LIOTHYRONINE SODIUM- liothyronine sodium tablet
Northstar Rx LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LIOTHYRONINE SODIUM TABLETS safely and effectively. See full prescribing information for LIOTHYRONINE SODIUM TABLETS.

LIOTHYRONINE SODIUM tablets, for oral use
Initial U.S. Approval: 1956

WARNING: NOT FOR TREATMENT OF OBESITY OR FOR WEIGHT LOSS

See full prescribing information for complete boxed warning.

- **Thyroid hormones, including liothyronine sodium, should not be used for the treatment of obesity or for weight loss.**
- **Doses beyond the range of daily hormonal requirements may produce serious or even life-threatening manifestations of toxicity (6, 7.7, 10).**

RECENT MAJOR CHANGES

Indications and Usage (1.1, 1.2, 1.3)	12/2018
Dosage and Administration (2.1, 2.2, 2.3, 2.4, 2.5, 2.6)	12/2018
Contraindications (4)	12/2018
Warnings and Precautions (5.1, 5.2, 5.3, 5.4, 5.5, 5.6)	12/2018

INDICATIONS AND USAGE

Liothyronine is an L-triiodothyronine (T3) indicated for:

- Hypothyroidism: As replacement in primary (thyroidal), secondary (pituitary), and tertiary (hypothalamic) congenital or acquired hypothyroidism (1.1)
- Pituitary Thyroid-Stimulating Hormone (TSH) Suppression: As an adjunct to surgery and radioiodine therapy in the management of well-differentiated thyroid cancer (1.2)
- Thyroid Suppression Test: As a diagnostic agent in suppression tests to differentiate suspected mild hyperthyroidism or thyroid gland autonomy (1.3)

Limitations of Use:
- Not indicated for suppression of benign thyroid nodules and nontoxic diffuse goiter in iodine-sufficient patients. (1)
- Not indicated for treatment of hypothyroidism during the recovery phase of subacute thyroiditis. (1)

DOSAGE AND ADMINISTRATION

- Administer liothyronine sodium tablets orally once daily and individual dosage according to patient response and laboratory findings (2.1)
- See full prescribing information for recommended dosage for hypothyroidism (2.2) TSH suppression in well-differentiated thyroid cancer (2.3) and for thyroid suppression test (2.4)
- When switching a patient to liothyronine sodium, discontinue levothyroxine therapy and initiate liothyronine sodium at a low dosage. Gradually increase the dose according to the patient's response (2.5)
- Adequacy of therapy determined with periodic monitoring of TSH and T3 levels as well as clinical status (2.6)

DOSAGE FORMS AND STRENGTHS

Tablets: 5 mcg, 25 mcg, 50 mcg (3) (3)

CONTRAINDICATIONS

Uncorrected adrenal cortical insufficiency (4) (4)

WARNINGS AND PRECAUTIONS

- Cardiac adverse reactions in the elderly and in patients with underlying cardiovascular disease: Initiate liothyronine sodium at less than the full replacement dose because of the increased risk of cardiac adverse reactions, including atrial fibrillation (2.3,5.1, 8.5)
- Myxedema coma: Do not use oral thyroid hormone drug products to treat myxedema coma. (5.2)
- Acute adrenal crisis in patients with concomitant adrenal insufficiency: Treat with replacement

glucocorticoids prior to initiation of liothyronine sodium treatment (5.3)
- Prevention of hyperthyroidism or incomplete treatment of hypothyroidism: Proper dose titration and careful monitoring is critical to prevent the persistence of hypothyroidism or the development of hyperthyroidism. (5.4)
- Worsening of diabetic control: Therapy in patients with diabetes mellitus may worsen glycemic control and result in increased antidiabetic agent or insulin requirements. Carefully monitor glycemic control after starting, changing, or discontinuing thyroid hormone therapy (5.5)
- Decreased bone mineral density associated with thyroid hormone over-replacement: Over-replacement can increase bone resorption and decrease bone mineral density. Give the lowest effective dose (5.6)

ADVERSE REACTIONS

Most common adverse reactions for liothyronine sodium are primarily those of hyperthyroidism due to therapeutic overdosage: arrhythmias, myocardial infarction, dyspnea, headache, nervousness, irritability, insomnia, tremors, muscle weakness, increased appetite, weight loss, diarrhea, heat intolerance, menstrual irregularities, and skin rash (6) (6)

To report SUSPECTED ADVERSE REACTIONS, contact Northstar Rx LLC @1-800-206-7821 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. (6)

DRUG INTERACTIONS

See full prescribing information for drugs that affect thyroid hormone pharmacokinetics and metabolism (e.g., absorption, synthesis, secretion, catabolism, protein binding, and target tissue response) and may alter the therapeutic response to liothyronine sodium (7) (7)

USE IN SPECIFIC POPULATIONS

Pregnancy may require the use of higher doses of thyroid hormone (2.2, 8.1)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 10/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: NOT FOR TREATMENT OF OBESITY OR FOR WEIGHT LOSS

- **Thyroid hormones, including liothyronine sodium, either alone or with other therapeutic agents, should not be used for the treatment of obesity or for 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 their anorectic effects *[see Adverse Reactions (6), Drug Interactions (7.7), and Overdosage (10)]* .**

1 INDICATIONS AND USAGE

1.1 Hypothyroidism

Liothyronine sodium tablets are indicated as a replacement therapy in primary (thyroidal), secondary (pituitary), and tertiary (hypothalamic) congenital or acquired hypothyroidism.

1.2 Pituitary Thyroid-Stimulating Hormone (TSH) Suppression

Liothyronine sodium tablets are indicated as an adjunct to surgery and radioiodine therapy in the management of well-differentiated thyroid cancer.

1.3 Thyroid Suppression Test

Liothyronine sodium tablets are indicated as a diagnostic agent in suppression tests to differentiate suspected mild hyperthyroidism or thyroid gland autonomy.

Limitations of Use

- Liothyronine sodium tablets are not indicated for suppression of benign thyroid nodules and nontoxic diffuse goiter in iodine-sufficient patients as there are no clinical benefits and overtreatment with liothyronine sodium may induce hyperthyroidism *[see Warnings and Precautions (5.4)]* .
- Liothyronine sodium tablets are not indicated for treatment of hypothyroidism during the recovery phase of subacute thyroiditis.

