Leroxy™-50

Levothyroxine Sodium 50 mcg

Presentations

Leroxy 50 mcg tablet: Each tablet contains 50 mcg of Levothyroxine Sodium BP.

Pharmacology

Levothyroxine is a synthetic thyroid hormone that is chemically identical to thyroxine (T4), which is naturally secreted by the follicular cells of the thyroid gland.Thyroid hormones exert their physiologic actions through control of DNA transcription and protein synthesis. Triiodothyronine (T3) and Levothyroxine (T4) diffuse into the cell nucleus and bind to thyroid receptor proteins attached to DNA. This hormone nuclear receptor complex activates gene transcription and synthesis of messenger RNA and cytoplasmic proteins. The physiological actions of thyroid hormones are produced predominantly by T3is derived from T4 by deiodination in peripheral tissues.

Pharmacokinetics

Absorption and Bioavailability: Absorption of orally administered T4 from the gastrointestinal (GI) tract ranges from 40% to 80%. The majority of the Levothyroxine dose is absorbed from the jejunum and upper ileum. The relative bioavailability of Levothyroxine sodium tablets, compared to an equal nominal dose of oral Levothyroxine sodium solution is approximately 93%.

Distribution

Circulating thyroid hormones are greater than 99% bound to plasma proteins, including thyroxine-binding globulin (TBG), thyroxine-binding prealbumin (TBPA) and albumin (TBA), whose capacities and affinities vary for each hormone. The higher affinity of both TBG and TBPA for T4 partially explains the higher serum levels, slower metabolic clearance, and longer half-life of T4 compared to T3. Protein-bound thyroid hormones exist in reverse equilibrium with small amounts of free hormone. Only unbound hormone is metabolically active.

Metabolism and Elimination

The major pathway of thyroid hormone metabolism is through sequential deiodination. Approximately 80% of circulating T3 is derived from peripheral T4 by monodeiodination. The liver is the major site of degradation for both T4 and T3, with T4 deiodination also occurring at a number of additional sites, including the kidney and other tissues. Thyroid hormones are also metabolized via conjugation with glucuronides and sulfates and excreted directly into the bile and gut where they undergo enterohepatic recirculation. Thyroid hormones are primarily eliminated by the kidneys. A portion of the conjugated hormone reaches the colon unchanged and is eliminated in the feces. Approximately 20% of T4 is eliminated in the stool. Urinary excretion of T4 decreases with age.

Indications and Usage

● Hypothyroidism ● Congenital hypothyroidism ● Thyroid-stimulating hormone (TSH) suppression

Contraindications

Levothyroxineis contraindicated in patients with: ● Hypersensitivity to drug & it's components ● Acute myocardial infarction ● Thyrotoxicosis ● Adrenal insufficiency.

Dosage

● Hypothyroidism

Adults: All dosages are highly individualized. Initially, 0.05 mg PO, increased in increments of 0.025 mg 2 to 3 weeks depending on cardiovascular status. Maintenance dosage is 0.2 mg daily, adjusted within first 4 weeks of therapy. For patients who can't tolerate oral doses, adjust I.M. or I.V. dose to about one-half of oral dosage.

● Severe Hypothyroidism in Patients with Cardiac Disease

Adult: Initially 25 mcg once daily. Adjusted in steps of 25 mcg every 4 weeks according to response. Maintaince dose is 50-200 mcg once daily, preferably taken 30 min before of breakfast with caffeine containing liquids or other medication.

