Baxter

Cernevit

MULTIVITAMIN INJECTION

Cernevit

Quality in every dose

– Manufacturing that adheres to most rigorous quality standards

– Registration license approved by key global regulatory bodies

– Commitment to continuous product improvement

– Global resources that help ensure consistency of supply

Baxter

A Company You Can Count On

– A leader in the healthcare industry for more than 80 years

– Dedicated sales professionals

– Medical and clinical support

– Customer service teams

Cernevit is registered in more than 50 countries with over 100 million doses infused since 2013.[1]

Cernevit

A 12-in-1 Spectrum of Essential Vitamins

12-in-1 lyophilised multivitamin formulation
Mixed micelle technology allows water- and lipid-soluble vitamins to be combined in a convenient single-dose vial[2,3]

Flexible, easy to reconstitute
Can be added to PN solutions with or without lipids, provided that compatibility and stability have been confirmed[3]

No refrigeration required*[3]
Enhanced convenience and access at point of care

*Can be stored at room temperature for up to 2 years when unopened.

Cernevit Composition[3]

Vitamin	B_1	B_2	B_3	B_5	B_6	Biotin	Folic Acid	B_{12}	C	A	D_3	E
Amount per Vial	3.51 mg	4.14 mg	46 mg	17.25 mg	4.53 mg	69 µg	414 µg	6 µg	125 mg	3500 IU	220 IU	11.2 IU

A simple reconstitution process

1. 

Aseptic conditions must be followed during reconstitution process and when CERNEVIT is administered as part of a PN admixture.[3]

2. 

Using a sterile syringe, inject 5 mL sterile water or 0.9% sodium chloride solution or 5% glucose solution into the vial.[3]

3. 

Mix gently until the lyophilised powder is completely dissolved. The obtained solution is yellow-orange in colour.* After adding CERNEVIT into the PN solution, check for any abnormal colour change[3].

*Reconstituted CERNEVIT can be stored at 2–8°C for up to 24 hours[3]

REFERENCES:

1. Baxter data on file.
2. Rifai K, et al. *Aliment Pharmacol Ther* 2006;23:1337-45.
3. Baxter Healthcare. CERNEVIT SmPC, 2019.

CERNEVIT, powder for solution for injection or infusion, orange yellow sterile cake of powder.

QUALITATIVE AND QUANTITATIVE COMPOSITION
One vial (5 ml) contains : Retinol (Vitamin A) in the form of retinol palmitate 3500 IU; Cholecalciferol (Vitamin D3) 220.000 IU; Alpha-tocopherol (Vitamin E) 11.200 IU; corresponding to DL alpha-tocopherol quantity 10.200 mg; Ascorbic acid (Vitamin C) 125.000 mg; Thiamine (Vitamin B1) 3.510 mg; in the form of cocarboxylase tetrahydrate 5.800 mg; Riboflavin (Vitamin B2) 4.140 mg; in the form of riboflavin sodium phosphate dehydrate 5.670 mg; Pyridoxine (Vitamin B6) 4.530 mg; in the form of pyridoxine hydrochloride 5.500 mg; Cyanocobalamin (Vitamin B12) 0.006 mg; Folic acid (Vitamin B9) 0.414 mg; Pantothenic acid (Vitamin B5) 17.250 mg; in the form of dexpanthenol 16.150 mg; Biotin (Vitamin B8) 0.069 mg; Nicotinamide (Vitamin PP) 46.000 mg

Other ingredients: Glycine 250.000mg, Glycocholic acid 140.000mg, soybean phosphatides112.500mg, sodium hydroxide, hydrochloric acid qs pH5.9

Pharmaceutical form and Description
Powder for solution for injection or infusion, orange yellow sterile cake of powder.

Uses
CERNEVIT is indicated for adults and children over 11 years of age. When the daily requirements of vitamins are required to be given to the patient by the parenteral route because oral administration is either contraindicated, impossible or insufficient (eg due to malnutrition, gastrointestinal malabsorption, etc).

Dosage and administration
Dosage
Adults and children aged over 11 years : 1 vial/day.