2 DOSAGE AND ADMINISTRATION

2.1 General Principles of Dosing

The dose of liothyronine sodium for hypothyroidism or pituitary Thyroid-Stimulating Hormone (TSH) suppression depends on a variety of factors including: the patient's age, body weight, cardiovascular status, concomitant medical conditions (including pregnancy), concomitant medications, co-administered food and the specific nature of the condition being treated *[see Dosage and Administration (2.2, 2.3, 2.4), Warnings and Precautions (5), and Drug Interactions (7)]*. Dosing must be individualized to account for these factors and dose adjustments made based on periodic assessment of the patient's clinical response and laboratory parameters *[see Dosage and Administration (2.4)]*.

Administer liothyronine sodium tablets orally once daily.

2.2 Recommended Dosage for Hypothyroidism

Adults

The recommended starting dosage is 25 mcg orally once daily. Increase the dose by 25 mcg daily every 1 or 2 weeks, if needed. The usual maintenance dose is 25 mcg to 75 mcg once daily.

For elderly patients or patients with underlying cardiac disease, start with liothyronine sodium tablets 5 mcg once daily and increase by 5 mcg increments at the recommended intervals.

Serum TSH is not a reliable measure of liothyronine sodium dose adequacy in patients with secondary or tertiary hypothyroidism and should not be used to monitor therapy.

Use the serum T3 level to monitor adequacy of therapy in this patient population.

Pediatric Patients

The recommended starting dosage is 5 mcg once daily, with a 5 mcg increase every 3 to 4 days until the desired response is achieved. Infants a few months old may require 20 mcg once daily for maintenance. At 1 year of age, 50 mcg once daily may be required. Above 3 years of age, the full adult dosage may be necessary *[see Use in Specific Populations (8.4)].*

Newborns (0 to 3 months) at Risk for Cardiac Failure:

Consider a lower starting dose in infants at risk for cardiac failure. Increase the dose as needed based on clinical and laboratory response.

Pediatric Patients at Risk for Hyperactivity:

To minimize the risk of hyperactivity in pediatric patients, start at one-fourth the recommended full replacement dose, and increase on a weekly basis by one-fourth the full recommended replacement dose until the full recommended replacement dose is reached.

Pregnancy

Pre-existing Hypothyroidism: Thyroid hormone dose requirements may increase during pregnancy. Measure serum TSH and free-T4 as soon as pregnancy is confirmed and, at minimum, during each trimester of pregnancy. In patients with primary hypothyroidism, maintain serum TSH in the trimester-specific reference range. For patients with serum TSH above the normal trimester-specific range, increase the dose of thyroid hormone and measure TSH every 4 weeks until a stable dose is reached and serum TSH is within the normal trimester-specific range. Reduce thyroid hormone dosage to pre-pregnancy levels immediately after delivery and measure serum TSH levels 4 to 8 weeks postpartum to ensure thyroid hormone dose is appropriate.

2.3 Recommended Dosage for TSH Suppression in Well-Differentiated Thyroid Cancer

The dose of liothyronine sodium should target TSH levels within the desired therapeutic range. This may require higher doses, depending on the target level for TSH suppression.

2.4 Recommended Dosage for Thyroid Suppression Test

The recommended dose is 75 mcg to 100 mcg daily for 7 days, with radioactive iodine uptake being determined before and after the 7 day administration of liothyronine sodium tablets. If thyroid function is normal, the radioiodine uptake will drop significantly after treatment. A 50% or greater suppression of uptake indicates a normal thyroid-pituitary axis.

2.5 Switching from Levothyroxine to Liothyronine Sodium

Liothyronine sodium has a rapid onset of action and residual effects of the other thyroid preparation may persist for the first several weeks after initiating liothyronine sodium therapy. When switching a patient to liothyronine sodium, discontinue levothyroxine therapy and initiate liothyronine sodium at a low dosage. Gradually increase the

liothyronine sodium dose according to the patient's response.

2.6 Monitoring TSH and Triiodothyronine (T3) Levels

Assess the adequacy of therapy by periodic assessment of laboratory tests and clinical evaluation. Persistent clinical and laboratory evidence of hypothyroidism despite an apparent adequate replacement dose of liothyronine sodium may be evidence of inadequate absorption, poor compliance, drug interactions, or a combination of these factors.

Adults

In adult patients with primary hypothyroidism, monitor serum TSH periodically after initiation of the therapy or any change in dose. To check the immediate response to therapy before the TSH has had a chance to respond or if your patient's status needs to be assessed prior to that point, measurement of total T3 would be most appropriate. In patients on a stable and appropriate replacement dose, evaluate clinical and biochemical response every 6 to 12 months and whenever there is a change in the patient's clinical status.

Pediatrics

In pediatric patients with hypothyroidism, assess the adequacy of replacement therapy by measuring serum TSH and T3 levels. For pediatric patients three years of age and older, the recommended monitoring is every 3 to 12 months thereafter, following dose stabilization until growth and puberty are completed. Poor compliance or abnormal values may necessitate more frequent monitoring. Perform routine clinical examination, including assessment of development, mental and physical growth, and bone maturation, at regular intervals.

While the general aim of therapy is to normalize the serum TSH level, TSH may not normalize in some patients due to *in utero* hypothyroidism causing a resetting of pituitary-thyroid feedback. Failure of the serum TSH to decrease below 20 IU per liter after initiation of liothyronine sodium therapy may indicate the child is not receiving adequate therapy. Assess compliance, dose of medication administered, and method of administration prior to increasing the dose of liothyronine sodium *[see Warnings and Precautions (5.1)* and *Use in Specific Populations (8.4)]*.

Secondary and Tertiary Hypothyroidism

Monitor serum T3 levels and maintain in the normal range.