● Congenital Hypothyroidism

Children over age 12: Up to 150 mcg or 2 to 3 mcg/kg P.O. daily
Children ages 6 to 12: 100 to 150 mcg P.O. daily
Children ages 1 to 6: 75 to 100 mcg P.O. daily
Infants ages 6 to 12 months: 50 to 75 mcg P.O. daily
Infants ages 3 to 6 months: 25 to 50 mcg P.O. daily
Infants up to 3 months: 10 to 15 mcg/kg P.O. daily

● Thyroid-Stimulating Hormone Suppression

Adults: 2.6 mcg/kg P.O. daily for 7 to 10 days

Administration

● Take tablets on an empty stomach 30 minutes to 1 hour before first meal of a day.
● If patient unable to swallow tablets, crush them and sprinkle into a small amount of food. For infants and children, dissolve tablets in a small amount of water, or breast milk and administer immediately.
● Avoid within 4 hours of bile acid sequestrates or antacids which interfere with Levothyroxine absorption.
● Levothyroxine sodium preparations aren't bioequivalent. Patient should consistently use the same brand or generic product, with dosing based on weight, age, general physical condition and duration of symptoms.

Adverse Effects

Adverse reactions associated with Levothyroxine therapy are primarily those of hyperthyroidism due to therapeutic over dosages. They include the following:

General: fatigue, increased appetite, weight loss, heat intolerance, fever, excessive sweating,

Central nervous system: headache, hyperactivity, nervousness, anxiety, irritability, emotional ability, insomnia.

Musculoskeletal: tremors, muscle weakness.

Cardiovascular: palpitations, tachycardia, arrhythmias, increased pulse and blood pressure, heart failure, angina, myocardial infarction, cardiac arrest etc.

Respiratory: dyspnea.

Gastrointestinal: diarrhea, vomiting, abdominal cramps and elevations in liver function tests etc.

Dermatologic: hair loss, flushing.

Endocrine: decreased bone mineral density.

Reproductive: menstrual irregularities, impaired fertility etc.

Overdosage

The signs and symptoms of over dosage are those of hyperthyroidism. In addition, confusion and disorientation may occur. Cerebral embolism, shock, coma, and death have been reported. Seizures have occurred in a child ingesting 18 mg of Levothyroxine. Symptoms may not necessarily be evidentor may not appear until several days after ingestion of Levothyroxine sodium.

Treatment of Overdosage

Levothyroxine sodium should be reduced in dose or temporarily discontinued if signs or symptoms of overdosage occur. For, acute massive overdosage it may be a life-threatening emergency, therefore, symptomatic and supportive therapy should be instituted immediately. If not contraindicated (e.g., by seizures, coma, or loss of the gag reflex), the stomach should be emptied by emesis or gastric lavage to decrease gastrointestinal absorption. Activated charcoal or cholestyramine may also be used to decrease absorption. Central and peripheral increased sympathetic activity may be treated by administering ?-receptor antagonists, e.g., propranolol, provided there are no medical contraindications to their use. Provide respiratory support as needed; control congestive heart failure and arrhythmia; control fever, hypoglycemia and fluid loss as necessary. Large doses of antithyroid drugs (e.g., Methimazole or Propylthiouracil) followed in one to two hours by large doses of iodine may be given to inhibit synthesis and release of thyroid hormones. Glucocorticoids may be given to inhibit the conversion of T4 to T3. Plasmapheresis, charcoal hemoperfusion and exchange transfusion have been reserved for cases in which continued clinical deterioration occurs despite conventional therapy. Because T4 is highly protein bound, very little drug will be removed by dialysis.

Precautions

General

Levothyroxine has a narrow therapeutic index. Regardless of the indication for use, careful dosage titration is necessary to avoid the consequences of over- or under-treatment. These consequences include, among others, effects on growth and development, cardiovascular function, bone metabolism, reproductive function, cognitive function, emotional state, gastrointestinal function, and on glucose and lipid metabolism.

Effects on Bone Mineral Density

In women, long-term Levothyroxine sodium therapy has been associated with increased bone resorption, thereby decreasing bone mineral density, especially in post-menopausal women on greater than replacement doses or in women who are receiving suppressive doses of Levothyroxine sodium. The increased bone resorption may be associated with increased serum levels and urinary excretion of calcium and phosphorous, elevations in bone alkaline phosphatase and suppressed serum parathyroid hormone levels. Therefore, it is recommended that patients receiving Levothyroxine sodium be given the minimum dose necessary to achieve the desired clinical and biochemical response.

