Cernevit™-12 (multivitamins for infusion)
For dilution in infusions only

Description
Cernevit™-12 (multivitamins for infusion) is a lyophilized, sterile powder containing both water soluble and fat soluble vitamins (except Vitamin K) combined with mixed micelles (glycocholic acid and lecithin) in a single-dose amber glass vial intended for intravenous infusion following reconstitution and further dilution.

Each single-dose vial of Cernevit™-12 (multivitamins for infusion) provides:

Retinol palmitate corresponding to Retinol (Vitamin A)	3500 IU
Cholecalciferol (Vitamin D_3)	200 IU
DL α-tocopherol	10.2 mg
corresponding to α-tocopherol (Vitamin E)	11.2 IU
Ascorbic Acid (Vitamin C)	125 mg
Nicotinamide (Vitamin B_3)	46 mg
Dexpanthenol	16.15 mg
corresponding to pantothenic acid (Vitamin B_5)	17.25 mg
Pyridoxine hydrochloride	5.5 mg
corresponding to pyridoxine (Vitamin B_6)	4.53 mg
Riboflavin sodium phosphate	5.67 mg
corresponding to riboflavin (Vitamin B_2)	4.14 mg
Cocarboxylase tetrahydrate	5.8 mg
corresponding to thiamine (Vitamin B_1)	3.51 mg
Folic Acid	414 mcg
D-Biotin	60 mcg
Cyanocobalamin (Vitamin B_{12})	5.5 mcg

Other Ingredients
Each vial is formulated to contain approximately:

Glycine	250 mg
Glycocholic acid	140 mg
Soybean lecithin	112.5 mg

Sodium hydroxide and/or Hydrochloric acid added to adjust pH to 5.9

Cernevit™-12 (multivitamins for infusion) makes available a combination of important water soluble and fat soluble vitamins in a physiologic micellar system specially formulated for incorporation into intravenous infusions. Glycocholic acid and lecithin, both possessing emulsifying properties, are combined to form mixed micelles allowing the water soluble and fat soluble vitamins to solubilize in one container. The lyophilization of Cernevit™-12 (multivitamins for infusion) produces a sterile dry powder intended for reconstitution, providing an aqueous solution. Glycine is incorporated for rapid reconstitution.

Indications and Usage
This formulation is indicated as a daily multivitamin maintenance dosage for adults and children aged 11 years and above receiving parenteral nutrition.

It 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.

This product (administered in intravenous fluids under proper dilution) contributes intake of these 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.

This product does not contain Vitamin K, which may have to be administered separately.

Clinical testing indicates that some patients do not maintain adequate levels of certain vitamins when this formulation in recommended amounts is the sole source of vitamins.. Although there was no clinical evidence of vitamin deficiency or toxicity, blood levels of Vitamin E and 1,25-OH Vitamin D were low and Vitamin A levels were high in a number of subjects who received this formulation as the only source of vitamins for 3 months. In addition, blood levels of Vitamin C, thiamine and folic acid declined or were low normal in some subjects who received a similar formulation as the only vitamin source for 4 to 6 months.[1] Therefore, in patients for whom total parenteral nutrition will be continued for long periods of time, serum levels of these vitamins should be monitored. 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
Known hypersensitivity to any of the vitamins in this product or a pre-existing hypervitaminosis.

Precautions
Folic acid may obscure pernicious anemia.

Drug Interactions: The dosage of drugs known to be influenced by folic acid and pyridoxine, for example phenytoin and phenobarbital, must be carefully monitored. Pyridoxine can reduce the effect of levodopa. Several drugs are known to influence the serum concentration of vitamins. An *in vitro* study[2] using therapeutic concentrations of glycocholic acid (0.177 mg glycocholate/mL human serum) demonstrated a 50-80% increase in the unbound (free) fraction of drugs known to bind α_1-acid glycoprotein (e.g., disopyramide, propranolol, quinidine, and prazosin). Although the *in vivo* response has not been determined, physicians should closely monitor patients for the possibility of an increase in the therapeutic response to drugs binding to α_1-acid glycoprotein. Consult appropriate references for drugs that bind to α_1-acid glycoprotein[3,4] and for listings of specific drug-vitamin interactions.

