ERMEZA- levothyroxine sodium solution
Viatris Specialty LLC

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

ERMEZA™ (levothyroxine sodium) oral solution
Initial U.S. Approval: 2000

WARNING: NOT FOR TREATMENT OF OBESITY OR FOR WEIGHT LOSS

See full prescribing information for complete boxed warning.

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

INDICATIONS AND USAGE

ERMEZA is levothyroxine sodium (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:

3. Not indicated for suppression of benign thyroid nodules and nontoxic diffuse goiter in iodine-sufficient patients
4. 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 levothyroxine absorption. (2.1)
- Administer orally using the appropriate syringe provided in the original carton. The 5 mL syringe should be used for doses up to 5 mL. The 10 mL syringe should be used for doses over 5 mL. (2.1, 2.4)
- Starting dose depends on a variety of factors, including age, body weight, cardiovascular status, and concomitant medical conditions. 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. (2.5)

DOSAGE FORMS AND STRENGTHS

Oral Solution: 150 mcg levothyroxine sodium per 5 mL (30 mcg levothyroxine sodium per mL) in 90 mL or 180 mL bottles (3)

CONTRAINDICATIONS

- Uncorrected adrenal insufficiency. (4)
- Hypersensitivity to glycerin and edetate disodium. (4)

WARNINGS AND PRECAUTIONS

- *Serious risks related to overtreatment or undertreatment of ERMEZA:* Titrate the dose of ERMEZA carefully and monitor response to titration. (5.1)
- *Cardiac adverse reactions in the elderly and in patients with underlying cardiovascular disease:* Initiate ERMEZA 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 ERMEZA 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 levothyroxine 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 Mylan at 1-877-446-3679 (1-877-4-INFO-RX) 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 (e.g., absorption, synthesis, secretion, metabolism, protein binding, and target tissue response) and may alter the therapeutic response to ERMEZA. (7)

USE IN SPECIFIC POPULATIONS

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

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

Revised: 4/2022

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: NOT FOR TREATMENT OF OBESITY OR FOR WEIGHT LOSS
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
2.1 Important Administration Instructions
2.2 Important Considerations for Dosing
2.3 Recommended Dosage and Titration
2.4 Converting Recommended Microgram Dosage to Milliliters
2.5 Monitoring TSH and/or Thyroxine (T4) Levels
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Serious Risks Related to Overtreatment or Undertreatment of ERMEZA
5.2 Cardiac Adverse Reactions in the Elderly and in Patients with Underlying Cardiovascular Disease
5.3 Myxedema Coma
5.4 Acute Adrenal Crisis in Patients with Concomitant Adrenal Insufficiency
5.5 Worsening of Diabetic Control

5.6 Decreased Bone Mineral Density Associated with Thyroid Hormone Over-Replacement
6 ADVERSE REACTIONS
7 DRUG INTERACTIONS
7.1 Drugs Known to Affect Thyroid Hormone Pharmacokinetics
7.2 Antidiabetic Therapy
7.3 Oral Anticoagulants
7.4 Digitalis Glycosides
7.5 Antidepressant Therapy
7.6 Ketamine
7.7 Sympathomimetics
7.8 Tyrosine-Kinase Inhibitors
7.9 Drug-Food Interactions
7.10 Drug-Laboratory Test Interactions
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation
8.4 Pediatric Use
8.5 Geriatric Use
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION
* 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 ERMEZA, 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

ERMEZA 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

ERMEZA 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:

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

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Instructions

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

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

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

Convert mcg dosage to mL using the following equation and round up or down to the nearest syringe graduation *[see Dosage and Administration (2.4)]:*

$$\frac{\text{Dosage (mcg)}}{30} = \text{Dosage (mL)}$$

Administer ERMEZA directly to the mouth using the 5 mL or 10 mL oral syringe provided in the original carton. A household teaspoon or tablespoon is not an adequate measuring device. Instruct patients to read the “Instructions for Use” carefully for complete directions on how to properly dose and administer ERMEZA.

2.2 Important Considerations for Dosing

ERMEZA oral solution may have a different concentration from other levothyroxine oral solution products. Use caution and consider the total dosage in terms of mcg and not volume (mL) when converting between ERMEZA and other levothyroxine oral solution products.

