

# PIL of METAX SL Tablet 1000 mcg for NPD.

Front

Size: 135 x 315 mm

Back

**METAX SL**<sup>TM</sup>  
(Mecobalamin)  
SUBLINGUAL  
TABLET

میٹکس

**COMPOSITION:**  
Each sublingual tablet contains:  
Mecobalamin (JP) ..... 1000 mcg.

**Product Specs. - Manufacturer Specs.**

**CLINICAL PARTICULARS:**

**Therapeutic Indications:**

**Mecobalamin is indicated for:**

- Vitamin B12 deficiency
  - Peripheral neuropathy
  - Diabetic neuropathy
  - Alcoholic neuropathy
  - Megaloblastic anaemia caused by vitamin B12 deficiency
  - Nutritional vitamin B12 deficiency
  - Neurological disorders associated with vitamin B12 deficiency
- Mecobalamin is involved in neuronal repair and regeneration and supports normal erythropoiesis.

**Posology and Method of Administration:**

**Adults:**

- Typical dose:  
• 1000 mcg once daily

OR

- 500-1500 mcg daily depending on clinical condition.

**Elderly:**

No specific dose adjustment required.

**Pediatric population:**

Use under medical supervision.

**Method of Administration:**

- Place tablet under the tongue
  - Allow it to dissolve completely
  - Do not chew or swallow immediately
- Sublingual administration allows rapid systemic absorption.

**CONTRAINDICATIONS:**

**Mecobalamin is contraindicated in patients with:**

- Hypersensitivity to Methylcobalamin or vitamin B12
- Leber's hereditary optic neuropathy
- Known cobalt hypersensitivity

**Special Warnings and Precautions for Use:**

**Use with caution in:**

- Patients with optic nerve disease
- Patients with hypokalemia
- Severe vitamin B12 deficiency requiring parenteral therapy

**Additional precautions:**

- High doses may mask folate deficiency
  - Long term therapy should be monitored by laboratory testing
- Vitamin B12 therapy may cause transient hypokalemia during rapid erythropoiesis.

**Interaction with Other Medicinal Products:**

**The following medicines may reduce vitamin B12 absorption or efficacy:**

- Metformin
  - Proton pump inhibitors
  - H2 receptor antagonists
  - Chloramphenicol
  - Colchicine
  - Neomycin
- Chronic alcohol intake may reduce therapeutic response.

**Fertility, Pregnancy and Lactation:**

**Pregnancy:**

Vitamin B12 is essential during pregnancy. Mecobalamin may be used when clinically indicated.

**Lactation:**

Vitamin B12 is excreted in breast milk but is considered safe at therapeutic doses.

**Fertility:**

No evidence suggests impairment of fertility.

**Effects on Ability to Drive and Use Machines:**

Mecobalamin has no or negligible effect on the ability to drive or operate machinery.

**Undesirable Effects:**

Mecobalamin is generally well tolerated.

**Common:**

- Nausea
- Headache
- Diarrhea
- Skin rash

**Rare:**

- Hypersensitivity reactions
- Pruritus
- Anaphylactic reactions

**Very Rare:**

- Peripheral edema
- Hypokalemia during rapid hematopoietic response

**Overdose:**

Vitamin B12 has very low toxicity.

Symptoms of overdose are rare.

**Treatment:**

- Symptomatic and supportive management.

**PHARMACOLOGICAL PROPERTIES:**

**Pharmacodynamic Properties:**

**Pharmacotherapeutic group:** Antianemic preparations - Vitamin B12

**ATC Code:** B03BA05

**Mechanism of Action:**

Mecobalamin (methylcobalamin) is the biologically active coenzyme form of vitamin B12 that participates in several essential biochemical reactions. It functions primarily as a cofactor for the enzyme methionine synthase, which catalyzes the conversion of:

**Homocysteine -> Methionine:**

**This reaction is essential for:**

- DNA synthesis
- RNA synthesis
- Myelin sheath formation
- Methylation reactions within the nervous system

**Through this mechanism, mecobalamin supports:**

- Normal hematopoiesis
- Neuronal regeneration
- Maintenance of central and peripheral nervous system function.

**Role in One-Carbon Metabolism:**

Mecobalamin participates in folate-dependent methyl transfer reactions required for nucleotide synthesis.

**Key actions include:**

- Conversion of 5-methyltetrahydrofolate to tetrahydrofolate
- Production of S-adenosylmethionine (SAM)
- Regulation of methylation of DNA, RNA, phospholipids, and neurotransmitters

SAM acts as a universal methyl donor involved in neuronal membrane integrity and neurotransmitter synthesis.

**Effects on Hematopoiesis:**

Vitamin B12 deficiency leads to impaired DNA synthesis, resulting in megaloblastic anaemia.

**Mecobalamin:**

- Restores normal erythroblast maturation
- Enhances DNA synthesis in bone marrow cells
- Increases reticulocyte production
- Improves hemoglobin synthesis

Correction of anaemia typically occurs within 4-8 weeks of therapy.

**Neurological Effects:**

Mecobalamin plays an important role in neuronal repair and regeneration.

