REXOM$_{TM}$ WINA NEURO TABLET

Name and Strength of Active Ingredient(s)
Each tablet contains:
Thiamine Hydrochloride (Vitamin B1) ……100mg
Pyridoxine Hydrochloride (Vitamin B6) ……..200mg
Cyanocobalamin (Vitamin B12)……..…….…….200 mcg

Description
Product Description
Pink colour, round with top-score tablet.

Pharmacodynamics
Rexom Wina Neuro Tablet contain a combination of neurotropic active substances of the vitamin B complex. The vitamins thiamine (B1), pyridoxine (B6) and cobalamin (B12) contained play a particular role as coenzymes in the intermediary metabolism of the central and peripheral nervous system.

Like all other vitamins, they are essential nutrients which the body cannot synthesize itself.

Therapeutic supply of vitamins B1, B6 and B12 may supplement inadequate nutritive vitamin intake and thus ensure the availability of the required quantities of coenzymes.
The therapeutic use of these vitamins in diseases of the nervous system serves, on the one hand, to compensate for concomitant deficiencies (possibly due to an increased requirement induced by the disease) and, on the other, to stimulate natural repair mechanisms.

Thiamine (vitamin B1)
Thiamine pyrophosphate (TPP) is the effective form of vitamin B1 and acts as a coenzyme for a number of enzymes (e.g. pyruvate dehydrogenase and transketolase). Accordingly, vitamin B1 is primarily involved in the carbohydrate metabolism; however, it also intervenes in the synthesis of lipids and amino acids. Nerve cells cover their energy requirement exclusively via enzymatic oxidation and decarboxylation of glucose, so that an adequate supply of vitamin B1 is of crucial importance. Thiamine is also involved in the conduction of nerve impulses.
Models used in animal studies have indicated analgetic activity for vitamin B1.

Manifestations of vitamin B1 deficiency are very multifaceted and can involve central and peripheral nervous system, the cardiovascular system, skin and other body systems. Specific symptoms can include polyneuropathy with paraesthesia (tingling, burning, numbness), hyperesthesia (increased sensitivity), muscle weakness, altered temperature sensitivity, oedema, and others.

Pyridoxine (vitamin B6)

Pyridoxal phosphate, the biologically active form of pyridoxine, is the determinative coenzyme in amino acid metabolism. It is involved in the formation of physiologically active amines (e.g. serotonin, histamine, adrenalin) through decarboxylation processes, as well as in anabolic and catabolic processes through transamination.

Pyridoxal phosphate plays an essential role in the nervous system, especially in the enzymatically controlled neurotransmitter metabolism. As a catalyst of the first biosynthesis steps of sphingosine, pyridoxal phosphate also has a key role in the metabolism of sphingolipids. Sphingolipids are essential constituents of the myelin sheaths of nerve cells. Animal experimental models have demonstrated that vitamin B6 has an analgesic effect.

Vitamin B6 deficiency can be associated with peripheral neuritis and neuropathy, paresthesia, burning, painful dysesthesia, disorders of oxalate metabolism, depression of immune responses, anemia, lesions of the mucous membranes and other symptoms.

Cobalamin (vitamin B12)

Vitamin B12 in its coenzyme forms (5-deoxyadenosyl cobalamin and methyl cobalamin) is involved in enzymatically catalysed intramolecular hydrogen displacements and in intramolecular transfers of methyl groups. Vitamin B12 is also involved in methionine synthesis (closely coupled to the synthesis of nucleic acids) and in lipid metabolism, via the conversion of propionic acid into succinic acid.

Vitamin B12 is involved in the methylation of the myelin basic protein, a constituent of the myelin sheaths of the nervous system. Methylation increases the lipophilic properties of the myelin basic protein, which favours increased integration in the myelin sheaths.

Vitamin B12 deficiency can result in neurological symptoms like paresthesia, numbness, gait impairment, impaired vibration sense, polyneuritis (particularly sensory, in the distal extremities), ataxia and others. Further symptoms can be anaemia, optic atrophy, altered mental status and others.

Combination of vitamins B1, B6 and B12

Neurotropic vitamins B1, B6 and B12 alone, and in combination as the result of biochemical synergy, have special significance for the metabolism of the nervous system, which justifies their combined use.

Further, in most of the patient populations such as elderly, diabetic patients and others, deficiency of all three neurotropic vitamins is present.

