SYNTHROID- levothyroxine sodium tablet
AbbVie Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use SYNTHROID safely and effectively. See full prescribing information for SYNTHROID.
SYNTHROID® (levothyroxine sodium) tablets, for oral use
Initial U.S. Approval: 2002

WARNING: NOT FOR TREATMENT OF OBESITY OR FOR WEIGHT LOSS

See full prescribing information for complete boxed warning.

- **Thyroid hormones, including SYNTHROID, 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, 10).**

RECENT MAJOR CHANGES

Dosage and Administration, Important Considerations for Dosing (2.2)	2/2024
Dosage and Administration, Monitoring TSH and/or Thyroxine (T4) Levels (2.4)	2/2024

INDICATIONS AND USAGE

SYNTHROID is a L-thyroxine (T4) indicated in adult and pediatric patients, including neonates, for:

- Hypothyroidism: As replacement therapy 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 thyrotropin-dependent well-differentiated thyroid cancer. (1)

Limitations of Use:

- Not indicated for suppression of benign thyroid nodules and nontoxic diffuse goiter in iodine-sufficient patients
- Not indicated for treatment of hypothyroidism during the recovery phase of subacute thyroiditis

DOSAGE AND ADMINISTRATION

- Administer once daily, preferably on an empty stomach, one-half to one hour before breakfast. (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)
- Advise patients to stop biotin and biotin-containing supplements at least 2 days before assessing TSH and/or T4 levels. (2.2)
- Starting dose depends on a variety of factors, including age, body weight, cardiovascular status, and concomitant medications. Peak therapeutic effect may not be attained for 4-6 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, 50, 75, 88, 100, 112, 125, 137, 150, 175, 200, and 300 mcg (3)

CONTRAINDICATIONS

- Uncorrected adrenal insufficiency. (4)

WARNINGS AND PRECAUTIONS

- *Serious risks related to overtreatment or undertreatment with SYNTHROID:* Titrate the dose of SYNTHROID carefully and monitor response to titration. (5.1)
- *Cardiac adverse reactions in the elderly and in patients with underlying cardiovascular disease:* Initiate

SYNTHROID at less than the full replacement dose because of the increased risk of cardiac adverse reactions, including atrial fibrillation. (2.3, 5.2, 8.5)
- *Myxedema coma:* Do not use oral thyroid hormone drug products to treat myxedema coma. (5.3)
- *Acute adrenal crisis in patients with concomitant adrenal insufficiency:* Treat with replacement glucocorticoids prior to initiation of SYNTHROID treatment. (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

Adverse reactions associated with SYNTHROID therapy are primarily those of hyperthyroidism due to therapeutic overdosage: 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 AbbVie Inc. at 1-800-633-9110 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 SYNTHROID. (7)

USE IN SPECIFIC POPULATIONS

Pregnancy may require the use of higher doses of SYNTHROID. (2.3, 8.1)
See 17 for PATIENT COUNSELING INFORMATION.

Revised: 2/2024

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 SYNTHROID, 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

Hypothyroidism

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

Pituitary Thyrotropin (Thyroid-Stimulating Hormone, TSH) Suppression

SYNTHROID is indicated in adult and pediatric patients, including neonates, as an adjunct to surgery and radioiodine therapy in the management of thyrotropin-dependent well-differentiated thyroid cancer.

Limitations of Use

- SYNTHROID 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 SYNTHROID may induce hyperthyroidism *[see Warnings and Precautions (5.1)]*.
- SYNTHROID is not indicated for treatment of hypothyroidism during the recovery phase of subacute thyroiditis.

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Instructions

Administer SYNTHROID as a single daily dose, on an empty stomach, one-half to one hour before breakfast.

Administer SYNTHROID at least 4 hours before or after drugs known to interfere with SYNTHROID absorption *[see Drug Interactions (7.1)]*.

Evaluate the need for dosage adjustments when regularly administering within one hour of certain foods that may affect SYNTHROID absorption *[see Dosage and Administration (2.2 and 2.3), Drug Interactions (7.9), and Clinical Pharmacology (12.3)]*.

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

2.2 Important Considerations for Dosing

The dosage of SYNTHROID 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), and Drug Interactions (7)]*. Dosing must be individualized to account for these factors and dosage adjustments made based on periodic assessment of the patient's clinical response and laboratory parameters *[see Dosage and Administration (2.4)]*.

For adult patients with primary hypothyroidism, titrate until the patient is clinically euthyroid and the serum TSH returns to normal *[see Dosage and Administration (2.3)]*.

For secondary or tertiary hypothyroidism, serum TSH is not a reliable measure of SYNTHROID dosage adequacy and should not be used to monitor therapy. Use the serum free-T4 level to titrate SYNTHROID dosing until the patient is clinically euthyroid and the serum free-T4 level is restored to the upper half of the normal range *[see Dosage and Administration (2.3)]*.

Inquire whether patients are taking biotin or biotin-containing supplements. If so, advise them to stop biotin supplementation at least 2 days before assessing TSH and/or T4 levels *[see Dosage and Administration (2.4) and Drug Interactions (7.10)].*

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

2.3 Recommended Dosage and Titration

Primary, Secondary, and Tertiary Hypothyroidism in Adults

The recommended starting daily dosage of SYNTHROID in adults with primary, secondary, or tertiary hypothyroidism is based on age and comorbid cardiac conditions, as described in Table 1. For patients at risk of atrial fibrillation or patients with underlying cardiac disease, start with a lower dosage and titrate the dosage more slowly to avoid exacerbation of cardiac symptoms. Dosage titration is based on serum TSH or free-T4 *[see Dosage and Administration (2.2)]*.

Table 1. SYNTHROID Dosing Guidelines for Hypothyroidism in Adults*

Patient Population	Starting Dosage	Dosage Titration Based on Serum TSH or Free-T4
Adults diagnosed with hypothyroidism	Full replacement dose is 1.6 mcg/kg/day. Some patients require a lower starting dose.	Titrate dosage by 12.5 to 25 mcg increments every 4 to 6 weeks, as needed until the patient is euthyroid.
Adults at risk for atrial fibrillation or with underlying cardiac disease	Lower starting dose (less than 1.6 mcg/kg/day)	Titrate dosage every 6 to 8 weeks, as needed until the patient is euthyroid.
Geriatric patients	Lower starting dose (less than 1.6 mcg/kg/day)	

* Dosages greater than 200 mcg/day are seldom required. An inadequate response to daily dosages greater than 300 mcg/day is rare and may indicate poor compliance, malabsorption, drug interactions, or a combination of these factors *[see Dosage and Administration (2.1) and Drug Interactions (7)]*.

