For dilution in intravenous infusions only.

Multi-12®

Multiple Vitamins for Infusion

Multi-12®
Multiple Vitamins for Infusion

For intravenous infusion after dilution only.

DESCRIPTION

Multi-12® is a sterile product consisting of two 5 mL single-dose vials labeled Vial 1 and Vial 2.

Each 5 mL of Vial 1* contains:

Ascorbic acid (Vitamin C)	100 mg
Vitamin A** (as palmitate)	3 300 IU
Vitamin D_3** (cholecalciferol)	200 IU
Thiamine (Vitamin B_1) (as the hydrochloride)	3 mg
Riboflavin (Vitamin B_2) (as riboflavin 5-phosphate sodium)	3.6 mg
Pyridoxine HCl (Vitamin B_6)	4 mg
Niacinamide	40 mg
Dexpanthenol (as *d*-pantothenyl alcohol)	15 mg
Vitamin E** (*dl*-α-tocopheryl acetate)	10 IU

* with 1.4 % polysorbate 80, sodium hydroxide for pH adjustment and water for injection.
** Polysorbate 80 is used to water solubilize the oil-soluble vitamins A, D and E.

Each 5 mL of Vial 2† contains:

Folic acid	400 mcg
Biotin	60 mcg
Vitamin B12 (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:
Multi-12® (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 and E have been solubilized in an aqueous medium with polysorbate 80, permitting intravenous administration of these vitamins.

INDICATIONS AND USAGE
Multi-12® is indicated as a daily multivitamin maintenance supplement for adults and children aged 11 and older receiving parenteral nutrition.

Multi-12® 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.

Multi-12® (administered in intravenous fluids under proper dilution) contributes intake of necessary vitamins, except vitamin K, 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.

Multi-12® does not contain vitamin K which may have to be administered separately.

Some patients do not maintain adequate levels of certain vitamins when a multiple vitamin preparation, such as **Multi-12®**, 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

Multi-12® 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, a vitamin contained in this formulation, and vitamin K, a vitamin which may be co-administered with this formulation. 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.

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 **Multi-12®**.

Drug – Drug/Solution Interactions:

Multi-12® (Multiple Vitamins for Infusion) as formulated does not contain vitamin K, however as vitamin K may sometimes be co-administered **caution should be exercised when administering vitamin K to patients on anticoagulant therapy. In such patients, vitamin K may antagonize the hypothrombinemic response to anticoagulant drugs, such as warfarin and its congeners. Therefore, periodic monitring of prothrombin/INR response is essential in determining the appropriate dosage of anticoagulant therapy.**

Multi-12® (Multiple Vitamins for Infusion) is not physically compatible with alkaline solutions or moderately alkaline drugs such as DIAMOX® (Acetazolamide), DIURIL® Intravenous Sodium (Chlorothiazide sodium), Aminophylline or sodium bicarbonate. ACHROMYCIN® (tetracycline HCl) may not be physically compatible with **Multi-12®**. 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 levodoopa by increasing its metabolism. Concomitant administration of hydralazine or isoniazid may increase pyridoxine requirements.

In patients with pernicious anemia, the hematologic response to vitamin B_{12} 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.

Viatmin 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 **Multi-12®** 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 **Multi-12®** .

Pregnancy: **Pregnancy Category C:** Animal reproduction studies have not been conducted with **Multi-12®** (Multiple Vitamins for Infusion). **Multi-12®** 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 **Multi-12®** 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. However, because many drugs are excreted in human milk, caution should be exercised when **Multi-12®** 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

Multi-12® is ready for immediate use in adults and children aged 11 years and older when added to intravenous infusion fluids.

Multi-12® should not be given as a direct, undiluted intravenous injection as it may give rise to dizziness, faintness and possible tissue irritation.

For intravenous feeding, one daily dose of Multi-12® (5 mL of Vial 1 plus 5 mL of Vial 2) 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 **Multi-12®** 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.

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

How Supplied

Multi-12® - NDC 54643-5641-1 , is available in boxes containing 2 vials - Vial 1 (5 mL) and Vial 2 (5 mL), both vials to be used for a single dose.

Multi-12® - NDC 54643-5641-0 , is available in boxes containing 10 vials - 5 each of Vial 1 (5 mL) and Vial 2 (5 mL), one Vial 1 plus one Vial 2 to be used for a single dose.

Rx only.

Distributed by: *(To be determined)*

Manufactured by:
Sabex Inc.
145 Jules-Leger Street
Boucherville, QC, Canada J4B 7K8

Issued: Month/Year

DRAFT INNER LABEL - MULTI-12® VIAL 1

Dilute Vials 1 and 2 in not less than 500 mL infusion fluid, both vials to be used for a single dose.

