LEVOTHYROXINE SODIUM

THYROXIL

50 mcg Tablet
100 mcg Tablet

THYROID HORMONE

℞

CYDC

COMPOSITION:
Each tablet contains:
Levothyroxine Sodium, BP ..... 50 mcg

Each tablet contains:
Levothyroxine Sodium, BP ..... 100 mcg
Lake Sunset Yellow ..... 400 mcg

PRODUCT DESCRIPTION:
Levothyroxine sodium (Thyroxil) 50 mcg Tablet: Pink colored, oval shaped bi-convex tablet having break line on one side and plain on other side.
Levothyroxine sodium (Thyroxil) 100 mcg Tablet: Pale orange colored, oval shaped bi-convex tablet having break line on one side and plain on other side.

PHARMACOLOGY:
Pharmacologic Category: Belongs to the class of thyroid hormones.
ATC code: H03AA01.

Pharmacodynamics:
Thyroxine (T4) is a naturally occurring hormone produced by the thyroid gland and converted to the more active hormone triiodothyronine (T3) in peripheral tissues. The precise signals controlling the conversion of T4 to T3 within the cell are not known. The thyroid hormones are required for normal growth and development, particularly of the nervous system. They increase the resting or basal metabolic rate of the whole organism and have stimulatory effects on the heart, skeletal muscle, liver and kidney.
Thyroid hormones enhance lipolysis and the utilization of carbohydrate. 100 microgram thyroxine is equivalent in activity to 20 to 30 microgram liothyronin/triiodothyronine or 60 mg Thyroid BP and/or local pharmacopoiea specification.
Pharmacokinetics:
Absorption: Following oral administration, the absorption of thyroxine is incomplete and variable, especially when taken with food. The amount absorbed increases during fasting conditions.
Distribution: Thyroxine is nearly totally bound to serum protein.
Metabolism: The main pathway for the metabolism of thyroxine (T4) is its conversion, by de-iodination, to the active metabolite triiodothyronine (T3). Further de-iodination of T4 and T3 leads to production of inactive products.
Elimination: Thyroxine is eliminated slowly from the body with a half-life of approximately seven days in a normal person. This may be reduced in hyperthyroid states or increased in hypothyroid patients. In man, approximately 20 to 40% of thyroxine is eliminated in the faeces and approximately 30 to 55% of a dose of thyroxine is excreted in the urine.

INDICATIONS:
- Control of hypothyroidism,
- Congenital hypothyroidism in infants,
- Acquired hypothyroidism in children and
- Juvenile myxedema

