

LEVOXYL- levothyroxine sodium tablet
Pfizer Laboratories Div Pfizer Inc

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use LEVOXYL safely and effectively. See full prescribing information for LEVOXYL.

LEVOXYL® (levothyroxine sodium) tablets, for oral use

Initial U.S. Approval: 2001

WARNING: NOT FOR TREATMENT OF OBESITY OR FOR WEIGHT LOSS

See full prescribing information for complete boxed warning.

- **Thyroid hormones, including LEVOXYL, 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).**

INDICATIONS AND USAGE

LEVOXYL is L-thyroxine (T4) indicated in pediatric and adult patients for:

- Hypothyroidism: As replacement in primary (thyroidal), secondary (pituitary), and tertiary (hypothalamic) congenital or acquired hypothyroidism. (1)
- Pituitary Thyrotropin (Thyroid-Stimulating Hormone, TSH) suppression: As an adjunct to surgery and radioiodine therapy in the management of well-differentiated thyroid cancer. (1)

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 once daily, on an empty stomach, one-half to one hour before breakfast with a full glass of water. (2.1)
- Administer at least 4 hours before or after drugs that are known to interfere with absorption. (2.1)
- Evaluate the need for dose adjustments when regularly administering within one hour of certain foods that may affect absorption. (2.1)
- Starting dose depends on a variety of factors, including age, body weight, cardiovascular status, concomitant medical conditions (including pregnancy), concomitant medications, co-administered food, and the specific nature of the condition being treated. Peak therapeutic effect may not be attained for 4 to 6 weeks. (2.2)
- See full prescribing information for dosing in specific patient populations. (2.3)
- Adequacy of therapy determined with periodic monitoring of TSH and/or T4 as well as clinical status. (2.4)

DOSAGE FORMS AND STRENGTHS

Tablets: 25 mcg, 50 mcg, 75 mcg, 88 mcg, 100 mcg, 112 mcg, 125 mcg, 137 mcg, 150 mcg, 175 mcg, 200 mcg (3)

CONTRAINDICATIONS

Uncorrected adrenal insufficiency. (4)

WARNINGS AND PRECAUTIONS

- *Cardiac adverse reactions in the elderly and in patients with underlying cardiovascular disease:* Initiate LEVOXYL 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 LEVOXYL 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** -----

Common adverse reactions for LEVOXYL are primarily those of hyperthyroidism due to therapeutic overdose: arrhythmias, myocardial infarction, dyspnea, muscle spasm, headache, nervousness, irritability, insomnia, tremors, muscle weakness, increased appetite, weight loss, diarrhea, heat intolerance, menstrual irregularities, and skin rash. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer, Inc. at 1-800-438-1985 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----- **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 LEVOXYL. (7)

----- **USE IN SPECIFIC POPULATIONS** -----

Pregnancy may require the use of higher doses of levothyroxine. (2.3, 8.1)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 12/2018

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FULL PRESCRIBING INFORMATION

WARNING: NOT FOR TREATMENT OF OBESITY OR FOR WEIGHT LOSS

- **Thyroid hormones, including LEVOXYL, 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), Overdosage (10)].**

1 INDICATIONS AND USAGE

Hypothyroidism

LEVOXYL is indicated in pediatric and adult patients as a replacement therapy in primary (thyroidal), secondary (pituitary), and tertiary (hypothalamic) congenital or acquired hypothyroidism.

Pituitary Thyrotropin (Thyroid-Stimulating Hormone, TSH) Suppression

LEVOXYL is indicated in pediatric and adult patients as an adjunct to surgery and radioiodine therapy in the management of well-differentiated thyroid cancer.

Limitations of Use:

- LEVOXYL is 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 LEVOXYL may induce hyperthyroidism [see Warnings and Precautions (5.4)].
- LEVOXYL is not indicated for treatment of hypothyroidism during the recovery phase of subacute thyroiditis.

2 DOSAGE AND ADMINISTRATION

2.1 General Administration Information

Administer LEVOXYL tablets orally as a single daily dose, on an empty stomach, one-half to one hour before breakfast with a full glass of water to avoid choking or gagging [see Adverse Reactions (6)].

Administer LEVOXYL at least 4 hours before or after drugs that are known to interfere with

LEVOXYL absorption [see *Drug Interactions (7.1)*].

Evaluate the need for dose adjustments when regularly administering within one hour of certain foods that may affect LEVOXYL absorption [see *Drug Interactions (7.9)*, *Clinical Pharmacology (12.3)*].

Administer LEVOXYL to infants and children who cannot swallow intact tablets by crushing the tablet, suspending the freshly crushed tablet in a small amount (5 mL to 10 mL or 1 teaspoon to 2 teaspoons) of water and immediately administering the suspension by spoon or dropper. Do not store the suspension. Do not administer in foods that decrease absorption of LEVOXYL, such as soybean-based infant formula [see *Drug Interactions (7.9)*].

2.2 General Principles of Dosing

The dose of LEVOXYL for hypothyroidism or pituitary 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 (2.3)*, *Warnings and Precautions (5)*, *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)*].

The peak therapeutic effect of a given dose of LEVOXYL may not be attained for 4 to 6 weeks.

2.3 Dosing in Specific Populations

Primary Hypothyroidism in Adults and in Adolescents in Whom Growth and Puberty Are Complete

Start LEVOXYL at the full replacement dose in otherwise healthy, non-elderly individuals who have been hypothyroid for only a short time (such as a few months). The average full replacement dose of LEVOXYL is approximately 1.6 mcg per kg per day (for example: 100 mcg per day to 125 mcg per day for a 70 kg adult).

Adjust the dose by 12.5 mcg to 25 mcg increments every 4 to 6 weeks until the patient is clinically euthyroid and the serum TSH returns to normal. Doses greater than 200 mcg per day are seldom required. An inadequate response to daily doses of greater than 300 mcg per day is rare and may indicate poor compliance, malabsorption, drug interactions, or a combination of these factors.

For elderly patients or patients with underlying cardiac disease, start with a dose of 12.5 mcg to 25 mcg per day. Increase the dose every 6 to 8 weeks, as needed until the patient is clinically euthyroid and the serum TSH returns to normal. The full replacement dose of LEVOXYL may be less than 1 mcg per kg per day in elderly patients.

In patients with severe longstanding hypothyroidism, start with a dose of 12.5 mcg to 25 mcg per day. Adjust the dose in 12.5 mcg to 25 mcg increments every 2 to 4 weeks until the patient is clinically euthyroid and the serum TSH level is normalized.

Secondary or Tertiary Hypothyroidism

Start LEVOXYL at the full replacement dose in otherwise healthy, non-elderly individuals. Start with a lower dose in elderly patients, patients with underlying cardiovascular disease or patients with severe longstanding hypothyroidism as described above. Serum TSH is not a reliable measure of LEVOXYL dose adequacy in patients with secondary or tertiary hypothyroidism and should not be used to monitor therapy. Use the serum free-T4 level to monitor adequacy of therapy in this patient population. Titrate LEVOXYL dosing per above instructions until the patient is clinically euthyroid and the serum free-T4 level is restored to the upper half of the normal range.

Pediatric Dosage - Congenital or Acquired Hypothyroidism

The recommended daily dose of LEVOXYL in pediatric patients with hypothyroidism is based on body weight and changes with age as described in Table 1. Start LEVOXYL at the full daily dose in most

pediatric patients. Start at a lower starting dose in newborns (0 to 3 months) at risk for cardiac failure and in children at risk for hyperactivity (see below). Monitor for clinical and laboratory response [see *Dosage and Administration (2.4)*].

Table 1: LEVOXYL Dosing Guidelines for Pediatric Hypothyroidism

Age	Daily Dose Per Kg Body Weight*
0 to 3 months	10 mcg/kg daily to 15 mcg/kg daily
3 to 6 months	8 mcg/kg daily to 10 mcg/kg daily
6 to 12 months	6 mcg/kg daily to 8 mcg/kg daily
1 to 5 years	5 mcg/kg daily to 6 mcg/kg daily
6 to 12 years	4 mcg/kg daily to 5 mcg/kg daily
Greater than 12 years but growth and puberty incomplete	2 mcg/kg daily to 3 mcg/kg daily
Growth and puberty complete	1.6 mcg/kg daily

* - The dose should be adjusted based on clinical response and laboratory parameters [see *Warnings and Precautions (5.4)*, *Drug Interactions (7.10)*, *Use in Specific Populations (8.4)*].

