

# T<sub>3</sub> CYTOMEL<sup>®</sup>

**Liothyronine sodium, USP 29, Ph.Eur.5.5, Micronized grade**

L-Tri-iodothyronine sodium

Thyroid drug

Molecular Formula: C<sub>15</sub>H<sub>11</sub>I<sub>3</sub>NNaO<sub>4</sub>,

Molecular Weight: 673.0 gm/mol.

## DESCRIPTION:

T<sub>3</sub>Cytomel<sup>®</sup>, brand of Liothyronine sodium tablets, is a synthetic form of a natural thyroid hormone, and is available as the sodium salt. Each tablet contains 100 microgram of Liothyronine sodium, USP 29, Ph.Eur.5.5, Micronized grade. It is designated chemically as Sodium 4-*O*-(4-hydroxy-3-iodophenyl)-3,5-di-iodo-L-Tyrosine.

It occurs as white or slightly coloured crystalline powder. Practically insoluble in water; slightly soluble in alcohol; It dissolves in dilute solutions of alkali hydroxides.

Each tablet also contains lactose monohydrate, sodium starch glycolate, polyvidone 25,000, microcrystalline cellulose and magnesium stearate as excipients. The 100 mcg tablet also contains yellow ferric oxide (E172) as colouring agent.

Thyroid hormones enhance oxygen consumption by most tissues in the body, increasing the basal metabolic rate and the rate of metabolism of carbohydrates, lipids, and proteins. Thyroid hormones have a profound influence on every organ in the body and are of particular importance in the development of the central nervous system.

## CLINICAL PHARMACOLOGY:

Liothyronine sodium (T<sub>3</sub>) is weakly bound to serum protein, leaving it readily available for use in body tissues. The onset of T<sub>3</sub> 100 is rapid, occurring within a few hours. Maximum pharmacological response occurs within 2 or 3 days, providing an early clinical response.

The biological half-life is about 2.5 days.

T<sub>3</sub> is absorbed 95% within 4 hours of oral administration. T<sub>3</sub> has a rapid inaction of activity which allows for quick dosage titration and allows better control of overdose effects, should they occur.

The higher affinity of T<sub>4</sub> for both thyroid-binding globulin and thyroid binding prealbumin versus T<sub>3</sub> explains the greater serum levels and longer half-life of the T<sub>4</sub> vs. T<sub>3</sub>. Both protein bound hormones exist in reverse equilibrium with a small amount of free hormones which account for the metabolic activity.

## INDICATIONS:

Thyroid hormone drugs are used for:

1. Replacement or supplementation therapy in patients with hypothyroidism of any etiology, except transient hypothyroidism during the recovery phase of subacute thyroiditis. This includes cretinism, myxedema, and ordinary hypothyroidism in patients of any age or state; primary hypothyroidism from function deficiency, primary atrophy, partial or total absence of the thyroid gland, or the effects of surgery, radiation, or drugs, with or without the presence of goiter; and secondary (pituitary), or tertiary (hypothalamic) hypothyroidism.
2. As pituitary thyroid stimulating hormones (TSH) suppressants, in the treatment or prevention of various types of euthyroid goiters, thyroid nodules, subacute or chronic lymphocytic thyroiditis, and multinodular goiter.
3. As diagnostic agents in diagnosing mild hyperthyroidism vs. thyroid gland autonomy.
4. T<sub>3</sub> Cytomel<sup>®</sup> can be used in patients allergic to desiccated thyroid or thyroid extract derived from pork or beef.

## CONTRAINDICATIONS:

Thyroid hormone preparations are generally contraindicated in patients.

1. With diagnosed but as yet uncorrected adrenal cortical insufficiency, untreated thyrotoxicosis or hyperthyroidism.
2. Hypersensitivity to any of their active or extraneous constituents. There is no well-documented evidence from the literature, however, of true allergic or idiosyncratic reactions to thyroid hormone.
3. Cardiovascular disorders including angina, heart failure, myocardial infarction and hypertension.