**Experimental and clinical studies demonstrate that mecobalamin:**

- Promotes axonal regeneration
- Enhances nerve conduction velocity
- Stimulates protein synthesis in neurons
- Facilitates remyelination of damaged nerves

**These effects contribute to improvement in:**

- Diabetic neuropathy
- Peripheral neuropathy
- Alcoholic neuropathy
- Entrapment neuropathies

**Neuroprotective Effects:**

**Mecobalamin has been shown to:**

- Promote synthesis of phospholipids in neuronal membranes
- Increase nucleic acid synthesis in nerve cells
- Improve axonal transport

In experimental models, mecobalamin reduces neuronal degeneration and supports regeneration following nerve injury.

**Effect on Homocysteine Metabolism:**

**Elevated homocysteine levels are associated with:**

- Cardiovascular disease
- Endothelial dysfunction
- Neurodegenerative disorders

Mecobalamin reduces plasma homocysteine by enhancing methionine synthase activity, thereby contributing to improved vascular and neurological health.

**Pharmacokinetic Properties:**

**Absorption:**

**Mecobalamin may be absorbed via:**

1. Sublingual absorption through oral mucosa
2. Gastrointestinal absorption via intrinsic factor-mediated transport

**Following oral or sublingual administration:**

- Absorption occurs in the terminal ileum through intrinsic factor-mediated uptake
- A small fraction is absorbed via passive diffusion

Sublingual formulations allow direct absorption into systemic circulation, bypassing partial gastrointestinal degradation.

**Pharmacokinetic characteristics:**

- Time to peak plasma concentration (T<sub>max</sub>): approximately 1-3 hours
- Bioavailability: limited but improved with sublingual delivery

Absorption efficiency decreases with increasing dose due to saturation of intrinsic factor transport mechanisms.

**Distribution:**

**Following systemic absorption, mecobalamin binds extensively to plasma transport proteins:**

- Transcobalamin II (TCII) - biologically active transport protein
- Haptocorrin (transcobalamin I) - storage transport protein

**Distribution characteristics:**

- Rapid uptake by liver, bone marrow, and nervous tissue

**Highest tissue concentrations in:**

- Liver
- Kidney
- Brain
- Peripheral nerves

The liver acts as the primary storage site, containing up to 90% of total body vitamin B12 stores.

Total body stores may range from 2-5 mg, sufficient for several years in healthy individuals.

**Cellular Uptake:**

Mecobalamin enters cells via receptor-mediated endocytosis of the transcobalamin II complex.

**Once inside the cell:**

- It is converted into coenzyme forms
- Incorporated into enzymatic reactions involved in methylation and DNA synthesis.

**Metabolism:**

Unlike cyanocobalamin, mecobalamin is already an active coenzyme form and therefore requires minimal metabolic conversion.

**In cells, vitamin B12 derivatives may interconvert between two active coenzyme forms:**

- Methylcobalamin - cytosolic reactions
- Adenosyl cobalamin - mitochondrial reactions

**These coenzymes participate in:**

- Methionine synthase reactions
- Methylmalonyl-CoA mutase activity.

**Elimination:**

**Mecobalamin elimination occurs primarily through:**

- Biliary excretion into feces
- Renal excretion via urine

A significant portion undergoes enterohepatic circulation, where vitamin B12 secreted in bile is reabsorbed in the intestine.

**Elimination characteristics:**

- Renal excretion increases after high doses
- Unbound vitamin B12 is rapidly excreted in urine.

**Half-Life:**

Vitamin B12 exhibits a long biological half-life due to extensive hepatic storage.

**Approximate parameters:**

- Plasma half-life: approximately 6 days
- Hepatic storage half-life: several months

This long half-life allows maintenance of adequate levels with intermittent dosing.

**Special Populations:**

**Renal Impairment:**

- Increased plasma concentrations may occur due to reduced renal elimination.

**Hepatic Impairment:**

- Minimal impact on pharmacokinetics due to large hepatic storage capacity.

**Elderly:**

- Reduced gastric acid production may impair absorption of dietary vitamin B12, making supplementation beneficial.

**INSTRUCTIONS:**

- Store below 30°C.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

**PRESENTATION:**

METAX SL 1000 mcg Tablet : Pack of 3 x 10 tablets.

Manufactured by

Phytocon International (Pvt.) Ltd.  
339-A, Sundar Industrial Estate, Rawind Road,  
Lahore, Pakistan.

Manufactured for

CCU Pharmaceuticals (Pvt.) Ltd.  
62 Industrial Estate, Kot Lakhpat, Lahore, Pakistan.

FOR FURTHER INFORMATION PLEASE CONTACT:

**CCU**

Pharmaceuticals

Distributed & Marketed by

Nexpharm Healthcare (Pvt.) Ltd.

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دراہیات:  
۳۰ روزہ یعنی گریڈ سے کم درجہ حرارت پر رکھیں۔  
گرمی، دھوپ اور نمی سے بچائیں۔  
بچوں کی پہنچ سے دور رکھیں۔  
صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