Administration
Method of reconstitution: see section Instruction for use and handling.
Intravenous route: By slow intravenous injection (at least 10 minutes) or by infusion in a solution of 5% glucose or 0.9% sodium chloride solution for infusion.
Cernevit may be included in the composition of nutritive mixtures combining carbohydrates, lipids, amino acids and electrolytes provided that compatibility and stability have been confirmed for each nutritive mixture, to meet nutrient needs and prevent deficiencies and complications from developing.
The total vitamin amounts from all sources such as nutritional sources, other vitamin supplements, or medications that contain vitamins as inactive ingredients (see Interaction with Other Medicaments and Other Forms of Interaction) should be considered.
The patient's clinical status and vitamin levels should be monitored to ensure maintenance of adequate levels.
It should be taken into account that some vitamins, especially A, B2, and B6 are sensitive to ultraviolet light (e.g., direct or indirect sun light). In addition, loss of vitamins A, B1, C, and E may increase with higher levels of oxygen in the solution. These factors should be considered if adequate vitamin levels are not achieved.

Contraindications
- hypersensitivity to the active substances, especially vitamin B1 or to any of the excipients, including soy protein/products (lecithin in mixed micelle is soy-derived) or peanut protein/products
- hypervitaminosis from any vitamin contained in this formulation
- neonates, infants and children less than 11 years old.

Special Warnings and Precautions for Use
WARNINGS
Hypersensitivity Reactions
- Severe systemic hypersensitivity reactions have been reported with Cernevit, other multivitamin preparations, and individual vitamins (including B1, B2, B12 and folic acid). Reactions with fatal outcome have been reported with Cernevit and other parenteral vitamin products (See Undesirable Effects).
- Cross-allergic reactions between soybean and peanut proteins have been observed.
- In some cases, the manifestations of a hypersensitivity reaction during intravenous administration of multivitamins may be rate related. If infused intravenously, Cernevit should be administered slowly. If injected intravenously, the injection must be administered slowly (over at least 10 minutes).
- The infusion or injection must be stopped immediately if signs or symptoms of a hypersensitivity reaction develop.
- Mild allergic reactions such as sneezing or mild asthma are warning signs that a further injection may give rise to anaphylactic shock.

Vitamin Toxicity
- The patient's clinical status and blood vitamin concentrations should be monitored to avoid overdose and toxic effects, especially with vitamins A, D and E, and in particular in patients who receive additional vitamins from other sources or use other agents that increase the risk of vitamin toxicity.
- Monitoring is particularly important in patients receiving long-term supplementation.

Hypervitaminosis A
- The risk for hypervitaminosis A and vitamin A toxicity (e.g., skin and bone abnormalities, diplopia, cirrhosis) is increased in, for example:
  - patients with protein malnutrition,
  - patients with renal impairment (even in the absence of vitamin A supplementation),
  - patients with hepatic impairment, - patients with small body size (e.g., paediatric patients), and
  - patients on chronic therapy.
- Acute hepatic disease in patients with saturated hepatic vitamin A stores can lead to the manifestation of vitamin A toxicity.

Refeeding Syndrome in Patients Receiving Parenteral Nutrition
Refeeding severely undernourished patients may result in refeeding syndrome that is characterized by the shift of potassium, phosphorus, and magnesium intracellularly as the patient becomes anabolic. Thiamine deficiency and fluid retention may also develop. Careful monitoring and slowly increasing nutrient intakes while avoiding overfeeding can prevent these complications. Should nutrient deficiencies occur, appropriate supplementation may be warranted.

Precipitates in Patients Receiving Parenteral Nutrition
Pulmonary vascular precipitates have been reported in patients receiving parenteral nutrition. In some cases, fatal outcomes have occurred. Excessive addition of calcium and phosphate increases the risk of the formation of calcium phosphate precipitates. Precipitates have been reported even in the absence of phosphate salt in the solution. Precipitation distal to the in-line filter and suspected precipitate formation in the blood stream have also been reported.

In addition to inspection of the solution, the infusion set and catheter should also periodically be checked for precipitates.

If signs of pulmonary distress occur, the infusion should be stopped and medical evaluation initiated.

PRECAUTIONS
Hepatic Effects
- Monitoring of liver function parameters is recommended in patients receiving Cernevit. Particularly close monitoring is recommended in patients with hepatic jaundice or other evidence of cholestasis.
  In patients receiving Cernevit, instances of liver enzyme increases have been reported, including isolated alanine aminotransferase (ALT) increases in patients with inflammatory bowel disease (see Undesirable Effects).
  In addition, an increase in bile acid levels (total and individual bile acids including glycocholic acid) have been reported in patients receiving Cernevit.
- Hepatobiliary disorders including cholestasis, hepatic steatosis, fibrosis and cirrhosis, possibly leading to hepatic failure, as well as cholecystitis and cholelithiasis are known to develop in some patients on parenteral nutrition (including vitamin supplemented parenteral nutrition). The etiology of these disorders is thought to be multifactorial and may differ between patients. Patients developing abnormal laboratory parameters or other signs of hepatobiliary disorders should be assessed early by a clinician knowledgeable in liver diseases in order to identify possible causative and contributory factors, and possible therapeutic and prophylactic interventions.