The dosage of ERMEZA 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 dose adjustments made based on periodic assessment of the patient's clinical response and laboratory parameters *[see Dosage and Administration (2.5)]*.

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 ERMEZA dosage adequacy and should not be used to monitor therapy. Use the serum free-T4 level to titrate ERMEZA 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)]*.

The peak therapeutic effect of a given dose of ERMEZA 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 ERMEZA 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. ERMEZA 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 ERMEZA 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. ERMEZA 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 ERMEZA in pregnant patients is described in Table 3.

Table 3. ERMEZA Dosing Guidelines for Hypothyroidism in Pregnant Patients

Patient Population	Starting Dosage	Dose Adjustment and

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

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

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

2.4 Converting Recommended Microgram Dosage to Milliliters

After determination of the recommended ERMEZA dosage in mcg *[see Dosage and Administration (2.3)]*, convert the required mcg dosage to mL using the following equation:

$$\frac{\text{Dosage (mcg)}}{30} = \text{Dosage (mL)}$$

Once the mcg dose has been converted to mL, it should be rounded up or down to the nearest syringe graduation (0.1 mL for doses up to 5 mL or 0.2 mL for doses up to 10 mL).

Example of dosing volumes in mL for the equivalent mcg dosages is shown in Table 4.

Table 4: Example Dosing Volumes (mL) for Equivalent Dosages (mcg)

Dose (mcg)	Dose (mL) using 5 mL syringe	Dose (mL) using 10 mL syringe
12.5	0.4	
25	0.8	

50	1.7	Do not use
75	2.5	
88	2.9	
100	3.3	
112	3.7	
125	4.2	
137	4.6	
150	5.0	
175	Do not use	5.8
200		6.6
300		10.0

The 5 mL syringe provided in the original carton should be used for doses up to 5 mL with each graduation mark representing 0.1 mL.

The 10 mL syringe provided in the original carton should be used for doses over 5 mL with each graduation mark representing 0.2 mL.

2.5 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 ERMEZA, may be evidence of inadequate absorption, poor compliance, drug interactions, or a combination of these factors.

The risk of thyroid imbalance can be linked to the switch between levothyroxine-containing products. Assess the adequacy of therapy by assessment of laboratory tests, and clinical evaluation is recommended.

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 dose, 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 ERMEZA 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 ERMEZA *[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

ERMEZA (levothyroxine sodium) Oral Solution, 150 mcg/ 5 mL (30 mcg/ mL) is a clear, colorless solution supplied in a 90 mL or 180 mL amber glass bottle with a child-resistant closure.

ERMEZA is to be used with the 5 mL or 10 mL oral syringe provided in the original carton.

4 CONTRAINDICATIONS

ERMEZA is contraindicated in patients with:

- Uncorrected adrenal insufficiency *[see Warnings and Precautions (5.4)]*.
- Hypersensitivity to glycerin and edetate disodium, inactive ingredients in ERMEZA *[see Adverse Reactions (6) and Pediatric Use (8.4)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Serious Risks Related to Overtreatment or Undertreatment of ERMEZA

ERMEZA has a narrow therapeutic index. Overtreatment or undertreatment with ERMEZA 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 ERMEZA 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 ERMEZA 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 ERMEZA 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 ERMEZA therapy. Monitor patients receiving concomitant ERMEZA and sympathomimetic agents for signs and symptoms of coronary insufficiency.

If cardiac symptoms develop or worsen, reduce the ERMEZA 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 ERMEZA *[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 ERMEZA *[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 ERMEZA that achieves the desired clinical and biochemical response to mitigate this risk.

6 ADVERSE REACTIONS

Adverse reactions associated with levothyroxine therapy are primarily those of hyperthyroidism due to therapeutic overdosage *[see Warnings and Precautions (5)*, *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 (e.g., absorption, synthesis, secretion, metabolism, protein binding, and target tissue response) and may alter the therapeutic response to ERMEZA (Tables 5 to 8).