DOSAGE AND ADMINISTRATION:
In younger patients, and in the absence of heart disease, a serum Levothyroxine (T4) level of 70 to 160 nanomols per liter, or a serum thyrotrophin level of less than 5 milli-units per liter should be targeted. A pre-therapy ECG is valuable because ECG changes due to hypothyroidism may be confused with ECG evidence of cardiac ischemia. If too rapid an increase in metabolism is produced (causing diarrhea, nervousness, rapid pulse, insomnia, tremors, and sometimes anginal pain where there is latent cardiac ischemia) dosage must be reduced, or withheld, for a day or two, and then re-started at a lower dose level.
Adults: Initially 50-100 micrograms daily (2 to 4 tablets daily), preferably taken before breakfast or your first meal of the day. Adjust at three to four week intervals by 50 micrograms until normal metabolism is steadily maintained. The final daily dose may be up to 100 to 200 micrograms.
Elderly: As for patients aged over 50 years.
For patients over 50 years, initially, it is not advisable to exceed 50 micrograms daily. In this condition, the daily dose may be increased by 50 micrograms at intervals of every 3-4 weeks, until stable thyroxine levels are attained. The final daily dose may be up to 50 to 200 micrograms.
Patients over 50 years with cardiac disease:
Where there is cardiac disease, 25 micrograms daily or 50 micrograms on alternate days is more suitable. In this condition, the daily dose may be increased by 25 micrograms at intervals of every 4 weeks, until stable thyroxine levels are attained. The final daily dose may be up to 50 to 200 micrograms.
For patients aged over 50 years, with or without cardiac disease, clinical response is probably a more acceptable criterion of dosage rather that serum levels.
Pediatric population:
The maintenance dose is generally 100 to 150 micrograms per square meter body surface area. The dose for children depends on their age, weight and the condition being treated. Regular monitoring using serum TSH levels, as in adults, is required to make sure he/she gets the right dose. Infants should be given the total daily dose at least half an hour before the first meal of the day.
Congenital hypothyroidism in infants:
For neonates and infants with congenital hypothyroidism, where rapid replacement is important, the initial recommended dosage is 10 to 15 micrograms per kg BW per day for the first 3 months. Thereafter, the dose should be adjusted individually according to the clinical findings, thyroid hormone, and TSH values.
Acquired hypothyroidism in children:
For children with acquired hypothyroidism, the initial recommended dosage is 12.5-50 micrograms per day. The dose should be increased gradually every 2 to 4 weeks according to the clinical findings and thyroid hormone and TSH values until the full replacement dose is reached. Infants should be given the total daily dose at least half an hour before the first meal of the day.
Juvenile myxedema in children:
The initial recommended dosage is 25 micrograms daily. In such conditions, the daily dose may be increased by 25 micrograms at intervals of every 2 - 4 weeks, until mild symptoms of hyperthyroidism is seen. The dose will then be reduced slightly. In children under 5 years of age, the administration of whole tablets is not recommended. It is also not recommended that tablets are crushed and dispersed in water or other liquids, owing to limited solubility, which could lead to dosing inaccuracy. In this age group, it is preferable to administer an approved oral solution of Levothyroxine.

Method of administration
Oral

CONTRAINDICATIONS:
- Hypersensitivity to the active substance or to certain excipients
- Thyrotoxicosis
- Adrenal gland disorder or adrenal insufficiency

Warnings and Precautions:
Laboratory monitoring: Levothyroxine sodium has a narrow therapeutic index. Appropriate Levothyroxine sodium dosage is based upon clinical assessment and laboratory monitoring of thyroid function tests. During the initial titration period, careful dosage titration and monitoring is necessary to avoid the consequences of under- or over-treatment. The symptoms of excessive Levothyroxine sodium dosage are the same as many features of endogenous thyrotoxicosis. Treatment with Levothyroxine sodium in patients with pan hypopituitarism or other causes predisposing to adrenal insufficiency may cause reactions, including dizziness, weakness, malaise, weight loss, hypotension and adrenal crisis. It is advisable to initiate corticosteroid therapy before giving Levothyroxine sodium in these cases. Special patient populations: The initial dose and any dose increments should be carefully chosen in the elderly and in patients with cardiac symptoms, diabetes mellitus or insipidus: too high initial dose or too rapid increase may cause or aggravate symptoms of angina, arrhythmias, myocardial infarction, cardiac failure or a sudden raise in blood pressure.
Levothyroxine sodium should not be used for the treatment of obesity or weight loss. In euthyroid patients, doses within the range of daily hormonal requirements are ineffective for weight reduction. Larger doses may produce serious or even life-threatening manifestations of toxicity, particularly when given in association with sympathomimetic amines such as those used for anorectic effects. Patients with myxedema have an increased sensitivity for thyroid hormones; in these patients the starting should be low with slow dossing increments. Thyroxine absorption is decreased in patients with malabsorption syndromes. It is advised to treat the malabsorption condition to ensure effective thyroxine treatment with regular thyroxine dose. During pregnancy, serum thyroxine levels may decrease with a concomitantly increase in serum TSH level to values outside the normal range. Patients taking levothyroxine should have their TSH measured during each trimester. An elevated serum TSH level should be corrected by an increase in the dose of levothyroxine. Since postpartum TSH serum levels are similar to preconception values, levothyroxine dosage can be reduced to the pre-pregnancy dose. 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 of in women who are receiving suppressive doses of levothyroxine. To minimize the risk of osteoporosis, dosage of levothyroxine sodium should be titrated to the lowest possible level.