Primary, Secondary, and Tertiary Hypothyroidism in Pediatric Patients

The recommended starting daily dosage of SYNTHROID in pediatric patients with primary, secondary, or tertiary hypothyroidism is based on body weight and changes with age as described in Table 2. Titrate the dosage (every 2 weeks) as needed based on

serum TSH or free-T4 until the patient is euthyroid *[see Dosage and Administration (2.2)]*.

Table 2. SYNTHROID Dosing Guidelines for Hypothyroidism in Pediatric Patients

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

* Adjust dosage based on clinical response and laboratory parameters *[see Dosage and Administration (2.4) and Use in Specific Populations (8.4)]*.

Pediatric Patients from Birth to 3 Months of Age at Risk for Cardiac Failure

Start at a lower starting dosage and increase the dosage 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, start at one-fourth the recommended full replacement dosage, and increase on a weekly basis by one-fourth the full recommended replacement dosage until the full recommended replacement dosage is reached.

Hypothyroidism in Pregnant Patients

For pregnant patients with pre-existing hypothyroidism, measure serum TSH and free-T4 as soon as pregnancy is confirmed and, at minimum, during each trimester of pregnancy. In pregnant patients with primary hypothyroidism, maintain serum TSH in the trimester-specific reference range.

The recommended daily dosage of SYNTHROID in pregnant patients is described in Table 3.

Table 3. SYNTHROID Dosing Guidelines for Hypothyroidism in Pregnant Patients

Patient Population	Starting Dosage	Dose Adjustment and Titration
Pre-existing primary hypothyroidism with serum TSH above	Pre-pregnancy dosage may	Increase SYNTHROID dosage by 12.5 to 25 mcg per day. Monitor TSH every 4 weeks until a stable dose is reached and serum TSH is within normal trimester-specific

serum TSH above normal trimester-specific range	increase during pregnancy	range. Reduce SYNTHROID dosage to pre-pregnancy levels immediately after delivery. Monitor serum TSH 4 to 8 weeks postpartum.
New onset hypothyroidism (TSH ≥ 10 mIU per liter)	1.6 mcg/kg/day	Monitor serum TSH every 4 weeks and adjust SYNTHROID dosage until serum TSH is within normal trimester-specific range.
New onset hypothyroidism (TSH < 10 mIU per liter)	1.0 mcg/kg/day	

TSH Suppression in Well-differentiated Thyroid Cancer in Adult and Pediatric Patients

The SYNTHROID dosage is based on the target level of TSH suppression for the stage and clinical status of thyroid cancer.

2.4 Monitoring TSH and/or Thyroxine (T4) Levels

Assess the adequacy of therapy by periodic assessment of laboratory tests and clinical evaluation.

Biotin supplementation may interfere with immunoassays for TSH, T4, and T3, resulting in erroneous thyroid hormone test results. Stop biotin and biotin-containing supplements for at least 2 days before assessing TSH and/or T4 levels *[see Drug Interactions (7.10)].*

Persistent clinical and laboratory evidence of hypothyroidism despite an apparent adequate replacement dose of SYNTHROID 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 dosage. In patients on a stable and appropriate replacement dosage, evaluate clinical and biochemical response every 6 to 12 months and whenever there is a change in the patient's clinical status.

Pediatric Patients

In patients with 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 pediatric patients 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 dosage 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.

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 SYNTHROID therapy and/or of the serum TSH to decrease

below 20 mIU per liter within 4 weeks may indicate the patient is not receiving adequate therapy. Assess compliance, dose of medication administered, and method of administration prior to increasing the dose of SYNTHROID *[see Warnings and Precautions (5.1) and 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

SYNTHROID tablets are available as follows (Table 4):

Table 4: SYNTHROID Tablet Strengths and Identifying Features

Tablet Strength	Tablet Color/Shape	Tablet Markings
25 mcg	Orange/Round	“SYNTHROID” and “25”
50 mcg	White/Round	“SYNTHROID” and “50”
75 mcg	Violet/Round	“SYNTHROID” and “75”
88 mcg	Olive/Round	“SYNTHROID” and “88”
100 mcg	Yellow/Round	“SYNTHROID” and “100”
112 mcg	Rose/Round	“SYNTHROID” and “112”
125 mcg	Brown/Round	“SYNTHROID” and “125”
137 mcg	Turquoise/Round	“SYNTHROID” and “137”
150 mcg	Blue/Round	“SYNTHROID” and “150”
175 mcg	Lilac/Round	“SYNTHROID” and “175”
200 mcg	Pink/Round	“SYNTHROID” and “200”
300 mcg	Green/Round	“SYNTHROID” and “300”

4 CONTRAINDICATIONS

SYNTHROID is contraindicated in patients with uncorrected adrenal insufficiency *[see Warnings and Precautions (5.4)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Serious Risks Related to Overtreatment or Undertreatment with SYNTHROID

SYNTHROID has a narrow therapeutic index. Overtreatment or undertreatment with SYNTHROID may have negative effects on growth and development, cardiovascular function, bone metabolism, reproductive function, cognitive function, gastrointestinal function, and glucose and lipid metabolism in adult or pediatric patients.

In pediatric patients with congenital and acquired hypothyroidism, undertreatment may adversely affect cognitive development and linear growth, and overtreatment is associated with craniosynostosis and acceleration of bone age *[see Use in Specific Populations (8.4)]*.

Titrate the dose of SYNTHROID carefully and monitor response to titration to avoid these effects *[see Dosage and Administration (2.4)]*. Consider the potential for food or drug interactions and adjust the administration or dosage of SYNTHROID as needed *[see Dosage and Administration (2.1), Drug Interactions (7.1), and Clinical Pharmacology (12.3)]*.

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

Over-treatment 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 SYNTHROID 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 SYNTHROID therapy. Monitor patients receiving concomitant SYNTHROID and sympathomimetic agents for signs and symptoms of coronary insufficiency.

If cardiac symptoms develop or worsen, reduce the SYNTHROID dose or withhold for one week and restart at a lower dose.

5.3 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.

5.4 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 SYNTHROID *[see Contraindications (4)]*.

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 SYNTHROID *[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 SYNTHROID that achieves the desired clinical and biochemical response to mitigate this risk.