3 DOSAGE FORMS AND STRENGTHS

Tablets available as follows:

- 5 mcg: white to off white, round, flat faced beveled edge, uncoated tablets, debossed with '582' on one side and plain on the other side.
- 25 mcg: white to off white, oval shaped, uncoated tablets, debossed with '583' on one side and scored on the other side.
- 50 mcg: white to off white, capsule shaped, beveled edge, uncoated tablets, debossed with '584' on one side and scored on the other side.

4 CONTRAINDICATIONS

Liothyronine sodium is contraindicated in patients with uncorrected adrenal insufficiency *[see Warnings and Precautions (5.3)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Cardiac Adverse Reactions in the Elderly and in Patients with Underlying Cardiovascular Disease

Overtreatment with thyroid hormone may cause an increase in heart rate, cardiac wall thickness, and cardiac contractility and may precipitate angina or arrhythmias, particularly in patients with cardiovascular disease and in elderly patients. Initiate liothyronine sodium therapy in this population at lower doses than those recommended in younger individuals or in patients without cardiac disease *[see Dosage and Administration (2.3) and Use in Specific Populations (8.5)].*

Monitor for cardiac arrhythmias during surgical procedures in patients with coronary artery disease receiving suppressive liothyronine sodium therapy. Monitor patients receiving concomitant liothyronine sodium and sympathomimetic agents for signs and symptoms of coronary insufficiency. If cardiovascular symptoms develop or worsen, reduce or withhold the liothyronine sodium dose for one week and restart at a lower dose.

5.2 Myxedema Coma

Myxedema coma is a life-threatening emergency characterized by poor circulation and hypometabolism, and may result in unpredictable absorption of thyroid hormone from the gastrointestinal tract. Use of oral thyroid hormone drug products is not recommended to treat myxedema coma. Administer thyroid hormone products formulated for intravenous administration to treat myxedema coma.

5.3 Acute Adrenal Crisis in Patients with Concomitant Adrenal Insufficiency

Thyroid hormone increases metabolic clearance of glucocorticoids. Initiation of thyroid hormone therapy prior to initiating glucocorticoid therapy may precipitate an acute adrenal crisis in patients with adrenal insufficiency. Treat patients with adrenal insufficiency with replacement glucocorticoids prior to initiating treatment with liothyronine sodium *[see Contraindications (4)].*

5.4 Prevention of Hyperthyroidism or Incomplete Treatment of Hypothyroidism

Liothyronine sodium has a narrow therapeutic index. Over- or undertreatment with liothyronine sodium may have negative effects on growth and development, cardiovascular function, bone metabolism, reproductive function, cognitive function, emotional state, gastrointestinal function, and on glucose and lipid metabolism. Titrate the dose of liothyronine sodium carefully and monitor response to titration to avoid these effects *[see Dosage and Administration (2.4)].* Monitor for the presence of drug or food interactions when using liothyronine sodium and adjust the dose as necessary *[see Drug Interactions (7) and Clinical Pharmacology (12.3)].*

5.5 Worsening of Diabetic Control

Addition of thyroid hormone therapy in patients with diabetes mellitus may worsen glycemic control and result in increased antidiabetic agent or insulin requirements. Carefully monitor glycemic control after starting, changing, or discontinuing liothyronine sodium *[see Drug Interactions (7.2)].*

5.6 Decreased Bone Mineral Density Associated with Thyroid Hormone Over-Replacement

Increased bone resorption and decreased bone mineral density may occur as a result of thyroid hormone over-replacement, particularly in post-menopausal women. 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. Administer the minimum dose of liothyronine sodium that achieves the desired clinical and biochemical response to mitigate against this risk.

6 ADVERSE REACTIONS

Adverse reactions associated with liothyronine sodium therapy are primarily those of hyperthyroidism due to therapeutic overdosage *[see Warnings and Precautions (5.4) and Overdosage (10)]*. 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 and cramps

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

Respiratory: dyspnea

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

Dermatologic: hair loss, flushing

Endocrine: decreased bone mineral density

Reproductive: menstrual irregularities, impaired fertility

Adverse Reactions in Pediatric Patients

Pseudotumor cerebri and slipped capital femoral epiphysis have been reported in pediatric patients receiving thyroid replacement therapy. Overtreatment may result in craniosynostosis in infants and premature closure of the epiphyses in pediatric patients with resultant compromised adult height.

Hypersensitivity Reactions

Hypersensitivity reactions to inactive ingredients have occurred in patients treated with thyroid hormone products. These include urticaria, pruritus, skin rash, flushing, angioedema, various gastrointestinal symptoms (abdominal pain, nausea, vomiting and

diarrhea), fever, arthralgia, serum sickness and wheezing.

7 DRUG INTERACTIONS

7.1 Drugs Known to Affect Thyroid Hormone Pharmacokinetics

Many drugs can exert effects on thyroid hormone pharmacokinetics (e.g. absorption, synthesis, secretion, catabolism, protein binding, and target tissue response) and may alter the therapeutic response to liothyronine sodium (see Tables 1 to 4).

Table 1: Drugs That May Decrease T3 Absorption (Hypothyroidism)

Potential impact: Concurrent use may reduce the efficacy of liothyronine sodium by binding and delaying or preventing absorption, potentially resulting in hypothyroidism.	
Drug or Drug Class	**Effect**
Bile Acid Sequestrants -Colesevelam -Cholestyramine -Colestipol Ion Exchange Resins -Kayexalate -Sevelamer	Bile acid sequestrants and ion exchange resins are known to decrease thyroid hormones absorption. Administer liothyronine sodium at least 4 hours prior to these drugs or monitor thyrotropin-stimulating hormone (TSH) levels.

