PRODUCT LITERATURE

BEVITA ELIXIR

Each 5 ml contains

Niacinamide BP	10 mg
Thiamine Hydrochloride BP	5 mg
Riboflavine Sodium Phosphate BP	1 mg
Pyridoxine Hydrochloride BP	1 mg
Calcium Pantothenate BP	1 mg
Cyanocobalamine BP	3 mcg

Preservative:

Propyl Paraben BP	0.01%w/v
Methyl Paraben BP	0.1%w/v
Sodium Benzoate BP	0.1%w/v

Product description
Orange coloured syrup

Pharmacodynamics and pharmacokinetics
None

Indication
For the prevention or/and treatment of vitamin deficiency states.

Recommended dose
To be taken 2 times a day.
Adult : 5-10ml (1-2 teaspoonfuls)
Children: 6-12 years: 5ml (1 teaspoonful)
2-5 years : 2.5ml (½ teaspoonfuls)

Route of administration
Oral

Contraindications
Risk-benefit should be considered when the following medical problems exist

- Thiamine
  -Sensitivity to thiamine
  -Wernicke's encephalopathy (intravenous glucose loading may precipitate or worsen this condition in thiamine deficient patients; thiamine should be administered prior to glucose)
- Pyridoxine
  -Sensitivity to pyridoxine
- Cyanocobalamin
  -Sensitivity to cyanocobalamin
- Nicotinamide
  -Arterial bleeding or haemorrhage or Glaucoma (these conditions may be exacerbated)
  -Diabetes mellitus (large doses of niacin may cause impaired glucose tolerance; adjustment of diet and/or hypoglycemic therapy may be necessary)
  -Gout (large doses may cause hyperuricemia
  -Hepatic disease (large doses may cause hepatic damage
  -Hepatobiliary disease, history of or Jaundice, history of (patients with a past history of these medical problems should be closely observed during niacin extended-release therapy; frequent monitoring of liver function tests and blood glucose is recommended)
  - Hypotension (may worsen due to vasodilating effects of niacin)
  - Peptic ulcer (large doses may activate peptic ulcer
  - Renal dysfunction (caution is advised when niacin extended- release is used in patients with renal dysfunction; increased drug exposure may result due to decreased renal elimination of niacin and metabolites)

Except under special circumstances, this medication should not be used when the following medical problems exists:
Note: These medical problems are contraindications for niacin extended-release due to the higher doses used to treat hyperlipidemia. These medical problems are relative contraindications (risk-benefit) for niacin used for prophylaxis and treatment of niacin deficiency.

- Arterial bleeding (niacin extended-release is contraindicated in patients with arterial bleeding)
- Hepatic dysfunction, active or
- Transaminases, serum, unexplained elevations (niacin extended-release is contraindicated in patients with significant or unexplained hepatic dysfunction)
  Hypersensitivity to niacin or niacinamide
- Peptic ulcer disease, active (niacin extended-release is contraindicated in patients with active peptic ulcer disease)

Riboflavin / Calcium Panthothenate

- Data not available

Warnings and precautions
Pediatrics

- Thiamine / Pyridoxine / Riboflavine / Nicotinamide / Cyanocobalamin / Calcium Panthothenate
  -Problems in pediatrics have not been documented with intake of normal daily recommended amounts.
- Nicotinaminde
  -Appropriate studies of niacin as an antihyperlipidemic have not been performed in the pediatric population.
  -However, use of niacin as an antihyperlipidemic in children under 2 years of age is not recommended since cholesterol is required for normal development.