6 ADVERSE REACTIONS

Adverse reactions associated with SYNTHROID therapy are primarily those of hyperthyroidism due to therapeutic overdosage *[see Warnings and Precautions (5) 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, muscle spasm
- *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, rash
- *Endocrine:* decreased bone mineral density
- *Reproductive:* menstrual irregularities, impaired fertility

Seizures have been reported rarely with the institution of 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 who have not undergone complete closure of the fontanelles, and in premature closure of the epiphyses in pediatric patients still experiencing growth 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.

7 DRUG INTERACTIONS

7.1 Drugs Known to Affect Thyroid Hormone Pharmacokinetics

Many drugs can exert effects on thyroid hormone pharmacokinetics and metabolism (e.g., absorption, synthesis, secretion, catabolism, protein binding, and target tissue response) and may alter the therapeutic response to SYNTHROID (Tables 5 to 8).

Table 5. Drugs That May Decrease T4 Absorption (Hypothyroidism)

Potential impact: Concurrent use may reduce the efficacy of SYNTHROID by binding and delaying or preventing absorption, potentially resulting in hypothyroidism.	
Drug or Drug Class	**Effect**
Phosphate Binders (e.g., calcium carbonate, ferrous sulfate, sevelamer, lanthanum)	Phosphate binders may bind to levothyroxine. Administer SYNTHROID at least 4 hours apart from these agents.
Orlistat	Monitor patients treated concomitantly with orlistat and SYNTHROID for changes in thyroid function.
Bile Acid Sequestrants (e.g., colesevelam, cholestyramine, colestipol) Ion Exchange Resins (e.g., Kayexalate)	Bile acid sequestrants and ion exchange resins are known to decrease levothyroxine absorption. Administer SYNTHROID at least 4 hours prior to these drugs or monitor TSH levels.
Proton Pump Inhibitors Sucralfate Antacids (e.g., 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 6. Drugs That May Alter 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 SYNTHROID 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 increase 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 free T4 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 7. 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 SYNTHROID 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 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 8. 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 $\geq$ 4	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

mg/day)	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 SYNTHROID 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 thyroid therapy is started, changed, or discontinued *[see Warnings and Precautions (5.5)]*.

7.3 Oral Anticoagulants

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

7.4 Digitalis Glycosides

SYNTHROID may reduce the therapeutic effects of digitalis glycosides. Serum digitalis glycoside levels may decrease 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 SYNTHROID 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. SYNTHROID may accelerate the onset of action of tricyclics. Administration of sertraline in patients stabilized on SYNTHROID may result in increased SYNTHROID requirements.

7.6 Ketamine

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

7.7 Sympathomimetics

Concurrent use of sympathomimetics and SYNTHROID 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 SYNTHROID absorption thereby necessitating adjustments in dosing *[see Dosage and Administration (2.1)]*. Soybean flour, cottonseed meal, walnuts, and dietary fiber may bind and decrease the absorption of SYNTHROID from the gastrointestinal tract. Grapefruit juice may delay the absorption of levothyroxine and reduce its bioavailability.

7.10 Drug-Laboratory Test Interactions

Thyroxine-binding Globulin (TBG)

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 concentration. 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.

Biotin

Biotin supplementation is known to interfere with thyroid hormone immunoassays that are based on a biotin and streptavidin interaction, which may result in erroneous thyroid hormone test results. Stop biotin and biotin-containing supplements for at least 2 days prior to thyroid testing.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

The clinical experience, including data from postmarketing studies, in pregnant women treated with oral levothyroxine to maintain euthyroid state have not reported increased rates of major birth defects, miscarriages, or other adverse maternal or fetal outcomes. 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 SYNTHROID dosage adjusted during pregnancy *(see Clinical Considerations)*. Animal reproductive studies have not been conducted with levothyroxine sodium. SYNTHROID 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. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. 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 SYNTHROID requirements. Serum TSH levels should be monitored and the SYNTHROID dosage adjusted during pregnancy. Since postpartum TSH levels are similar to preconception values, the SYNTHROID dosage should return to the pre-pregnancy dose immediately after delivery *[see Dosage and Administration (2.3)].*

8.2 Lactation

Risk Summary

Published studies report that levothyroxine is present in human milk following the administration of oral levothyroxine. No adverse effects on the breastfed infant have been reported and there is no information on the effects of levothyroxine on milk production. Adequate levothyroxine treatment during lactation may normalize milk production in hypothyroid lactating mothers with low milk supply. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for SYNTHROID and any potential adverse effects on the breastfed infant from SYNTHROID or from the underlying maternal condition.

8.4 Pediatric Use

SYNTHROID is indicated in patients from birth to less than 17 years of age:

- As a replacement therapy in primary (thyroidal), secondary (pituitary), and tertiary (hypothalamic) congenital or acquired hypothyroidism.
- As an adjunct to surgery and radioiodine therapy in the management of thyrotropin-dependent well-differentiated thyroid cancer.

Rapid restoration of normal serum T4 concentrations is essential for preventing the adverse effects of congenital hypothyroidism on cognitive development as well as on overall physical growth and maturation. Therefore, initiate SYNTHROID therapy immediately upon diagnosis. Levothyroxine is generally continued for life in these patients *[see Warnings and Precautions (5.1)]*.

Closely monitor infants during the first 2 weeks of SYNTHROID therapy for cardiac overload and arrhythmias.

8.5 Geriatric Use

Because of the increased prevalence of cardiovascular disease among the elderly, initiate SYNTHROID at less than the full replacement dose *[see Dosage and Administration (2.3) and Warnings and Precautions (5.2)]*. 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

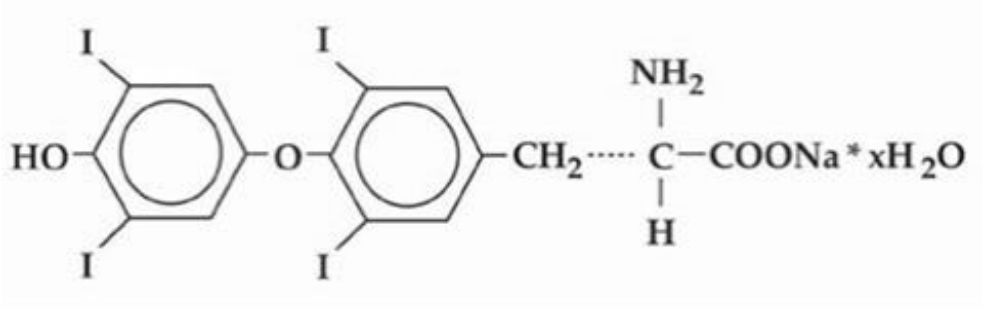
The signs and symptoms of overdosage are those of hyperthyroidism *[see Warnings and Precautions (5) and Adverse Reactions (6)]*. In addition, confusion and disorientation may occur. Cerebral embolism, shock, coma, and death have been reported. Seizures occurred in a 3-year-old child ingesting 3.6 mg of levothyroxine. Symptoms may not necessarily be evident or may not appear until several days after ingestion of levothyroxine sodium.

