

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

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FINAL PRINTED LABELING

APPROVED

For dilution in intravenous infusions only.

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Multi-12[®]
Multiple Vitamins for Infusion

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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 <i>d</i> -pantothenyl alcohol).....	15 mg
Vitamin E** (<i>dl</i> - 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.

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 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.

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 levodopa 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 **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.
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