## PRECAUTIONS:

1. T<sub>3</sub>Cytomel<sup>®</sup> have been used in the treatment of obesity. In euthyroid patients, doses within the normal range of hormonal requirements are ineffective for weight reduction. Larger doses may produce serious or even life-threatening manifestations of toxicity, particularly when given with sympathomimetic amines concomitantly.
2. T<sub>3</sub>Cytomel<sup>®</sup> should not be used without verification of the integrity of the cardiovascular system, particular coronary arteries; especially in patients with angina pectoris and in the elderly where occult cardiac disease is more probable.
3. Patients with greater risk profiles should begin treatment with doses of 5mcg per day and titration at 2-week intervals until the desired clinical range is achieved. Myxedematous patients are very sensitized to thyroid hormones and must be started at a very low dose. If achieving a euthyroid state requires exacerbation of cardiovascular disease, dosage should be reduced.
4. Nephrosis and morphological hypogonadism should be ruled out prior to treatment.
5. Hypopituitarism and adrenal deficiency must be corrected prior to T<sub>3</sub>Cytomel<sup>®</sup> use.
6. Prolonged hypothyroidism can result in decreased adrenocortical activity commensurate with lowered metabolic rate. When thyroid replacement therapy is initiated, metabolism increases at a greater rate than adrenocortical activity; which may trigger adrenocortical insufficiency. In these severe and prolonged hypothyroidism cases; supplementation with adrenocortical steroids may be necessary.
7. T<sub>3</sub>Cytomel<sup>®</sup> may trigger a hyperthyroid state or may aggravate existing hyperthyroidism.
8. T<sub>3</sub>Cytomel<sup>®</sup> in patients with diabetes mellitus or insipidus or adrenal cortical insufficiency may aggravate the intensity of their symptoms. Dosage adjustments and other measures may be required to control these endocrine diseases. If thyroid medication is stopped, a downward readjustment of insulin or other hypoglycemic agents may be necessary to avoid hypoglycemia. Monitor urinary and serum glucose during treatment. Myxedema coma requires simultaneous administration of glucocorticoids.
9. Hypothyroidism decreases and hyperthyroidism increases the sensitivity to oral

anticoagulants. PT should be closely monitored in these patients when treated with thyroid hormones and dosage adjustment of oral anticoagulants may be required in accordance with serum PT in INR requirements.

10. Excessive doses of T<sub>3</sub>Cytomel<sup>®</sup> in infants may produce craniosynostosis.

11. T<sub>3</sub>Cytomel<sup>®</sup> is excreted primarily by the kidneys; patients with impaired renal functions should be monitored.

12. Caution should be used with nursing mothers as limited amounts of T<sub>3</sub>Cytomel<sup>®</sup> are excreted in human milk.

13. Dosage should be reduced or temporarily discontinued upon signs and symptoms of overdose. In normal patients, the hypothalamic-pituitary thyroid-axis is restored in 6 to 8 weeks are thyroid suppression.

14. T<sub>3</sub>Cytomel<sup>®</sup> may occasionally precipitate or exacerbate a pre-existing myasthenic syndrome.

15. The iron deficiency anemia with primary hypothyroidism patient developed palpitations and restlessness on treatment with T<sub>3</sub>Cytomel<sup>®</sup>. The drug had to be stopped. Upon correct of anemia with ferrous sulfate, all will be able to tolerate T<sub>3</sub>Cytomel<sup>®</sup>.

## Information for the Patient

Patients on T<sub>3</sub>Cytomel<sup>®</sup> and parents of pediatric patients on thyroid therapy should be informed that:

1. Replacement therapy is to be taken essentially for life, with the exception of cases of transient hypothyroidism, usually associated with thyroiditis and in those patients receiving a therapeutic trial of the drug.
2. They should immediately report during the course of therapy any signs or symptoms of thyroid hormone toxicity e.g. chest pain, increased pulse rate, palpitations, excessive sweating, heat intolerance, nervousness, or any other unusual event.
3. In case of concomitant diabetes mellitus, the daily dosage of antidiabetic medication may need readjustment as thyroid hormone replacement is achieved. If thyroid medication is stopped, a downward readjustment of the dosage of insulin or oral hypoglycemic agent may be necessary to avoid hypoglycemia. At all times, close monitoring of urinary glucose levels is mandatory in such patients.
4. In case of concomitant oral anticoagulant therapy, the prothrombin time should be measured frequently to determine if the dosage of oral anticoagulants is to be readjusted.
5. Partial loss of hair may be experienced by pediatric patients in the first few months of thyroid therapy, but this is usually a transient phenomenon and later recovery is usually the rule.