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

Consider a lower starting dose in newborns at risk for cardiac failure. Increase the dose every 4 to 6 weeks 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: LEVOXYL 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 LEVOXYL by 12.5 mcg daily to 25 mcg daily and measure TSH every 4 weeks until a stable LEVOXYL dose is reached and serum TSH is within the normal trimester-specific range. Reduce LEVOXYL dosage to pre-pregnancy levels immediately after delivery and measure serum TSH levels 4 to 8 weeks postpartum to ensure LEVOXYL dose is appropriate.

New Onset Hypothyroidism: Normalize thyroid function as rapidly as possible. In patients with moderate to severe signs and symptoms of hypothyroidism, start LEVOXYL at the full replacement dose (1.6 mcg per kg body weight per day). In patients with mild hypothyroidism (TSH less than 10 mIU per liter) start LEVOXYL at 1 mcg per kg body weight per day. Evaluate serum TSH every 4 weeks and adjust LEVOXYL dosage until a serum TSH is within the normal trimester-specific range [see *Use in Specific Populations (8.1)*].

TSH Suppression in Well-Differentiated Thyroid Cancer

The dose of LEVOXYL should target TSH levels within the desired therapeutic range. This may require a LEVOXYL dose of greater than 2 mcg per kg per day, depending on the target level for TSH suppression.

2.4 Monitoring TSH and/or Thyroxine (T4) 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 LEVOXYL 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 levels after an interval of 6 to 8 weeks after any change in dose. 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 patients with congenital hypothyroidism, assess the adequacy of replacement therapy by measuring both serum TSH and total or free-T4. Monitor TSH and total or free-T4 in children as follows: 2 and 4 weeks after the initiation of treatment, 2 weeks after any change in dosage, and then every 3 to 12 months thereafter following dose stabilization until growth is 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 T4 to increase into the upper half of the normal range within 2 weeks of initiation of LEVOXYL therapy and/or of the serum TSH to decrease below 20 mIU per liter within 4 weeks 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 LEVOXYL [see *Warnings and Precautions (5.4)*, *Use in Specific Populations (8.4)*].

Secondary and Tertiary Hypothyroidism

Monitor serum free-T4 levels and maintain in the upper half of the normal range in these patients.

3 DOSAGE FORMS AND STRENGTHS

LEVOXYL tablets are oval, color-coded and, potency marked available as follows:

Strength (mcg)	Color	Tablet Markings
25	Orange	25
50	White	50
75	Purple	75
88	Olive	88
100	Yellow	100
112	Rose	112
125	Light Brown	125
137	Dark Blue	137
150	Blue	150
175	Turquoise	175
200	Pink	200

4 CONTRAINDICATIONS

Levothyroxine 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 levothyroxine 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 LEVOXYL 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), Use in Specific Populations (8.5)*].

Monitor for cardiac arrhythmias during surgical procedures in patients with coronary artery disease receiving suppressive LEVOXYL therapy. Monitor patients receiving concomitant LEVOXYL and sympathomimetic agents for signs and symptoms of coronary insufficiency. If cardiovascular symptoms develop or worsen, reduce or withhold the LEVOXYL 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 levothyroxine sodium 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 LEVOXYL [*see Contraindications (4)*].

5.4 Prevention of Hyperthyroidism or Incomplete Treatment of Hypothyroidism

LEVOXYL has a narrow therapeutic index. Over- or undertreatment with LEVOXYL 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 LEVOXYL 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 LEVOXYL and adjust the dose as necessary [*see Drug Interactions (7), Clinical Pharmacology (12.3)*].

5.5 Worsening of Diabetic Control

Addition of levothyroxine 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 LEVOXYL [*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 levothyroxine 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 LEVOXYL that achieves the desired clinical and biochemical response to mitigate against this risk.

6 ADVERSE REACTIONS

Common adverse reactions with LEVOXYL therapy are primarily those of hyperthyroidism due to therapeutic overdosage [see *Warnings and Precautions (5.4), 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

Seizures have been reported rarely with levothyroxine therapy.

Adverse Reactions in Pediatric Patients

Pseudotumor cerebri and slipped capital femoral epiphysis have been reported in pediatric patients receiving levothyroxine therapy. Overtreatment may result in craniosynostosis in infants and premature closure of the epiphysis 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. Hypersensitivity to levothyroxine itself is not known to occur.

Choking and Gagging on LEVOXYL Tablets

There have been reports of choking, gagging, tablet stuck in throat, and dysphagia with LEVOXYL tablets, predominately when LEVOXYL tablets were not taken with water [see *Dosage and Administration (2.1)*].

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 LEVOXYL (see Tables 2 – 5).

Table 2: Drugs That May Decrease T4 Absorption (Hypothyroidism)

Potential impact: Concurrent use may reduce the efficacy of LEVOXYL by binding and delaying or preventing absorption, potentially resulting in hypothyroidism.	
Drug or Drug Class	Effect
Calcium Carbonate Ferrous Sulfate	Calcium carbonate may form an insoluble chelate with levothyroxine, and ferrous sulfate likely forms a ferric-thyroxine complex. Administer LEVOXYL at least 4 hours apart from these agents.

Orlistat	Monitor patients treated concomitantly with orlistat and LEVOXYL for changes in thyroid function.
Bile Acid Sequestrants -Colesevelam -Cholestyramine -Colestipol Ion Exchange Resins -Kayexalate -Sevelamer	Bile acid sequestrants and ion exchange resins are known to decrease levothyroxine absorption. Administer LEVOXYL at least 4 hours prior to these drugs or monitor thyroid-stimulating hormone (TSH) levels.
Other drugs: Proton Pump Inhibitors Sucralfate Antacids - Aluminum & Magnesium Hydroxides - Simethicone	Gastric acidity is an essential requirement for adequate absorption of levothyroxine. Sucralfate, antacids and proton pump inhibitors may cause hypochlorhydria, affect intragastric pH, and reduce levothyroxine absorption. Monitor patients appropriately.

Table 3: Drugs That May Alter Thyroxine (T4) and 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.
Potential impact (below): Administration of these agents with LEVOXYL results in an initial transient increase in FT4. Continued administration results in a decrease in serum T4 and normal FT4 and TSH concentrations.	
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 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 Anti-inflammatory 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 levothyroxine, 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 4: Drugs That May Alter Hepatic Metabolism of T4 (Hypothyroidism)

Potential impact: Stimulation of hepatic microsomal drug-metabolizing enzyme activity may cause increased hepatic degradation of levothyroxine, resulting in increased LEVOXYL 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 levothyroxine.

Table 5: 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 slightly, TSH levels remain normal, and patients are clinically euthyroid. It should be noted that actions of particular beta-adrenergic antagonists may be impaired when the 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: 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 LEVOXYL 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 LEVOXYL is started, changed, or discontinued [see Warnings and Precautions (5.5)].

7.3 Oral Anticoagulants

LEVOXYL 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 LEVOXYL dose is increased. Closely monitor coagulation tests to permit appropriate and timely dosage adjustments.

7.4 Digitalis Glycosides

LEVOXYL 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 LEVOXYL 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. LEVOXYL may accelerate the onset of action of tricyclics. Administration of sertraline in patients stabilized on LEVOXYL may result in increased LEVOXYL requirements.

7.6 Ketamine

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

7.7 Sympathomimetics

Concurrent use of sympathomimetics and LEVOXYL 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-Food Interactions

Consumption of certain foods may affect LEVOXYL absorption thereby necessitating adjustments in dosing [see *Dosage and Administration (2.1)*]. Soybean flour (infant formula), cotton seed meal, walnuts, and dietary fiber may bind and decrease the absorption of LEVOXYL from the GI tract. Grapefruit juice may delay the absorption of levothyroxine and reduce its bioavailability.