Reduce the SYNTHROID dosage or discontinue temporarily 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

SYNTHROID (levothyroxine sodium tablets, USP) is L-thyroxine (T4) and contains synthetic crystalline L-3,3',5,5'-tetraiodothyronine sodium salt. Synthetic T4 is chemically identical to that produced in the human thyroid gland. Levothyroxine (T4) sodium has an empirical formula of $C_{15}H_{10}I_4N\ NaO_4 \bullet\ H_2O$, molecular weight of 798.86 (anhydrous), and structural formula as shown:



SYNTHROID 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, 200 mcg, and 300 mcg. Each SYNTHROID tablet contains the inactive ingredients acacia, confectioner's sugar (contains corn starch), lactose monohydrate, magnesium stearate, povidone, and talc. SYNTHROID tablets contain no ingredients made from a gluten-containing grain (wheat, barley, or rye). Each tablet strength meets USP Dissolution Test 3. Table 9 provides a listing of the color additives by tablet strength:

Table 9: SYNTHROID Tablet Color Additives

Strength (mcg)	Color additive(s)
25	FD&C Yellow No. 6 Aluminum Lake*
50	None
75	FD&C Red No. 40 Aluminum Lake, FD&C Blue No. 2 Aluminum Lake
88	FD&C Blue No. 1 Aluminum Lake, FD&C Yellow No. 6 Aluminum Lake*, D&C Yellow No. 10 Aluminum Lake

100	D&C Yellow No. 10 Aluminum Lake, FD&C Yellow No. 6 Aluminum Lake*
112	D&C Red No. 27 & 30 Aluminum Lake
125	FD&C Yellow No. 6 Aluminum Lake*, FD&C Red No. 40 Aluminum Lake, FD&C Blue No. 1 Aluminum Lake
137	FD&C Blue No. 1 Aluminum Lake
150	FD&C Blue No. 2 Aluminum Lake
175	FD&C Blue No. 1 Aluminum Lake, D&C Red No. 27 & 30 Aluminum Lake
200	FD&C Red No. 40 Aluminum Lake
300	D&C Yellow No. 10 Aluminum Lake, FD&C Yellow No. 6 Aluminum Lake*, FD&C Blue No. 1 Aluminum Lake

* Note – FD&C Yellow No. 6 is orange in color.

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 SYNTHROID dose is absorbed from the jejunum and upper ileum. The relative bioavailability of SYNTHROID tablets, compared to an equal nominal dose of oral levothyroxine sodium solution, is approximately 93%. 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 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 (see Table 10). 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 10. 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

Long-term carcinogenicity studies in animals to evaluate the carcinogenic potential of levothyroxine have not been performed. Studies to evaluate mutagenic potential and animal fertility have not been performed.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

SYNTHROID (levothyroxine sodium, USP) tablets are supplied as follows (Table 11):

Table 11: SYNTHROID Tablet Presentations

Strength (mcg)	Color/Shape	Tablet Markings	NDC# for bottles of 90	NDC # for bottles of 1000	NDC # for unit dose cartons of 100
25	Orange/Round	“SYNTHROID” and “25”	0074-4341-90	0074-4341-19	--
50	White/Round	“SYNTHROID” and “50”	0074-4552-90	0074-4552-19	0074-4552-11
75	Violet/Round	“SYNTHROID” and “75”	0074-5182-90	0074-5182-19	0074-5182-11
88	Olive/Round	“SYNTHROID” and “88”	0074-6594-90	0074-6594-19	--
100	Yellow/Round	“SYNTHROID” and “100”	0074-6624-90	0074-6624-19	0074-6624-11
112	Rose/Round	“SYNTHROID” and “112”	0074-9296-90	0074-9296-19	--
125	Brown/Round	“SYNTHROID” and “125”	0074-7068-90	0074-7068-19	0074-7068-11
137	Turquoise/Round	“SYNTHROID” and “137”	0074-3727-90	0074-3727-19	--
150	Blue/Round	“SYNTHROID” and “150”	0074-7069-90	0074-7069-19	0074-7069-11
175	Lilac/Round	“SYNTHROID” and “175”	0074-7070-90	0074-7070-19	--
200	Pink/Round	“SYNTHROID” and “200”	0074-7148-90	0074-7148-19	0074-7148-11
300	Green/Round	“SYNTHROID” and “300”	0074-7149-90	0074-7149-19	--

Storage and Handling

Store SYNTHROID at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) (see USP Controlled Room Temperature).

SYNTHROID tablets should be protected from light and moisture.

17 PATIENT COUNSELING INFORMATION

Inform the patient of the following information to aid in the safe and effective use of SYNTHROID:

Dosing and Administration

- Instruct patients to take SYNTHROID only as directed by their healthcare provider.
- Instruct patients to take SYNTHROID as a single dose, preferably on an empty stomach, one-half to one hour before breakfast.
- Inform patients that agents such as iron and calcium supplements and antacids can decrease the absorption of levothyroxine. Instruct patients not to take SYNTHROID tablets within 4 hours of these agents.
- Instruct patients to notify their healthcare provider if they are pregnant or

breastfeeding or are thinking of becoming pregnant while taking SYNTHROID.

Important Information

- Inform patients that it may take several weeks before they notice an improvement in symptoms.
- Inform patients that the levothyroxine in SYNTHROID 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 SYNTHROID 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 discontinue biotin or any biotin-containing supplements for at least 2 days before thyroid function testing is conducted.
- Instruct patients to notify their physician of any other medical conditions they 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 they are taking SYNTHROID. 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 that they are taking SYNTHROID 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 SYNTHROID therapy, but this is usually temporary.

AbbVie Inc.

North Chicago, IL 60064 U.S.A.

