THIAMINE MONONITRATE (Vit. B1)
PYRIDOXINE HCl (Vit. B6)
CYANOCOBALAMIN (Vit. B12)
PARACETAMOL

POLYNERV™ FORTE

Film-Coated Tablet

Vitamins/Analgesic

FORMULATION:

Each film-coated tablet contains:

Thiamine Mononitrate (Vit. B1), USP	150 mg
Pyridoxine HCl (Vit. B6)	100 mg
Cyanocobalamin (Vit. B12)	3000 mcg
Paracetamol	600 mg

PRODUCT DESCRIPTION:

POLYNERV™FORTE Tablet is an old rose, biconvex, film-coated tablet bisected on one side.

POLYNERV™FORTE is a high potency formulation of the neurotropic vitamins B1, B6 and B12, reinforced with an analgesic, paracetamol. This unique formulation helps provide adequate nourishment of the different body systems especially the central and peripheral nervous systems and alleviate various painful conditions including neuromuscular illnesses. The vitamin B components of **POLYNERV™FORTE** catalyze various basic biochemical processes required in promoting nervous system physiology. Paracetamol, with its pain relieving actions, complements the nerve soothing actions of vitamins B1, B6 and B12.

PHARMACODYNAMICS AND PHARMACOKINETICS:

Vitamins B1, B6 and B12 are important co-factors in maintaining normal nerve metabolism. Any metabolic disorder that may result from the deficiency of these factors and or concomitant nerve injury may cause peripheral neuropathies.

Since pain often accompanies peripheral neuropathies, paracetamol, a proven safe and dependable analgesic, in combination with B-complex provide support in the management of neuromuscular diseases.

Thiamine (Vitamin B1) functions as a coenzyme of carbohydrate metabolism. It is specifically involved in the decarboxylation of alpha-ketoacids such as pyruvate and alpha-ketoglutarate. Impaired oxidation of the alpha-ketoacids leads to the accumulation of metabolites which are toxic to the cells of the central nervous system (CNS). Thiamine promotes efficient metabolism of glucose and the conversion of glucose into other substances such as ribose, a major component of DNA and RNA. Thiamine activates production of energy from glucose and storage of energy as fat, making energy available to support the normal cellular processes. Thiamine is essential for the normal functions of the gastrointestinal, cardiovascular and nervous systems of the body. The muscle cells of the heart, blood vessels, and the secretory glands of the gastrointestinal tract depend on the energy derived from the metabolism of glucose which thiamine catalyzes. A lack of thiamine leads to weakness in these muscles. The cells of the CNS also depend exclusively on glucose as its source of energy. When there is thiamine deficiency, glucose utilization by nervous tissues decreases, and the communication in many different portions of the CNS is disrupted. Independent of its coenzyme function, thiamine also acts as a modulator in the transmission of neural impulses.

Pyridoxine (Vitamin B6) participates in many cellular reactions of lipid and amino acid metabolism. The active form of B6, pyridoxal phosphate, acts as a coenzyme in several metabolic transformations of amino acids, which are in turn needed for tissue building and repair, and in the synthesis of blood elements and certain compounds like neurotransmitters. Pyridoxine is of particular importance in the synthesis of neurotransmitters, which are required for the normal activity of the nervous system. A deficiency of pyridoxine causes abnormal CNS function, with hyperirritability, neuritis, and even convulsions. Vitamin B6 is required in the synthesis of precursors necessary for hemoglobin production.

POLYNERV™FORTE contains high amount of cyanocobalamin (Vitamin B12), a coenzyme involved in several, metabolic pathways. Among the important actions of cyanocobalamin is to act as a coenzyme of nucleic acid metabolism, reducing ribonucleotides to deoxyribonucleotides, a step that is essential in the replication and formation of new cells. Cyanocobalamin is likewise an important co-factor in the formation and maturation of red blood cells in the bone marrow. Cyanocobalamin is also involved in the formation of myelin sheaths in the nervous tissues. A deficiency of cyanocobalamin may cause demyelination of the large nerve fibers of the spinal cord. The inhibition of normal fatty acid synthesis in the brain and nerve tissues may also lead to faulty structure and impaired functions manifested as neurological symptoms.

Paracetamol relieves pain by blocking the production of prostaglandin, the chemical that causes pain, through the inhibition of the enzyme cyclooxygenase.

INDICATIONS:

- Neuropathies caused by certain disease states such as diabetes mellitus and cardiac disorders.
- Alcoholic neuropathy
- Acute and chronic painful paresthesias
- Neuralgias (e.g., ischialgia, trigeminal neuralgia and lumbalgia) and in cases of peripheral nerve impingement (i.e., carpal tunnel syndrome, cervical shoulder-arm syndrome, cervical spondylosis and herniated disc with root impingement), trauma (e.g., nerve transection, crash injuries and traction injuries), or infection (e.g., herpes zoster or shingles).

DOSAGE AND ADMINISTRATION:

For therapeutic use, 2-4 tablets should be administered daily or as prescribed by the physician. Chronic cases which may require longer therapy must be under the supervision of a physician.

CONTRAINDICATIONS/PRECAUTIONS/WARNINGS:

Contraindicated in patients with history of hypersensitivity to paracetamol and any of the components.

Paracetamol should be given with care to patients with impaired kidney or liver function. It should also be given with care to patients with alcohol dependence, chronic malnutrition, or dehydration.