Table 2: Drugs That May Alter Triiodothyronine (T3) Serum Transport Without Affecting Free Thyroxine (FT4) Concentration (Euthyroidism)

Drug or Drug Class	**Effect**
Clofibrate Estrogen-containing oral contraceptives Estrogens (oral) Heroin / Methadone 5-Fluorouracil Mitotane Tamoxifen	These drugs may increase serum thyroxine-binding globulin (TBG) concentration.
Androgens / Anabolic Steroids Asparaginase Glucocorticoids Slow-Release Nicotinic Acid	These drugs may decrease serum TBG concentration.
Salicylates (>2 g/day)	Salicylates inhibit binding of T4 and T3 to TBG and transthyretin. An initial increase in serum FT4 is followed by return of FT4 to normal levels

Salicylates (>2 g/day)	with sustained therapeutic serum salicylate concentrations, although total T4 levels may decrease by as much as 30%.
Other drugs: Carbamazepine Furosemide (>80 mg IV) Heparin Hydantoins Non-Steroidal Antiinflammatory Drugs - Fenamates	These drugs may cause protein binding site displacement. Furosemide has been shown to inhibit the protein binding of T4 to TBG and albumin, causing an increased free-T4 fraction in serum. Furosemide competes for T4-binding sites on TBG, prealbumin, and albumin, so that a single high dose can acutely lower the total T4 level. Phenytoin and carbamazepine reduce serum protein binding of thyroid hormones, and total and FT4 may be reduced by 20% to 40%, but most patients have normal serum TSH levels and are clinically euthyroid. Closely monitor thyroid hormone parameters.

Table 3: Drugs That May Alter Hepatic Metabolism of Thyroid hormones

Potential impact: Stimulation of hepatic microsomal drug-metabolizing enzyme activity may cause increased hepatic degradation of thyroid hormones, resulting in increased liothyronine sodium requirements.	
Drug or Drug Class	**Effect**
Phenobarbital Rifampin	Phenobarbital has been shown to reduce the response to thyroxine. Phenobarbital increases L-thyroxine metabolism by inducing uridine 5'-diphospho-glucuronosyltransferase (UGT) and leads to a lower T4 serum levels. Changes in thyroid status may occur if barbiturates are added or withdrawn from patients being treated for hypothyroidism. Rifampin has been shown to accelerate the metabolism of thyroid hormones.

Table 4: Drugs That May Decrease Conversion of T4 to T3

Potential impact: Administration of these enzyme inhibitors decreases the peripheral conversion of T4 to T3, leading to decreased T3 levels. However, serum T4 levels are usually normal but may occasionally be slightly increased.	
Drug or Drug Class	**Effect**
Beta-adrenergic antagonists (e.g., Propranolol >160 mg/day)	In patients treated with large doses of propranolol (>160 mg/day), T3 and T4 levels change, TSH levels remain normal, and patients are clinically euthyroid. Actions of particular beta-adrenergic antagonists may be impaired when a hypothyroid patient is converted to the euthyroid state.

Glucocorticoids (e.g., Dexamethasone ≥4 mg/day)	Short-term administration of large doses of glucocorticoids may decrease serum T3 concentrations by 30% with minimal change in serum T4 levels. However, long-term glucocorticoid therapy may result in slightly decreased T3 and T4 levels due to decreased TBG production (see above).
Other drugs: Amiodarone	Amiodarone inhibits peripheral conversion of levothyroxine (T4) to triiodothyronine (T3) and may cause isolated biochemical changes (increase in serum free-T4, and decreased or normal free-T3) in clinically euthyroid patients.

7.2 Antidiabetic Therapy

Addition of liothyronine sodium therapy in patients with diabetes mellitus may worsen glycemic control and result in increased antidiabetic agent or insulin requirements. Carefully monitor glycemic control, especially when liothyronine sodium is started, changed, or discontinued *[see Warnings and Precautions (5.5)]*.

7.3 Oral Anticoagulants

Liothyronine sodium increases the response to oral anticoagulant therapy. Therefore, a decrease in the dose of anticoagulant may be warranted with correction of the hypothyroid state or when the liothyronine sodium dose is increased. Closely monitor coagulation tests to permit appropriate and timely dosage adjustments.

7.4 Digitalis Glycosides

Liothyronine sodium may reduce the therapeutic effects of digitalis glycosides. Serum digitalis glycoside levels may be decreased when a hypothyroid patient becomes euthyroid, necessitating an increase in the dose of digitalis glycosides.

7.5 Antidepressant Therapy

Concurrent use of tricyclic (e.g., amitriptyline) or tetracyclic (e.g., maprotiline) antidepressants and liothyronine sodium 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 central nervous system stimulation. Liothyronine sodium may accelerate the onset of action of tricyclics. Administration of sertraline in patients stabilized on liothyronine sodium may result in increased liothyronine sodium requirements.

7.6 Ketamine

Concurrent use of ketamine and liothyronine sodium may produce marked hypertension and tachycardia. Closely monitor blood pressure and heart rate in these patients.

7.7 Sympathomimetics

Concurrent use of sympathomimetics and liothyronine sodium may increase the effects of sympathomimetics or thyroid hormone. Thyroid hormones may increase the risk of

coronary insufficiency when sympathomimetic agents are administered to patients with coronary artery disease.

7.8 Tyrosine-Kinase Inhibitors

Concurrent use of tyrosine-kinase inhibitors such as imatinib may cause hypothyroidism. Closely monitor TSH levels in such patients.

7.9 Drug-Laboratory Test Interactions

Consider changes in TBG concentration when interpreting T4 and T3 values. Measure and evaluate unbound (free) hormone in this circumstance. Pregnancy, infectious hepatitis, estrogens, estrogen-containing oral contraceptives, and acute intermittent porphyria increase TBG concentrations. Nephrosis, severe hypoproteinemia, severe liver disease, acromegaly, androgens and corticosteroids decrease TBG concentration. Familial hyper- or hypo-thyroxine binding globulinemias have been described, with the incidence of TBG deficiency approximating 1 in 9000.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Experience with liothyronine use in pregnant women, including data from post-marketing studies, have not reported increased rates of major birth defects or miscarriages *(see Data).* There are risks to the mother and fetus associated with untreated hypothyroidism in pregnancy. Since TSH levels may increase during pregnancy, TSH should be monitored and liothyronine sodium dosage adjusted during pregnancy *(see Clinical Considerations)*. There are no animal studies conducted with liothyronine during pregnancy. Liothyronine sodium should not be discontinued during pregnancy and hypothyroidism diagnosed during pregnancy should be promptly treated.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Clinical Considerations

Disease-associated maternal and/or embryo/fetal risk

Maternal hypothyroidism during pregnancy is associated with a higher rate of complications, including spontaneous abortion, gestational hypertension, pre-eclampsia, stillbirth, and premature delivery. Untreated maternal hypothyroidism may have an adverse effect on fetal neurocognitive development.

