CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

202231Orig1s000

LABELING

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
See full prescribing information for complete boxed warning.
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, 500 mcg. (3)

----------CONTRAINDICATIONS----------
None

----------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.

To report SUSPECTED ADVERSE REACTIONS, contact APP Pharmaceuticals, LLC, Medical Affairs Department at 1-800-551-7176 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------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: [June 2011]

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

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 100 mcg per mL for the 100 mcg, 200 mcg and 500 mcg vials, respectively. Reconstituted drug product is preservative free. Use immediately after reconstitution. 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

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.