# VITAMIN B-COMPLEX + VITAMIN E

Each film-coated tablet contains:

d-Alpha Tocopheryl Acid Succinate (Vitamin E) ..... 100 IU
Thiamine Mononitrate (Vitamin $B_1$) ..... 300 mg
Pyridoxine Hydrochloride (Vitamin $B_6$) ..... 100 mg
Cyanocobalamin (Vitamin $B_{12}$) ..... 1 mg

# NEUROGEN-E®

## Film-coated Tablet
## Vitamins

PRODUCT DESCRIPTION
This product is a maroon, elliptical-shaped, film-coated tablet plain on both sides.

WHAT IS IN THE MEDICINE?
This product contains B-complex vitamins (vitamins $B_1$, $B_6$ and $B_{12}$) and vitamin E. B-complex vitamins are required for the normal function of the nervous system and are used as adjunct in the management of various neuromuscular disorders. Together with B-complex vitamins, vitamin E helps maintain membrane integrity in all cells of the body including the nerve tissues by acting as the body's major lipid-soluble antioxidant.
B-complex vitamins and vitamin E have the following known neuromuscular functions/effects:

| NUTRIENTS | NEUROMUSCULAR FUNCTION |
|---|---|
| Thiamine ($B_1$) | Involved in the production and release of acetylcholine, a neurotransmitter required in conveying signals between nerve cells |
| Pyridoxine ($B_6$) | Required in the formation of neurotransmitters such as serotonin, gamma amino butyric acid (GABA), dopamine, and epinephrine to facilitate normal nervous system function. |
| Cyanocobalamin ($B_{12}$) | Required for the synthesis of myelin, the white sheath that surrounds nerve fibers |
| Vitamin E | Helps maintain membrane integrity in all cells of the body including nerve tissues by acting as the body's major lipid-soluble chain-blocking antioxidant |

STRENGTH OF THE MEDICINE
Please see FORMULATION .

WHAT IS THE MEDICINE USED FOR?
- For the treatment of deficiencies in vitamins $B_1$, $B_6$, $B_{12}$, and E manifested as:
  - Muscle pain, loss of reflexes in the hands, knees, ankles, calves and feet and abnormal touch sensation (burning and pricking)
- For the treatment of conditions responsive to high dose vitamins $B_1$, $B_6$, $B_{12}$ and E which include the following:
  - Polyneuropathy (multiple disturbances in the function of the brain or spinal cord that may affect the nerves and muscles of the body)
  - Diabetic neuropathy (disturbances in the function of the brain or spinal cord that may affect the nerves and muscles of the body associated with diabetes mellitus)
  - Neuralgia (nerve pain)
  - Neuritis (inflammation of the nerves)
  - Wernicke's disease (an alcohol-induced thiamine deficiency characterized by mental confusion, staggering, and constant rapid eye movements)
  - Beri-beri [thiamine deficiency manifested as muscle weakness, loss of appetite, nerve degeneration (inability of nerves to function properly)]
  - Sideroblastic anemia (any of a heterogeneous group of anemias with diverse clinical manifestations)
  - Pernicious anemia [a type of megaloblastic anemia usually seen in older adults, caused by impaired intestinal absorption of vitamin $B_{12}$ due to lack of availability of intrinsic factor; characterized by pallor (paleness), achlorhydria (absence of hydrochloric acid from maximally stimulated gastric secretions), glossitis (inflammation of the tongue), weakness, and neurologic manifestations]

HOW MUCH AND HOW OFTEN SHOULD YOU USE THIS MEDICINE?
Orally one tablet daily.
Or, as directed by a doctor.

WHEN SHOULD YOU NOT TAKE THIS MEDICINE?
- If you are allergic to any ingredient in the product
- Cyanocobalamin is contraindicated in patients who have experienced hypersensitivity reactions to cobalt.
- Cyanocobalamin should not be used in patients with early Leber's disease (hereditary optic nerve atrophy), since rapid wasting of the optic nerve has been reported following its administration to these patients.

UNDESIRABLE EFFECTS
The nutrients in this product are relatively nontoxic and are usually well tolerated. However, the following undesirable effects may occur particularly when the nutrients are used at high doses.

Vitamin $B_1$
There have been no reported undesirable effects with thiamine.