Dose adjustments during pregnancy and the postpartum period

Pregnancy may increase liothyronine sodium requirements. Serum TSH levels should be monitored and the liothyronine sodium dosage adjusted during pregnancy. Since postpartum TSH levels are similar to preconception values, the liothyronine sodium dosage should return to the pre-pregnancy dose immediately after delivery *[see Dosage and Administration (2.3)].*

Data

Human Data

Liothyronine is approved for use as a replacement therapy for hypothyroidism. Data from post-marketing studies have not reported increased rates of fetal malformations, miscarriages, or other adverse maternal or fetal outcomes associated with liothyronine use in pregnant women.

8.2 Lactation

Risk Summary

Limited published studies report that liothyronine is present in human milk. However, there is insufficient information to determine the effects of liothyronine on the breastfed infant and no available information on the effects of liothyronine on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for liothyronine sodium and any potential adverse effects on the breastfed infant from liothyronine sodium or from the underlying maternal condition.

8.4 Pediatric Use

The initial dose of liothyronine sodium varies with age and body weight. Dosing adjustments are based on an assessment of the individual patient's clinical and laboratory parameters *[see Dosage and Administration (2.3, 2.4)]*.

In pediatric patients in whom a diagnosis of permanent hypothyroidism has not been established, discontinue thyroid hormone for a trial period, but only after the child is at least 3 years of age. Obtain serum TSH, T4, and T3 levels at the end of the trial period, and use laboratory test results and clinical assessments to guide diagnosis and treatment, if warranted *[see Dosage and Administration (2.6)].*

Congenital Hypothyroidism *[see Dosage and Administration (2.2, 2.6)]*

Rapid restoration of normal serum T4 concentrations is essential for preventing the adverse effects of congenital hypothyroidism on intellectual development as well as on overall physical growth and maturation. Therefore, initiate thyroid hormone immediately upon diagnosis. Thyroid hormone is generally continued for life in these patients.

Closely monitor infants during the first 2 weeks of thyroid hormone therapy for cardiac overload, arrhythmias, and aspiration from avid suckling.

Closely monitor patients to avoid undertreatment or overtreatment. Undertreatment may have deleterious effects on intellectual development and linear growth. Overtreatment is associated with craniosynostosis in infants, may adversely affect the tempo of brain maturation, and may accelerate the bone age and result in premature epiphyseal closure and compromised adult stature *[see Dosage and Administration (2.6) and Adverse Reactions (6)]*.

Acquired Hypothyroidism in Pediatric Patients

Closely monitor patients to avoid undertreatment and overtreatment. Undertreatment may result in poor school performance due to impaired concentration and slowed mentation and in reduced adult height. Overtreatment may accelerate the bone age and result in premature epiphyseal closure and compromised adult stature.

Treated children may manifest a period of catch-up growth, which may be adequate in some cases to normalize adult height. In children with severe or prolonged hypothyroidism, catch-up growth may not be adequate to normalize adult height *[see Adverse Reactions (6)]*.

8.5 Geriatric Use

Because of the increased prevalence of cardiovascular disease among the elderly, initiate liothyronine sodium at less than the full replacement dose *[see Dosage and Administration (2.3) and Warnings and Precautions (5.1)]*. Atrial arrhythmias can occur in elderly patients. Atrial fibrillation is the most common of the arrhythmias observed with thyroid hormone overtreatment in the elderly.

10 OVERDOSAGE

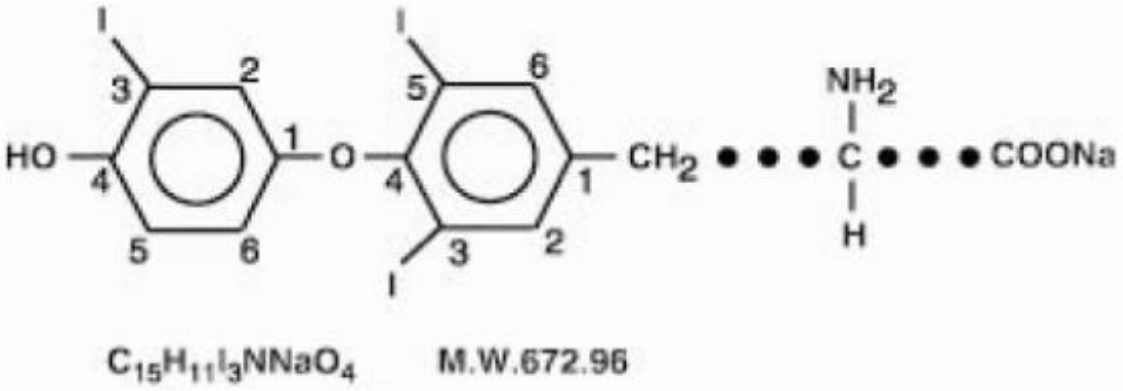
The signs and symptoms of overdosage are those of hyperthyroidism *[see Warnings and Precautions (5.4) and Adverse Reactions (6)]*. In addition, confusion and disorientation may occur. Cerebral embolism, seizure, shock, coma, and death have been reported. Symptoms may not necessarily be evident or may not appear until several days after ingestion.

Reduce the liothyronine sodium dose or temporarily discontinued if signs or symptoms of overdosage occur. Initiate appropriate supportive treatment as dictated by the patient's medical status.

For current information on the management of poisoning or overdosage, contact the National Poison Control Center at 1-800-222-1222 or www.poison.org.

11 DESCRIPTION

Liothyronine sodium tablets, USP contain the active ingredient, liothyronine (L-triiodothyronine or LT_3), a synthetic form of a thyroid hormone liothyronine in sodium salt form. It is chemically designated as L-Tyrosine, *O*-(4-hydroxy-3-iodophenyl)-3,5-diiodo-, monosodium salt. The molecular formula, molecular weight and structural formula of liothyronine sodium are given below.