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

Potential impact: Concurrent use may reduce the efficacy of ERMEZA 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 ERMEZA at least 4 hours apart from these agents.
Orlistat	Monitor patients treated concomitantly with orlistat and ERMEZA for changes in thyroid function.
Bile Acid Sequestrants	Bile acid sequestrants and ion exchange

-Colesevelam -Cholestyramine -Colestipol Ion Exchange Resins -Kayexalate	resins are known to decrease levothyroxine absorption. Administer ERMEZA at least 4 hours prior to these drugs or monitor 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 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 ERMEZA 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 ERMEZA 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 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 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 drugs: Amiodarone	Amiodarone inhibits peripheral conversion of levothyroxine (T4) to triiodothyronine (T3) and may

	cause isolated biochemical changes (increase in serum free-T4, and decrease or normal free-T3) in clinically euthyroid patients.

7.2 Antidiabetic Therapy

Addition of ERMEZA 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

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

7.4 Digitalis Glycosides

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

7.6 Ketamine

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

7.7 Sympathomimetics

Concurrent use of sympathomimetics and ERMEZA 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 ERMEZA absorption thereby necessitating adjustments in dosing *[see Dosage and Administration (2.1)]*. Soybean products, such as infant formula and soybean flour, cottonseed meal, walnuts, and dietary fiber may bind and decrease the absorption of ERMEZA from the gastrointestinal 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 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.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

The clinical experience, including data from post-marketing studies in pregnant women treated with oral levothyroxine, to maintain a 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 hypothyroidism in pregnancy. Since TSH levels may increase during pregnancy, TSH should be monitored, and ERMEZA dosage adjusted during pregnancy *(see Clinical Considerations)*. Animal reproduction studies have not been conducted with levothyroxine sodium. ERMEZA 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 ERMEZA requirements. Serum TSH levels should be monitored, and the ERMEZA dosage adjusted during pregnancy. Since postpartum TSH levels are similar to preconception values, the ERMEZA 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 sodium. 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 ERMEZA and any potential adverse effects on the breastfed infant from ERMEZA or from the underlying maternal condition.

8.4 Pediatric Use

ERMEZA 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.

Glycerin has the potential to cause gastrointestinal irritation resulting in vomiting and/or osmotic diarrhea. Patients in the first 3 months of life may be particularly susceptible to serious fluid and electrolyte complications from glycerin-induced gastrointestinal irritation. Closely monitor patients from birth to 3 months of age receiving ERMEZA for signs and symptoms of gastrointestinal irritation.

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 ERMEZA therapy immediately upon diagnosis. Levothyroxine is generally continued for life in these patients *[see Warnings and Precautions (5.1)]*.

Closely monitor patients during the first 2 weeks of ERMEZA therapy for cardiac overload and arrhythmias.

8.5 Geriatric Use

Because of the increased prevalence of cardiovascular disease among the elderly, initiate ERMEZA 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.

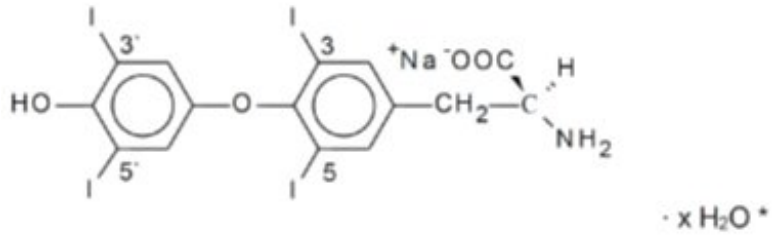
10 OVERDOSAGE

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 ERMEZA 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

ERMEZA (levothyroxine sodium) oral solution contains synthetic L-3,3', 5,5'-tetraiodothyronine sodium salt [levothyroxine (T4) sodium]. Synthetic T4 is chemically identical to that produced in the human thyroid gland, and is very slightly soluble in water. Levothyroxine (T4) sodium hydrate has an empirical formula of $C_{15}H_{10}I_4NNaO_4$ with x ≈ 5*, molecular weight of 798.86 (anhydrous), and structural formula as shown:



ERMEZA oral solution is supplied in the following strength: 150 mcg/5 mL (30 mcg/mL). ERMEZA oral solution contains the following inactive ingredients: edetate disodium, glycerin, and purified water.