7.10 Drug-Laboratory Test Interactions

Consider changes in TBG concentration when interpreting T4 and T3 values. Measure and evaluate unbound (free) hormone and/or determine the free T4 index (FT4I) 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 levothyroxine 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 thyroid-stimulating hormone (TSH) levels may increase during pregnancy, TSH should be monitored and LEVOXYL dosage adjusted during pregnancy (*see Clinical Considerations*). There are no animal studies conducted with levothyroxine during pregnancy. LEVOXYL 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 LEVOXYL requirements. Serum TSH level should be monitored and the LEVOXYL dosage adjusted during pregnancy. Since postpartum TSH levels are similar to preconception values, the LEVOXYL dosage should return to the pre-pregnancy dose immediately after delivery [*see Dosage and Administration (2.3)*].

Data

Human Data

Levothyroxine is approved for use as a replacement therapy for hypothyroidism. There is a long experience of levothyroxine use in pregnant women, including data from post-marketing studies that have not reported increased rates of fetal malformations, miscarriages or other adverse maternal or fetal outcomes associated with levothyroxine use in pregnant women.

8.2 Lactation

Risk Summary

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

8.4 Pediatric Use

The initial dose of LEVOXYL 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 children in whom a diagnosis of permanent hypothyroidism has not been established, discontinue LEVOXYL for a trial period, but only after the child is at least 3 years of age. Obtain serum T4 and TSH levels at the end of the trial period, and use laboratory test results and clinical assessments to guide diagnosis and treatment, if warranted.

Congenital Hypothyroidism [*see Dosage and Administration (2.3, 2.4)*]

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 LEVOXYL therapy immediately upon diagnosis. Levothyroxine is generally continued for life in these patients.

Closely monitor infants during the first 2 weeks of LEVOXYL 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.

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.

8.5 Geriatric Use

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

10 OVERDOSAGE

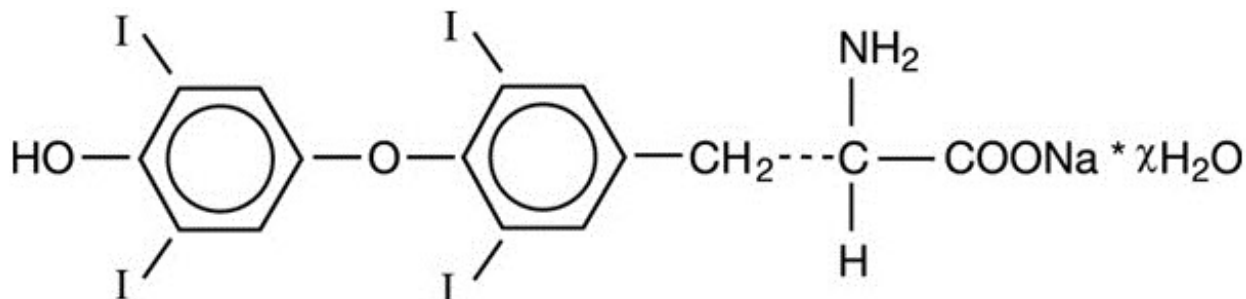
The signs and symptoms of overdosage are those of hyperthyroidism [see *Warnings and Precautions (5.4)*, *Adverse Reactions (6)*]. In addition, confusion and disorientation may occur. Cerebral embolism, shock, coma, and death have been reported. Seizures occurred in a 3-year-old child ingesting 3.6 mg of levothyroxine. Symptoms may not necessarily be evident or may not appear until several days after ingestion of levothyroxine sodium.

Reduce the LEVOXYL 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.poisson.org.

11 DESCRIPTION

LEVOXYL contains the active ingredient, levothyroxine, asynthetic crystalline levothyroxine (T₄) in sodium salt form. It is chemically designated as L-3,3',5,5'-tetraiodothyronine monosodium hydrate. Synthetic T₄ is identical in chemical structure to the T₄ produced in the human thyroid gland. Levothyroxine sodium has an empirical formula of C₁₅H₁₀I₄N NaO₄ · H₂O, molecular weight of 798.85 g/mol (anhydrous), and structural formula as shown:



LEVOXYL tablets for oral administration are supplied in the following strengths: 25 mcg, 50 mcg, 75 mcg, 88 mcg, 100 mcg, 112 mcg, 125 mcg, 137 mcg, 150 mcg, 175 mcg, and 200 mcg.

Inactive Ingredients

Calcium sulfate dihydrate, croscarmellose sodium, magnesium stearate, microcrystalline cellulose, and

sodium bicarbonate. The following are the coloring additives per tablet strength:

Strength (mcg)	Color additive(s)
25	FD&C Yellow No. 6 Aluminum Lake
50	None
75	FD&C Blue No. 1 Aluminum Lake, D&C Red No. 30 Aluminum Lake
88	FD&C Yellow No. 6 Aluminum Lake, FD&C Blue No. 1 Aluminum Lake, D&C Yellow No. 10 Aluminum Lake
100	FD&C Yellow No. 6 Aluminum Lake, D&C Yellow No. 10 Aluminum Lake
112	FD&C Yellow No. 6 Aluminum Lake, FD&C Red No. 40 Aluminum Lake, D&C Red No. 30 Aluminum Lake
125	FD&C Red No. 40 Aluminum Lake, D&C Yellow No. 10 Aluminum Lake
137	FD&C Blue No. 1 Aluminum Lake
150	FD&C Blue No. 1 Aluminum Lake, D&C Red No. 30 Aluminum Lake
175	FD&C Blue No. 1 Aluminum Lake, D&C Yellow No. 10 Aluminum Lake
200	D&C Red No. 30 Aluminum Lake, D&C Yellow No. 10 Aluminum Lake

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

Oral levothyroxine sodium is a synthetic T4 hormone that exerts the same physiologic effect as endogenous T4, thereby maintaining normal T4 levels when a deficiency is present.

12.3 Pharmacokinetics

Absorption

Absorption of orally administered T4 from the gastrointestinal tract ranges from 40% to 80%. The majority of the levothyroxine dose is absorbed from the jejunum and upper ileum. The relative bioavailability of LEVOXYL tablets, compared to an equal nominal dose of oral levothyroxine sodium solution, is approximately 95% to 98%. T4 absorption is increased by fasting, and decreased in malabsorption syndromes and by certain foods such as soybeans. Dietary fiber decreases bioavailability of T4. Absorption may also decrease with age. In addition, many drugs and foods affect T4 absorption [see *Drug Interactions (7)*].

Distribution

Circulating thyroid hormones are greater than 99% bound to plasma proteins, including thyroxine-binding globulin (TBG), thyroxine-binding prealbumin (TBPA), and thyroxine-binding 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. Many drugs and physiologic conditions affect the binding of thyroid hormones to serum proteins [see *Drug Interactions (7)*]. Thyroid hormones do not readily cross the placental barrier [see *Use in Specific Populations (8.1)*].

Elimination

Metabolism

T4 is slowly eliminated (Table 7). 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. Approximately 80% of the daily dose of T4 is deiodinated to yield equal amounts of T3 and reverse T3 (rT3). T3 and rT3 are 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. Approximately 20% of T4 is eliminated in the stool. Urinary excretion of T4 decreases with age.

Table 7: Pharmacokinetic Parameters of Thyroid Hormones in Euthyroid Patients

Hormone	Ratio in Thyroglobulin	Biologic Potency	t_{1/2} (days)	Protein Binding (%)[*]
Levothyroxine (T4)	10–20	1	6–7 [†]	99.96
Liothyronine (T3)	1	4	≤2	99.5

* Includes TBG, TBPA, and TBA

† 3 to 4 days in hyperthyroidism, 9 to 10 days in hypothyroidism

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 levothyroxine sodium.

16 HOW SUPPLIED/STORAGE AND HANDLING

LEVOXYL (levothyroxine sodium) tablets are oval, color-coded and, potency marked available as follows:

Strength (mcg)	Color	Tablet Markings	NDC - bottles of 100	NDC - bottles of 1000

25	Orange	25	60793-850-01	60793-850-10
50	White	50	60793-851-01	60793-851-10
75	Purple	75	60793-852-01	60793-852-10
88	Olive	88	60793-853-01	60793-853-10
100	Yellow	100	60793-854-01	60793-854-10
112	Rose	112	60793-855-01	60793-855-10
125	Light Brown	125	60793-856-01	60793-856-10
137	Dark Blue	137	60793-857-01	60793-857-10
150	Blue	150	60793-858-01	60793-858-10
175	Turquoise	175	60793-859-01	60793-859-10
200	Pink	200	60793-860-01	60793-860-10

STORAGE CONDITIONS

Store between 68°F–77°F (20°C–25°C) with excursions permitted between 59°F–86°F (15°C–30°C). Store LEVOXYL away from heat, moisture, and light.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Dosing and Administration

- Instruct patients to take LEVOXYL only as directed by their healthcare provider.
- Instruct patients to take LEVOXYL as a single dose, preferably on an empty stomach, one-half to one hour before breakfast with a full glass of water to avoid choking or gagging.
- Inform patients that agents such as iron and calcium supplements and antacids can decrease the absorption of levothyroxine. Instruct patients not to take LEVOXYL tablets within 4 hours of these agents.
- Instruct patients to notify their healthcare provider should they become pregnant or breastfeeding or are thinking of becoming pregnant, while taking LEVOXYL.