Use in Patients with Impaired Hepatic Function
Patients with hepatic impairment may need individualized vitamin supplementation. Particular attention should be placed on preventing vitamin A toxicity, because the presence of liver disease is associated with increased susceptibility to vitamin A toxicity, in particular in combination with chronic excessive alcohol consumption (See also Hypervitaminosis A and Hepatic Effects above).

Use in Patients with Impaired Renal Function
Patients with renal impairment may need individualized vitamin supplementation, depending on the degree of renal impairment and the presence of concomitant medical conditions. In patients with severe renal impairment, particular attention should be placed on maintaining adequate vitamin D status and preventing vitamin A toxicity, which may develop in such patients with low-dose vitamin A supplementation or even without supplementation.

Pyridoxine (vitamin B6) hypervitaminosis and toxicity (peripheral neuropathy, involuntary movements) have been reported in patients on chronic haemodialysis receiving intravenous multivitamins containing 4 mg pyridoxine administered three times a week.

General Monitoring Clinical status and vitamin levels should be monitored in patients receiving parenteral multivitamins as the only source of vitamins for extended periods of time. It is particularly important to monitor for adequate supplementation of, for example:
- Vitamin A in patients with pressure ulcers, wounds, burns, short bowel syndrome or cystic fibrosis
- Vitamin B1 in dialysis patients
- Vitamin B2 in cancer patients
- Vitamin B6 in patients with renal impairment
- Individual vitamins whose requirements may be increased due to interactions with other medicines (see Interaction with Other Medicaments and Other Forms of Interaction)

Deficiency of one or more vitamins must be corrected by specific supplementation.

Vitamin K
Cernevit does not contain Vitamin K. Vitamin K must be administered separately if necessary.

Use in Patients with Vitamin B12 Deficiency
Evaluation of vitamin B12 status is recommended before starting supplementation with Cernevit in patients at risk for vitamin B12 deficiency and/or when supplementation with Cernevit over several weeks is planned.
After several days of administration, both the individual amounts of cyanocobalamin (vitamin B12) and folic acid in Cernevit may be sufficient to result in an increase in red blood cell count, reticulocyte count, and haemoglobin values in some patients with vitamin B12 deficiency-associated megaloblastic anaemia. This may be masking an existing vitamin B12 deficiency. Effective treatment of vitamin B12 deficiency requires higher doses of cyanocobalamin than provided in Cernevit.
Folic acid supplementation in patients with vitamin B12 deficiency, who do not also receive vitamin B12, does not prevent the development or progression of neurologic manifestations associated with the vitamin B12 deficiency. It has been suggested that neurologic deterioration may even be accelerated.
When interpreting levels of vitamin B12, it should be taken into account that recent intake of vitamin B12 may result in normal levels despite a tissue deficiency.

Laboratory Test Interferences
Biotin
Biotin may interfere with laboratory tests that are based on a biotin/streptavidin interaction, leading to either falsely decreased or falsely increased test results, depending on the assay. The risk of interference is higher in children and patients with renal impairment and increases with higher doses. When interpreting results of laboratory tests, possible biotin interference has to be taken into consideration, especially if a lack of coherence with the clinical presentation is observed (e.g. thyroid test results mimicking Graves' disease in asymptomatic patients taking biotin or false negative troponin test results in patients with myocardial infarction taking biotin). Alternative tests not susceptible to biotin interference should be used, if available, in cases where interference is suspected. The laboratory personnel should be consulted when ordering laboratory tests in patients taking biotin.

Ascorbic acid
Depending on the reagents used, the presence of ascorbic acid in blood and urine may cause false high or low glucose readings in some urine and blood glucose testing systems, including test strips and handheld glucose meters. The technical information for any laboratory test should be consulted to determine the potential interference from vitamins.

Sodium Content
Cernevit contains 24 mg sodium (1 mmoL) per vial. This should be taken into consideration if patients are on a controlled sodium diet.

Paediatric Use
Cernevit is indicated in paediatric patients over 11 years of age (see also Hypervitaminosis A above).

Geriatric Use
In general, dosage adjustments for an elderly patient should be considered (reducing the dose and/or extending the dosing intervals) reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or drug therapy.