20083657

NDC 0074-4552-11

Synthroid®

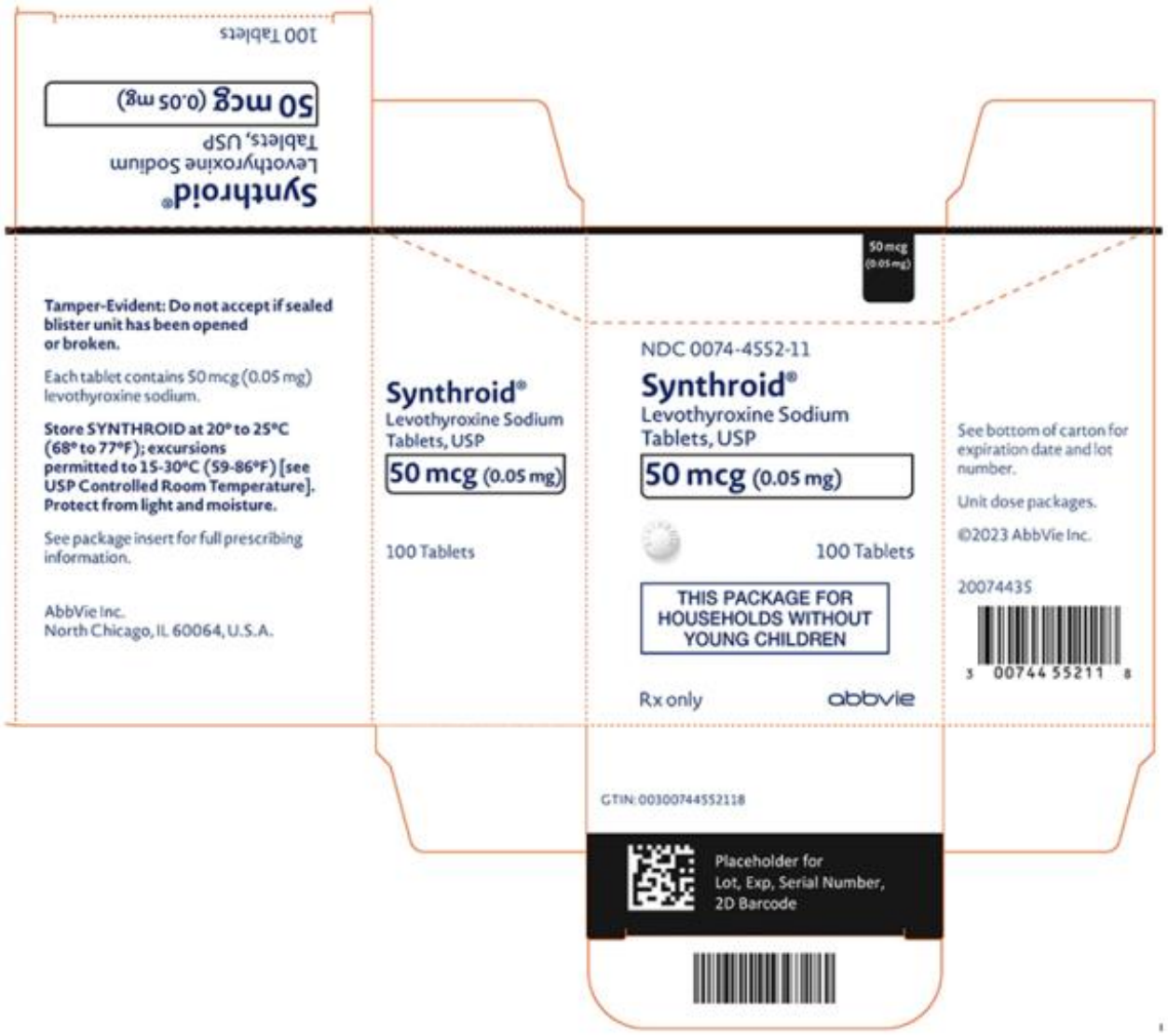
Levothyroxine Sodium
Tablets, USP

50 mcg (0.05 mg)

100 Tablets

THIS PACKAGE FOR HOUSEHOLDS WITHOUT YOUNG CHILDREN

Rx only **abbvie**



NDC 0074-6624-11

Synthroid®

Levothyroxine Sodium
Tablets, USP

100 mcg (0.1 mg)

100 Tablets

THIS PACKAGE FOR HOUSEHOLDS WITHOUT YOUNG CHILDREN

Rx only **abbvie**

NDC 0074-7148-11

Synthroid®

Levothyroxine Sodium
Tablets, USP

200 mcg (0.2 mg)

100 Tablets

THIS PACKAGE FOR HOUSEHOLDS WITHOUT YOUNG CHILDREN

Rx only **abbvie**

NDC 0074-3727-90

Synthroid®

Levothyroxine Sodium Tablets, USP

137 mcg (0.137 mg)

90 Tablets

Rx only **abbvie**

NDC 0074-4341-19

Synthroid®

Levothyroxine
Sodium Tablets,
USP

25 mcg
(0.025 mg)

1000 Tablets

Rx only **abbvie**

NDC 0074-5182-19

Synthroid®

Levothyroxine

Sodium Tablets,
USP

75 mcg
(0.075 mg)

1000 Tablets

Rx only **abbvie**

NDC 0074-6594-90

Synthroid®

Levothyroxine
Sodium Tablets,
USP

88 mcg
(0.088 mg)

90 Tablets

Rx only **abbvie**

NDC 0074-7068-19

Synthroid®

Levothyroxine
Sodium Tablets,
USP

125 mcg
(0.125 mg)

1000 Tablets

Rx only **abbvie**

NDC 0074-7069-90

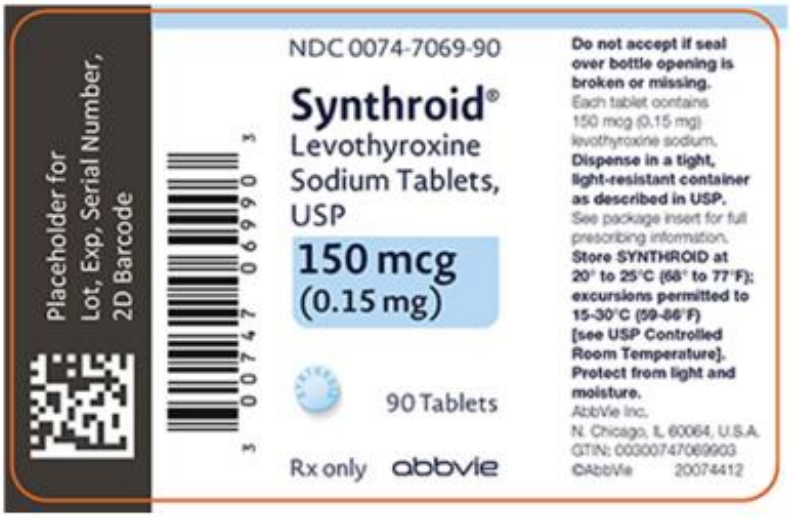
Synthroid®

Levothyroxine
Sodium Tablets,
USP

150 mcg
(0.15 mg)