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 ERMEZA dose is absorbed from the jejunum and upper ileum. 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 (see Table 9). 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 9. Pharmacokinetic Parameters of Thyroid Hormones in Euthyroid Patients

Hormone	Ratio in	Biologic	Half-Life	Protein Binding

	Thyroglobulin	Potency	(days)	(%)*
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

ERMEZA (levothyroxine sodium) Oral Solution, 150 mcg/ 5 mL (30 mcg/ mL) is a clear, colorless solution supplied in a 90 mL or 180 mL amber glass bottle with a child-resistant closure. A 5 mL with 0.1 mL graduation and a 10 mL with 0.2 mL graduation oral syringe are provided within the carton to accurately measure the prescribed dose. It is available as follows:

NDC 49502-378-75: 75 mL of oral solution filled in 90 mL size amber glass bottles.

NDC 49502-378-15: 150 mL of oral solution filled in 180 mL size amber glass bottles.

Storage and Handling

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

ERMEZA oral solution should be protected from light.

Store and dispense in original bottle. Use within 90 days of opening the bottle.

17 PATIENT COUNSELING INFORMATION

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

Dosing and Administration

- Instruct patients to take ERMEZA only as directed by their healthcare provider.
- Instruct patients to take ERMEZA once daily, preferably on an empty stomach, one-half to one hour before breakfast.
- Instruct patients to always use the 5 mL or 10 mL oral syringe provided in the original carton when administering ERMEZA to ensure that the dose is measured

and administered accurately. Instruct patients to read the “Instructions for Use” carefully for complete directions on how to properly dose and administer ERMEZA.
- Inform patients that agents such as iron and calcium supplements and antacids can decrease the absorption of levothyroxine. Instruct patients not to take ERMEZA 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 ERMEZA.

Important Information

- Inform patients that it may take several weeks before they notice an improvement in symptoms.
- Inform patients that the levothyroxine in ERMEZA 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 ERMEZA 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 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 ERMEZA. 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 ERMEZA 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 ERMEZA therapy, but this is usually temporary.

Manufactured for:
Mylan Specialty L.P.
Morgantown, WV 26505 U.S.A.

Manufactured by:
DPT Laboratories, Ltd.
San Antonio, TX 78215 U.S.A.

LEVOOSN:R1

PATIENT INFORMATION

ERMEZA™ [er-meh-zah]
(levothyroxine sodium)
oral solution

What is the most important information I should know about ERMEZA?
Do not use ERMEZA to treat weight problems or weight loss.

What is ERMEZA?
ERMEZA is a prescription medicine that contains a hormone called levothyroxine which is normally produced by the thyroid gland. ERMEZA is used in adults and children, including newborns:

- to replace or give extra levothyroxine when the thyroid does not produce enough of this hormone; or
- with surgery and radiodine therapy to manage a type of thyroid cancer called thyroid-dependent well-differentiated thyroid cancer.

ERMEZA 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 take ERMEZA:

- if your adrenal glands are not working well and you have not been treated for this problem; or
- if you are allergic to glycerin or edetate disodium, the inactive ingredients in ERMEZA.

Before you take ERMEZA, tell your doctor about all of your medical conditions, including if you:

- have or have had heart problems.
- have or have had thyroid nodules.
- have adrenal or pituitary gland problems.
- have any food or drug allergies.
- have 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).
- plan to have surgery.
- are pregnant or plan to become pregnant. Your doctor may need to change your ERMEZA dose while you are pregnant.
- are breastfeeding. Levothyroxine can pass into your breast milk.

Talk to your doctor about the best way to feed your baby if you take ERMEZA. Tell your doctor about all the medicines you are taking including prescription and over-the-counter medicines, vitamins and herbal supplements. ERMEZA may affect the way other medicines work, and other medicines may affect how ERMEZA works so your doctor may have to adjust the amount of medicines you take. You can ask your doctor or pharmacist for a list of medicines that interact with ERMEZA.

How should I take ERMEZA?