Pre-clinical Safety Data: No additional data of relevance.
Effects on Ability to Drive and Use Machines: From the pharmacokinetic and pharmacodynamic properties of thyroxine, treatment with Levothyroxine sodium would not be expected to interfere with ability to drive or operate machinery.

PREGNANCY AND LACTATION:
Levothyroxine sodium has been taken by a large number of pregnant women and women of childbearing age without any form of definite disturbances in the reproductive process having been observed so far. Thyroid, hypo- or hyperactivity in the mother may, however, unfavorably influence the fetal outcome or well-being. Thyroxine is excreted in breast milk in low concentrations and this may be sufficient to interfere with neonatal screening for hypothyroidism.

INTERACTIONS:
Levothyroxine sodium increases the effect of anticoagulants and it may be necessary to reduce the dose of anticoagulant if excessive hypoprothrombinemia and bleeding are to be avoided. Phenytoin levels may be increased by Levothyroxine sodium.
Interactions affecting thyroxine: Anticonvulsants such as carbamazepine and phenytoin enhance the metabolism of thyroid hormones and may displace them from plasma proteins. Initiation or discontinuation of anticonvulsant therapy may alter Levothyroxine sodium dose requirements.
Enzyme inducers like rifampicin and barbiturates increase the metabolism and excretion of thyroxine, resulting in increased Levothyroxine sodium requirements. If co-administered with cardiac glycosides, adjustment of dosage of cardiac glycoside may be necessary.
The effects of sympathomimetic agents are also enhanced.
Levothyroxine sodium increases receptor sensitivity to catecholamines thus accelerating the response to tricyclic antidepressants.
Interactions decreasing thyroxine absorption: Cholestyramine, calcium-, aluminum-, magnesium-, iron supplements, aluminum hydroxide, polystyrene sulfonates, sucralfate, lanthanum, bile acid sequesterants (e.g. colestipol), anion/cation exchange resins (e.g. kayexalate, sevelamer), calcium carbonate, and ferrous sulphate and proton pump inhibitors decrease the absorption of thyroxin. Separate the dosages of thyroxine and the previously mentioned medicines as much as possible to avoid interaction in the stomach or the small bowel. Soy-containing compounds and high-fiber diets can decrease the intestinal absorption of thyroxine. Therefore, a dosage adjustment of Levothyroxine sodium may be necessary, in particular at the beginning or after termination of nutrition with soy supplements. Co-administration of oral contraceptives, as well as a number of other drugs, including estrogen, tamoxifen, clofibrate, methadone, and 5-fluorouracil may increase serum concentration of thyroxine-binding globulin, and therefore increase Levothyroxine sodium dosage requirements. Reports indicate that some HMG-CoA reductase inhibitors (statins) may increase thyroid hormone requirements in patients receiving thyroxine therapy. It is unknown if this occurs with all statins. Close monitoring of thyroid function and appropriate thyroxine dose adjustments may be necessary when thyroxine and statins are co-prescribed. Treatment with some tyrosine kinase inhibitors (e.g., imatinib and sunitinib) was associated with increased Levothyroxine sodium dosage requirements in hypothyroid patients. Medicines that (partially) inhibit the peripheral transformation of T4 to T3 like propranolol, amiodarone, lithium, iodide, oral contrast agents, propylthiouracil and glucocorticoids lower the T3 level and therefore also the therapeutic effect. The concurrent use of sertraline can reduce serum levels of thyroxine (with concomitant increased TSH levels).
Interactions affecting other drugs: Thyroxine can increase the need for insulin or oral antidiabetics in patients with diabetes. Lowering the dose of thyroxine can cause hypoglycemia if the insulin or oral antidiabetics dose remains unchanged.
Laboratory test interactions: A number of drugs may decrease serum concentration of thyroxine-binding globulin, and therefore decrease thyroxine dosage requirements, including androgens and anabolic steroids.
False low plasma concentrations have been observed with concurrent anti-inflammatory treatment such as phenylbutazone or acetylsalicylic acid and thyroxine therapy. Administration of acetylsalicylic acid together with thyroxine results in an initial transient increase in serum free T4. Continued administration results in normal free T4 and TSH concentrations, and therefore, patients become clinically euthyroid. A number of drugs may affect thyroid function tests and this should be borne in mind when monitoring a patient on Levothyroxine sodium therapy.