Vitamin $B_6$
Although vitamin $B_6$ is generally considered to be relatively nontoxic, adverse neurologic effects have been reported following chronic administration of large pyridoxine dosages, e.g., more than 500 mg daily (see also SIGNS AND SYMPTOMS OF OVERDOSAGE). Nausea, headache, paresthesia (tingling or pricking sensation), sleepiness, and increased serum aspartate aminotransferase (AST, a liver enzyme) and decreased serum folic acid concentrations have been reported. Allergic reactions have been reported occasionally in patients receiving the vitamin.
Adverse neurologic effects have also been reported rarely after chronic administration of lower dosages (e.g., more than 200 mg daily) of pyridoxine.

Vitamin $B_{12}$
Vitamin $B_{12}$ may occasionally cause diarrhea and skin itching. Signs of polycythemia vera may be unmasked. Megadoses may exacerbate acne.

Vitamin E
Vitamin E (e.g., at dosages exceeding 300 IU daily) has rarely caused nausea, diarrhea, abdominal pain/intestinal cramps, fatigue/weakness, headache, dizziness, blurred vision, emotional disturbances, and rash. Myopathy (muscle disorder), hypertension, thrombophlebitis (vein inflammation related to a blood clot), gonadal dysfunction, breast soreness/gynecomastia, creatinuria (increased concentration of creatine in the urine), increased serum creatine kinase, serum cholesterol, and triglycerides; increased urinary estrogens and androgens; and thyroid problems have also been noted. These effects generally disappeared after discontinuing the vitamin.

Doses of vitamin E greater than 1,000 mg (equivalent to 1,490 IU) daily for prolonged periods have occasionally been associated with increased bleeding tendency in vitamin K-deficient patients such as those taking oral anticoagulants. It has also been suggested that it may increase the risk of thrombosis in some patients, such as those taking estrogens.

WHAT OTHER MEDICINE OR FOOD SHOULD BE AVOIDED WHILE TAKING THIS MEDICINE?
The following interactions have been noted particularly when the nutrients are used at high doses:

Vitamin $B_1$:
- Neuromuscular blocking agents (e.g., tubocurarine chloride, metocurine iodide, pancuronium bromide, and vecuronium bromide): These may be enhanced by high doses of vitamin $B_1$ (>500 mg daily), although the clinical significance of this is unknown.

Vitamin $B_6$:
- Cycloserine, hydralazine, isoniazid, penicillamine: These medicines may cause anemia or peripheral neuritis by acting as pyridoxine antagonists.
- Estrogen, isonicotinic acid hydrazide, theophylline: These may increase requirement for vitamin $B_6$.
- Levodopa: The effects of levodopa are reversed by pyridoxine (even doses as low as 5 mg daily); vitamin $B_6$ supplements should be avoided.
- Phenobarbital, phenytoin: Vitamin $B_6$ (200 mg daily for 1 month) resulted in a 50% decrease in serum levels of these drugs.

Vitamin $B_{12}$:
- Aminoglycoside antibiotics, chloramphenicol, colchicine, extended-release potassium preparations, aminosalicylic acid and its salts, anticonvulsants (e.g., phenytoin, phenobarbital, primidone), histamine H2-receptor antagonists, metformin, methyldopa, cobalt irradiation of the small bowel, and alcohol (excessive intake): These may decrease the absorption of vitamin $B_{12}$.
- Nitrous oxide: Prolonged nitrous oxide anesthesia inactivates vitamin $B_{12}$.
- Oral contraceptives, proton pump inhibitors (long-term treatment): These may reduce blood levels of vitamin $B_{12}$.