90 Tablets

Rx only **abbvie**



NDC 0074-7070-19

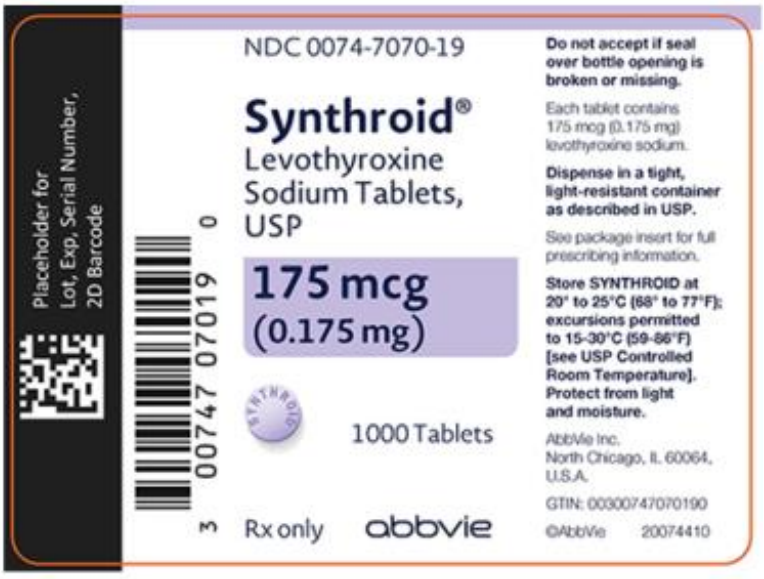
Synthroid®

Levothyroxine
Sodium Tablets,
USP

175 mcg
(0.175 mg)

1000 Tablets

Rx only **abbvie**



NDC 0074-7149-90

Synthroid®

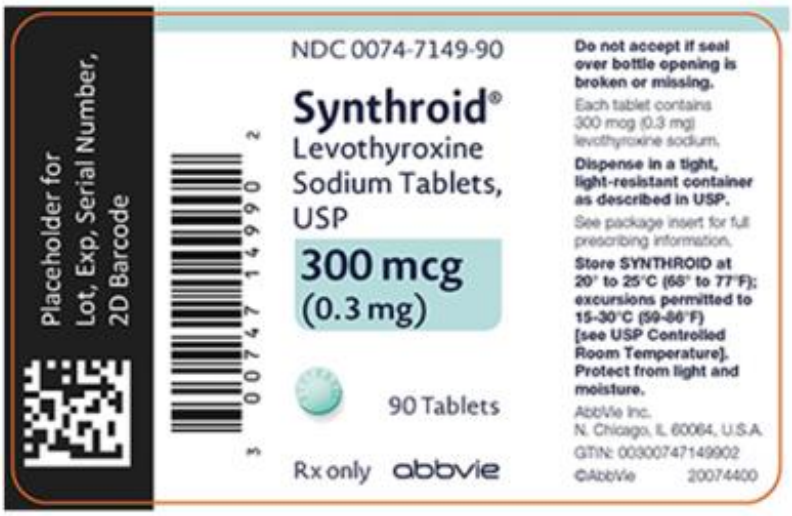
Levothyroxine
Sodium Tablets,

USP

300 mcg
(0.3 mg)

90 Tablets

Rx only **abbvie**



NDC 0074-9296-19

Synthroid®

Levothyroxine
Sodium Tablets,
USP

112 mcg
(0.112 mg)

1000 Tablets

Rx only **abbvie**

NDC 0074-4552-90

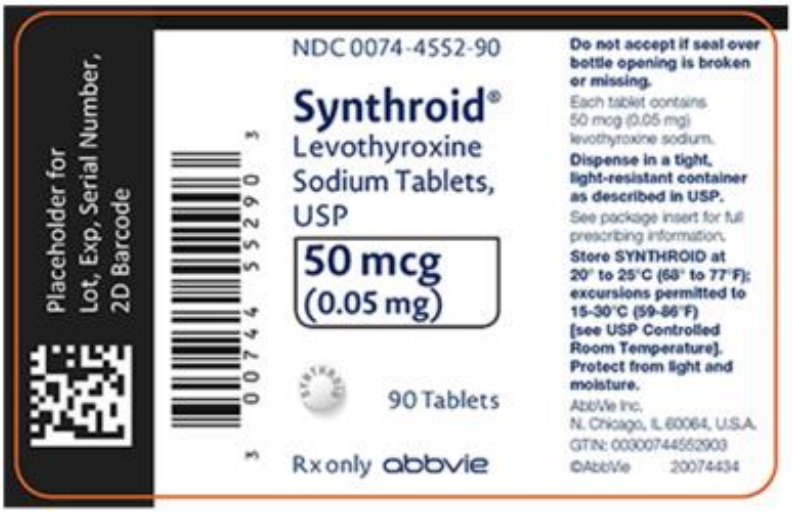
Synthroid®

Levothyroxine
Sodium Tablets,
USP

50 mcg
(0.05 mg)

90 Tablets

Rx only **abbvie**



NDC 0074-7148-90

Synthroid®

Levothyroxine
Sodium Tablets,
USP

200 mcg
(0.2 mg)

90 Tablets

Rx only **abbvie**

NDC 0074-6624-90

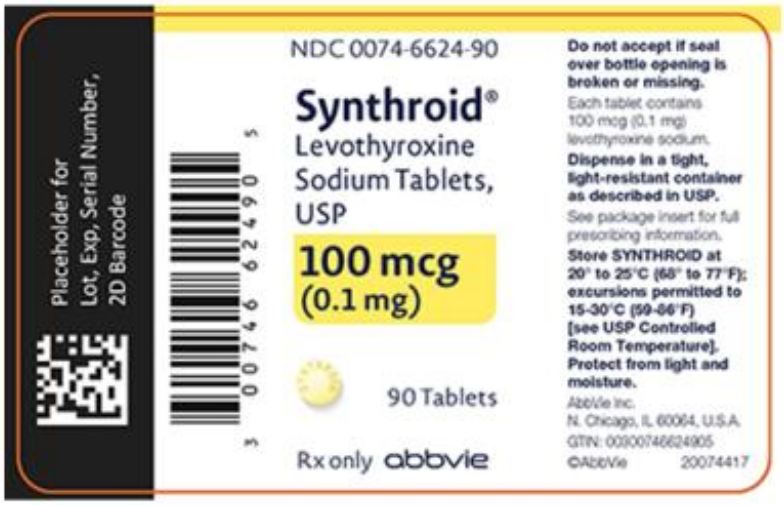
Synthroid®

Levothyroxine
Sodium Tablets,
USP

100 mcg
(0.1 mg)