Usual dosage: See Package Insert.

Manufactured by:
Sabex Inc.
Boucherville, Qc, Canada J4B 7K8

Lot.
Exp.

5 mL

MULTI-12®
Multiple Vitamins for Infusion

VIAL 1

For intravenous infusion after dilution only.

Single Dose Vial - Sterile

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

Rx only.

Each 5 mL of Vial 1 contains:

Vitamin C	100 mg
Vitamin A	3 300 I.U.
Vitamin D	200 I.U.
Thiamine (B_1)	3 mg
Riboflavin (B_2)	3.6 mg
Pyridoxine HCl (B_6)	4 mg
Niacinamide	40 mg
Dexpanthenol	15 mg
Vitamin E (*dl*-α-tocopheryl acetate)	10 I.U.

with 1.4 % polysorbate 80, sodium hydroxide for pH adjustment and water for injection.

DRAFT INNER LABEL - MULTI-12® VIAL 2

Dilute Vials 1 and 2 in not less than 500 mL infusion fluid, both vials to be used for a single dose.

Usual dosage: See Package Insert.

Manufactured by:
Sabex Inc.
Boucherville, Qc, Canada J4B 7K8

Lot.
Exp.

5 mL

MULTI-12®
Multiple Vitamins for Infusion

VIAL 2

For intravenous infusion after dilution only.

Single Dose Vial – Sterile

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

Rx only.

Each 5 mL of Vial 2 contains:
Folic acid.....400 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 OUTER LABEL - MULTI-12® (SINGLE DOSE PACKAGE SIZE)

(TOP FLAP)

MULTI-12®

Multiple Vitamins for Infusion

(SIDE PANEL)

The contents of both vials should be added to not less than 500 mL infusion fluid.

Each vial contains a sufficient amount to permit withdrawal and administration of 5 mL.

Usual dosage: See Package Insert.

Distributed by: ***(To be determined)***

Manufactured by:
Sabex Inc.
Boucherville, Qc, Canada J4B 7K8

Lot.
Exp.

(FRONT PANEL)

NDC 54643 5641 1 Sterile

MULTI-12®

Multiple Vitamins for Infusion

For intravenous infusion after dilution only.
Contents: Vial 1 (5 mL) and Vial 2 (5 mL).
Both vials to be used for a single dose.

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

Rx only.

(BACK PANEL)

MULTI-12®

Multiple Vitamins for Infusion

Each 5 mL of Vial 1 contains:

Vitamin C	100 mg
Vitamin A	3 300 I.U.
Vitamin D	200 I.U.
Thiamine (B_1)	3 mg
Riboflavin (B_2)	3.6 mg
Pyridoxine HCl (B_6)	4 mg
Niacinamide	40 mg
Dexpanthenol	15 mg
Vitamin E (*dl*-α-tocopheryl acetate)	10 I.U.

with 1.4 % polysorbate 80, sodium hydroxide for pH adjustment and water for injection.

Each 5 mL of Vial 2 contains:

Folic acid	400 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.

FINAL COPY- LABELS: 00-05-16

DRAFT OUTER LABEL - MULTI-12® (5 SINGLE DOSE PACKAGE SIZE)

(TOP FLAP)

MULTI-12®
Multiple Vitamins for Infusion

(SIDE PANEL)

The contents of both vials should be added to not less than 500 mL infusion fluid.

Each vial contains a sufficient amount to permit withdrawal and administration of 5 mL.

Usual dosage: See Package Insert.

Distributed by: ***(To be determined)***

Manufactured by:
Sabex Inc.
Boucherville, Qc, Canada J4B 7K8

Lot.
Exp.

(FRONT PANEL)

NDC 54643 5641 0 Sterile

MULTI-12®
Multiple Vitamins for Infusion

For intravenous infusion after dilution only.
Contains 5 each of Vial 1 (5 mL) and Vial 2 (5 mL). One vial of each to be used for a single dose.

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

Rx only.

(BACK PANEL)

MULTI-12®
Multiple Vitamins for Infusion

Each 5 mL of Vial 1 contains:

Vitamin C	100 mg
Vitamin A	3 300 I.U.
Vitamin D	200 I.U.
Thiamine (B_1)	3 mg
Riboflavin (B_2)	3.6 mg
Pyridoxine HCl (B_6)	4 mg
Niacinamide	40 mg
Dexpanthenol	15 mg
Vitamin E (*dl*-α-tocopheryl acetate)	10 I.U.

with 1.4 % polysorbate 80, sodium hydroxide for pH adjustment and water for injection.

Each 5 mL of Vial 2 contains:

Folic acid	400 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.

FINAL COPY- LABELS: 00-05-16