Important Information

- Inform patients that it may take several weeks before they notice an improvement in symptoms.
- Inform patients that the levothyroxine in LEVOXYL 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 LEVOXYL 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 you may have, 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 LEVOXYL. If they have diabetes, instruct patients to monitor their blood and/or urinary glucose levels as directed by their physician and immediately report any changes to their physician. If patients are taking anticoagulants, their clotting status should be checked frequently.
- Instruct patients to notify their physician or dentist if they are taking LEVOXYL 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.

- Inform patients that partial hair loss may occur rarely during the first few months of LEVOXYL therapy; this is usually temporary.

This product's label may have been updated. For the current prescribing information, please visit www.pfizer.com.



LAB-0709-2.0

Patient Information
LEVOXYL® (Lev-OX-il)
(levothyroxine sodium)
tablets, for oral use

What is the most important information I should know about LEVOXYL?

- **Do not use LEVOXYL to treat weight problems or weight loss.**
- **Do not take more LEVOXYL than your healthcare provider prescribes for you to take. Over dosage or taking too much LEVOXYL may cause life-threatening side effects or death.**

What is LEVOXYL?

LEVOXYL is a prescription medicine that contains a hormone called levothyroxine, which is similar to the hormone produced by your thyroid gland. LEVOXYL is used to treat children and adults:

- to replace or give extra levothyroxine in people whose thyroid does not produce enough of this hormone.
- who need surgery and radioiodine therapy to manage a type of thyroid cancer called well-differentiated thyroid cancer.

LEVOXYL should not be used to treat people who are recovering from swelling of the thyroid gland (thyroiditis) and whose bodies do not produce enough levothyroxine for a short time.

Do not use LEVOXYL if your adrenal glands are not working well and you have not been treated for this problem.

Before you take LEVOXYL, tell your healthcare provider about all of your medical conditions, including if you:

- have or had heart problems.
- have or had thyroid nodules.
- have adrenal or pituitary gland problems.
- have any food or drug allergies.
- have a low red blood cell count (anemia).
- have diabetes.
- have weak bones (osteoporosis).
- have or had a history of blood clotting problems.
- have recently received radiation therapy with iodine (such as I-131).
- are pregnant or plan to become pregnant. Your healthcare provider may need to increase your LEVOXYL while you are pregnant.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-

counter medicines, vitamins and herbal supplements. LEVOXYL may affect the way other medicines work, and other medicines may affect how LEVOXYL works. You can ask your healthcare provider or pharmacist for a list of medicines that interact with LEVOXYL.

Tell every healthcare provider including your dentist who treats you that you are taking LEVOXYL before any surgery.

How should I take LEVOXYL?

- Take LEVOXYL exactly as your healthcare provider tells you to take it.
- Your healthcare provider will tell you how much LEVOXYL to take each day.
- Take your dose of LEVOXYL on an empty stomach, at least **30 minutes to 1 hour** before breakfast with a full glass of water to avoid choking or gagging.
- Giving LEVOXYL to infants and children who cannot swallow tablets:
 - Crush the tablet.
 - Place the freshly crushed tablet in a small amount (5 mL to 10 mL or 1 teaspoon to 2 teaspoons) of water.
 - Immediately give the medicine by spoon or dropper.
 - **Do not** store the mixed medicine. **Do not** give in foods that decrease the absorption of LEVOXYL, such as soybean-based infant formula.
- Your healthcare provider may change your dose if needed.
- Certain medicines can interfere with how LEVOXYL is absorbed by your body. Take or give LEVOXYL:
 - **at least 4 hours before or after** medicines that contain calcium carbonate or iron (ferrous sulfate).
 - **at least 4 hours before** medicines that contain bile acid sequestrants or ion exchange resins.

Know the medicines that you take. Ask your healthcare provider or pharmacist for a list of these medicines, if you are not sure.

- Certain foods and drinks including soybean flour, cotton seed meal, walnuts, grapefruit juice and dietary fiber can affect your treatment and dose of LEVOXYL. Talk to your healthcare provider if you eat or drink these foods.
- Your healthcare provider should do certain blood tests while you are taking LEVOXYL and may change your daily dose of LEVOXYL as needed. You should not stop taking LEVOXYL or change your dose unless your healthcare provider tells you to.
- It may take weeks before you notice your symptoms getting better. Keep using this medicine even if you feel well.
- You may have to take medicine for the rest of your life to replace the thyroid hormone your body cannot produce.
- If you take too much LEVOXYL or overdose, call your healthcare provider or poison control center at 1-800-222-1222, or go to the nearest hospital emergency room right away.

What are the possible side effects of LEVOXYL?

LEVOXYL can cause serious side effects, including:

- **heart problems. You may experience an increased heart rate, chest pain and irregular heartbeat.** Your risk of developing heart problems may be greater if you are elderly, have heart problems, or if you take too much LEVOXYL. Your healthcare provider may reduce your dose or stop treatment with LEVOXYL for a while if you develop heart problems.
- **worsening diabetic control.** If you are a diabetic, it may be harder to control your blood sugar levels causing hyperglycemia while taking LEVOXYL. Check your blood sugar levels closely after starting, changing, or stopping treatment with LEVOXYL, and tell your healthcare provider if there are any changes. Your healthcare provider may have to change your diabetes treatment plan.
- **weak or brittle bones.** Your risk of developing weak or brittle bones may be greater if you are post-menopausal and are taking high doses of LEVOXYL for a long period.

The most common side effects of LEVOXYL include:

- irregular heartbeat
- chest pain
- shortness of breath
- leg cramps
- headache
- nervousness
- hives or skin rash
- irritability
- sleep problems (insomnia)
- tremors
- muscle weakness
- change in appetite
- weight loss
- vomiting
- diarrhea
- sweating a lot
- heat intolerance
- fever
- changes in menstrual period

Other side effects may include:

- partial hair loss during the first months of treatment with LEVOXYL. This usually lasts a short period of time.

These are not all the possible side effects of LEVOXYL. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How do I store LEVOXYL?

- Store LEVOXYL at room temperature between 68°F to 77°F (20°C to 25°C).
- Store LEVOXYL away from heat, light and moisture.
- **Keep LEVOXYL and all other medicines out of the reach of children.**

General information about the safe and effective use LEVOXYL.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use LEVOXYL for a condition for which it was not prescribed. Do not give your LEVOXYL to other people, even if they have the same symptoms that you have. It may harm them. You can ask your healthcare provider or pharmacist for information about LEVOXYL that was written for health professionals.

What are the ingredients in LEVOXYL?

Active ingredient: levothyroxine sodium

Inactive ingredients: microcrystalline cellulose, croscarmellose sodium, magnesium stearate, calcium sulfate dihydrate, sodium bicarbonate, coloring additives.

Gluten content: This product is gluten-free.

This product's label may have been updated. For current full prescribing information, please visit www.pfizer.com.



