



New Zealand Data Sheet

APO-B COMPLEX

Thiamine mononitrate 5mg, Riboflavin 2mg, Nicotinamide 20mg
and Pyridoxine hydrochloride 2mg, tablets

Presentation

APO-B COMPLEX tablets are round, 7mm in diameter, biconvex with a brown coating. The tablets are identified "B" on one side and plain on the other side. Each tablet contains 5mg Thiamine mononitrate, 2mg Riboflavin, 20mg Nicotinamide, 2mg Pyridoxine hydrochloride and typically weighs 136mg.

Uses

Actions

APO-B COMPLEX tablets contain four water-soluble B complex vitamins. Thiamine (vitamin B₁) is an essential co-enzyme carbohydrate metabolism; riboflavin (vitamin B₂) is required for tissue respiration and maintaining erythrocyte integrity; nicotinamide is involved in electron transfer reactions in the respiratory chain and pyridoxine hydrochloride (vitamin B₆) is principally involved in amino acid metabolism but is also required in carbohydrate and fat metabolism but for the formation of hemoglobin. Deficiencies may occur due to an inadequate diet, due to increased requirements e.g. pregnancy or may be induced by trauma, disease or drugs.

Pharmacokinetics

Small amounts of thiamine are absorbed from the gastrointestinal tract mainly from the duodenum by both active and passive processes. However absorption of doses greater than 5mg is limited. It is widely distributed to most body tissue and appears in breast milk. Body stores (as the phosphorylated form) are approximately 30mg with a 1mg daily turnover. Storage is mainly in skeletal muscles, heart, liver, kidneys and brain. Amounts of thiamine in excess of the body's requirements are excreted in the urine as either unchanged thiamine or as metabolites. Thiamine is metabolised in the liver. It is transformed by phosphorylation into active co-enzyme thiamine pyrophosphate. Dephosphorylation can occur in the kidneys and probably other organs and excess quantities of the free vitamin and the metabolites are excreted in the urine. The urinary excretion depends in part on the urine volume and during diuresis large amounts of thiamine may be lost. Small quantities are excreted in the sweat.

Riboflavin is readily absorbed from the upper gastrointestinal tract except in the presence of malabsorption syndromes. The extent of gastrointestinal absorption is increased when it is administered with food but is decreased in patients with hepatitis, cirrhosis and biliary obstruction. Riboflavin is widely distributed to body tissues but little is stored in the body. Riboflavin is inactive until phosphorylated to flavin mononucleotide (FMN) in gastrointestinal mucosal cells, erythrocytes and the liver. FMN is converted to another co-enzyme flavin adenine dinucleotide (FAD). Free vitamin B₂ is present in the retina and about 60% of FMN and FAD are bound to plasma proteins. The biological half-life is about 66-84 minutes following either oral or i.m. administration of a single dose to healthy individuals. Riboflavin is excreted in the urine partly as metabolites. Excretion appears to involve renal tubular secretion as well as glomerular filtration. Amounts in excess of the body's requirements are excreted in urine. Riboflavin crosses the placenta and is distributed into breast milk.

Nicotinamide is readily absorbed from the gastrointestinal tract after oral administration and is widely distributed in the body tissues. It is metabolised in the liver to N-methylnicotinamide, and the 2-pyridone and 4-pyridone derivatives with some nicotinuric acid also being formed before being excreted in the urine. Small amounts of unchanged nicotinamide are excreted in the urine unchanged however the amount excreted unchanged is increased with larger doses.



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Pyridoxine is readily absorbed from the gastrointestinal tract after oral administration and converted to the active forms pyridoxal phosphate and pyridoxamine phosphate. They are stored mainly in the liver where there is metabolisation to 4-pyridoxic acid and other inactive metabolites which are excreted in the urine. As the dose increases proportionally greater amounts are excreted unchanged in the urine. Vitamin B₆ crosses the placenta and also appears in breast milk.

Indications

Prevention and treatment of vitamin B complex deficiency.

Dosage and Administration

In preventing vitamin deficiencies adequate dietary intake is preferred over supplementation whenever possible.

The usual dosage is 1 tablet three times daily which may be increased to 2 tablets three times daily.

Contraindications

Hypersensitivity to any of the B group vitamins contained in this preparation.

Patients with known lactose intolerance.

Known Hypersensitivity to any of the components

Warnings and Precautions

Multiple vitamin deficiencies should be suspected in any case of dietary inadequacy.

Thiamine:

Simple vitamin B₁ deficiency is rare. Serious sensitivity reactions can occur with deaths having resulted from i.v. use.

Riboflavin:

Vitamin B₂ usually well tolerated and non-toxic.

Nicotinamide:

Patients with gall bladder disease or a history of jaundice, liver disease or peptic ulcer should be closely monitored. Liver function tests should be conducted frequently in the initial stages of therapy and periodically thereafter. Nicotinamide may cause hyperglycemia. Period blood glucose monitoring is advised especially in the early phase of therapy.