Patients with Underlying Cardiovascular Disease

Exercise caution when administering Levothyroxine to patients with cardiovascular disorders and to the elderly in whom there is an increased risk of occult cardiac disease. In these patients, Levothyroxine therapy should be initiated at lower doses than those recommended in younger individuals or in patients without cardiac disease. If cardiac symptoms develop or worsen, the Levothyroxine dose should be reduced or withheld for one week and then cautiously restarted at a lower dose. Overtreatment with Levothyroxine sodium may have adverse cardiovascular effects such as an increase in heart rate, cardiac wall thickness and cardiac contractility and may precipitate angina or arrhythmias. Patients with coronary artery disease who are receiving Levothyroxine therapy should be monitored closely during surgical procedures, since the possibility of precipitating cardiac arrhythmias may be greater in those treated with Levothyroxine. Concomitant administration of Levothyroxine and sympathomimetic agents to patients with coronary artery disease may precipitate coronary insufficiency.

Patients with Nontoxic Diffuse Goiter or Nodular Thyroid Disease

Exercise caution when administering Levothyroxine to patients with nontoxic diffuse goiter or nodular thyroid disease in order to prevent precipitation of thyrotoxicosis. If the serum TSH is already suppressed, Levothyroxine sodium should not be administered

Associated Endocrine Disorders

Hypothalamic/Pituitary Hormone Deficiencies

In patients with secondary or tertiary hypothyroidism, additional hypothalamic/pituitary hormone deficiencies should be considered.

Autoimmune Polyglandular Syndrome

Occasionally, chronic autoimmune thyroiditis may occur in association with other autoimmune disorders such as adrenal insufficiency, pernicious anemia, and insulin-dependent diabetes mellitus. Patients with concomitant adrenal insufficiency should be treated with replacement glucocorticoids prior to initiation of treatment with Levothyroxine sodium. Patients with diabetes mellitus may require upward adjustments of their antidiabetic therapeutic regimens when treated with Levothyroxine.

Other Associated Medical Conditions

Infants with congenital hypothyroidism appear to be at increased risk for other congenital anomalies with cardiovascular anomalies (pulmonary stenosis, atrial septal defect and ventricular septal defect) being the most common association.

Interactions

Drug-Drug Interaction

Aminoglutethimide, amiodarone, anabolic steroids, antithyroid drugs, asparaginase, barbiturates, carbamazepine, chloral hydrate, cholestyramine, clofibrate, colestipol, corticosteroids, danazol, diazepam, estrogens,ethionamide, fluorouracil, insulin, lithium, methadone, mitotane, nitroprusside, oxyphenbutazone,phenytoin, propranolol, salicylates (large doses), sulfonylureas, thiazides: altered thyroid function test results Antacids, bile acid sequestrants: interference with Levothyroxine absorption Anticoagulants: increased anticoagulant action Beta-adrenergic blockers: decreased beta blocker action Cardiac glycosides: decreased cardiac glycoside blood levels Cholestyramine, colestipol:Levothyroxine inefficacy Theophyllines: decreased theophylline clearance.

Drug-Food Interaction

Foods high in iron or fiber & soybeans-decreased drug absorption.

Pregnancy Category

US FDA Approved Pregnancy Category A.

Nursing Mothers

Although thyroid hormones are excreted only minimally in human milk, caution should be exercised when Levothyroxine is administered to a nursing woman. However, adequate replacement doses of Levothyroxine are generally needed to maintain normal lactation.

Pharmaceutical Precautions

Store in a cool dry place, protected from light and moisture. Keep out of reach of children.

Commercial Packs

Leroxy 50 mcg tablet: Each box contains 10 X10 tablets in blister pack.

Manufactured by :

POPULAR

POPULAR PHARMACEUTICALS LTD.
TONGI, GAZIPUR, BANGLADESH