Geriatrics

- Thiamine / Pyridoxine / Riboflavine / Nicotinamide / Calcium Panthothenate
  -Problems in geriatrics have not been documented with intake of normal daily recommended amounts.
- Thiamine
  -Studies have shown that the elderly may have impaired thiamine

Interactions with other medicaments

- Thiamine / Cyanocobalamin / Calcium Panthothenate
  Data not available
- Pyridoxine:
  - Cycloserine or Ethionamide or Hydralazine or Immunosuppress (such as: Azathioprine, Chlorambucil, Corticosteroids, Corticotropin (ACTH), Cyclophosphamide, Cyclosporine, Mercaptopurine, or Isoniazid or Penicillamine) (may cause anemia or peripheral neuritis by acting as pyridoxine antagonists or increasing renal excretion of pyridoxine; recommended intakes for pyridoxine may be increased in patients receiving these medications)
  -Estrogens or Contraceptives, estrogen-containing, oral (may increase recommended intakes for pyridoxine)
  -Levodopa (concurrent use with pyridoxine is not recommended since levodopa's antiparkinsonian effects are reversed by as little as 5 mg of pyridoxine orally; this problem does not occur with the carbidopa-levodopa combination)
- Riboflavine
  -Alcohol (impairs intestinal absorption of riboflavin)
  -Antidepressants, tricyclic or Phenothiazines (requirements for riboflavin may be increased in patients receiving these medications)
  -Probenecid (concurrent use decreases gastrointestinal absorption of riboflavin; requirements for riboflavin may be increased in patients receiving probenecid)
- Nicotinamide
  - Alcohol (niacin extended-release and concomitant alcohol may result in increased adverse effects, such as flushing and pruritus)
  - Anticoagulants (caution should be used with concomitant use with niacin extended-release; prothrombin time and platelet count monitoring is recommended
  - Antihypertensives (niacin may potentiate the effects of ganglionic blocking agents and vasoactive therapy resulting in postural hypotension)
  - Aspirin (concomitant use may decrease the metabolic clearance of nicotinic acid
  - Bile Acid Sequestrants (as great an interval as possible should elapse between the ingestion of bile acid binding resins and the administration of niacin
  -Chenodiol or
- Ursodiol (effect may be decreased when chenodiol or ursodiol is used concurrently with antihyperlipidemics, which tend to increase cholesterol saturation of bile)
  - HMG-CoA reductase inhibitors (concurrent use with niacin may be associated with an increased risk of rhabdomyolysis and acute renal failure; combined therapy with lovastatin, pravastatin, or simvastatin should include careful monitoring for symptoms of myopathy or rhabdomyolysis)
  - Vasoactive drugs, such as: Adrenergic blocking agents or Calcium channel blockers, or Nitrates (caution should be used when niacin extended-release is used in patients with unstable angina or in the acute phase of myocardial infarction, especially patients also receiving vasoactive drugs; may result in increased risk of hypotension)
  - Vitamins or Other supplements containing niacin or related compounds such as nicotinamide (may potentiate the adverse effects of niacin extended-release)

Pregnancy/Reproduction
Pregnancy/Reproduction

- Thiamine / Pyridoxine / Riboflavine / Nicotinamide / Calcium Panthothenate
  -Problems in humans have not been documented with intake of normal daily recommended amounts.
- Pyridoxine
  -However, exposure to large doses of pyridoxine in utero may result in a pyridoxine dependency syndrome in the neonate.
  Adequate and well-controlled studies in humans and animals have not been done at doses typically used for lipid disorders.
- Nicotinamide
  -If a women receiving niacin extended-release for primary hypercholesterolemia (Types IIa or IIb) becomes pregnant, the drug should be discontinued. If a woman being treated with niacin extended- release for hypertriglyceridemia (Types IV or V) conceives, the benefits and risks of continued therapy should be assessed per individual.
- Cyanocobalamin
  -Adequate and well-controlled studies have not been done in humans. Diagnostic testing should be postponed, if possible, until after delivery since cyanocobalamin crosses the placenta and is taken up by the fetus.
  -To avoid the possibility of radiation exposure to the fetus, in those circumstances where the patient's pregnancy status is uncertain, a pregnancy test will help to prevent inadvertent administration of this preparation during pregnancy.

Studies have not been done in animals.
FDA Pregnancy Category C.