Animal studies have shown that this combination of neurotropic B vitamins accelerates regenerative processes in damaged nerve fibres, which finally leads to enhanced restoration of function and muscle innervation. In the model of experimental diabetes in rats, administration of B complex vitamins prevented or attenuated the characteristic nerve damage, so that deterioration of the functional properties was counteracted (antineuropathic effect).

Further, the combination of B1, B6 and B12 has been proven to have a synergistic effect when combined with NSAIDs in the treatment of pain.

Pharmacokinetics
Combined administration of vitamins B1, B6 and B12 is not expected to have a negative effect on the pharmacokinetics of the individual vitamins.

Thiamine(vitamin B1) :
Has after oral administration a dose-dependent dual transport mechanism:
Active absorption up to concentrations of 2 µmol and passive diffusion in concentrations over 2 µmol).
There is almost no absorption in the stomach and in distal segments of the small intestine. Thiamine formed by the large intestinal flora is not absorbed. Absorption of thiamine takes place after phosphorylation in the epithelial cells; a carrier mechanism is assumed to be involved in the passage through the intestinal wall.

After absorption by the intestinal mucosa, thiamine is transported to the liver via the portal circulation. In the liver, thiamine is phosphorylated to thiamine pyrophosphate (TPP) and thiamine triphosphate (TTP) by means of thiamine kinase.

The biological half-life of thiamine in humans is about 9.5 to 18.5 days, with an elimination half-life is approx. 4 hours.
The human body can store approx. 30 mg thiamine. On account of the rapid metabolisation, the
reserve capacity, at 4-10 days, is very limited.

Pyridoxine(vitamin B6):
Pyridoxine is absorbed very rapidly, mainly in the upper gastrointestinal tract, and is excreted with a maximum between 2 and 5 hours.
Vitamins are bound to albumin. Vitamin B6 passes into the spinal fluid, is secreted into breast milk, and permeates the placenta. The principal excretion product is 4-pyridoxic acid; the amount of the latter depending on the vitamin B6 dose taken up.

Vitamin B6 is phosphorylated mainly in the liver, forming the biologically active pyridoxal phosphate. To cross cell membranes, phosphorylated vitamin B6 must be hydrolysed by alkaline phosphatase to free vitamin B6. Transport into the cells is by simple diffusion followed by rephosphorylation, and a specialized intestinal carrier-mediated system for pyridoxine uptake has been discussed recently. Peak concentrations are reached after 3.5 to 4 hours. The biological half-life of pyridoxal phosphate is about 15 - 25 days. The storage capacity for vitamin B6 is 14 to 42 days.
Approx. 40 to 150 mg can be stored, 1.7 to 3.6 mg is excreted in the urine per day.

Cobalamin (vitamin B12):
Cobalamin is absorbed from the gastrointestinal tract by means of 2 mechanisms:
- release through gastric acid and immediate binding to the intrinsic factor. A maximum of 1.5-2 µg of oral vitamin B12 is absorbed via this mechanism
- independently of the intrinsic factor through passive influx in the blood

At doses over 1.5 µg the latter mechanism increases in significance.
Patients with pernicious anaemia absorb approx. 1% of oral doses of 100 µg and over.
Vitamin B12 is stored predominantly in the liver, the daily requirement is 1 µg.
The turnover rate is 2.5 µg B12 per day, or 0.05% of the stored quantity. The biological half-life is about 1 year.
Vitamin B12 is mainly secreted into bile and largely reabsorbed during the enterohepatic circulation.

Indications
Deficiency or raised requirements of vitamin B1, B6 & B12.
Mononeuropathies & polyneuropathies eg. diabetic, alcoholic & toxic neuropathies.
Neuritis & neuralgia of the spinal nerves, especially facial paresis, cervical syndrome, low back pain and ischialgia.

Recommended Dose
One tablet once daily. In individual cases, the dose may be increased to one tablet 3 times daily.
The tablets are to be swallowed whole with plenty of liquid after meals.

Duration of administration
The physician in charge should decide on the duration of administration.
After a maximum period of four weeks, it should be decided whether to reduce the dose.

Not to be used in children and adolescents (<18 years).

Route of Administration
Oral.

Contraindications
- Hypersensitivity to the active substances or to any of the excipients
- Must not be used in children and adolescents due to their high active substance content.

Warning and Precautions
The clinical picture as well as the laboratory parameters of funicular myelosis or of pernicious anaemia can lose specificity by administration of vitamin B12.