- ERMEZA is for oral use only. **Do not** inhale, inject, or place ERMEZA in the eyes.
- **See the detailed "Instructions for Use" that come with ERMEZA for information on the right way to take your dose of ERMEZA.**
- Take ERMEZA exactly as your doctor tells you to take it.
- Your doctor will tell you how much ERMEZA to take each day.
- Your doctor may change your dose, if needed.
- Take your dose of ERMEZA 1 time each day 30 minutes to 1 hour before breakfast on an empty stomach.
- Certain medicines can interfere with how levothyroxine is absorbed by your body. Take ERMEZA:
    - **at least 4 hours before or after** you take medicines that contain calcium carbonate or iron (ferrous sulfate); and
    - **at least 4 hours before** you take medicines that contain bile acid sequestrants or ion exchange resins. **Know the medicines you take. Ask your doctor or pharmacist for a list of these medicines, if you are not sure.**
- Certain foods including soybean products (such as infant formula and soybean flour), cotton seed meal, walnuts, dietary fiber, and grapefruit juice can affect your treatment and dose of ERMEZA. Talk to your doctor if you eat or drink these foods.
- Use ERMEZA within **90 days** of opening the bottle.
- Your doctor should do certain blood tests while you are taking ERMEZA and may change your daily dose of ERMEZA as needed. Keep taking ERMEZA unless your doctor tells you to stop or to change your dose.

It may take weeks before you notice your symptoms getting better. **Keep using this medicine even if you feel well.** In case of overdose, get medical help or contact a live Poison Control expert at 1-800-222-1222. Advice is also available online at www.poison.org.

What are the possible side effects of ERMEZA?
ERMEZA may 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, you have heart problems, or you take too much ERMEZA. Your doctor may reduce your dose or stop treatment with ERMEZA for a while if you develop heart problems.
- **worsening diabetic control.** If you are diabetic, it may be harder to control your blood sugar levels causing hyperglycemia while taking ERMEZA. Check your blood sugar levels closely after starting, changing, or stopping treatment with ERMEZA. Your doctor 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 or you take too much ERMEZA.

The most common side effects of ERMEZA include:

- fast or irregular heartbeat
- chest pain
- irritability
- sleep problems (insomnia)
- vomiting
- diarrhea
- sweating a lot

- shortness of breath
- leg cramps
- headache
- nervousness
- hives or skin rash
- tremors
- muscle weakness
- change in appetite
- weight loss or weight gain
- heat intolerance
- fever
- changes in menstrual period

Other side effects may include partial hair loss during the first months of treatment with ERMEZA. This usually lasts a short period of time (temporary).

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

How should I store ERMEZA?

- Store ERMEZA at room temperature between 68°F to 77°F (20°C to 25°C).
- Protect from light.
- Store ERMEZA in the original bottle. Use ERMEZA within **90 days** of opening the bottle.

Keep ERMEZA and all medicines out of the reach of children.

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

What are the ingredients in ERMEZA oral solution?
Active ingredient: levothyroxine sodium
Inactive ingredients: edetate disodium, glycerin, and purified water

Manufactured for: Mylan Specialty L.P., Morgantown, WV 26505 U.S.A.

For more information, call Mylan at 1-877-446-3679 (1-877-4-INFO-RX).

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

Issued: 4/2022
PL:LEVOOSN:R1

INSTRUCTIONS FOR USE

ERMEZA™ [er-meh-zah]
(levothyroxine sodium oral solution)

Read this Instructions for Use before you start taking ERMEZA and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