Cyanocobalamin should not be given to patients with suspected vitamin B12 deficiency without first confirming the diagnosis. Use of doses greater than 10 mcg daily may produce a hematological response in patients with folate deficiency and indiscriminate use may mask the precise diagnosis. Regular monitoring of blood is advisable.

Cyanocobalamin should not be used for Leber's disease or tobacco amblyopia since these optic neuropathies may degenerate further.

PREGNANCY AND LACTATION:

Vitamins B1, B6, B12 and Paracetamol can be given safely for pregnant and lactating women.
Though some have expressed concern over inhibition of breast milk secretion by pyridoxine, others have cautioned that pyridoxine deficiency may cause seizures in the neonate.

ADVERSE DRUG REACTIONS:

Adverse effects of paracetamol are rare and usually mild, although hematological reactions including thrombocytopenia, leucopenia, pancytopenia, neutropenia, and agranulocytosis have been reported.

Paracetamol use has been associated with development of rashes and other hypersensitivity reactions characterized by urticaria, dyspnea, hypotension and angioedema. Fixed drug eruptions and toxic epidermal necrolysis have also been reported.

Results of few studies have suggested that long-term use of paracetamol may be associated with an increased risk for developing hematologic malignancies, hypertension, hearing loss and asthma. Paracetamol has also been associated with accumulation of pyroglutamic acid, resulting in pyroglutamic aciduria and high anion gap metabolic acidosis.

Adverse effects with thiamine are rare, but hypersensitivity reactions have occurred, mainly after parenteral doses.

Long-term (2 to 40 months) use of large doses of pyridoxine (2 to 6 g daily) is associated with the development of severe peripheral neuropathies.

Allergic hypersensitivity reactions have occurred rarely after cyanocobalamin and include skin reactions such as rash and itching, and anaphylaxis. Patients who are hypersensitive to cyanocobalamin injection may however be able to take oral cyanocobalamin. Other adverse effects reported with cyanocobalamin include gastrointestinal disturbances, fever, chills, hot flushing, dizziness, malaise, acneiform and bullous eruptions, and tremor.

DRUG INTERACTIONS:

The risk of paracetamol toxicity may be increased in patients receiving other potentially hepatotoxic drugs or drugs that induce liver microsomal enzymes. The absorption of paracetamol may be accelerated by drugs such as metoclopramide. Excretion may be decreased when given with probenecid. Cholestyramine reduces the absorption of paracetamol if given within 1 hour of paracetamol. Drugs that increase the requirements for pyridoxine include hydralazine, isoniazid, penicillamine and oral contraceptives. Pyridoxine reduces the activity of altretamine and decreases serum concentrations of phenobarbital and phenytoin.

Drugs that may reduce the absorption of vitamin B12 from the gastrointestinal tract include neomycin, aminosalicylic acid, histamine-2 receptor antagonists, omeprazole, and colchicine. The effect of vitamin B12 in anemia may be attenuated by parenteral chloramphenicol.

OVERDOSAGE AND TREATMENT:

Toxic doses of paracetamol may cause severe hepatocellular necrosis and renal tubular necrosis. Hepatotoxicity may occur after ingestion of more than 150 mg/kg, or rarely, as little as 75 mg/kg, of paracetamol within a 24-hour period. Early signs of overdosage such as nausea, vomiting, lethargy and sweating usually settle within 24 hours. Abdominal pain may be the first indication of liver damage although it is not apparent for 24 to 48 hours and may be delayed for up to 4 to 6 days after ingestion. Liver damage is generally at a maximum 72 to 96 hours after ingestion. Hepatic failure, encephalopathy, coma, and death may result. Complications of hepatic failure include acidosis, cerebral edema, hemorrhage, hypoglycemia, hypotension, infection, and renal failure.

Prompt treatment is essential, even when there are no obvious symptoms, and patients should be admitted to the hospital for full supportive measures. Activated charcoal may be used to reduce gastrointestinal absorption if it can be given within 1 hour of the overdose and if more than 150 mg/kg of paracetamol has been ingested. However, if acetylcysteine or methionine antidote is to be given orally, the charcoal is best cleared from the stomach to prevent it from reducing the absorption of the antidote. The plasma-paracetamol concentration should be determined as soon as possible, but not within 4 hours of ingestion. Antidote treatment should be started as soon as possible after suspected paracetamol ingestion and should not be delayed while awaiting the results of plasma assays. Once the results become available; treatment may be stopped if the initial concentration was below the nomogram reference line. Acetylcysteine is usually the antidote of choice but the route of administration varies. Acetylcysteine is most effective when given during the first 8 hours after taking the overdose and the effect diminishes progressively thereafter. Methionine is also most effective when given as early as possible after paracetamol overdosage.

The plasma-paracetamol concentrations considered as indication for antidote treatment should be halved in patients receiving enzyme-inducing drugs such as rifampicin, carbamazepine, phenobarbital, phenytoin, or primidone. Severe hepatotoxicity at therapeutic doses or moderate overdoses of paracetamol has been reported in patients receiving isoniazid, alone or with other drugs for tuberculosis.

No cases of Vitamin B1 overdose have been reported. Vitamin B6 overdose is rare, two cases that caused central nervous system toxicity have been reported. Overdose of Vitamin B12 is also rare. Although an overdose is highly unlikely, call the doctor right away if you have any reason to suspect that one has occurred.

AVAILABILITY:

Aluminum - OPA / Alu / PVC Blister Pack x 10's (Box of 100)

CAUTION:

Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

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STORE AT TEMPERATURES NOT EXCEEDING 30°C.

For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph

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