

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use M.V.I.-12™ safely and effectively. See full prescribing information for M.V.I.-12.

M.V.I.-12 (multiple vitamins without vitamin K injection), for intravenous use
Initial U.S. Approval: 1953

INDICATIONS AND USAGE

M.V.I.-12 is indicated for prevention of vitamin deficiency in adults and pediatric patients aged 11 years and above who are on warfarin anticoagulant therapy receiving home parenteral nutrition. (1)

DOSAGE AND ADMINISTRATION

- M.V.I.-12 is a combination product that contains the following vitamins: ascorbic acid, vitamin A, vitamin D, thiamine, riboflavin, pyridoxine, niacinamide, dextranthenol, vitamin E, folic acid, biotin, and vitamin B₁₂ (2.1)
- Recommended daily dosage is 10 mL (2.2)
- Administer by intravenous infusion after dilution (2.1)
- M.V.I.-12 Pharmacy Bulk Package consists of two vials labeled Vial 1 and Vial 2. Aseptically transfer the contents of Vial 1 to Vial 2. The mixed solution (100 mL) will provide ten 10 mL single doses to patients in a pharmacy admixture program. Use within 4 hours of puncture (2.1, 2.3)
- Prior to intravenous administration, dilute the once daily dose of 10 mL by adding to at least 500 to 1,000 mL intravenous parenteral nutrition solution containing dextrose or saline (2.3)
- After dilution in an intravenous infusion, refrigerate resulting solution unless used immediately. Use solution within 24 hours after dilution (2.3)
- Monitor blood vitamin concentrations (2.4)
- See Full Prescribing Information for drug incompatibilities (2.5)

DOSAGE FORMS AND STRENGTHS

- Injection: Pharmacy bulk package consists of two vials labeled Vial 1 (50 mL) and Vial 2 (50 mL) (3)
- See Full Prescribing Information for vitamin strengths (3, 11)

CONTRAINDICATIONS

- Hypersensitivity to any of the vitamins or excipients (4)
- Existing hypervitaminosis (4)

WARNINGS AND PRECAUTIONS

- Risk of Aluminum Toxicity:** For at risk patients (renal failure or those with prolonged therapy), periodically monitor aluminum levels with prolonged administration (5.1)
- Low Vitamin A Levels:** Monitor vitamin A levels (5.2)
- Allergic Reactions:** to thiamine may occur (5.3)

- Hypervitaminosis A:** Patients with renal failure or liver disease may be at higher risk (5.4)
- Interferes with Megaloblastic Anemia Diagnosis:** Avoid use during testing for this disorder (5.5)
- Risk of Vitamin Deficiencies or Excess:** Monitor blood vitamin concentrations (5.6)
- False Negative Urine Glucose Tests:** May occur due to vitamin C (5.7)

ADVERSE REACTIONS

Adverse reactions have included anaphylactoid reactions, rash, erythema, pruritus, headache, dizziness, agitation, anxiety, diplopia (6)

To report SUSPECTED ADVERSE REACTIONS, contact Hospira, Inc. at 1-800-441-4100, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Effect of M.V.I.-12 on other drugs:

- Phenytoin:** Folic acid may decrease phenytoin blood levels and increase the risk of seizure frequency (7.1)
- Methotrexate:** Folic acid may decrease response to methotrexate (7.1)
- Levodopa:** Pyridoxine may decrease blood levels of levodopa and levodopa efficacy may decrease (7.1)
- Antibiotics:** Thiamine, riboflavin, pyridoxine, niacinamide, and ascorbic acid decrease activities of erythromycin, kanamycin, streptomycin, doxycycline, and lincomycin (7.1)
- Bleomycin:** Ascorbic acid and riboflavin may reduce the activity of bleomycin (7.1)

Effects of other drugs on M.V.I.-12:

- Hydralazine, Isoniazid:** Concomitant administration of hydralazine or isoniazid may increase pyridoxine requirements (7.2)
- Chloramphenicol:** In patients with pernicious anemia, hematologic response to vitamin B₁₂ may be inhibited by concomitant administration of chloramphenicol (7.2)
- Phenytoin:** May decrease folic acid concentrations (7.2)

USE IN SPECIFIC POPULATIONS

- Pregnant and Nursing Mothers:** Pregnant and nursing women should follow the U.S. Recommended Daily Allowances for their condition, because their vitamin requirements may exceed those of nonpregnant and nonlactating women (8.1, 8.3)
- Pediatric Use:** Safety and effectiveness in pediatric patients below the age of 11 years have not been established (8.4)
- Renal Impairment:** Monitor renal function, calcium, phosphorus and vitamin A levels (8.6)
- Hepatic Impairment:** Monitor vitamin A levels (8.7)

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

M.V.I.-12™ is indicated for the prevention of vitamin deficiency in adults and pediatric patients aged 11 years and above on warfarin anticoagulant therapy receiving parenteral nutrition.

