

METAX SLTM

(M e c o b a l a m i n)

SUBLINGUAL
TABLET

COMPOSITION:
Each sub lingual 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
- H2receptor 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_{max}): 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:

1. 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
- Methyl malonyl-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.

DOSAGE:
Place one tablet under the tongue and allow it to dissolve completely, once daily after meal, or as directed by the physician.

INSTRUCTIONS:

- Store below 30°C.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.

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

Manufactured by:
Phytocon International (Pvt.) Ltd.
339-A, Sundar Industrial Estate, Raiwind Road,
Lahore, Pakistan.

Manufactured for:
CCL Pharmaceuticals (Pvt.) Ltd.
62 Industrial Estate, Kot Lakhpat, Lahore, Pakistan.

FOR FURTHER INFORMATION PLEASE CONTACT:



Distributed by:
Nexpharm Healthcare (Pvt.) Ltd.
65 Industrial Estate, Kot Lakhpat, Lahore, Pakistan.

خوراک:

کھانے کے بعد روزانہ ایک گولی زبان کے نیچے رکھ کر استعمال کریں،

یا معالج کے مشورے کے مطابق استعمال کریں۔

ہدایات:

۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

گرمی، دھوپ اور نمی سے بچائیں۔

بچوں کی پہنچ سے دور رکھیں۔