If symptoms of peripheral sensory neuropathy (paraesthesia) occur, the dosage should be reviewed and treatment with the medicinal product discontinued, if necessary. Neuropathies have been observed under long-term intake (over 6-12 months) of daily dosages exceeding 50 mg vitamin B6 as well as in short-term intake (over 2 months) of more than 1 g vitamin B6 per day. Therefore, regular monitoring is recommended under long-term treatment.

Interactions with Other Medicaments
Thiamine is inactivated by 5-fluorouracil as the latter competitively inhibits the phosphorylation of thiamine to thiamine pyrophosphate.

Antacids diminish the absorption of thiamine.

Loop diuretics, e.g. furosemide that inhibit tubular reabsorption may cause increased excretion of thiamine in long-term therapy and, thus, lowering of the thiamine serum level.

If taken simultaneously with L-dopa, vitamin B6 can lessen the dopa effect.

The simultaneous administration of pyridoxine antagonists (e.g. isoniazide (INH), hydralazine, Dpenicillamine or cycloserine) may decrease the efficacy of vitamin B6 (pyridoxine).
Long term use of acid-lowering agents may lead to vitamin B12 deficiency.
Alcohol and black tea diminish the absorption of thiamine.

Beverages containing sulphite (e.g. wine) enhance thiamine degradation.

Pregnancy & Lactation
Pregnancy
During pregnancy and the nursing period the generally recommended daily dosage of vitamin B1 is 1.4 mg and of vitamin B6 1.9 mg.
These dosages may be exceeded in pregnant patients with manifest vitamin B1 and B6 deficiencies only as the safety of doses higher than the recommended daily dosage has not yet been demonstrated. There are only insufficient animal studies on the effect of this medicinal product on pregnancy, embryo-foetal, prenatal and postnatal development. The possible risk for human beings is not known. The treating physician should decide about the use of this product during pregnancy after carefully weighing the risk-to-benefit ratio.

Breast-feeding
Vitamins B1, B6 and B12 are secreted into human breast milk. High concentrations of vitamin B6 i.e. > 600 mg daily, can inhibit the production of breast milk. Data on the extent of secretion into breast milk from animal studies are not available. Therefore, the advantages of breastfeeding for the infant should be carefully weighed against the therapeutic benefit for the women in order to decide to either discontinue breast-feeding or therapy with Rexom Wina Neuro Tablet.

Side Effects
Nervous system disorders:
Long-term intake (> 6-12 months) of a daily dosage > 50 mg vitamin B6 may cause peripheral sensory neuropathy.

Gastrointestinal disorders:
Gastrointestinal complaints such as nausea, vomiting, diarrhoea and abdominal pain.

Immune system disorders:
Hypersensitivity reactions such as sweating, tachycardia and skin reactions like itching and urticaria.

Renal and urinary disorders:

Chromaturia ("reddish urine", appeared during the first 8 hours after an administration and typically resolves within 48 hours).

Symptoms and Treatment of Overdose

Vitamin B1:

Thiamine has a broad therapeutic range. Very high doses (over 10 g) have a ganglion-blocking effect, similar to that of curare, and suppress the conduction of nerve impulses.

Vitamin B6:

The toxic potential of vitamin B6 can be considered as very low. Long-term intake (> 6-12 months) of a daily dosage > 50 mg vitamin B6 may, however, cause peripheral sensory neuropathy and other sensorial neuropathy syndromes. These symptoms improve gradually upon vitamin discontinuation.

Continuous intake of vitamin B6 at a daily dosage of more than 1 g over more than two months may produce neurotoxic effects.

Neuropathies with ataxia and sensitivity disorders, cerebral convulsions with EEG changes as well as, in individual cases, hypochromic anaemia and seborrhoeic dermatitis have been described after administration of more than 2 g daily.

Vitamin B12:

Allergic reactions, eczematous skin changes and a benign form of acne have been observed after high parenteral doses (in rare cases also after oral doses).

Effects on Ability to Drive and Use Machine

Rexom Wina Neuro Tablet do not affect the capability to drive a vehicle or to operate machinery.

Storage Condition

Store below 30°C. Keep container tightly closed. Protect from light.

Presentation:

Rexom Wina Neuro Tablet is also packed in 30's, 60's and 100's per white HDPE bottle with white HDPE screw cap with PE wad, torque seal. Packed with one packet of silica gel. 100 tablet are for export only.

Registration Number:

MAL19991911X

Manufactured by & Product Registration Holder:

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Date of Revision:
29 July 2025