LEVOTHYROXINE SODIUM- levothyroxine sodium anhydrous injection, powder, lyophilized, for solution

Fresenius Kabi USA, LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION

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

Levothyroxine Sodium for Injection
Initial U.S. Approval: 1969

WARNING: NOT FOR TREATMENT OF OBESITY OR FOR WEIGHT LOSS

Thyroid hormones, including Levothyroxine Sodium for Injection, should not be used for the treatment of obesity or for weight loss. (5.3)
Larger doses may produce serious or even life threatening manifestations of toxicity. (6)

INDICATIONS AND USAGE

Levothyroxine Sodium is an L-thyroxine product. Levothyroxine (T_4) Sodium for Injection is indicated for the treatment of myxedema coma. **(1)**

Important Limitations of Use:

The relative bioavailability of this drug has not been established. Use caution when converting patients from oral to intravenous levothyroxine.

DOSAGE AND ADMINISTRATION

- An initial intravenous loading dose of Levothyroxine Sodium for Injection between 300 to 500 mcg followed by once daily intravenous maintenance doses between 50 and 100 mcg should be administered, as clinically indicated, until the patient can tolerate oral therapy. (**2.1**)
- Reconstitute the lyophilized Levothyroxine Sodium for Injection by aseptically adding 5 mL of 0.9% Sodium Chloride Injection, USP. Shake vial to ensure complete mixing. Reconstituted drug product is preservative free. Use immediately after reconstitution. Discard any unused portion. (**2.3**)
- Do not add to other IV fluids. (**2.3**)

DOSAGE FORMS AND STRENGTHS

Lyophilized powder for injection in single use vials: 100 mcg, 200 mcg and 500 mcg. (**3**)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

- Excessive bolus doses of Levothyroxine Sodium for Injection (> 500 mcg) are associated with cardiac complications, particularly in the elderly and in patients with an underlying cardiac condition. Initiate therapy with doses at the lower end of the recommended range. (**5.1**)
- Close observation of the patient following the administration of Levothyroxine Sodium for Injection is advised. (**5.1**)
- Levothyroxine Sodium for Injection therapy for patients with previously undiagnosed endocrine disorders, including adrenal insufficiency, hypopituitarism, and diabetes insipidus, may worsen symptoms of these endocrinopathies. (**5.2**)

ADVERSE REACTIONS

Excessive doses of L-thyroxine can predispose to signs and symptoms compatible with hyperthyroidism. (6)
(6)

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Kabi USA, LLC, Medical Affairs Department at 1-800-551-7176 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. (6)

DRUG INTERACTIONS

Many drugs 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 Levothyroxine Sodium for Injection. (**7**, **12.3**)

USE IN SPECIFIC POPULATIONS

- Elderly and those with underlying cardiovascular disease should receive doses at the lower end of the recommended range. (**8.5**)

Revised: 12/2013

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FULL PRESCRIBING INFORMATION

WARNING: NOT FOR TREATMENT OF OBESITY OR FOR WEIGHT LOSS
Thyroid hormones, including Levothyroxine Sodium for Injection, should not be used for the treatment of obesity or for weight loss. (5.3)
Larger doses may produce serious or even life threatening manifestations of toxicity. (6)

1 INDICATIONS AND USAGE

Levothyroxine Sodium for Injection is indicated for the treatment of myxedema coma. Important Limitations of Use: The relative bioavailability between Levothyroxine Sodium for Injection and oral levothyroxine products has not been established. Caution should be used when switching patients from oral levothyroxine products to Levothyroxine Sodium for Injection as accurate dosing conversion has not been studied.

2 DOSAGE AND ADMINISTRATION

2.1 Dosage

An initial intravenous loading dose of Levothyroxine Sodium for Injection between 300 to 500 mcg, followed by once daily intravenous maintenance doses between 50 and 100 mcg, should be administered, as clinically indicated, until the patient can tolerate oral therapy. The age, general physical condition, cardiac risk factors, and clinical severity of myxedema and duration of myxedema symptoms should be considered when determining the starting and maintenance dosages of Levothyroxine Sodium for Injection.

Levothyroxine Sodium for Injection produces a gradual increase in the circulating concentrations of the hormone with an approximate half-life of 9 to 10 days in hypothyroid patients. Daily administration of Levothyroxine Sodium for Injection should be maintained until the patient is capable of tolerating an oral dose and is clinically stable. For chronic treatment of hypothyroidism, an oral dosage form of levothyroxine should be used to maintain a euthyroid state. Relative bioavailability between Levothyroxine Sodium for Injection and oral levothyroxine products has not been established. Based on medical practice, the relative bioavailability between oral and intravenous administration of Levothyroxine Sodium for Injection is estimated to be from 48 to 74%. Due to differences in absorption characteristics of patients and the oral levothyroxine product formulations, TSH and thyroid hormone levels should be measured a few weeks after initiating oral levothyroxine and dose adjusted accordingly.

2.2 Dosing in the Elderly and in Patients with Cardiovascular Disease

Intravenous levothyroxine may be associated with cardiac toxicity—including arrhythmias, tachycardia, myocardial ischemia and infarction, or worsening of congestive heart failure and death—in the elderly and in those with underlying cardiovascular disease. Therefore, cautious use, including doses in the lower end of the recommended range, may be warranted in these populations.