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

2 DOSAGE AND ADMINISTRATION

2.1 Important Dosage and Administration Instructions

M.V.I.-12 is a combination product that contains the following vitamins: ascorbic acid, vitamin A, vitamin D, thiamine, riboflavin, pyridoxine, niacinamide, dexpanthenol, vitamin E, folic acid, biotin, and vitamin B₁₂.

M.V.I.-12 is supplied as a pharmacy bulk package for intravenous use intended for administration by intravenous infusion after dilution:

M.V.I.-12 Pharmacy Bulk Package: consists of two pharmacy bulk vials which must be mixed prior to use. The mixed solution will provide ten 10 mL single doses which must be diluted prior to intravenous administration. Pharmacy bulk package of M.V.I.-12 is intended for dispensing of single doses to multiple patients in a pharmacy admixture program and is restricted to the preparation of admixtures for infusion [*see Dosage and Administration (2.3)*].

Do not administer M.V.I.-12 as a direct, undiluted intravenous injection as it may cause dizziness, faintness, and tissue irritation.

2.2 Dosage Information

The recommended daily dosage volume is 10 mL. One daily dose (10 mL) is diluted by adding directly to a specified volume of an intravenous fluid [*see Dosage and Administration (2.3)*].

Patients with multiple vitamin deficiencies or with increased vitamin requirements may need multiple daily dosages as indicated or additional doses of individual vitamins.

2.3 Preparation and Administration Instructions

- Handling of M.V.I.-12 solution, including preparation of the pharmacy bulk pack, should be restricted to a suitable work area, such as a laminar flow hood (or an equivalent clean air compounding area).
- Aseptically transfer the contents of Vial 1 (50 mL) into Vial 2 (50 mL). The mixed solution (100 mL) will provide ten 10 mL single doses to patients in a pharmacy admixture program.
- Each bulk vial closure shall be penetrated only one time with a suitable sterile transfer device or dispensing set that allows measured dispensing of the contents.
- Once closure system has been penetrated, complete dispensing from the pharmacy bulk vial within 4 hours. Mixed solution may be stored for up to 4 hours refrigerated.
- Discard unused portion.
- Visually inspect for particulate matter and discoloration prior to administration.
- Utilizing a suitable sterile automated compounding device or dispensing pin for accuracy, aseptically transfer each 10 mL dose into a plastic or glass bottle containing at least 500 to 1,000 mL intravenous parenteral nutrition solution containing dextrose or saline.

- After M.V.I.-12 is diluted in an intravenous infusion, refrigerate the resulting solution unless it is to be used immediately, and use the solution within 24 hours after dilution.
- Minimize exposure to light because some of the vitamins in M.V.I.-12, particularly A, D and riboflavin, are light sensitive.

2.4 Monitoring Vitamin Blood Levels

Blood vitamin concentrations should be monitored to ensure maintenance of adequate levels, particularly in patients receiving parenteral multivitamins as the only source of vitamins for long periods of time.

2.5 Drug Incompatibilities

- M.V.I.-12 is not physically compatible with moderately alkaline solutions such as a sodium bicarbonate solution and other alkaline drugs such as acetazolamide sodium, aminophylline, ampicillin sodium, and chlorothiazide sodium.
- Folic acid is unstable in the presence of calcium salts such as calcium gluconate.
- Vitamin A and thiamine in M.V.I.-12 may react with bisulfite solutions such as sodium bisulfite or vitamin K bisulfate. Patients should be monitored for vitamin A and thiamine deficiencies. Do not add M.V.I.-12 directly to intravenous fat emulsions.
- Consult appropriate references for listings of physical and chemical compatibility of solutions and drugs with M.V.I.-12. In such circumstances, admixture or Y-site administration with M.V.I.-12 should be avoided.

3 DOSAGE FORMS AND STRENGTHS

M.V.I.-12 is an injection available as:

Pharmacy bulk package consisting of two vials labeled Vial 1 and Vial 2. Vial 1 is an amber vial containing a clear, amber to orange colored solution. Vial 2 is an amber vial containing a clear to light straw colored solution. Both vials must be mixed prior to use. The mixed solution (100 mL) will provide ten 10 mL single doses [*see Dosage and Administration (2.3)*].

See Description section for vitamin strengths [*see Description (11)*].

4 CONTRAINDICATIONS

M.V.I.-12 is contraindicated in patients who have:

- A history of known hypersensitivity to any of the vitamins or excipients in M.V.I.-12 [*see Warnings and Precautions (5.3), Adverse Reactions (6)*].
- An existing hypervitaminosis

5 WARNINGS AND PRECAUTIONS

5.1 Aluminum Toxicity

M.V.I.-12 contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration in patients with renal impairment. Premature neonates are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which contain aluminum.

Patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than 4 to 5 micrograms per kg per day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration. To prevent aluminum toxicity monitor periodically aluminum levels with prolonged parenteral administration of M.V.I.-12.

5.2 Risk of Low Vitamin A Levels

Vitamin A may adhere to plastic, resulting in lower vitamin A concentrations after administration of M.V.I.-12. Therefore, blood vitamin concentrations should be periodically monitored and the administration of additional therapeutic doses of Vitamin A may be required.

5.3 Allergic Reactions to Thiamine

Allergic reactions such as urticaria, periorbital and digital edema, have been reported following intravenous administration of thiamine, which is found in M.V.I.-12. There have been rare reports of anaphylactoid reactions following intravenous doses of thiamine. No fatal anaphylactoid reactions associated with M.V.I.-12 have been reported.

5.4 Hypervitaminosis A

Hypervitaminosis A, manifested by nausea, vomiting, headache, dizziness, blurred vision, has been reported in patients with renal failure receiving 1.5 mg/day retinol and in patients with liver disease. Therefore, supplementation of renal failure patients and patients with liver diseases with vitamin A, an ingredient found in M.V.I.-12, should be undertaken with caution [*see Use in Specific Populations (8.6 and 8.7)*]. Blood levels of Vitamin A should be monitored periodically.

5.5 Interference with Diagnosis of Megaloblastic Anemia Patients

Avoid the use of M.V.I.-12 in patients with suspected or diagnosed megaloblastic anemia prior to blood sampling for the detection of the folic acid and cyanocobalamin deficiencies. M.V.I.-12 contains folic acid and cyanocobalamin which can mask serum deficits of folic acid and cyanocobalamin in patients with megaloblastic anemia.

5.6 Potential to Develop Vitamin Deficiencies or Excesses

In patients receiving parenteral multivitamins, such as with M.V.I.-12, blood vitamin concentrations should be periodically monitored to determine if vitamin deficiencies or excesses are developing. M.V.I.-12 may not correct long-standing specific vitamin deficiencies. The administration of additional doses of specific vitamins may be required [*see Dosage and Administration (2.2)*].

5.7 Interference with Urine Glucose Testing

M.V.I.-12 contains Vitamin C which is also known as ascorbic acid. Ascorbic acid in the urine may cause false negative urine glucose determinations.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other section of the labeling.

- Allergic Reactions to Thiamine [*see Warnings and Precautions (5.4)*].
- Hypervitaminosis A [*see Warnings and Precautions (5.5)*].

The following adverse reactions associated with the use of M.V.I.-12 were identified in clinical studies or postmarketing reports. Because some of these reactions were reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Dermatologic: rash, erythema, pruritus

CNS: headache, dizziness, agitation, anxiety

Ophthalmic: diplopia

7 DRUG INTERACTIONS

7.1 Effect of M.V.I.-12 on Other Drugs

Phenytoin: Folic acid may increase phenytoin metabolism and lower the serum concentration of phenytoin resulting in increased seizure activity.

Methotrexate: Folic acid may decrease a patient's response to methotrexate therapy.

Levodopa: Pyridoxine may increase the metabolism of levodopa (decrease blood level of levodopa) and decrease its efficacy.

Antibiotics: Thiamine, riboflavin, pyridoxine, niacinamide, and ascorbic acid decrease antibiotic activities of erythromycin, kanamycin, streptomycin, doxycycline, and lincomycin.

Bleomycin: Ascorbic acid and riboflavin inactivate bleomycin *in vitro*, thus the activity of bleomycin may be reduced.

7.2 Effect of Other Drugs on M.V.I.-12

Hydralazine or Isoniazid: Concomitant administration of hydralazine or isoniazid may increase pyridoxine requirements.

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

Phenytoin: Phenytoin may decrease serum folic acid concentrations.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

M.V.I.-12 has not been studied in pregnant women. Pregnant women should follow the U.S. Recommended Daily Allowances for pregnancy, because their vitamin requirements may exceed those of nonpregnant women.

8.3 Nursing Mothers

M.V.I.-12 has not been studied in lactating women. Lactating women should follow the U.S. Recommended Daily Allowances for their condition, because their vitamin requirements may exceed those of nonlactating women. Caution should be exercised when M.V.I.-12 is administered to a nursing woman.

8.4 Pediatric Use

M.V.I.-12 is indicated for the prevention of vitamin deficiency in pediatric patients age 11 years and above on warfarin anticoagulant therapy receiving parenteral nutrition. Safety and effectiveness of M.V.I.-12 in pediatric patients below the age of 11 years have not been established.

8.5 Geriatric Use

Reported clinical experience has not identified differences in responses between the elderly and younger patients.