$C_{15}H_{11}I_3NNaO_4$ M.W.672.96

Liothyronine sodium tablets, USP contain liothyronine sodium, USP equivalent to

liothyronine in 5 mcg, 25 mcg, and 50 mcg. Inactive ingredients consist of calcium sulfate dihydrate, corn starch, gelatin, stearic acid, sucrose and talc.

FDA approved dissolution method differ from the USP dissolution method.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Thyroid hormones exert their physiologic actions through control of DNA transcription and protein synthesis. Triiodothyronine (T3) and L-thyroxine (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 T3, the majority of which (approximately 80%) is derived from T4 by deiodination in peripheral tissues.

12.2 Pharmacodynamics

The onset of activity of liothyronine sodium occurs within a few hours. Maximum pharmacologic response occurs within 2 or 3 days.

12.3 Pharmacokinetics

Absorption

T3 is almost totally absorbed, 95 percent in 4 hours. The hormones contained in the natural preparations are absorbed in a manner similar to the synthetic hormones.

Distribution

Liothyronine sodium (T3) is not firmly bound to serum protein. The higher affinity of levothyroxine (T4) for both thyroid-binding globulin and thyroid-binding prealbumin as compared to triiodothyronine (T3) partially explains the higher serum levels and longer half-life of the former hormone. Both protein-bound hormones exist in reverse equilibrium with minute amounts of free hormone, the latter accounting for the metabolic activity.

Elimination

Metabolism

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. T3 is further deiodinated to diiodothyronine. Thyroid hormones are also metabolized via conjugation with glucuronides and sulfates and excreted directly into the bile and gut where they undergo enterohepatic recirculation.

Excretion

Thyroid hormones are primarily eliminated by the kidneys. A portion of the conjugated hormone reaches the colon unchanged and is eliminated in the feces. The biological half-

life is about 2-1/2 days.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal studies have not been performed to evaluate the carcinogenic potential, mutagenic potential or effects on fertility of liothyronine sodium.

16 HOW SUPPLIED/STORAGE AND HANDLING

Liothyronine sodium tablets, USP are supplied as follows:

5 mcg tablets are white to off white, round, flat faced beveled edge, uncoated tablets, debossed with '582' on one side and plain on the other side.

NDC 16714-166-01 in bottles of 100 tablets with child-resistance closure

25 mcg tablets are white to off white, oval shaped, uncoated tablets, debossed with '583' on one side and scored on the other side.

NDC 16714-167-01 in bottles of 100 tablets with child-resistance closure

50 mcg tablets are white to off white, capsule shaped, beveled edge, uncoated tablets, debossed with '584' on one side and scored on the other side.

NDC 16714-168-01 in bottles of 100 tablets with child-resistance closure

Store between 15°C and 30°C (59°F and 86°F).

17 PATIENT COUNSELING INFORMATION

Dosing and Administration

- Instruct patients that liothyronine sodium tablets should only be taken as directed by their healthcare provider.
- Instruct patients to notify their healthcare provider should they become pregnant or breastfeeding or are thinking of becoming pregnant, while taking liothyronine sodium tablets.

Important Information

- Inform patients that the liothyronine in liothyronine sodium tablets is intended to replace a hormone that is normally produced by the thyroid gland. Generally replacement therapy is to be taken for life.
- Inform patients that liothyronine sodium tablets should not be used as a primary or adjunctive therapy in a weight control program.
- Instruct patients to notify their healthcare provider if they are taking any other medications, including prescription and over-the-counter preparations.
- Instruct patients to notify their healthcare provider of any other medical conditions, particularly heart disease, diabetes, clotting disorders, and adrenal or pituitary gland problems, as the dose of medications used to control these other conditions may need to be adjusted while taking liothyronine sodium tablets. If patents are taking anticoagulants (blood thinners), their clotting status should be checked frequently.

- Instruct patients to notify their physician or dentist if they are taking liothyronine sodium tablets prior to any surgery.

Adverse Reactions

- Instruct patients to notify their healthcare provider if they experience any of the following symptoms: rapid or irregular heartbeat, chest pain, shortness of breath, leg cramps, headache, nervousness, irritability, sleeplessness, tremors, change in appetite, weight gain or loss, vomiting, diarrhea, excessive sweating, heat intolerance, fever, changes in menstrual periods, hives or skin rash, or any other unusual medical event *[see Adverse Reactions (6)]*.
- Inform patients that partial hair loss may occur rarely during the first few months of liothyronine sodium tablets therapy; this is usually temporary *[see Adverse Reactions (6)]*.

Manufactured for:

Northstar Rx LLC

Memphis, TN 38141

Manufactured by:

Zydus Lifesciences Ltd.,

Ahmedabad, India

Iss. 10/22

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

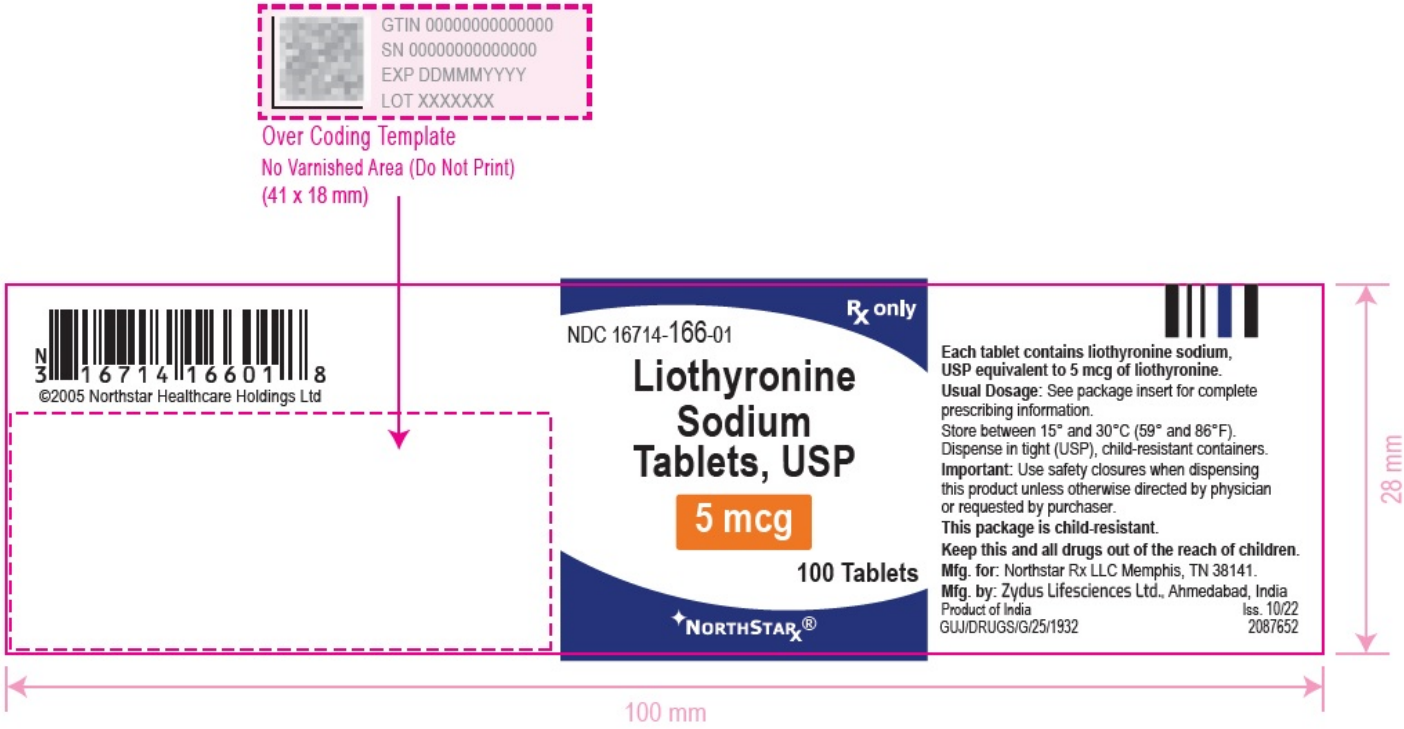
NDC 16714-166-01

Liothyronine Sodium Tablets, USP

5 mcg

100 Tablets

Rx only



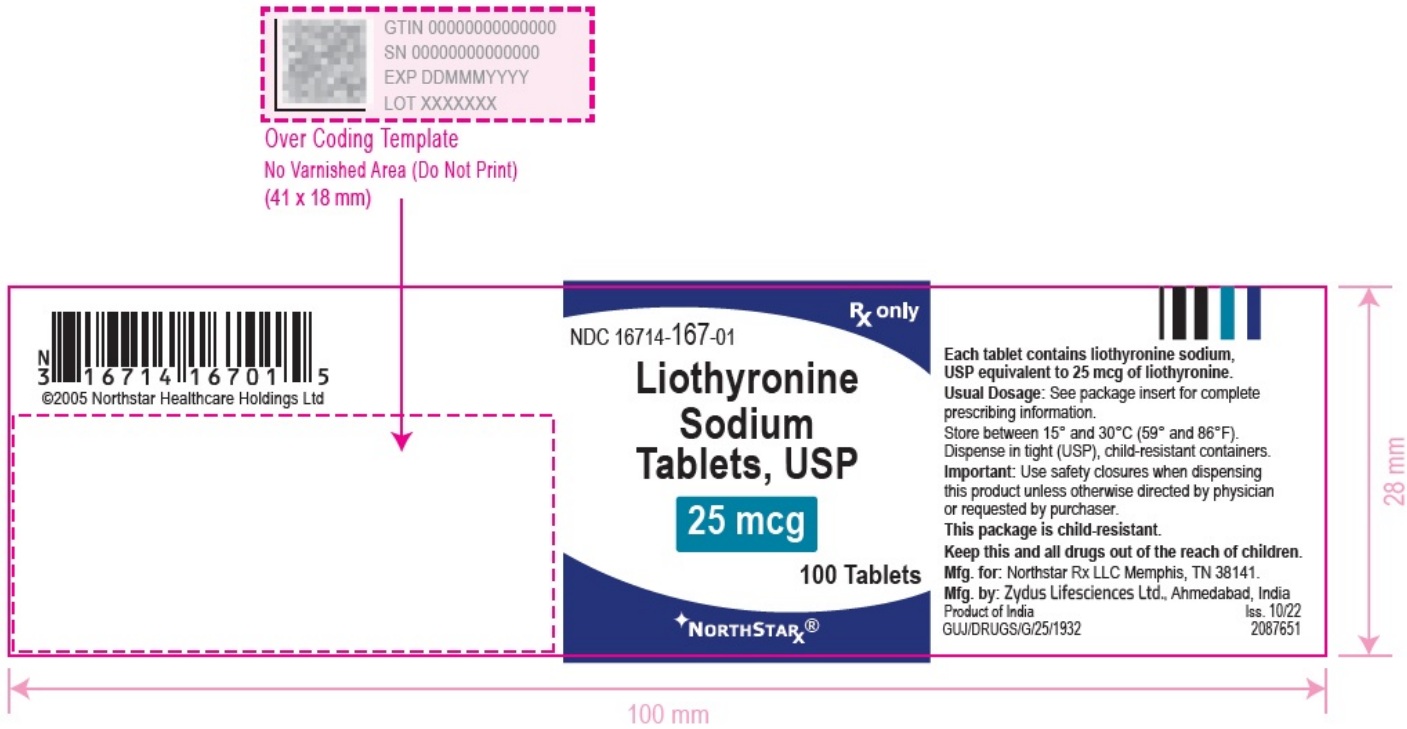
NDC 16714-167-01

Liothyronine Sodium Tablets, USP

25 mcg

100 Tablets

Rx only



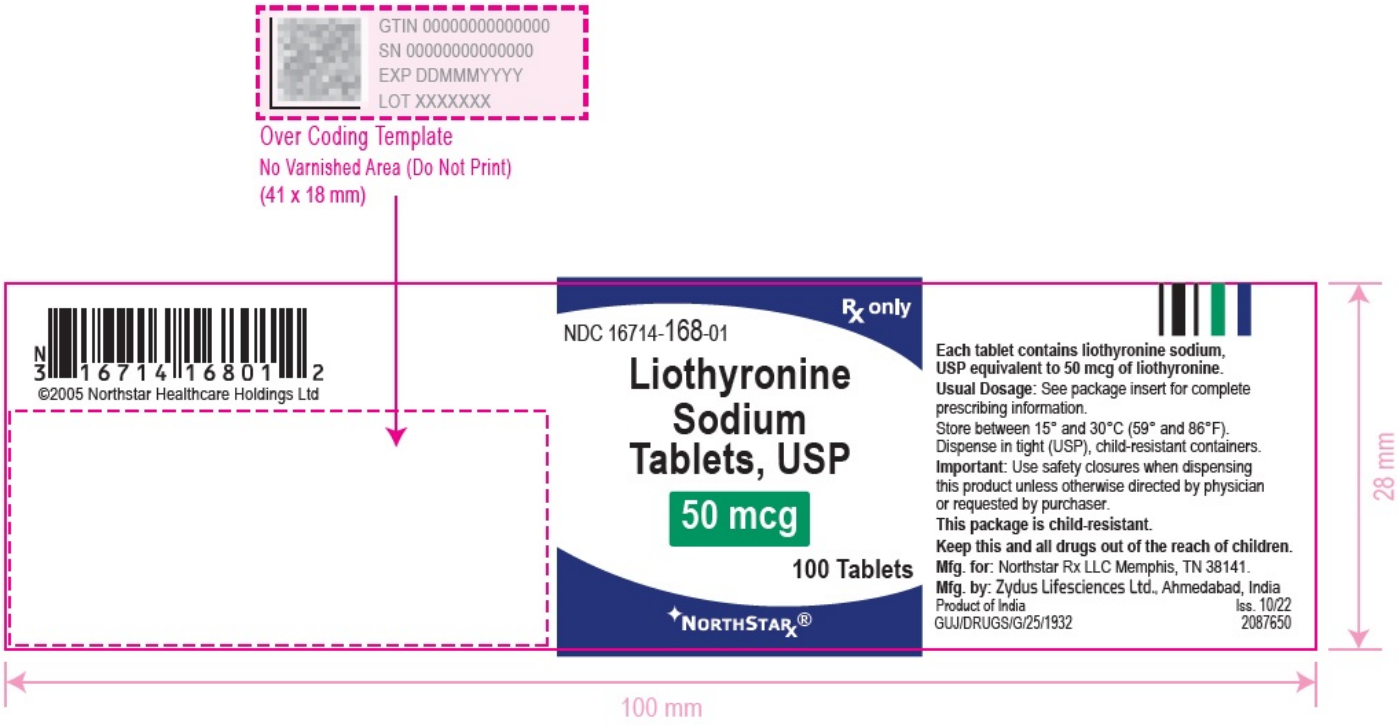
NDC 16714-168-01

Liothyronine Sodium Tablets, USP

50 mcg

100 Tablets

Rx only



LIOTHYRONINE SODIUM

liothyronine sodium tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:16714-166
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
LIOTHYRONINE SODIUM (UNII: GCA9VV7D2N) (LIOTHYRONINE - UNII:06LU7C9H1V)	LIOTHYRONINE	5 ug

Inactive Ingredients	
Ingredient Name	**Strength**
CALCIUM SULFATE DIHYDRATE (UNII: 4846Q921YM)	
STARCH, CORN (UNII: O8232NY3SJ)	

GELATIN (UNII: 2G86QN327L)	
STEARIC ACID (UNII: 4ELV7Z65AP)	
SUCROSE (UNII: C151H8M554)	
TALC (UNII: 7SEV7J4R1U)	

Product Characteristics

Color	WHITE (white to off white)	**Score**	no score
Shape	ROUND	**Size**	6mm
Flavor		**Imprint Code**	582
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:16714-166-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	05/05/2021	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA214803	05/05/2021	

LIOTHYRONINE SODIUM

liothyronine sodium tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:16714-167
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LIOTHYRONINE SODIUM (UNII: GCA9VV7D2N) (LIOTHYRONINE - UNII:06LU7C9H1V)	LIOTHYRONINE	25 ug

Inactive Ingredients

Ingredient Name	Strength
CALCIUM SULFATE DIHYDRATE (UNII: 4846Q921YM)	