2.3 Reconstitution Directions

Reconstitute the lyophilized Levothyroxine Sodium for Injection by aseptically adding 5 mL of 0.9% Sodium Chloride Injection, USP only. Shake vial to ensure complete mixing. The resultant solution will have a final concentration of approximately 20 mcg per mL, 40 mcg per mL and and 100 mcg per mL for the 100 mcg, 200 mcg and 500 mcg vials, respectively. Reconstituted drug product is preservative free and is stable for 4 hours. Discard any unused portion. DO NOT ADD LEVOTHYROXINE SODIUM FOR INJECTION TO OTHER IV FLUIDS. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container

permit.

3 DOSAGE FORMS AND STRENGTHS

Levothyroxine Sodium for Injection is supplied as a lyophilized powder at three strengths in single use amber-colored vials: 100 mcg, 200 mcg and 500 mcg.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Risk of Cardiac Complications in Elderly and in Patients with Cardiovascular Disease

Excessive bolus dosing of Levothyroxine Sodium for Injection (greater than 500 mcg) are associated with cardiac complications, particularly in the elderly and in patients with an underlying cardiac condition. Adverse events that can potentially be related to the administration of large doses of Levothyroxine Sodium for Injection include arrhythmias, tachycardia, myocardial ischemia and infarction, or worsening of congestive heart failure and death. Cautious use, including doses in the lower end of the recommended range, may be warranted in these populations. Close observation of the patient following the administration of Levothyroxine Sodium for Injection is advised.

5.2 Need for Concomitant Glucocorticoids and Monitoring for Other Diseases in Patients with Endocrine Disorders

Occasionally, chronic autoimmune thyroiditis, which can lead to myxedema coma, may occur in association with other autoimmune disorders such as adrenal insufficiency, pernicious anemia, and insulin-dependent diabetes mellitus. Patients should be treated with replacement glucocorticoids prior to initiation of treatment with Levothyroxine Sodium for Injection, until adrenal function has been adequately assessed. Failure to do so may precipitate an acute adrenal crisis when thyroid hormone therapy is initiated, due to increased metabolic clearance of glucocorticoids by thyroid hormone. With initiation of Levothyroxine Sodium for Injection, patients with myxedema coma should also be monitored for previously undiagnosed diabetes insipidus.

5.3 Not Indicated for Treatment of Obesity

Thyroid hormones, including Levothyroxine Sodium for Injection, 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) and Overdosage (10)]*.

6 ADVERSE REACTIONS

Excessive doses of levothyroxine can predispose to signs and symptoms compatible with hyperthyroidism. The signs and symptoms of thyrotoxicosis include, but are not limited to: exophthalmic goiter, weight loss, increased appetite, palpitations, nervousness, diarrhea, abdominal cramps, sweating, tachycardia, increased pulse and blood pressure, cardiac arrhythmias, angina pectoris, tremors, insomnia, heat intolerance, fever, and menstrual irregularities.

7 DRUG INTERACTIONS

Many drugs affect thyroid hormone pharmacokinetics and metabolism (e.g., synthesis, secretion, catabolism, protein binding, and target tissue response) and may alter the therapeutic response to Levothyroxine Sodium for Injection. In addition, thyroid hormones and thyroid status have varied effects on the pharmacokinetics and actions of other drugs (see Section 12.3).

7.1 Antidiabetic Therapy

Addition of levothyroxine to antidiabetic or insulin therapy may result in increased antidiabetic agent or insulin requirements. Careful monitoring of diabetic control is recommended, especially when thyroid therapy is started, changed, or discontinued.

7.2 Oral Anticoagulants

Levothyroxine 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 Levothyroxine Sodium for Injection dose is increased. Prothrombin time should be closely monitored to permit appropriate and timely dosage adjustments.

7.3 Digitalis Glycosides

The therapeutic effects of digitalis glycosides may be reduced by levothyroxine. Serum digitalis glycoside levels may be decreased when a hypothyroid patient becomes euthyroid, necessitating an increase in the dose of digitalis glycosides.

7.4 Antidepressant Therapy

Concurrent use of tricyclic (e.g., amitriptyline) or tetracyclic (e.g., maprotiline) antidepressants and levothyroxine 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 CNS stimulation; onset of action of tricyclics may be accelerated. Administration of sertraline in patients stabilized on levothyroxine may result in increased levothyroxine requirements.

7.5 Ketamine

Concurrent use may produce marked hypertension and tachycardia; cautious administration to patients receiving thyroid hormone therapy is recommended.

7.6 Sympathomimetics

Concurrent use 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.

7.7 Drug-Laboratory Test Interactions

Changes in thyroxine binding globulin (TBG) concentration must be considered when interpreting levothyroxine and triiodothyronine values, which necessitates measurement and evaluation of unbound (free) hormone and/or determination of the free levothyroxine index. Pregnancy, infectious hepatitis, estrogens, estrogen containing oral contraceptives, and acute intermittent porphyria increase TBG concentrations. Decreases in TBG concentrations are observed in nephrosis, severe hypoproteinemia, severe liver disease, acromegaly, and after androgen or corticosteroid therapy. 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

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