**WARNINGS:** Keep out of the reach of children. In case of accidental ingestion, contact a physician immediately.

**Drugs with thyroid hormone activity, alone or together with other therapeutic agents, have been used for the treatment of obesity. 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 their anorectic effects.**

## OVERDOSAGE:

Treatment of acute massive thyroid hormone overdose is focused on reducing gastrointestinal absorption of the drug and counteracting central and peripheral effects; principally those of increased sympathetic activity. Vomiting may be induced initially if further gastrointestinal absorption can be reasonably prevented and barring contraindications such as coma, convulsions, or loss of the gagging reflex. Treatment is symptomatic and supportive. Oxygen may be administered and ventilation maintained. Cardiac glycosides may be indicated if congestive heart failure develops. Measures to control fever, hypoglycemia, and fluid loss should be instituted if needed. Adrenergic agents, such as propranolol, have been used in the treatment of increased sympathetic activity. Propranolol may be administered intravenously at a dose of 1 to 3 mg over a 10-minute period or orally, 80 to 160 mg/day, especially when no contraindications exist for its use.

## DRUG INTERACTION:

1. Patients on oral anticoagulant therapy require close monitoring especially when T<sub>3</sub>Cytomel<sup>®</sup> is started or stopped. Dosages of anticoagulants may require adjustment to re-titrate PT and INR to clinically desirable state.
2. Diabetics: T<sub>3</sub>Cytomel<sup>®</sup> may alter the metabolism of oral hypoglycemic agents or may change insulin sensitivity in patients with diabetes mellitus which may require adjustment of dosage of insulin and other hypoglycemic drugs.
3. Avoid concomitant use with other CNS stimulants; particularly sympathomimetic amines.
4. Cholestyramine dosing must be 4-5 hours apart from T<sub>3</sub>Cytomel<sup>®</sup> dosing due to its ability to block T<sub>3</sub> and T<sub>4</sub> intestinal binding.
5. Oral contraceptives/Estrogen: May increase serum thyroxine-binding globulin. Thyroid requirements may change in female patients receiving estrogen therapy. Women without a functioning thyroid gland who are on replacement therapy may need to increase thyroid dosage if estrogens are administered.
6. Tricyclic Antidepressants (TCA): Use of thyroid products with imipramine and other TCAs may increase receptor sensitivity and enhance antidepressant activity. Transient cardiac arrhythmias have been observed in these patients and well as enhancement of thyroid hormone activity.
7. T<sub>3</sub>Cytomel<sup>®</sup> may potentiate the toxic effects of digitalis.
8. Ketamine use by patients on thyroid therapy may result in severe hypertension and tachycardia. Be prepared to treat hypertension in these patients.
9. Vasopressors: T<sub>3</sub> increases the adrenergic effect of catecholamine such as epinephrine and norepinephrine. Injection of these drugs in patients receiving T<sub>3</sub> therapy may increase risk of coronary insufficiency. Careful observation is required.

## ADVERSE REACTIONS:

Chest pain, increased pulse rate, palpitations, excessive sweating, cardiac arrhythmias, hypertension, heat intolerance, nervousness, or any other unusual event. Rare congestive heart failure.

## PATIENT MONITORING:

Thyroid hormones treatment should be preceded by a full clinical analysis with appropriate laboratory tests as determined by the treating physician. TSH suppression testing may be used to evaluate the effectiveness of any thyroid preparation. Bound T<sub>3</sub> and Bound T<sub>4</sub> serum

assays are less clinically useful than Free T<sub>3</sub> and Free T<sub>4</sub> testing; particularly in patients on concomitant androgen treatment which may alter bound T<sub>3</sub> and bound T<sub>4</sub> serum concentrations.

Serum testing should include at a minimum: Free T<sub>3</sub>, Free T<sub>4</sub>, TSH, FTI, RT3, and anti-TPO.

Laboratory tests should be repeated and dosages titrated until the clinically desirable euthyroid state is reached.

Many drugs are known to interfere with thyroid laboratory testing including but not limited to: androgens, corticosteroids, estrogens, oral contraceptives, iodine-containing preparations, and preparations contain salicylates.

#### **DOSAGE AND ADMINISTRATION:**

The dosage of thyroid hormones is determined by the indication and must in every case be individualized according to patient response and laboratory findings.

T<sub>3</sub>Cytomel<sup>®</sup> is intended for oral administration; once-a-day dosage is recommended. Although T<sub>3</sub>Cytomel<sup>®</sup> has a rapid cutoff; its metabolic effects persist for a few days following discontinuance.

#### **Mild Hypothyroidism:**

Recommended starting dosage is 25 mcg (¼ tablet of T<sub>3</sub>Cytomel<sup>®</sup>) daily. Daily dosage then may be increased by up to 25 mcg (¼ tablet of T<sub>3</sub>Cytomel<sup>®</sup>) every 1 or 2 weeks. Usual maintenance dose is 25 to 75mcg daily.