LAB-0710-1.0
December 2018

For more information, go to www.levoxy.com, or call 1-866-295-7600

This Patient Information has been approved by the U.S. Food and Drug Administration

Issued:Dec 2018

PRINCIPAL DISPLAY PANEL - 25 mcg Tablet Bottle Label

NDC 60793-850-01

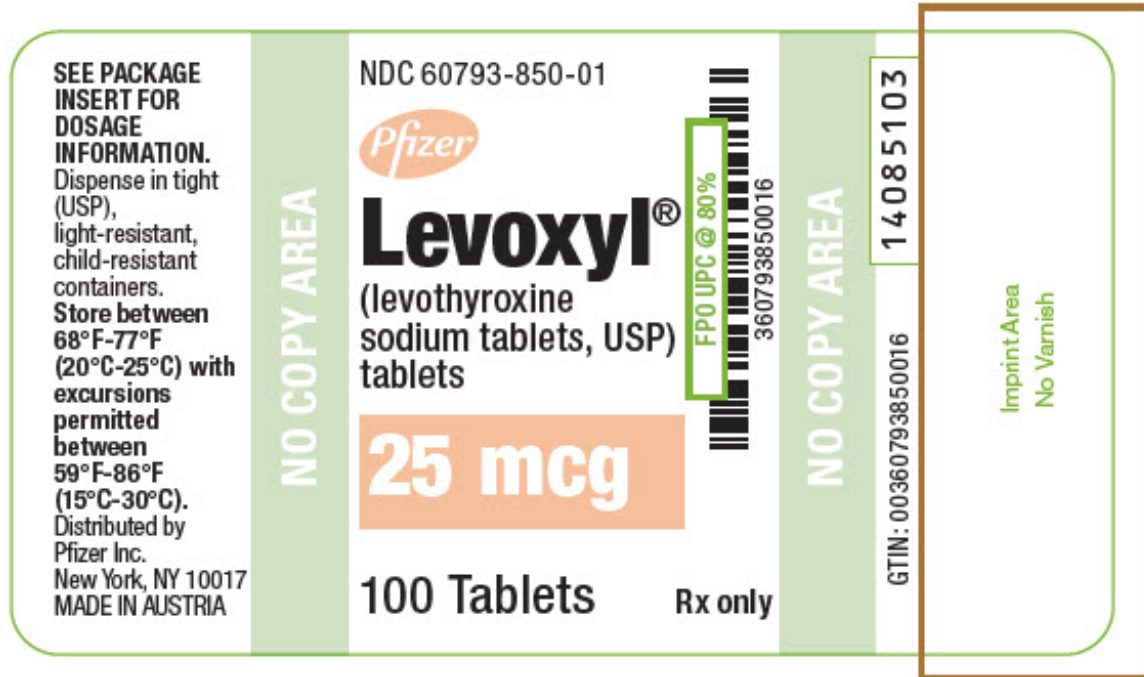
Pfizer

Levoxyl®
(levothyroxine
sodium tablets, USP)
tablets

25 mcg

100 Tablets

Rx only



PRINCIPAL DISPLAY PANEL - 50 mcg Tablet Bottle Label

NDC 60793-851-01

Pfizer

Levoxyl®
(levothyroxine
sodium tablets, USP)
tablets

50 mcg

100 Tablets

Rx only

SEE PACKAGE INSERT FOR DOSAGE INFORMATION.
 Dispense in tight (USP), light-resistant, child-resistant containers.
 Store between 68°F-77°F (20°C-25°C) with excursions permitted between 59°F-86°F (15°C-30°C).
 Distributed by Pfizer Inc.
 New York, NY 10017
 MADE IN AUSTRIA

NO COPY AREA

NDC 60793-851-01

Pfizer

Levoxyl®
 (levothyroxine sodium tablets, USP) tablets

50 mcg

100 Tablets Rx only

FPO UPC @ 80%
 360793851013

NO COPY AREA

GTIN: 00360793851013 **14084603**

Imprint Area
 No Varnish

PRINCIPAL DISPLAY PANEL - 75 mcg Tablet Bottle Label

NDC 60793-852-01

Pfizer

Levoxyl®
 (levothyroxine sodium tablets, USP) tablets

75 mcg

100 Tablets

Rx only

SEE PACKAGE INSERT FOR DOSAGE INFORMATION.
 Dispense in tight (USP), light-resistant, child-resistant containers.
 Store between 68°F-77°F (20°C-25°C) with excursions permitted between 59°F-86°F (15°C-30°C).
 Distributed by Pfizer Inc.
 New York, NY 10017
 MADE IN AUSTRIA

NO COPY AREA

NDC 60793-852-01

Pfizer

Levoxyl®
 (levothyroxine sodium tablets, USP) tablets

75 mcg

100 Tablets Rx only

FPO UPC @ 80%
 360793852010

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GTIN: 00360793852010 **14085003**

Imprint Area
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PRINCIPAL DISPLAY PANEL - 88 mcg Tablet Bottle Label

