Thyrin®

Levothyroxine Sodium

COMPOSITION
Thyrin® 25 Tablet: Each tablet contains Levothyroxine Sodium BP 25 mcg.
Thyrin® 50 Tablet: Each tablet contains Levothyroxine Sodium BP 50 mcg.
Thyrin® 75 Tablet: Each tablet contains Levothyroxine Sodium BP 75 mcg.

PHARMACOLOGY
Levothyroxine is a synthetic form of the thyroid hormone, thyroxine (T_4, a tetra-iodinated tyrosine derivative) that is made and released by the thyroid gland. In the liver and kidney, T_4 is converted to T_3, the active metabolite. In order to increase solubility, the thyroid hormones attach to thyroid hormone binding proteins, thyroxine-binding globulin, and thyroxine-binding prealbumin (transthyretin). Transport and binding to thyroid hormone receptors in the cytoplasm and nucleus then takes place. Thus by acting as a replacement for natural thyroxine, symptoms of thyroxine deficiency are relieved.

INDICATION
Hypothyroidism
As replacement or supplemental therapy in congenital or acquired hypothyroidism of any etiology, except transient hypothyroidism during the recovery phase of subacute-thyroiditis.

Specific indications: Primary (thyroidal), secondary (pituitary), and tertiary (hypothalamic) hypothyroidism and subclinical hypothyroidism.

Pituitary TSH Suppression
In the treatment or prevention of various types of euthyroid goiters, subacute or chronic lymphocytic thyroiditis (Hashimoto's thyroiditis), multinodular goiter and, as an adjunct to surgery and radioiodine therapy in the management of thyrotropin-dependent well-differentiated thyroid cancer.

DOSAGE AND ADMINISTRATION
In order to avoid irregular absorption, **Thyrin**® tablets should be taken preferably at a fixed time on an empty stomach. Concomitant intake of food may decrease the absorption of Levothyroxine. Dosing must be individualized and adjustments to be made based on periodic assessment of the patient's clinical response and laboratory parameters.

Adult Dosage:
Initial starting dose: 25-50 mcg/day, with gradual increments in dose at 6-8 week intervals, as needed. The Levothyroxine Sodium dose is generally adjusted in 12.5-25 mcg increments until the patient with primary hypothyroidism is clinically euthyroid and the serum TSH has normalized.

In patients with severe hypothyroidism: Initial dose is 12.5-25 mcg/day with increases of 25 mcg/day every 2-4 weeks, accompanied by clinical and laboratory assessment, until the TSH level is normalized.

In patients with secondary (pituitary) or tertiary (hypothalamic) hypothyroidism: Levothyroxine Sodium dose should be titrated until the patient is clinically euthyroid and the serum free - T_4 level is restored to the upper half of the normal range.

For patients older than 50 years or for patients under 50 years of age with underlying cardiac disease: An initial dose of 25-50 mcg/day is recommended with gradual increments in dose at 6-8 week intervals.

Pediatric Dosage
Newborns: The recommended starting dose is 10-15 mcg/kg/day. A lower starting dose should be considered in infants at risk for cardiac failure, and the dose should be increased in 4-6 weeks as needed based on clinical and laboratory response to treatment. In infants with very low (< 5 mcg/dL) or undetectable serum T_4 concentrations, the recommended initial starting dose is 50 mcg/day of Levothyroxine Sodium.

Infants and Children: In children with chronic or severe hypothyroidism, initial dose of 25 mcg/day with increments of 25 mcg every 2-4 weeks until the desired effect is achieved.
Hyperactivity in an older child can be minimized if the starting dose is one-fourth of the recommended full replacement dose, and the dose is then increased on a weekly basis by an amount equal to one-fourth the full-recommended replacement dose until the full recommended replacement dose is reached.
Daily dose per kg body weight:

0-3 months: 10-15 mcg/kg/day
3-6 months: 8-10 mcg/kg/day
6-12 months: 6-8 mcg/kg/day
1-5 years: 5-6 mcg/kg/day
6-12 years: 4-5 mcg/kg/day
>12 years but growth and puberty incomplete: 2-3 mcg/kg/day
Growth and puberty complete: 1.7 mcg/kg/day

The dose should be adjusted based on clinical response and laboratory parameters.

CONTRAINDICATION
Untreated subclinical or overt thyrotoxicosis of any etiology and acute myocardial infarction.

PRECAUTION
Levothyroxine has a narrow therapeutic index. So, careful dose titration is necessary to avoid the consequences of over- or under-treatment. Caution is needed when administering Levothyroxine to patients with cardiovascular disorders, to the elderly in whom there is an increased risk of occult cardiac disease & for patients with nontoxic diffuse goiter or nodular thyroid disease in order to prevent precipitation of thyrotoxicosis

PREGNANCY AND LACTATION
Pregnancy - Category A. Pregnancy may increase Levothyroxine requirements.

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

DRUG INTERACTION
Concurrent use of tri/tetracyclic antidepressants and Levothyroxine may increase the therapeutic and toxic effects of both drugs, possibly due to increased receptor sensitivity to catecholamines. Toxic effects may include increased risk of cardiac arrhythmias and CNS stimulation; onset of action of tricyclics may be accelerated. Administration of sertraline in patients stabilized on Levothyroxine may result in increased Levothyroxine requirements. Addition of Levothyroxine to antidiabetic or insulin therapy may result in increased antidiabetic agent or insulin requirements. Careful monitoring of diabetic control is recommended, especially when thyroid therapy is started, changed, or discontinued. Serum digitalis glycoside levels may be reduced in hyperthyroidism or when the hypothyroid patient is converted to the euthyroid state. Therapeutic effect of digitalis glycosides may be reduced.

ADVERSE EFFECT
Adverse reactions associated with Levothyroxine therapy are primarily those of hyperthyroidism due to therapeutic overdose .They include the following:
General: Fatigue, increased appetite, weight loss, heat intolerance, fever, excessive sweating;
Central nervous system: headache, hyperactivity, nervousness, anxiety, irritability, emotional lability, insomnia.
Musculoskeletal: Tremors, muscle weakness.
Cardiovascular: Palpitations, tachycardia, arrhythmias, increased pulse and blood pressure,
Respiratory: Dyspnea.
Gastrointestinal: Diarrhea, vomiting, abdominal cramps
Dermatologic: Hair loss, flushing

OVERDOSE
The signs and symptoms of overdose are those of hyperthyroidism – agitation, confusion, irritability, hyperactivity, headache, sweating, mydriasis, tachycardia, arrhythmias, tachypnoea, pyrexia, increased bowel movements and convulsions. Cerebral embolism, shock, coma, and death have been reported. Symptoms may not necessarily be evident or may not appear until several days after ingestion of Levothyroxine Sodium.
Treatment of Overdose : Levothyroxine Sodium should be reduced in dose or temporarily discontinued if signs or symptoms of overdosage occur. Treatment is symptomatic.

STORAGE
Store below 25° C & dry place, protect from light. Keep out of reach of children.

HOW SUPPLIED
Thyrin® 25 Tablet: Each Box contains 90 tablets in blister pack.
Thyrin® 50 Tablet: Each Box contains 90 tablets in blister pack.
Thyrin® 75 Tablet: Each Box contains 60 tablets in blister pack.

Manufactured by
SQUARE
PHARMACEUTICALS PLC.
BANGLADESH