- **Keep ERMEZA and all medicines out of reach of children.**

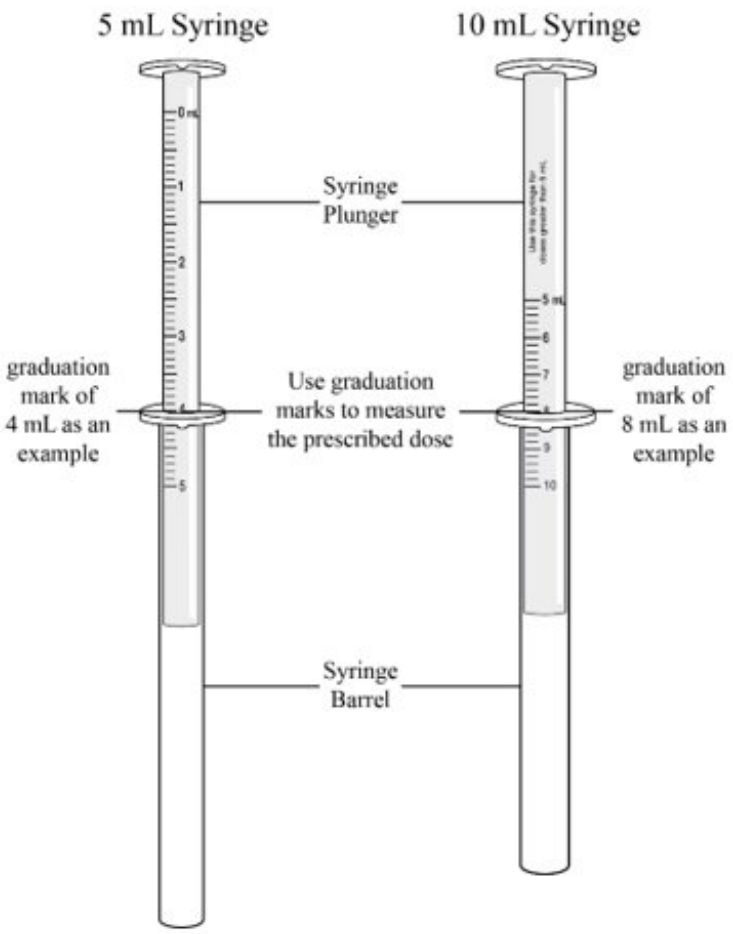
- Be sure that you read, understand and follow these instructions carefully to ensure correct dosing of the oral solution.

- Always check the expiration date of your ERMEZA before use. **Do not** use if the expiration date has passed.

- Throw away (discard) any unused ERMEZA after **90 days** of first opening the bottle.

- Store ERMEZA at room temperature between 68°F to 77°F (20°C to 25°C) with the oral syringes in the original carton.

Figure A: The diagram of 2 oral syringes



Important Information You Need to Know Before Taking ERMEZA.

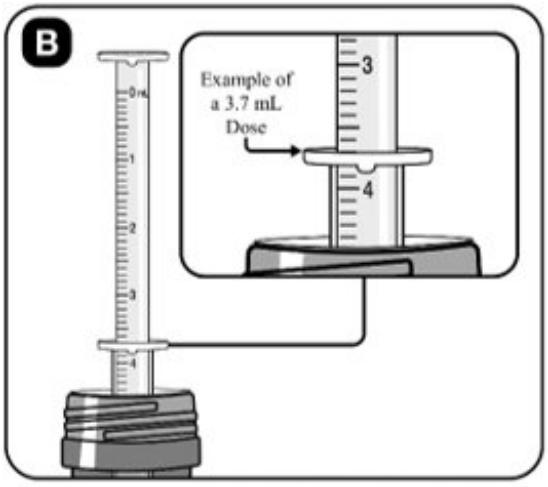
For oral use only (take by mouth).

Two ERMEZA syringes are provided in the carton (see Figure A):

- 5 mL syringe for doses up to 5 mL. Each graduation mark represents 0.1 mL. Figure A shows a graduation mark of 4 mL as an example.
- 10 mL syringe for doses over 5 mL. Each graduation mark represents 0.2 mL. Figure A shows a graduation mark of 8 mL as an example.

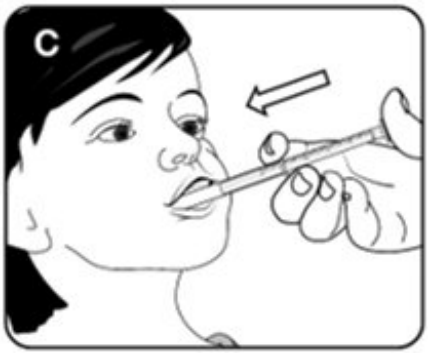
Do not wash the syringes in a dishwasher, use warm water only.