NDC 60793-853-01

Pfizer

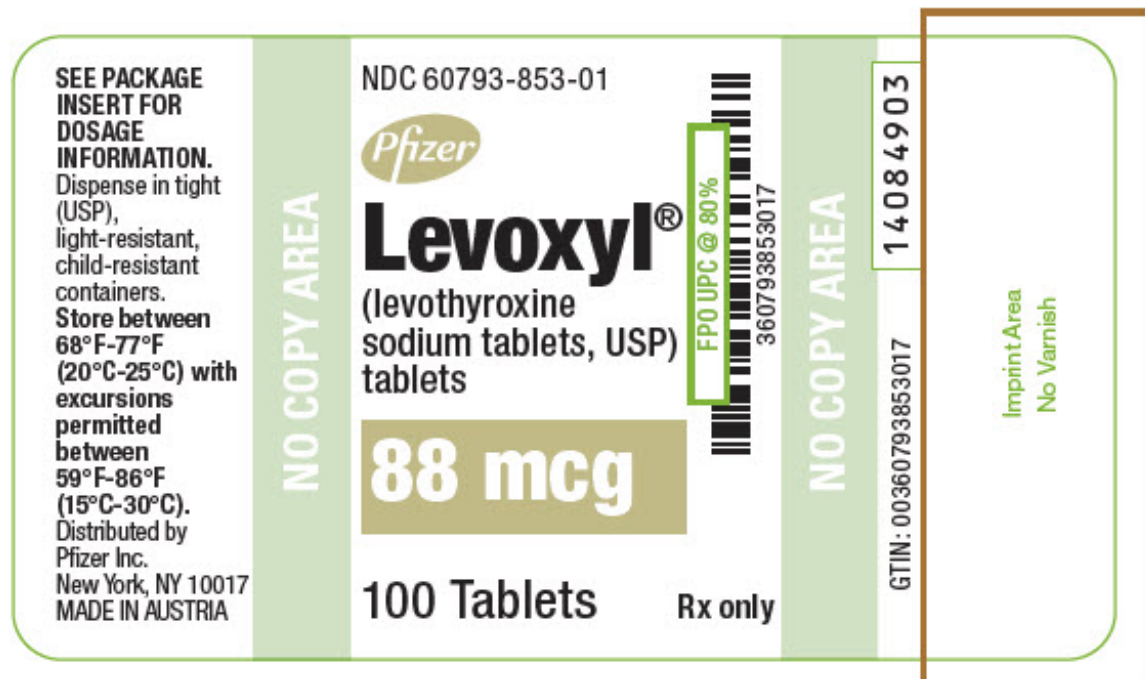
Levoxyl®

(levothyroxine
sodium tablets, USP)
tablets

88 mcg

100 Tablets

Rx only



PRINCIPAL DISPLAY PANEL - 100 mcg Tablet Bottle Label

NDC 60793-854-01

Pfizer

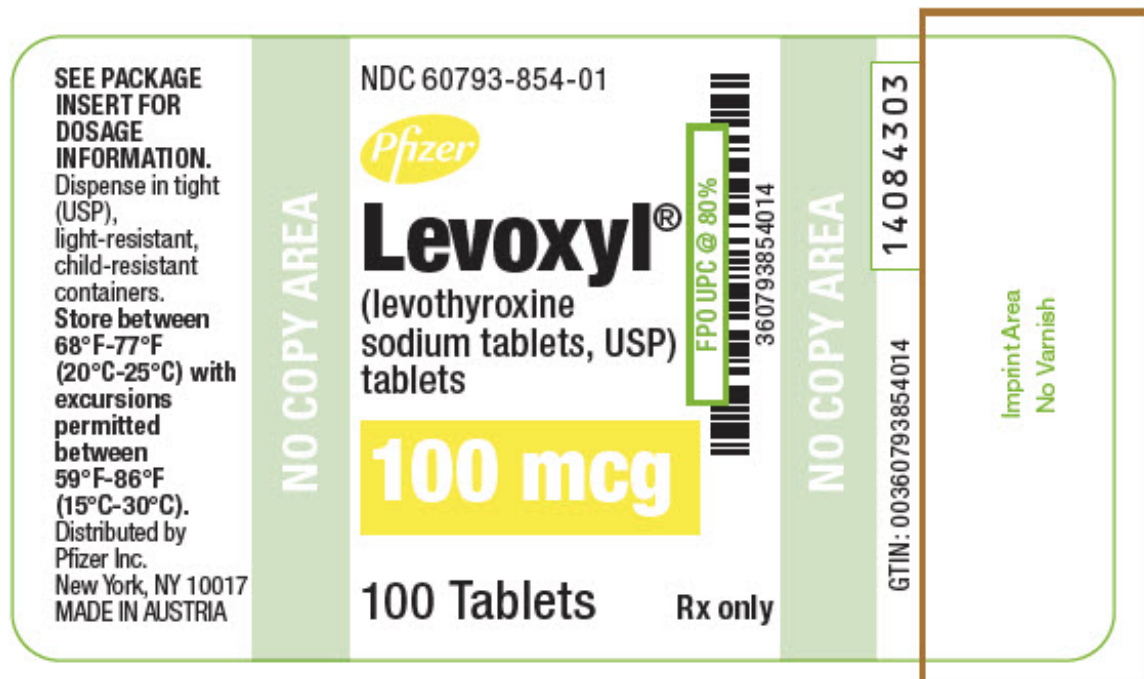
Levoxyl®

(levothyroxine
sodium tablets, USP)
tablets

100 mcg

100 Tablets

Rx only



PRINCIPAL DISPLAY PANEL - 112 mcg Tablet Bottle Label

NDC 60793-855-01

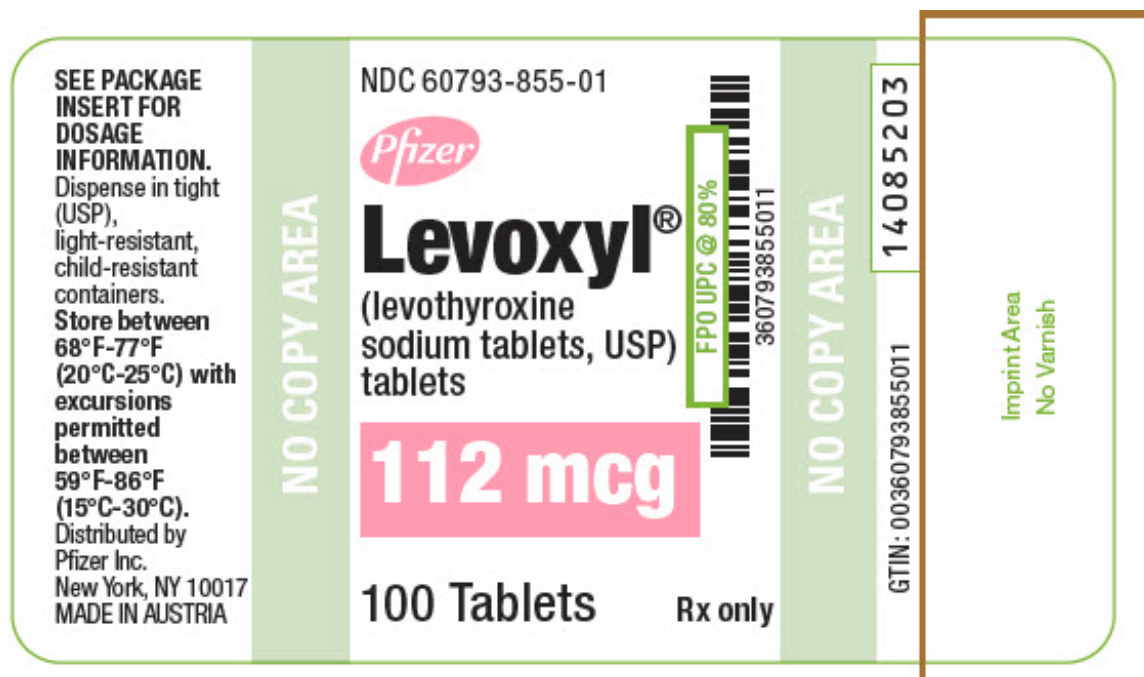
Pfizer

Levoxyl®
(levothyroxine sodium tablets, USP) tablets

112 mcg

100 Tablets

Rx only



PRINCIPAL DISPLAY PANEL - 125 mcg Tablet Bottle Label

NDC 60793-856-01

Pfizer

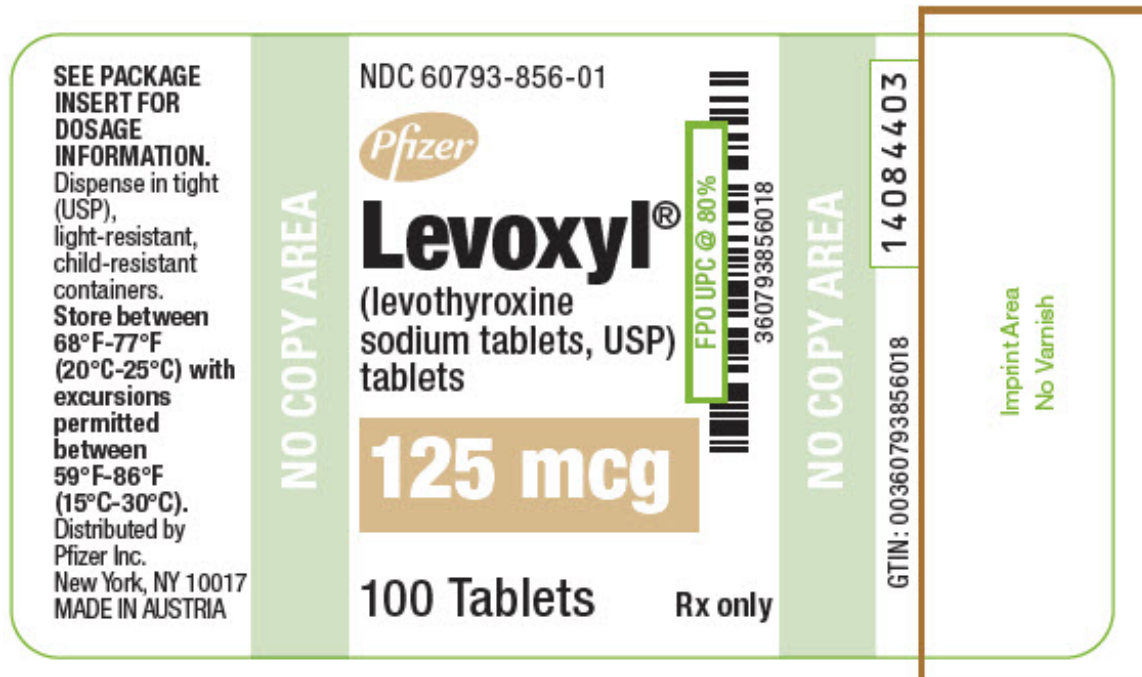
Levoxyl®

(levothyroxine
sodium tablets, USP)
tablets

125 mcg

100 Tablets

Rx only



PRINCIPAL DISPLAY PANEL - 137 mcg Tablet Bottle Label

NDC 60793-857-01

Pfizer

Levoxyl®

(levothyroxine
sodium tablets, USP)
tablets

137 mcg

100 Tablets

Rx only

SEE PACKAGE INSERT FOR DOSAGE INFORMATION.
 Dispense in tight (USP), light-resistant, child-resistant containers.
 Store between 68°F-77°F (20°C-25°C) with excursions permitted between 59°F-86°F (15°C-30°C).
 Distributed by Pfizer Inc. New York, NY 10017
 MADE IN AUSTRIA