ADVERSE DRUG REACTIONS:
The following effects are indicative of excessive dosage and usually disappear on reduction of dosage or withdrawal of treatment for a few days. The frequency classification for these adverse reactions is not known due to a lack of robust clinical trial data to accurately determine frequency estimates.
Immune system disorders: Hypersensitivity reactions such as skin rash and pruritus.
Metabolism and nutrition disorders: Increased appetite, abnormal loss of weight.
Endocrine disorders: Hyperthyroidism.
Gastrointestinal disorders: Abdominal cramps, nausea, vomiting, diarrhea.
Nervous system disorders: Headache, tremors, seizure. Rare cases of pseudotumor cerebri (benign intracranial hypertension) have been reported especially in children.
Cardiac disorders: Anginal pain, cardiac arrhythmias, palpitations, tachycardia, increased blood pressure, heart failure, myocardial infarction.
Respiratory, thoracic and mediastinal disorders: Dyspnea.
Skin and subcutaneous tissue disorders: Sweating, alopecia.
Vascular disorders: Flushing.
Musculoskeletal and connective tissue disorders: Cramps in the skeletal muscle, muscular weakness. Excessive dose may result in premature closure of epiphyses in children with compromised adult height.
Congenital, familial and genetic disorders: Excessive dose may result in craniosynostosis in infants.
Psychiatric disorders: Anxiety, emotional lability, nervousness, excitability, insomnia, restlessness.
Reproductive system and breast disorders: Menstrual irregularity, impaired fertility.
General disorders and administration site conditions: Fatigue, heat intolerance, fever.

OVERDOSE AND TREATMENT:
Symptoms and Signs: In addition to exaggeration of side effects, the following symptoms may for example be seen: agitation, confusion, irritability, hyperactivity, headache, sweating, mydriasis, tachycardia, arrhythmias, tachypnea, pyrexia, increased bowel movements and convulsions. The appearance of clinical hyperthyroidism may be delayed for up to five days. Thyrotoxicosis crisis has been occasionally reported following massive or chronic intoxication, leading to cardiac arrhythmias, heart failure and coma.
Treatment: The goal of therapy is restoration of clinical and biochemical euthyroid state by omitting or reducing Levothyroxine sodium dosage, and other measures as needed depending on clinical status. Treatment is symptomatic, and tachycardia has been controlled in adults by 40 mg doses of propranolol given every 6 h and other symptoms by diazepam and/or chlorpromazine as appropriate.

STORAGE CONDITION:
Store at a temperature not exceeding 30°C. Protect from light and moisture.
Keep out of the reach of children.

SHELF-LIFE: 24 months

PACKAGING PRESENTATION:
Levothyroxine sodium 50 mcg Tablet (THYROXIL): Alu/Amber Colored PVC Blister Pack x 10's (Box of 50's)
Levothyroxine sodium 100 mcg Tablet (THYROXIL): Alu/Amber PVC Blister Pack x 10's (Box of 50's)

CAUTION:
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

ADR REPORTING STATEMENT
For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph
Patient should seek medical attention immediately at the first sign of any adverse drug reaction.

Manufactured by:
STERIL-GENE LIFE SCIENCES (P) LTD.
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PRODUCT NAME	REGISTRATION NUMBER	DATE OF FIRST AUTHORIZATION
Levothyroxine sodium (Thyroxil) 50 mcg Tablet	DRP-13157-02	18 April 2024
Levothyroxine sodium (Thyroxil) 100 mcg Tablet	DRP-14067-01	28 March 2024

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