Step 1: Preparing the Dose



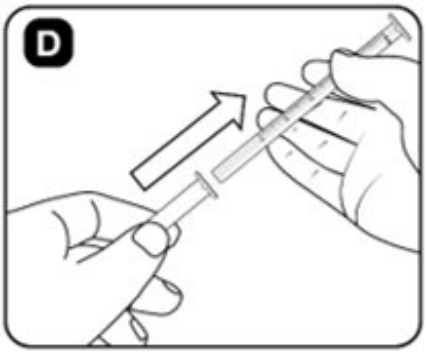
- Hold the bottle firmly with 1 hand and then push down on the bottle cap and turn it counterclockwise to remove it.
- Ensure the syringe plunger is pushed all the way into the barrel to remove any air from the syringe.
- Place the oral syringe provided into the medicine within the bottle (See Figure B).
- Pull back the plunger, ensuring the end remains in the medicine, until the graduation mark for the dose prescribed by your healthcare provider lines up with the top surface of the syringe barrel (See Figure B). Figure B shows a dose of 3.7 mL as an example.
- If you see any large air bubbles in the barrel of the syringe, hold the syringe over the bottle to remove them and repeat Step 1.

Step 2: Taking ERMEZA



- Place the end of the oral syringe into the corner of the mouth toward the inside cheek (See Figure C).
- Slowly push the plunger down until the syringe is empty.
- Replace cap onto bottle and screw in a clockwise direction until tight.

Step 3: Cleaning and Storage



- Pull plunger straight out of the oral syringe barrel (See Figure D). Rinse the barrel and plunger with warm water and leave to air dry.
- When dry, place the plunger back inside the oral syringe barrel and put back inside the carton supplied and store at room temperature between 68°F to 77°F (20°C to 25°C).

For more information, call Mylan at 1-

877-446-3679 (1-877-4-INFO-RX).

Manufactured for:
Mylan Specialty L.P.
Morgantown, WV 26505 U.S.A.

Manufactured by:
DPT Laboratories, Ltd.
San Antonio, TX 78215 U.S.A.

This Instructions for Use has been approved by the U.S. Food and Drug Administration.
Issued: 4/2022

141152-0422

IFU:LEVOOSN:R1

PRINCIPAL DISPLAY PANEL – 150 mcg/5 mL

NDC 49502-378-75 Rx only

Ermeza™
(levothyroxine sodium)
Oral Solution
150 mcg/5 mL
(30 mcg/mL)

For Oral Administration Only

Please read the Instructions for Use before administering Ermeza.

One 5 mL oral syringe and one 10 mL oral syringe provided.

Store and dispense in original bottle.

75 mL

Each 5 mL contains:
Levothyroxine sodium, USP
150 mcg

Usual Dosage: See accompanying prescribing information.

Keep this and all medication out of the reach of children.

Store at 20°C to 25°C (68°F to 77°F), excursions permitted between 15°C to 30°C (59°F to 86°F). [See USP Controlled Room Temperature.]

Protect from light.