NO COPY AREA

NDC 60793-857-01

Pfizer

Levoxyl®
 (levothyroxine sodium tablets, USP) tablets

137 mcg

100 Tablets Rx only

FPO UPC @ 80%
 360793857015

NO COPY AREA

GTIN: 00360793857015

14085303

Imprint Area
 No Varnish

PRINCIPAL DISPLAY PANEL - 150 mcg Tablet Bottle Label

NDC 60793-858-01

Pfizer

Levoxyl®
 (levothyroxine sodium tablets, USP) tablets

150 mcg

100 Tablets

Rx only

SEE PACKAGE INSERT FOR DOSAGE INFORMATION.
 Dispense in tight (USP), light-resistant, child-resistant containers.
 Store between 68°F-77°F (20°C-25°C) with excursions permitted between 59°F-86°F (15°C-30°C).
 Distributed by Pfizer Inc. New York, NY 10017
 MADE IN AUSTRIA

NO COPY AREA

NDC 60793-858-01

Pfizer

Levoxyl®
 (levothyroxine sodium tablets, USP) tablets

150 mcg

100 Tablets Rx only

FPO UPC @ 80%
 360793858012

NO COPY AREA

GTIN: 00360793858012

14084503

Imprint Area
 No Varnish

PRINCIPAL DISPLAY PANEL - 175 mcg Tablet Bottle Label

NDC 60793-859-01

Pfizer

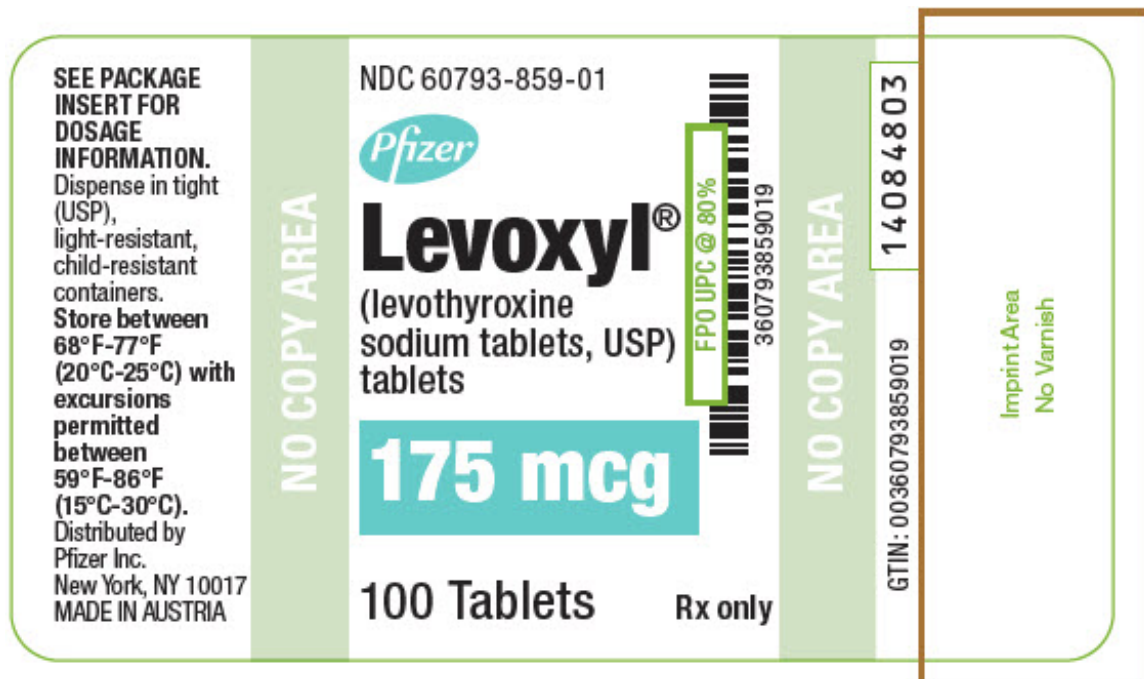
Levoxyl®

(levothyroxine
sodium tablets, USP)
tablets

175 mcg

100 Tablets

Rx only



PRINCIPAL DISPLAY PANEL - 200 mcg Tablet Bottle Label

NDC 60793-860-01

Pfizer

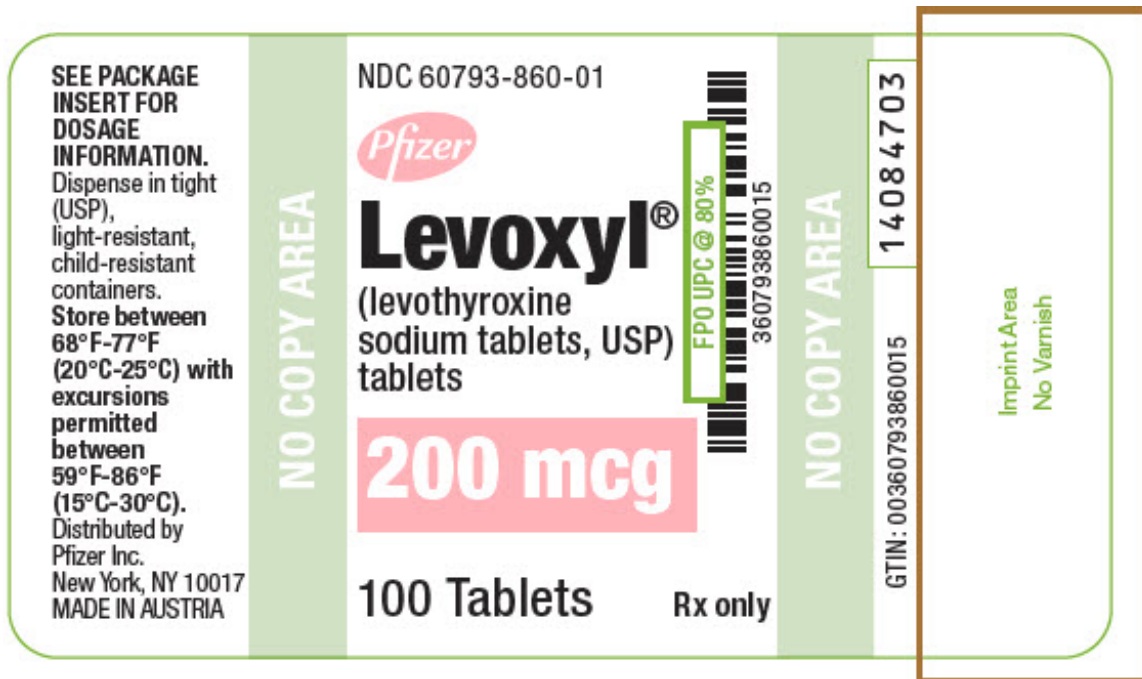
Levoxyl®

(levothyroxine
sodium tablets, USP)
tablets

200 mcg

100 Tablets

Rx only



LEVOXYL

levothyroxine sodium tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:60793-850
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LEVO THYRO XINE SODIUM (UNII: 9J765S329G) (LEVO THYRO XINE - UNII:Q51BO43MG4)	LEVO THYRO XINE SODIUM ANHYDROUS	25 ug

Inactive Ingredients

Ingredient Name	Strength
SODIUM BICARBONATE (UNII: 8MDF5V39QO)	
CALCIUM SULFATE DIHYDRATE (UNII: 4846Q921YM)	

Product Characteristics

Color	ORANGE	Score	2 pieces
Shape	OVAL	Size	10mm
Flavor		Imprint Code	Levoxyl;dp;25
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
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1	NDC:60793-850-10	1000 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	
2	NDC:60793-850-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	

Marketing Information			
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021301	05/25/2001	

LEVOXYL				
levothyroxine sodium tablet				
Product Information				
Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:60793-851	
Route of Administration	ORAL			
Active Ingredient/Active Moiety				
	Ingredient Name	Basis of Strength	Strength	
	LEVOTHYROXINE SODIUM (UNII: 9J765S329G) (LEVOTHYROXINE - UNII:Q51BO43MG4)	LEVOTHYROXINE SODIUM ANHYDROUS	50 ug	
Inactive Ingredients				
	Ingredient Name	Strength		
	CALCIUM SULFATE DIHYDRATE (UNII: 4846Q921YM)			
	SODIUM BICARBONATE (UNII: 8MDF5V39QO)			
Product Characteristics				
Color	WHITE	Score	2 pieces	
Shape	OVAL	Size	10mm	
Flavor		Imprint Code	Levoxyl;dp;50	
Contains				
Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:60793-851-10	1000 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	
2	NDC:60793-851-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	
Marketing Information				
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date	
NDA	NDA021301	05/25/2001		