Folic acid has been reported to be unstable in the presence of calcium gluconate. Bisulfites have been reported to affect the stability of Vitamin A, thiamine, and ascorbic acid.[5] The pH of the parenteral nutrition admixture may affect the stability of Vitamin C and thiamine.[5] Bleomycin can be inactivated by ascorbic acid and riboflavin. Several vitamins have been reported to decrease the activity of certain antibiotics. Admixture or Y-site administration of alkaline drugs through a vitamin infusion should be avoided. Cernevit™-12 (multivitamins for infusion) should not be admixed directly into a lipid emulsion. Cernevit™-12 (multivitamins for infusion) may be combined with parenteral nutrition containing a lipid emulsion. The prime destabilizers of emulsions are excessive acidity (low pH) and inappropriate electrolyte content. Careful consideration should be given to additions of divalent cations (Ca++ and Mg++) which have been shown to cause emulsion instability. Consult the current literature for physical compatibility of drugs with parenteral nutrition.

Carcinogenesis, Mutagenesis, and Impairment of Fertility: Carcinogenicity, mutagenicity and fertility studies have not been performed with Cernevit™-12 (multivitamins for infusion).

Pregnancy

Pregnancy Category C: The use of Cernevit™-12 (multivitamins for infusion) has not been studied in human pregnancy. Animal reproduction studies have not been conducted with Cernevit™-12 (multivitamins for infusion). It is also not known whether Cernevit™-12 (multivitamins for infusion) should be given to a pregnant woman or can affect reproduction capacity. Cernevit™-12 (multivitamins for infusion) 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.

Nursing mothers: Lactating women should follow the U.S. Recommended Daily Allowances for their condition, because their vitamin requirements 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 Cernevit™-12 (multivitamins for infusion) is administered to a nursing mother.

Pediatric use: Safety and efficacy of Cernevit™-12 (multivitamins for infusion) administration to children <11 years of age has not been established. Cernevit™-12 (multivitamins for infusion) is not recommended for use in children <11 years of age because it lacks Vitamin K and contains an inadequate amount of Vitamin D compared to that recommended by the Nutrition Advisory Group (NAG) of the Department of Food and Nutrition, American Medical Association (AMA) for children in this age group receiving total parenteral nutrition.[6]

Adverse Reactions
Anaphylactic reactions have been reported following large intravenous doses of thiamine. There have been very rare reports of anaphylactic reactions following IV injection of Cernevit™-12 (multivitamins for infusion) over 1-4 minutes. Urticaria and rash have also been associated with Cernevit™-12 (multivitamins for infusion).

Overdosage
Accumulation of Vitamin A and Vitamin D are possible with prolonged administration of high doses. Signs and symptoms of excess, such as hypercalcemia, should be monitored.

Dosage and Administration
The single-dose vial of Cernevit™-12 (multivitamins for infusion) is reconstituted by adding 5 mL of Sterile Water for Injection into the vial and gently mixing to dissolve the lyophilized powder. The resultant solution should be administered by intravenous infusion. After reconstitution, Cernevit™-12 (multivitamins for infusion) should be used immediately or stored under refrigeration for no more than 24 hours. To minimize vitamin losses in parenteral nutrition admixtures, add the vitamins immediately prior to administration and complete administration within 24 hours.[5] Discard any unused portion. Many parenteral vitamins are light sensitive and exposure to light should be minimized.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Use of a final filter is recommended during administration of all parenteral solutions where possible.

Adults and Children aged 11 years and above
Adults and children aged 11 years and above should receive the contents of one vial (5 mL) per day.

How Supplied
Cernevit™-12 (multivitamins for infusion) is supplied in a single-dose amber glass vial as follows:

100 vials/case	2A6736	NDC 64371-869-60

Storage
Store between 4°C (39°F) – 25°C (77°F). Protect from light and heat. Do not freeze.

References

1 Shils ME, Baker H, Frank O. Blood vitamin levels of long-term adult home total parenteral nutrition patients: the efficacy of the AMA-FDA parenteral multivitamin formulation. J Paren Enteral Nutr. 1985;9(2):179-88.
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4 Kremer JM, Wilting J, Janssen LH. Drug binding to human alpha-1-acid glycoprotein in health and disease. Pharmacol Rev. 1988;40(1):1-47.
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6 Multivitamin preparations for parenteral use a statement by the Nutrition Advisory Group. J Paren Enteral Nutr. 1979;3(4):258-62.

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