90 Tablets

Rx only **abbvie**



SYNTHROID

levothyroxine sodium tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0074-4341
Route of Administration	ORAL		

Active Ingredient/Active Moiety

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

Inactive Ingredients

Ingredient Name	Strength
ACACIA (UNII: 5C5403N26O)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	
TALC (UNII: 7SEV7J4R1U)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	
SUCROSE (UNII: C151H8M554)	

Product Characteristics

Color	orange	**Score**	2 pieces
Shape	ROUND	**Size**	7mm
Flavor		**Imprint Code**	SYNTHROID;25
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0074-4341-13	100 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	04/13/2012
2	NDC:0074-4341-90	90 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	
3	NDC:0074-4341-19	1000 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	
4	NDC:0074-4341-72	2 in 1 CARTON	06/03/2016	
4		7 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021402	07/24/2002	

SYNTHROID

levothyroxine sodium tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0074-4552
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
ACACIA (UNII: 5C5403N26O)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
TALC (UNII: 7SEV7J4R1U)	
SUCROSE (UNII: C151H8M554)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	

Product Characteristics

Color	white	**Score**	2 pieces
Shape	ROUND	**Size**	7mm
Flavor		**Imprint Code**	SYNTHROID;50
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0074-4552-13	100 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	05/18/2012
2	NDC:0074-4552-90	90 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	
3	NDC:0074-4552-19	1000 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	
4	NDC:0074-4552-11	10 in 1 BOX, UNIT-DOSE	07/24/2002	
4		10 in 1 BLISTER PACK; Type 0: Not a Combination Product		
5	NDC:0074-4552-71	4 in 1 CARTON	07/24/2002	12/20/2012
5		7 in 1 BLISTER PACK; Type 0: Not a Combination Product		
6	NDC:0074-4552-72	2 in 1 CARTON	07/24/2002	
6		7 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021402	07/24/2002	

SYNTHROID

levothyroxine sodium tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0074-5182
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
ACACIA (UNII: 5C5403N26O)	
SUCROSE (UNII: C151H8M554)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	
TALC (UNII: 7SEV7J4R1U)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
FD&C BLUE NO. 2 (UNII: L06K8R7DQK)	

Product Characteristics

Color	purple (Violet)	**Score**	2 pieces
Shape	ROUND	**Size**	7mm
Flavor		**Imprint Code**	SYNTHROID;75
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0074-5182-13	100 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	04/25/2012
2	NDC:0074-5182-90	90 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	
3	NDC:0074-5182-71	4 in 1 CARTON	07/24/2002	12/12/2012

3		7 in 1 BLISTER PACK; Type 0: Not a Combination Product		
4	NDC:0074-5182-19	1000 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	
5	NDC:0074-5182-11	10 in 1 BOX, UNIT-DOSE	07/24/2002	
5		10 in 1 BLISTER PACK; Type 0: Not a Combination Product		
6	NDC:0074-5182-72	2 in 1 CARTON	07/24/2002	
6		7 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021402	07/24/2002	

SYNTHROID

levothyroxine sodium tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0074-6594
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
ACACIA (UNII: 5C5403N26O)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
TALC (UNII: 7SEV7J4R1U)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	
D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)	
SUCROSE (UNII: C151H8M554)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	

Product Characteristics

Color	green (Olive)	**Score**	2 pieces

Shape	ROUND	**Size**	7mm
Flavor		**Imprint Code**	SYNTHROID;88
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0074-6594-13	100 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	05/02/2012
2	NDC:0074-6594-90	90 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	
3	NDC:0074-6594-71	4 in 1 CARTON	07/24/2002	01/01/2019
3		7 in 1 BLISTER PACK; Type 0: Not a Combination Product		
4	NDC:0074-6594-19	1000 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	
5	NDC:0074-6594-72	2 in 1 CARTON	07/24/2002	
5		7 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021402	07/24/2002	

SYNTHROID

levothyroxine sodium tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0074-6624
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
ACACIA (UNII: 5C5403N26O)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
TALC (UNII: 7SEV7J4R1U)	

D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	
SUCROSE (UNII: C151H8M554)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	

Product Characteristics

Color	yellow	**Score**	2 pieces
Shape	ROUND	**Size**	7mm
Flavor		**Imprint Code**	SYNTHROID;100
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0074-6624-13	100 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	05/21/2012
2	NDC:0074-6624-90	90 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	
3	NDC:0074-6624-19	1000 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	
4	NDC:0074-6624-11	10 in 1 BOX, UNIT-DOSE	07/24/2002	
4		10 in 1 BLISTER PACK; Type 0: Not a Combination Product		
5	NDC:0074-6624-71	4 in 1 CARTON	07/24/2002	01/01/2019
5		7 in 1 BLISTER PACK; Type 0: Not a Combination Product		
6	NDC:0074-6624-72	2 in 1 CARTON	07/24/2002	
6		7 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021402	07/24/2002	

SYNTHROID

levothyroxine sodium tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0074-9296
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LEVOTHYROXINE SODIUM (UNII: 9J765S329G) (LEVOTHYROXINE - UNII:Q51BO43MG4)	LEVOTHYROXINE SODIUM ANHYDROUS	112 ug

Inactive Ingredients

Ingredient Name	Strength
ACACIA (UNII: 5C5403N26O)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
TALC (UNII: 7SEV7J4R1U)	
D&C RED NO. 27 (UNII: 2LRS185U6K)	
D&C RED NO. 30 (UNII: 2S42T2808B)	
SUCROSE (UNII: C151H8M554)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	

Product Characteristics

Color	red (Rose)	**Score**	2 pieces
Shape	ROUND	**Size**	7mm
Flavor		**Imprint Code**	SYNTHROID;112
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0074-9296-13	100 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	04/15/2011
2	NDC:0074-9296-90	90 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	
3	NDC:0074-9296-19	1000 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	
4	NDC:0074-9296-71	4 in 1 CARTON	07/24/2002	01/11/2013
4		7 in 1 BLISTER PACK; Type 0: Not a Combination Product		
5	NDC:0074-9296-72	2 in 1 CARTON	07/24/2002	
5		7 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021402	07/24/2002	