8.6 Renal Impairment

M.V.I.-12 has not been studied in patients with renal impairment. Monitor renal function, calcium, phosphorus and vitamin A levels in patients with renal impairment [*see Warning and Precautions (5.1, 5.4)*].

8.7 Hepatic Impairment

M.V.I.-12 has not been studied in patients with hepatic impairment. Monitor vitamin A level in patients with liver disease or high alcohol consumption [*see Warning and Precautions (5.4)*].

10 OVERDOSAGE

Signs and symptoms of acute or chronic overdosage may be those of individual M.V.I.-12 component toxicity. There is no clinical experience with M.V.I.-12 overdosage.

11 DESCRIPTION

M.V.I.-12 Pharmacy Bulk Package: A sterile product consisting of two Type 1, amber glass vials labeled Vial 1 (50 mL) and Vial 2 (50 mL). The mixed solution will provide ten single doses of 10 mL each.

Table 1 provides the strengths of the vitamins provided in vial 1 and vial 2:

Table 1: M.V.I.-12 FORMULATION (INTENDED FOR AGES 11 AND OLDER)

Vial 1*	
Ingredient	Amount per Unit Dose
Fat Soluble Vitamins**	
Vitamin A (retinol)	1 mg (3,300 USP units)
Vitamin D (ergocalciferol)	5 mcg (200 USP units)
Vitamin E (dl-alpha-tocopheryl acetate)	10 mg (10 USP units)
Water Soluble Vitamins	
Vitamin C (ascorbic acid)	200 mg
Niacinamide	40 mg
Vitamin B ₂ (as riboflavin 5-phosphate sodium)	3.6 mg
Vitamin B ₁ (thiamine)	6 mg
Vitamin B ₆ (pyridoxine HCl)	6 mg
Dexpanthenol (d-pantothenyl alcohol)	15 mg

* With 30% propylene glycol and 2% gentisic acid ethanolamide as stabilizers and preservatives; sodium hydroxide for pH adjustment; 1.6% polysorbate 80; 0.028% polysorbate 20; 0.002% butylated hydroxytoluene; 0.0005% butylated hydroxyanisole.

** Fat-soluble vitamins A, D, and E are water solubilized with polysorbate 80.

Vial 2*	
Ingredient	Amount per Unit Dose
Biotin	60 mcg
Folic acid	600 mcg
Vitamin B ₁₂ (cyanocobalamin)	5 mcg

* With 30% propylene glycol; and citric acid, sodium citrate, and sodium hydroxide for pH adjustment

“Aqueous” multivitamin formula for intravenous infusion: M.V.I.-12 (multiple vitamins without vitamin K injection) makes available a combination of fat-soluble and water-soluble vitamins in an aqueous solution, formulated for incorporation into intravenous infusions. The liposoluble vitamins A, D, and E have been solubilized in an aqueous medium with polysorbate 80, permitting intravenous administration of these vitamins.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity, mutagenicity and fertility studies were not performed.

16 HOW SUPPLIED/STORAGE AND HANDLING

M.V.I.-12 is an injection available as:

M.V.I.-12 Pharmacy Bulk Package

Unit of Sale	Intermediate Multi-Pack	Each (Vial 1 and Vial 2)
NDC 61703-423-83 Case of 2 Boxes of 10 vials (5 vial 1 and 5 vial 2)	NDC 61703-423-78 Box of 10 vials (5 Vial 1 and 5 Vial 2)	Vial 1: NDC 61703-423-73 Vial 2: NDC 61703-423-93 50 mL (Vial 1 and Vial 2) multiple dose vial

Vial 1 is an amber vial containing a clear, amber to orange colored solution. Vial 2 is an amber vial containing a clear to light straw colored solution. Mix contents of Vial 1 and Vial 2 to provide ten 10 mL single doses [see *Dosage and Administration (2.3)*].

See Description section for vitamin strengths [see *Description (11)*].

Minimize the exposure of M.V.I.-12 to the light, because vitamins A, D and riboflavin are light sensitive.

Store at 2-8°C (36-46°F).

17 PATIENT COUNSELING INFORMATION

Instruct patients (if age appropriate) and caregivers:

- To watch for and immediately report signs of allergic reactions (i.e. urticaria, periorbital and digital edema).
- To watch for and immediately report signs of hypervitaminosis A, manifested by nausea, vomiting, headache, dizziness, blurred vision, if patients have renal impairment.
- To report other adverse reactions such as rash, erythema, pruritus, headache, dizziness, agitation, anxiety, and diplopia.
- About the significance of periodic monitoring of blood vitamin concentrations to determine if vitamin deficiencies or excesses are developing.
- About the need to monitor renal function, calcium, phosphorus, aluminum and vitamin A levels in patients with renal impairment.

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