Fertility, pregnancy and lactation
Physicians should carefully consider the potential risks and benefits for each specific patient before prescribing CERNEVIT.
No safety data from Clinical trials are available to date therefore it is recommended to use CERNEVIT during pregnancy and breastfeeding only if absolutely necessary (only if the potential benefits are higher than the foetal risks).
CERNEVIT contains vitamin A. Taking into account that normal nutrition covers the daily vitamin A needs (found in liver, liver products, milk, dairy products, margarine, eggs, salad oils), daily doses sometimes exceed the daily needs (especially when liver of liver products are consumed). Certain data show that high vitamin A doses in pregnant women (1 st trimester) and women who want to become pregnant should not exceed 10 000 IU/day. This should be taken into consideration when CERNEVIT is administered with a large amount of food containing vitamin A.
The risk of vitamin A overdose in the neonate should be evaluated before using CERNEVIT in breastfeeding women.
Fertility There are no adequate data from the use of CERNEVIT with regards to fertility in male or female patients.

Interaction with Other Medicaments and Other Forms of Interaction
Interactions between specific vitamins in Cernevit and other agents should be managed accordingly.

Effects on the ability to drive and use machines
There is no information on the effects of Cernevit on the ability to operate an automobile or other heavy machinery.

Undesirable Effects
Adverse drug reactions (ADRs) that occurred after administration of Cernevit are presented with their relative frequencies; these include ADRs documented in clinical trials and those from post-marketing reports. Cernevit was administered during 3 clinical trials to 267 adult patients requiring a parenteral vitamin supplement.
Frequencies of ARs are reported, using the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1000 to <1/100); rare (≥1/10000 to <1/1000); very rare (<1/10000); and unknown (cannot be estimated from the available data).

Overdosage
Acute or chronic overdose of vitamins (in particular A, B6, D, and E) can cause symptomatic hypervitaminosis.
Clinical signs of acute overdose of vitamin A (doses exceeding 150,000 IU):
- Gastrointestinal disorders, headache, raised intracranial pressure (swollen fontanelle in infants), papilloedema, psychiatric disorders, irritability, or even convulsions, delayed generalized desquamation.

Clinical signs of chronic intoxication (prolonged vitamin A supplementation with supraphysiological doses in non-deficient subjects)
- Liver disorders, raised intracranial pressure, cortical hyperostosis of long bones and premature epiphyseal fusion, cephalitis, pruritus, vomiting, dryness of mucous membranes. The diagnosis is generally based on the presence of tender or painful subcutaneous swellings in the extremities of the limbs. X-rays demonstrate diaphyseal periosteal thickening of the ulna, fibula, clavicles and ribs.
  The risk of overdose is particularly high if a patient receives vitamins from multiple sources and overall supplementation of a vitamin does not match the patient's individual requirements, and in patients with increased susceptibility to hypervitaminosis

Actions to be taken in the event of acute or chronic overdose
- Stop administration of CERNEVIT, reduce calcium intake, increase diuresis and rehydrate.

Pharmacological Properties
Pharmacodynamic properties

ADDITIVES FOR INTRAVENOUS SOLUTIONS/VITAMINS, (ATC Code: B05XC)

CERNEVIT contains 9 hydrosoluble vitamins and 3 liposoluble vitamins, essential to the metabolism of adults and children aged over 11, except for vitamin K.
The pharmacodynamic properties of CERNEVIT are those of the individual 12 vitamins in its composition.

Pharmacokinetic properties
Not available.

Preclinical safety data
Not available.

Packing
Box of 10 vials

Storage
Store below 25°C, keep container in the outer carton. Protect from heat and light. To be used only as directed by medical practitioner. Reconstituted solution should be kept refrigerated (2° 8°C) for no more than 24 hours.
The product after reconstitution should be used immediately.
From microbiological point of view, the product should be used immediately after reconstitution.

Shelf life
2 years

Incompatibility statement
- In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.
- Additives may be incompatible with parenteral nutrition containing Cernevit. If co-administration of drugs that are incompatible at the Y-site is necessary, administer via separate IV lines.
- Vitamin A and thiamine in Cernevit may react with bisulfites in parenteral nutrition solutions (e.g., as a result of admixtures) leading to degradation of vitamin A and thiamine.
- An increase in pH of a solution may increase the degradation of some vitamins. This should be considered when adding alkaline solutions to the admixture containing Cernevit.
- Folic acid stability can be impaired with increased calcium concentrations in an admixture.

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For Healthcare Professionals Only.

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