LEVOXYL

levothyroxine sodium tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:60793-852
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LEVOTHYROXINE SODIUM (UNII: 9J765S329G) (LEVOTHYROXINE - UNII:Q51BO43MG4)	LEVOTHYROXINE SODIUM ANHYDROUS	75 ug

Inactive Ingredients

Ingredient Name	Strength
SODIUM BICARBONATE (UNII: 8MDF5V39QO)	
CALCIUM SULFATE DIHYDRATE (UNII: 4846Q921YM)	

Product Characteristics

Color	PURPLE	Score	2 pieces
Shape	OVAL	Size	10mm
Flavor		Imprint Code	Levo xyl;dp;75
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:60793-852-10	1000 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	
2	NDC:60793-852-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021301	05/25/2001	

LEVOXYL

levothyroxine sodium tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:60793-853
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LEVOTHYROXINE SODIUM (UNII: 9J765S329G) (LEVOTHYROXINE - UNII:Q51BO43MG4)	LEVOTHYROXINE SODIUM ANHYDROUS	88 ug

Inactive Ingredients

Ingredient Name	Strength
CALCIUM SULFATE DIHYDRATE (UNII: 4846Q921YM)	
SODIUM BICARBONATE (UNII: 8MDF5V39QO)	

Product Characteristics

Color	GREEN (Olive)	Score	2 pieces
Shape	OVAL	Size	10mm
Flavor		Imprint Code	Levoxyl;dp;88
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:60793-853-10	1000 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	
2	NDC:60793-853-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021301	05/25/2001	

LEVOXYL

levothyroxine sodium tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:60793-854
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LEVOTHYROXINE SODIUM (UNII: 9J765S329G) (LEVOTHYROXINE - UNII:Q51BO43MG4)	LEVOTHYROXINE SODIUM ANHYDROUS	100 ug

Inactive Ingredients

Ingredient Name		Strength		
SODIUM BICARBONATE (UNII: 8MDF5V39QO)				
CALCIUM SULFATE DIHYDRATE (UNII: 4846Q921YM)				
Product Characteristics				
Color	YELLOW	Score	2 pieces	
Shape	OVAL	Size	10mm	
Flavor		Imprint Code	Levo xyl;dp;100	
Contains				
Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:60793-854-10	1000 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	
2	NDC:60793-854-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	
Marketing Information				
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date	
NDA	NDA021301	05/25/2001		

LEVOXYL			
levothyroxine sodium tablet			
Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:60793-855
Route of Administration	ORAL		
Active Ingredient/Active Moiety			
Ingredient Name	Basis of Strength	Strength	
LEVO THYRO XINE SODIUM (UNII: 9J765S329G) (LEVO THYRO XINE - UNII:Q51BO43MG4)	LEVO THYRO XINE SODIUM ANHYDROUS	112 ug	
Inactive Ingredients			
Ingredient Name	Strength		
SODIUM BICARBONATE (UNII: 8MDF5V39QO)			
CALCIUM SULFATE DIHYDRATE (UNII: 4846Q921YM)			
Product Characteristics			
Color	PINK (ROSE)	Score	2 pieces
Shape	OVAL	Size	10mm
Flavor		Imprint Code	Levo xyl;dp;112

Contains**Packaging**

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:60793-855-10	1000 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	
2	NDC:60793-855-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021301	05/25/2001	

LEVOXYL

levothyroxine sodium tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:60793-856
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LEVO THYRO XINE SODIUM (UNII: 9J765S329G) (LEVO THYRO XINE - UNII:Q51BO43MG4)	LEVO THYRO XINE SODIUM ANHYDROUS	125 ug

Inactive Ingredients

Ingredient Name	Strength
SODIUM BICARBONATE (UNII: 8MDF5V39QO)	
CALCIUM SULFATE DIHYDRATE (UNII: 4846Q921YM)	

Product Characteristics

Color	BROWN	Score	2 pieces
Shape	OVAL	Size	10mm
Flavor		Imprint Code	Levoxyl;dp;125
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:60793-856-10	1000 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	
2	NDC:60793-856-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021301	05/25/2001	

LEVOXYL

levothyroxine sodium tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:60793-857
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LEVOTHYROXINE SODIUM (UNII: 9J765S329G) (LEVOTHYROXINE - UNII:Q51BO43MG4)	LEVOTHYROXINE SODIUM ANHYDROUS	137 ug

Inactive Ingredients

Ingredient Name	Strength
SODIUM BICARBONATE (UNII: 8MDF5V39QO)	
CALCIUM SULFATE DIHYDRATE (UNII: 4846Q921YM)	

Product Characteristics

Color	BLUE (DARK BLUE)	Score	2 pieces
Shape	OVAL	Size	10mm
Flavor		Imprint Code	Levoxyl;dp;137
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:60793-857-10	1000 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	
2	NDC:60793-857-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021301	05/25/2001	

LEVOXYL

levothyroxine sodium tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:60793-858
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LEVOTHYROXINE SODIUM (UNII: 9J765S329G) (LEVOTHYROXINE - UNII:Q51BO43MG4)	LEVOTHYROXINE SODIUM ANHYDROUS	150 ug

Inactive Ingredients

Ingredient Name	Strength
SODIUM BICARBONATE (UNII: 8MDF5V39QO)	
CALCIUM SULFATE DIHYDRATE (UNII: 4846Q921YM)	

Product Characteristics

Color	BLUE	Score	2 pieces
Shape	OVAL	Size	10mm
Flavor		Imprint Code	Levoxyl;dp;150
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:60793-858-10	1000 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	
2	NDC:60793-858-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021301	05/25/2001	

LEVOXYL

levothyroxine sodium tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:60793-859
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
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LEVOTHYROXINE SODIUM (UNII: 9J765S329G) (LEVOTHYROXINE - UNII:Q51BO43MG4)		LEVOTHYROXINE SODIUM ANHYDROUS	175 ug	
Inactive Ingredients				
Ingredient Name			Strength	
SODIUM BICARBONATE (UNII: 8MDF5V39QO)				
CALCIUM SULFATE DIHYDRATE (UNII: 4846Q921YM)				
Product Characteristics				
Color	TURQUOISE	Score	2 pieces	
Shape	OVAL	Size	10mm	
Flavor		Imprint Code	Levoxyl;dp;175	
Contains				
Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:60793-859-10	1000 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	
2	NDC:60793-859-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	
Marketing Information				
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date	
NDA	NDA021301	05/25/2001		

LEVOXYL			
levothyroxine sodium tablet			
Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:60793-860
Route of Administration	ORAL		
Active Ingredient/Active Moiety			
Ingredient Name		Basis of Strength	Strength
LEVOTHYROXINE SODIUM (UNII: 9J765S329G) (LEVOTHYROXINE - UNII:Q51BO43MG4)		LEVOTHYROXINE SODIUM ANHYDROUS	200 ug
Inactive Ingredients			
Ingredient Name			Strength
SODIUM BICARBONATE (UNII: 8MDF5V39QO)			
CALCIUM SULFATE DIHYDRATE (UNII: 4846Q921YM)			

Product Characteristics

Color	PINK	Score	2 pieces
Shape	OVAL	Size	10mm
Flavor		Imprint Code	Levoxyl;dp;200
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:60793-860-10	1000 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	
2	NDC:60793-860-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	05/25/2001	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021301	05/25/2001	

Labeler - Pfizer Laboratories Div Pfizer Inc (134489525)

Establishment

Name	Address	ID/FEI	Business Operations
UPM Pharmaceuticals		032125469	ANALYSIS(60793-850, 60793-851, 60793-852, 60793-853, 60793-854, 60793-855, 60793-856, 60793-857, 60793-858, 60793-859, 60793-860), LABEL(60793-850, 60793-851, 60793-852, 60793-853, 60793-854, 60793-855, 60793-856, 60793-857, 60793-858, 60793-859, 60793-860), MANUFACTURE(60793-850, 60793-851, 60793-852, 60793-853, 60793-854, 60793-855, 60793-856, 60793-857, 60793-858, 60793-859, 60793-860), PACK(60793-850, 60793-851, 60793-852, 60793-853, 60793-854, 60793-855, 60793-856, 60793-857, 60793-858, 60793-859, 60793-860)

Revised: 5/2019

Pfizer Laboratories Div Pfizer Inc