Pyridoxine:

Vitamin B₆ usually well tolerated and is relatively non-toxic. Long-term administration of high doses (2-6g daily) is associated with the development of severe peripheral neuropathies.

There have been reports of doses of 500mg daily having a toxic effect.

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Use in Pregnancy and Lactation

No adverse effects have been reported with the intake of normal daily requirements during pregnancy. However, Riboflavin and Pyridoxine do cross the placenta. Daily dietary requirements of pyridoxine may increase slightly during pregnancy but the use of high doses during pregnancy has been implicated in some cases of pyridoxine dependent syndrome in infants.

No adverse effects have been reported with the intake of normal daily requirements during lactation. Vitamins B₁, B₂ and B₆ are excreted in breast milk.

Effects on ability to drive and use machines

Presumed to be safe or unlikely to produce an effect on the ability to drive or use machinery.

Adverse Effects

Thiamine:

Feeling of warmth, pruritus, urticaria, weakness, sweating, nausea, restlessness, tightness of the throat, angioneurotic oedema, cyanosis, pulmonary oedema, hemorrhage into the gastrointestinal tract, collapse and death have been rarely reported, mainly following repeated I.V. administration due to anaphylactoid reactions.

Riboflavin:

Riboflavin is usually well tolerated and non-toxic. Because of its fluorescent yellow colour, large doses may cause yellow discolouration of the urine.

Nicotinamide:

Parental solutions of B complex vitamins containing nicotinamide may cause flushing, itching or burning of the skin in patients susceptible to the effects of nicotinamide.

Nicotinamide has also caused hyperhidrosis, nausea and abdominal cramps.

Pyridoxine:

Nausea, headache, paresthesia, somnolence and low serum folic acid concentrations have been reported. Vitamin B₆ is relatively nontoxic at normal doses however long-term administration of high doses (2-6g daily) is associated with the development of severe peripheral neuropathies.

There have been reports of doses of 500mg daily having a toxic effect.

Transient dependency symptoms may occur upon withdrawal of therapy at a dose of 200mg/day for over 1 month. The significance of this is not known however for patients on large doses for long period of time withdrawal of therapy should probably be gradual.

Adverse reactions may be expected, based on other water soluble vitamin compounds. The adverse reactions may include: allergic reactions including anaphylaxis, dermatological reactions including flushing, erythema & pruritus and CNS reactions including headache, dizziness and agitation.



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Interactions

Thiamine:

None have been reported.

Riboflavin:

Alcohol impairs intestinal absorption of riboflavin.

Phenothiazines and Tricyclic antidepressants may inhibit the conversion of vitamin B₂ to the active coenzyme form. Requirements of vitamin B₂ may be increased in patients receiving these drugs. The extent of gastrointestinal absorption of vitamin B₂ is decreased when it is used concomitantly with probenecid.

Nicotinamide:

Dosage adjustment of insulin or oral antihyperglycaemic agents may be required in some diabetic patients. The clearance of Primidone and carbamazepine may be reduced with the concomitant use of nicotinamide leading to an increase in the plasma concentration of these drugs.

Pyridoxine:

Pyridoxine increases the peripheral metabolism of levodopa. When levodopa is combined with carbidopa this effect is prevented.

Isoniazid, cycloserine, pyrazinamide and penicillamine may antagonise the effects of pyridoxine and lead to a secondary deficiency.

It has been reported that pyridoxine decreases serum concentrations of phenobarbitone.

Patients taking oestrogens e.g. oral contraceptives have higher vitamin B₆ requirements.

Overdosage

Thiamine, Riboflavin and Nicotinamide:

Overdosage has not been reported and intake in excess of the body's requirements is excreted in the urine. Should overdosage occur and adverse reactions result, treatment should be supportive and symptomatic. Fluid intake should be maintained.

Possible symptoms of nicotinamide overdosage include pruritis, vomiting, diarrhoea, dyspepsia and severe abdominal cramps.

Pyridoxine:

Sensory neuropathy can occur following long term administration of large doses. Withdrawal should be started but should probably be gradual to prevent the occurrence of transient dependency symptoms.

Pharmaceutical Precautions

Store at or below 30°C. Protect from heat, light and moisture.

Keep container tightly closed.

Shelf life: 48 months from date of manufacture.



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Medicine Classification

General Sale Medicine

Package Quantities

Bottles of 500 tablets

Further Information

Tablets contain lactose.

Pyridoxine has been widely used in premenstrual syndrome despite controversy over its effectiveness. Doses of up to 100mg daily from either the onset of symptoms or for 14 days prior to the start of menstruation have been used. Concerns exist about the possibility of neurotoxicity occurring.

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