Vitamin E
- Anticoagulants: Vitamin E reportedly may have anti-vitamin K effects; concomitant intake of anticoagulants (e.g., warfarin) and vitamin E may result in hemorrhage (bleeding).
- Antiplatelets: High doses of vitamin E may also potentiate the effects of antiplatelets (e.g., aspirin, clopidogrel, ticlopidine) and herbs with antithrombotic activity such as garlic and ginkgo.
- Anticonvulsants (e.g., phenobarbital, phenytoin, carbamazepine): These may lower plasma levels of vitamin E.
- Oral contraceptives: These may lower plasma levels of vitamin E.
- Cholestyramine, colestipol, isoniazid, mineral oil, neomycin, orlistat, or sucralfate: These may decrease/impair the absorption of vitamin E. Allow as much time as possible between doses.
- Digoxin: Vitamin E may reduce the requirement for digoxin. Monitoring is recommended.
- Insulin: Vitamin E may reduce the requirement for insulin. Monitoring is recommended.
- Dietary fiber supplementation: This may decrease the antioxidative effect of a supplement containing vitamin E (alpha-tocopherol).
- Others: Vitamin E may enhance the side effects of some drugs (i.e., amiodarone, ciclosporin, and zidovudine).

Interference with Laboratory Tests:
- Vitamin $B_1$ has been reported to interfere with the results of the following laboratory tests: phosphotungstate method for determination of uric acid; urine spot test with Ehrlich's reagent for urobilinogen; spectrophotometric determination of serum theophylline concentrations.
- Vitamin $B_6$ has reportedly resulted in a false-positive determination for urobilinogen in the spot test using Ehrlich's reagent.
- Antibiotics may interfere with microbiological assay for serum and erythrocyte vitamin $B_{12}$ (false low results).

WHAT SHOULD YOU DO IF YOU MISS A DOSE?
If you miss a dose, just take the next dose and the subsequent doses at the usual recommended schedule, i.e., once a day. Do not double the dose.

HOW SHOULD YOU KEEP THIS MEDICINE?
- Keep the product out of reach and sight of children.
- Store at temperatures not exceeding 30 °C.
- Protect from light.

SIGNS AND SYMPTOMS OF OVERDOSAGE
Vitamin $B_6$
Long term administration (i.e., 2 months or longer) of large (megadose) dosages (e.g., 2 g or more daily) of pyridoxine can cause sensory neuropathy or neuronopathy syndromes. Other side effects reported with megadoses of pyridoxine include peripheral neuropathy, unsteady gait (manner of walking), loss of limb reflexes/numbness and tingling in feet and hands, hyperesthesia (increased physical sensitivity), muscle weakness, impaired or absent tendon reflexes; bone pain, headache, dizziness, sleepiness, nausea, upset stomach, breast tenderness, photosensitivity on sun exposure, and exacerbation of acne.
Vitamin E
There are no available data on acute overdosage with vitamin E. However, large doses have occasionally been associated with side effects (see UNDESIRABLE EFFECTS).

WHAT TO DO WHEN YOU HAVE USED MORE THAN THE RECOMMENDED DOSAGE?
If you have taken more than the recommended dosage, consult a doctor.

CARE THAT SHOULD BE TAKEN WHEN TAKING THIS MEDICINE
- High doses of vitamin E (i.e., doses greater than 100 IU) should be used with caution in patients on warfarin. Monitoring of international normalized ratio (INR) and adjusting of warfarin dose (if indicated) are recommended. Likewise, those with vitamin K deficiencies, such as patients with liver failure, should be cautious in taking high doses of vitamin E.
- Vitamin E should be used with extreme caution in those with any lesions that have a tendency to bleed (e.g., bleeding peptic ulcers), those with a history of hemorrhagic stroke, and those with inherited bleeding disorders (e.g., hemophilia).
- Vitamin E supplements should be avoided in cases of iron-deficiency anemia (vitamin E may impair hematological response to iron) and hyperthyroidism.
- Do not use more than the recommended dose.
- Do not use after the expiry date on the label.

WHEN SHOULD YOU CONSULT YOUR DOCTOR?
- Consult a doctor before using this product if you:
  - have a history of stroke or risk factors for stroke;
  - have any coagulation (blood clotting) problem or you are taking anticoagulants (e.g., warfarin)
- If any undesirable effect occurs.

DATE OF REVISION OF PATIENT INFORMATION LEAFLET: August 2018

DATE OF FIRST AUTHORIZATION: 19 May 2008

AVAILABILITY
Available in Box of 8`s and 100`s (flex foil x 4`s)

For suspected adverse drug reaction, seek medical attention immediately and report to the FDA at www.fda.gov.ph AND Unilab at (+632) 858-1000 or productsafety@unilab.com.ph. By reporting undesirable effects, you can help provide more information on the safety of this medicine.

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