 with Vial 2 to provide 10 single doses.

Store under refrigeration, 2-8 °C (36-46 °F).

Distributed by:

BAXTER HEALTHCARE CORPORATION
Clintec Nutrition Division
Deerfield, IL 60015 USA

Manufactured by:

SAB-PHARMA INC.
145 Jules-Leger Street
Boucherville, QC, Canada J4B 7K8

Issued: Month/Year

INFUVITE® is a registered trademark of Sab-Pharma Inc.

DRAFT INNER LABEL - INFUVITE® ADULT (Pharmacy Bulk Package) VIAL 1

Transfer the contents of Vial 1 into Vial 2 to provide ten 10 mL single doses. Each 10 mL single dose should be added to not less than 500 mL of infusion fluid.

Once closure system has been compromised, withdrawal of container contents should be completed within 4 hours.

DISCARD UNUSED PORTION

USUAL DOSAGE: See Package Insert.

Lot.
Exp.

NDC 54643 5649 2
50 mL

Product Code 56492

**INFUVITE® ADULT
PHARMACY BULK PACKAGE**

Multiple Vitamins for Infusion

VIAL 1

For intravenous infusion after dilution only.

**PHARMACY BULK PACKAGE
NOT FOR DIRECT INFUSION**

Sterile

Store under refrigeration, 2-8 °C (36-46 °F)

Protect from light.

Rx only.



Each 5 mL in Vial 1 contains:

Vitamin C.....	200 mg
Vitamin A.....	3 300 I.U.
Vitamin D.....	200 I.U.
Thiamine (B ₁).....	6 mg
Riboflavin (B ₂).....	3.6 mg
Pyridoxine HCl (B ₆).....	6 mg
Niacinamide.....	40 mg
Dexpanthenol.....	15 mg
Vitamin E (<i>dl</i> - α -tocopheryl acetate).....	10 I.U.
Vitamin K.....	150 mcg

with 1.4 % polysorbate 80, sodium hydroxide and/or hydrochloric acid for pH adjustment and water for injection.

Dist By:
BAXTER HEALTHCARE CORPORATION
Deerfield, IL 60015 USA

*NOTE TO REVIEWER: THE TEST TO QUANTIFY THE ALUMINUM LEVELS IN INFUVITE® ADULT (PHARMACY BULK PACKAGE) IS CURRENTLY ONGOING. AS SOON AS THE TESTS ARE COMPLETE, SABEX 2002 INC. WILL MODIFY THIS LABEL AND FORWARD THE LABEL AND RESULTS TO THE FDA AS AN OFFICIAL SUPPLEMENT TO THIS APPLICATION.

Draft Labels

Preparation date: August 2, 2002
Revision date: May 16, 2003

DRAFT INNER LABEL - INFUVITE® ADULT (Pharmacy Bulk Package) VIAL 2

Transfer the contents of Vial 1 into Vial 2 to provide ten 10 mL single doses. Each 10 mL single dose should be added to not less than 500 mL of infusion fluid.

Once closure system has been compromised, withdrawal of container contents should be completed within 4 hours.

DISCARD UNUSED PORTION

USUAL DOSAGE: See Package Insert.

Lot.
Exp.

NDC 54643 5649 2
50 mL Fill in 100 mL Vial

Product Code 56492

Each 5 mL in Vial 2 contains:

Folic acid..... 600 mcg
Biotin..... 60 mcg
Cyanocobalamin (B₁₂)..... 5 mcg
with 30 % propylene glycol, citric acid and/or sodium citrate for pH adjustment and water for injection.

**INFUVITE® ADULT
PHARMACY BULK PACKAGE**

Multiple Vitamins for Infusion

VIAL 2

For intravenous infusion after dilution only.

**PHARMACY BULK PACKAGE
NOT FOR DIRECT INFUSION**

Sterile

Store under refrigeration, 2-8 °C (36-46 °F)

Protect from light

Rx only.



Dist. By:
BAXTER HEALTHCARE CORPORATION
Deerfield, IL 60015 USA

***NOTE TO REVIEWER: THE TEST TO QUANTIFY THE ALUMINUM LEVELS IN INFUVITE® ADULT (PHARMACY BULK PACKAGE) IS CURRENTLY ONGOING. AS SOON AS THE TESTS ARE COMPLETE, SABEX 2002 INC. WILL MODIFY THIS LABEL AND FORWARD THE LABEL AND RESULTS TO THE FDA AS AN OFFICIAL SUPPLEMENT TO THIS APPLICATION.**

Draft Labels

*Preparation date: August 2, 2002
Revision date: May 16, 2003*

DRAFT OUTER LABEL - INFUVITE® ADULT (Pharmacy Bulk Package)

(SIDE PANEL)

Transfer the contents of Vial 1 into Vial 2 to provide ten 10 mL single doses. Each 10 mL single dose should be added to not less than 500 mL of infusion fluid.

Once closure system has been compromised, withdrawal of container contents should be completed within 4 hours.

Usual dosage: See Package Insert.
DISCARD UNUSED PORTION

Distributed by:
BAXTER HEALTHCARE CORPORATION
Clintec Nutrition Division
Deerfield, IL 60015 USA

Manufactured by:
SAB-PHARMA INC.
Boucherville, QC, Canada J4B 7K8

Lot.
Exp.

(TOP FLAP)

INFUVITE® ADULT
Pharmacy Bulk Package
Multiple Vitamins for Infusion

(FRONT PANEL)
NDC 54643 5649 2
Product Code 56492

Sterile

INFUVITE® ADULT
PHARMACY BULK PACKAGE
Multiple Vitamins for Infusion

PHARMACY BULK PACKAGE
NOT FOR DIRECT INFUSION

For intravenous infusion after dilution only.
Contents: Vial 1 (50 mL) and Vial 2 (50 mL Fill per
100 mL Vial).
Both vials combined produce 10 single doses.

Store under refrigeration, 2-8 °C (36-46 °F)

Rx only.



(BACK PANEL)

INFUVITE® ADULT
PHARMACY BULK PACKAGE
Multiple Vitamins for Infusion

Each 5 mL of Vial 1 contains:

Vitamin C.....	200 mg
Vitamin A.....	3 300 I.U.
Vitamin D.....	200 I.U.
Thiamine (B ₁).....	6 mg
Riboflavin (B ₂).....	3.6 mg
Pyridoxine HCl (B ₆).....	6 mg
Niacinamide.....	40 mg
Dexpanthenol.....	15 mg
Vitamin E (<i>dl</i> - α -tocopheryl acetate).....	10 I.U.
Vitamin K.....	150 mcg

with 1.4 % polysorbate 80, sodium hydroxide and/or hydrochloric acid for pH adjustment and water for injection.

Each 5 mL of Vial 2 contains:

Folic acid.....	600 mcg
Biotin.....	60 mcg
Cyanocobalamin (B ₁₂).....	5 mcg

with 30 % propylene glycol, citric acid and/or sodium citrate for pH adjustment and water for injection.

Draft Labels

Preparation date: August 2, 2002
Revision date: May 16, 2003

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/s/

• David Orloff
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