SYNTHROID

levothyroxine sodium tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0074-7068
Route of Administration	ORAL		

Active Ingredient/Active Moiety

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

Inactive Ingredients

Ingredient Name	Strength
ACACIA (UNII: 5C5403N26O)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
TALC (UNII: 7SEV7J4R1U)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
SUCROSE (UNII: C151H8M554)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	

Product Characteristics

Color	brown	**Score**	2 pieces
Shape	ROUND	**Size**	7mm
Flavor		**Imprint Code**	SYNTHROID;125
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0074-7068-13	100 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	04/14/2012
2	NDC:0074-7068-90	90 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	
3	NDC:0074-7068-71	4 in 1 CARTON	07/24/2002	01/01/2019
3		7 in 1 BLISTER PACK; Type 0: Not a Combination Product		
4	NDC:0074-7068-19	1000 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	
5	NDC:0074-7068-11	10 in 1 BOX, UNIT-DOSE	07/24/2002	
5		10 in 1 BLISTER PACK; Type 0: Not a Combination Product		
	NDC:0074			

6	NDC:0074-7068-72	2 in 1 CARTON	07/24/2002	
6		7 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021402	07/24/2002	

SYNTHROID

levothyroxine sodium tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0074-3727
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
ACACIA (UNII: 5C5403N26O)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
TALC (UNII: 7SEV7J4R1U)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
SUCROSE (UNII: C151H8M554)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	

Product Characteristics

Color	blue (Turquoise)	**Score**	2 pieces
Shape	ROUND	**Size**	7mm
Flavor		**Imprint Code**	SYNTHROID;137
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0074-3727-13	100 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	04/15/2011

2	NDC:0074-3727-90	90 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	
3	NDC:0074-3727-71	4 in 1 CARTON	07/24/2002	11/28/2011
3		7 in 1 BLISTER PACK; Type 0: Not a Combination Product		
4	NDC:0074-3727-19	1000 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	
5	NDC:0074-3727-72	2 in 1 CARTON	07/24/2002	
5		7 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021402	07/24/2002	

SYNTHROID

levothyroxine sodium tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0074-7069
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
ACACIA (UNII: 5C5403N26O)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
TALC (UNII: 7SEV7J4R1U)	
FD&C BLUE NO. 2 (UNII: L06K8R7DQK)	
SUCROSE (UNII: C151H8M554)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	

Product Characteristics

Color	blue	**Score**	2 pieces
Shape	ROUND	**Size**	7mm
Flavor		**Imprint Code**	SYNTHROID;150

Contains	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0074-7069-90	90 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	
2	NDC:0074-7069-71	4 in 1 CARTON	07/24/2002	05/25/2012
2		7 in 1 BLISTER PACK; Type 0: Not a Combination Product		
3	NDC:0074-7069-19	1000 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	
4	NDC:0074-7069-11	10 in 1 BOX, UNIT-DOSE	07/24/2002	
4		10 in 1 BLISTER PACK; Type 0: Not a Combination Product		
5	NDC:0074-7069-72	2 in 1 CARTON	07/24/2002	
5		7 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021402	07/24/2002	

SYNTHROID

levothyroxine sodium tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0074-7070
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LEVOTHYROXINE SODIUM (UNII: 9J765S329G) (LEVOTHYROXINE - UNII:Q51BO43MG4)	LEVOTHYROXINE SODIUM ANHYDROUS	175 ug

Inactive Ingredients

Ingredient Name	Strength
ACACIA (UNII: 5C5403N26O)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
TALC (UNII: 7SEV7J4R1U)	

FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
D&C RED NO. 27 (UNII: 2LRS185U6K)	
D&C RED NO. 30 (UNII: 2S42T2808B)	
SUCROSE (UNII: C151H8M554)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	

Product Characteristics

Color	purple (Lilac)	**Score**	2 pieces
Shape	ROUND	**Size**	7mm
Flavor		**Imprint Code**	SYNTHROID;175
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0074-7070-13	100 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	03/06/2012
2	NDC:0074-7070-90	90 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	
3	NDC:0074-7070-71	4 in 1 CARTON	07/24/2002	01/10/2013
3		7 in 1 BLISTER PACK; Type 0: Not a Combination Product		
4	NDC:0074-7070-19	1000 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	
5	NDC:0074-7070-72	2 in 1 CARTON	07/24/2002	07/03/2015
5		7 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021402	07/24/2002	

SYNTHROID

levothyroxine sodium tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0074-7148
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
ACACIA (UNII: 5C5403N26O)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
TALC (UNII: 7SEV7J4R1U)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
SUCROSE (UNII: C151H8M554)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	

Product Characteristics

Color	pink	**Score**	2 pieces
Shape	ROUND	**Size**	7mm
Flavor		**Imprint Code**	SYNTHROID;200
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0074-7148-90	90 in 1 BOTTLE; Type 0: Not a Combination Product	02/24/2002	
2	NDC:0074-7148-19	1000 in 1 BOTTLE; Type 0: Not a Combination Product	02/24/2002	
3	NDC:0074-7148-71	4 in 1 CARTON	02/24/2002	08/01/2012
3		7 in 1 BLISTER PACK; Type 0: Not a Combination Product		
4	NDC:0074-7148-11	10 in 1 BOX, UNIT-DOSE	02/24/2002	
4		10 in 1 BLISTER PACK; Type 0: Not a Combination Product		
5	NDC:0074-7148-72	2 in 1 CARTON	02/24/2002	07/09/2015
5		7 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021402	02/24/2002	

SYNTHROID

levothyroxine sodium tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0074-7149
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LEVOTHYROXINE SODIUM (UNII: 9J765S329G) (LEVOTHYROXINE - UNII:Q51BO43MG4)	LEVOTHYROXINE SODIUM ANHYDROUS	300 ug

Inactive Ingredients

Ingredient Name	Strength
ACACIA (UNII: 5C5403N26O)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
TALC (UNII: 7SEV7J4R1U)	
D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
SUCROSE (UNII: C151H8M554)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	

Product Characteristics

Color	green	**Score**	2 pieces
Shape	ROUND	**Size**	7mm
Flavor		**Imprint Code**	SYNTHROID;300
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0074-7149-90	90 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	
2	NDC:0074-7149-19	1000 in 1 BOTTLE; Type 0: Not a Combination Product	07/24/2002	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021402	07/24/2002	

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