Breast-feeding

- Thiamine /Pyridoxine / Riboflavine / Nicotinamide / Calcium Panthothenate
  Problems in humans have not been documented with intake of normal daily recommended amounts.
- Nicotinamide
  However, niacin has been reported to be distributed in human milk. Because of the potential for serious adverse reactions in nursing infants from lipid-altering doses of nicotinic acid, a decision should be made whether to discontinue nursing or to discontinue therapy, taking into account the importance of therapy to the mother.
- Cyanocobalamin
  Cyanocobalamin is excreted in breast milk in very small concentrations. Although discontinuation of breastfeeding is not essential, because of the potential risk to the

infant from radiation exposure, temporary discontinuation of nursing is recommended for a short period of time.

Side effects
Those indicating need for medical attention
Incidence rare

- Thiamine
  Anaphylactic reaction (coughing; difficulty in swallowing; hives; itching of skin; swelling of face, lips, or eyelids; wheezing or difficulty in breathing) usually after a large intravenous dose

- Pyridoxine :
  Doses of 200 mg per day for over 30 days have been reported to produce a pyridoxine dependency syndrome.
  High doses of pyridoxine (2 to 6 grams per day) taken for several months have caused a severe sensory neuropathy, progressing from unstable gait and numb feet to numbness and clumsiness of hands. This condition seems to be reversible on withdrawal of pyridoxine, although some residual weakness has been observed.
- Riboflavine
  While toxicity with high doses of riboflavin has not been reported, high doses of other water-soluble vitamins have been known to cause problems.
  Large doses of riboflavin may cause yellow discoloration of urine.
- Nicotinamide
  Allergic reaction, anaphylactic (skin rash or itching; wheezing); after intravenous administration
  Those indicating need for medical attention only if they continue or are bothersome
- Incidence less frequent, with niacin only
  -Feeling of warmth, flushing or redness of skin, especially on face and neck, headache pain, abdominal, rash, rhinits is (stuffy nose; runny nose; sneezing)

- With high oral doses with niacin only.
  -Cardiac arrhythmias (unusually fast, slow, or irregular heartbeat) diarrhoea, dizziness or faintness, dryness of skin or eyes, hyperglycaemia (frequent urination or unusual thirst); may occasionally be fatal, hyperuricemia (joint pain; side, lower back, or stomach pain; swelling of feet or lower legs), myalgia (fever; muscle aching or cramping; unusual tiredness or weakness), nausea or vomiting, peptic ulcer, aggravation of (stomach pain), pruritus (itching of skin); may be severe

Note: Rarely, along with markedly elevated creatine kinase (CK) concentrations, fever, muscle aching or cramping, or unusual tiredness or weakness may be symptoms of myositis or rhabdomyolysis; incidence may be increased in patients treated concurrently with lovastatin, pravastatin, or simvastatin.

- Cyanocobalamin
  Data not available
- Calcium Panthothenate
  None

Symptoms and Treatment of Overdose
Thiamine / Pyridoxine / Riboflavine / Nicotinamide / Cyanocobalamin / Calcium Panthothenate

Data not available

Packing
Packed in plastic container of 100 ml

Storage Condition
Store below 30^{o}C, in a dry place, protected from direct light.
Keep away from reach of children.
Jauhkan daripada kanak- kanak.

SHAKE WELL BEFORE USE

Shelf life
2 years from date manufacturing date

Name and Address of Product Registration Holder/ Distributor:
ZONTRON PHARMACEUTICALS SDN.BHD. (445695-T)
Lot 10 & 11, PERDA Industrial Park,
Lorong IKS Simpang Ampat B,
14100 Simpang Ampat,
S.P.S Pulau Pinang, Malaysia

Name and Address of Manufacturer:
TERAPUTICS SDN. BHD. (590500-W)
Lot 10 & 11, PERDA Industrial Park,
Lorong IKS Simpang Ampat B,
14100 Simpang Ampat,
S.P.S., Pulau Pinang, Malaysia

Malaysian Drug Registration No.
MAL19950116XCZ

Date of Revision: 16/04/2020