The rapid onset and dissipation of action of T<sub>3</sub>Cytomel<sup>®</sup>, as compared with levothyroxine sodium (T<sub>4</sub>), has led some clinicians to prefer its use in patients who might be more susceptible to the untoward effects of thyroid medication. However, the wide swings in serum T<sub>3</sub> levels that follow its administration and the possibility of more pronounced cardiovascular side effects tend to counterbalance the stated advantages.

T<sub>3</sub>Cytomel<sup>®</sup> may be used in preference to levothyroxine (T<sub>4</sub>) during radioisotope scanning procedures, since induction of hypothyroidism in those cases is more abrupt and can be of shorter duration. It may also be preferred when impairment of peripheral conversion of T<sub>4</sub> to T<sub>3</sub> is suspected.

#### **Myxedema:**

Recommended starting dosage is 5 mcg daily. This may be increased by 5 to 10 mcg daily every 1 or 2 weeks. When 25 mcg (¼ tablet of T<sub>3</sub>Cytomel<sup>®</sup>) daily is reached, dosage may be increased by 5 to 25 mcg every 1 or 2 weeks until a satisfactory therapeutic response is attained. Usual maintenance dose is 50 (½ tablet of T<sub>3</sub>Cytomel<sup>®</sup>) to 100 mcg daily.

#### **Myxedema Coma:**

Myxedema coma is usually precipitated in the hypothyroid patient of long standing by intercurrent illness or drugs such as sedatives and anesthetics and should be considered a medical emergency.

#### **Congenital Hypothyroidism:**

Recommended starting dosage is 5 mcg daily, with a 5 mcg increment every 3 to 4 days until the desired response is achieved. Infants a few months old may require only 20 mcg daily for maintenance. At 1 year, 50 mcg (½ tablet of T<sub>3</sub>Cytomel<sup>®</sup>) daily may be required. Above 3 years, full adult dosage may be necessary.

#### **Simple (non-toxic) Goiter:**

Recommended starting dosage is 5 mcg daily. This dosage may be increased by 5 to 10 mcg daily every 1 or 2 weeks. When 25 mcg daily is reached, dosage may be increased every week or two by 12.5 or 25 mcg. Usual maintenance dosage is 75 mcg (¾ tablet of T<sub>3</sub>Cytomel<sup>®</sup>) daily.

**In the elderly or in pediatric patients**, therapy should be started with 5 mcg daily and increased only by 5 mcg increments at the recommended intervals.

**When switching a patient to T<sub>3</sub>Cytomel<sup>®</sup> from thyroid, L-thyroxine or thyroglobulin**, discontinue the other medication, initiate T<sub>3</sub>Cytomel<sup>®</sup> at a low dosage, and increase gradually according to the patient's response. When selecting a starting dosage, bear in mind that this drug has a rapid onset of action, and that residual effects of the other thyroid preparation may persist for the first several weeks of therapy.

#### **Thyroid Suppression Therapy:**

Administration of thyroid hormone in doses higher than those produced physiologically by the gland results in suppression of the production of endogenous hormone. This is the basis for the thyroid suppression test and is used as an aid in the diagnosis of patients with signs of mild hyperthyroidism in whom baseline laboratory tests appear normal or to demonstrate thyroid gland autonomy in patients with Graves' ophthalmopathy. I<sup>131</sup> uptake is determined before and after the administration of the exogenous hormone. A 50% or greater suppression of uptake indicates a normal thyroid-pituitary axis and thus rules out thyroid gland autonomy.

T<sub>3</sub>Cytomel<sup>®</sup> is given in doses of 75 to 100 mcg/day for 7 days, and radioactive iodine uptake is determined before and after administration of the hormone. If thyroid function is under normal control, the radioiodine uptake will drop significantly after treatment. T<sub>3</sub>Cytomel<sup>®</sup> should be administered cautiously to patients in whom there is a strong suspicion of thyroid gland autonomy, in view of the fact that the exogenous hormone effects will be additive to the endogenous source.

#### **HOW SUPPLIED:**

T<sub>3</sub>Cytomel<sup>®</sup> 100 microgram per tablet is supplied in bottle of 100 yellow tablets.

For shelf-life please refer to the imprint on the pack.

Keep out of reach of children.

Should be at controlled room temperatures 15-30°C (59-86°F)

Protect from sun light

This drug has not been shown to be safe and effective for the enhancement of athletic performance!

**Manufactured and Distributed by: LA Pharma S.r.l.**

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