STARCH, CORN (UNII: O8232NY3SJ)	
GELATIN (UNII: 2G86QN327L)	
STEARIC ACID (UNII: 4ELV7Z65AP)	
SUCROSE (UNII: C151H8M554)	
TALC (UNII: 7SEV7J4R1U)	

Product Characteristics			
Color	WHITE (white to off white)	**Score**	2 pieces
Shape	OVAL	**Size**	7mm
Flavor		**Imprint Code**	583
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:16714-167-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	05/05/2021	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA214803	05/05/2021	

LIOTHYRONINE SODIUM

liothyronine sodium tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:16714-168
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
LIOTHYRONINE SODIUM (UNII: GCA9VV7D2N) (LIOTHYRONINE - UNII:06LU7C9H1V)	LIOTHYRONINE	50 ug

Inactive Ingredients	
Ingredient Name	**Strength**
CALCIUM SULFATE DIHYDRATE (UNII: 4846Q921YM)	
STARCH, CORN (UNII: O8232NY3SJ)	
GELATIN (UNII: 2G86QN327L)	
STEARIC ACID (UNII: 4ELV7Z65AP)	
SUCROSE (UNII: C151H8M554)	
TALC (UNII: 7SEV7J4R1U)	

Product Characteristics			
Color	WHITE (white to off white)	**Score**	2 pieces

Shape	OVAL	**Size**	7mm
Flavor		**Imprint Code**	584
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:16714-168-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	05/05/2021	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA214803	05/05/2021	

Labeler - Northstar Rx LLC (830546433)

Registrant - Zydus Lifesciences Global FZE (850107010)

Establishment

Name	Address	ID/FEI	Business Operations
Zydus Lifesciences Limited		863362789	ANALYSIS(16714-166, 16714-167, 16714-168) , MANUFACTURE(16714-166, 16714-167, 16714-168)

Revised: 8/2024 Northstar Rx LLC