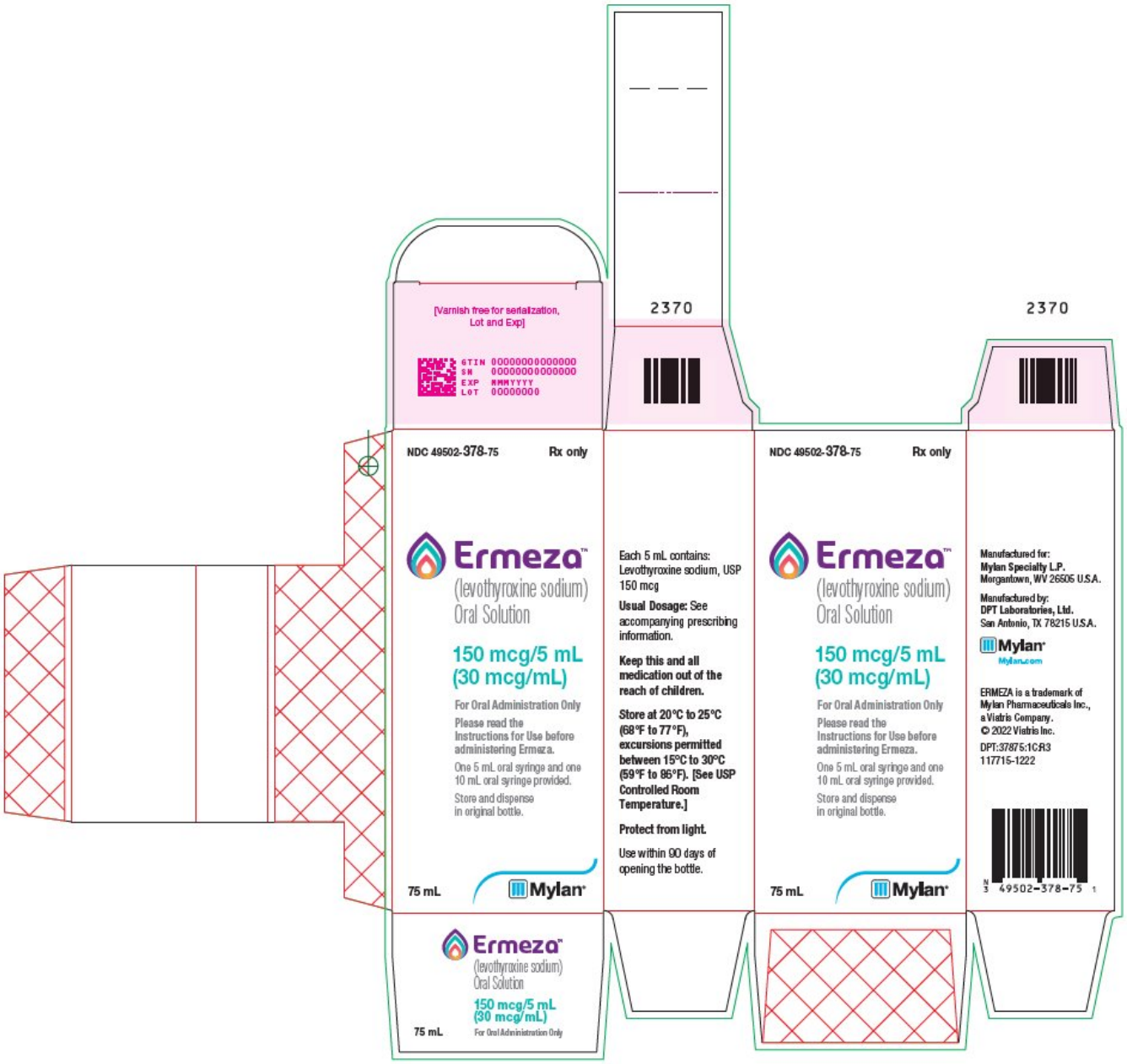
Use within 90 days of opening the bottle.

Manufactured for:
Mylan Specialty L.P.
Morgantown, WV 26505 U.S.A.

Manufactured by:
DPT Laboratories, Ltd.
San Antonio, TX 78215 U.S.A.

Mylan.com

DPT:37875:1C:R3
117715-1222



ERMEZA

levothyroxine sodium solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:49502-378
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
LEVOTHYROXINE SODIUM (UNII: 9J765S329G) (LEVOTHYROXINE - UNII:Q51BO43MG4)	LEVOTHYROXINE SODIUM ANHYDROUS	30 ug in 1 mL

Inactive Ingredients

Ingredient Name	Strength
EDETATE DISODIUM (UNII: 7FLD91C86K)	
GLYCERIN (UNII: PDC6A3C0OX)	
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:49502-378-75	1 in 1 CARTON	12/14/2022	07/31/2026
1		75 mL in 1 BOTTLE, GLASS; Type 1: Convenience Kit of Co-Package		
2	NDC:49502-378-15	1 in 1 CARTON	12/14/2022	07/31/2026
2		150 mL in 1 BOTTLE, GLASS; Type 1: Convenience Kit of Co-Package		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA215809	12/14/2022	07/31/2026

Labeler - Viatris Specialty LLC (117455616)

Revised: 4/2022

Viatris Specialty LLC