CLINICAL UPDATE

Brand Name	Tirosint®
Generic Name	levothyroxine
Drug Manufacturer	Teva Pharmaceuticals USA, Inc.

Clinical Update

TYPE OF CLINICAL UPDATE

New Dosage Form (capsules) and First Time Generic

FDA APPROVAL DATE

October 28, 2020

LAUNCH DATE

November 3, 2020

REVIEW DESIGNATION

N/A

TYPE OF REVIEW

Abbreviated New Drug Application (ANDA): 211369

DISPENSING RESTRICTIONS

N/A

Overview

INDICATION(S) FOR USE

L-thyroxine (T4) indicated for adults and pediatric patients 6 years and older with:

• Hypothyroidism - As replacement therapy in primary (thyroidal), secondary (pituitary), and tertiary (hypothalamic) congenital or acquired hypothyroidism.

• 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.

Limitations of Use:

• Not indicated for suppression of benign thyroid nodules and nontoxic diffuse goiter in iodine-sufficient patients.

• Not indicated for treatment of transient hypothyroidism during the recovery phase of subacute thyroiditis.

MECHANISMS 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.

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DOSAGE FORM(S) AND STRENGTH(S)

Capsules: 13, 25, 50, 75, 88, 100, 112, 125, 137, 150, 175, 200 mcg

DOSE & ADMINISTRATION

Administer once daily, on an empty stomach, one-half to one hour before breakfast.

• Administer at least 4 hours before or after drugs that are known to interfere with absorption.

• Evaluate the need for dose adjustments when regularly administering within an hour of certain foods that may affect TIROSINT absorption.

• Swallow Tirosint® capsules whole, do not cut, crush, or chew.

• Starting dose depends on a variety of factors, including age, body weight, cardiovascular status, concomitant medical conditions (including pregnancy), concomitant medications, co-administered food, and the specific nature of the condition being treated. Peak therapeutic effect may not be attained for 4-6 weeks.

• Adequacy of therapy determined with periodic monitoring of TSH and/or T4 as well as clinical status.

EFFICACY

This retrospective, 1:1 propensity score–matched longitudinal cohort study used the OptumLabs Data Warehouse administrative claims database linked to laboratory results from commercially insured and Medicare Advantage enrollees throughout the United States. Eligible patients were adults (aged ≥18 years) with thyrotropin levels ranging from 4.5 to 19.9 mIU/L who initiated use of generic or brand-name levothyroxine from January 1, 2008, to October 1, 2017. Data were analyzed from August 13, 2018, to October 25, 2019.

Proportion of patients with normal vs markedly abnormal thyrotropin levels (<0.1 or >10 mIU/L) within 3 months and with stable thyrotropin levels within 3 months after the thyrotropin value fell into the normal range.

A total of 17,598 patients were included (69.0% female; 74.0% White; mean [SD] age, 55.1 [16.0] years), of whom 15 299 filled generic and 2299 filled brand-name levothyroxine prescriptions during the study period. Among 4570 propensity score–matched patients (mean [SD] age, 50.3 [13.8] years; 3457 [75.6%] female; 3510 [76.8%] White), the proportion with normal thyrotropin levels within 3 months of filling levothyroxine prescriptions was similar for patients who received generic vs brand-name levothyroxine (1722 [75.4%; 95% CI, 71.9%-79.0%] vs 1757 [76.9%; 95% CI, 73.4%-80.6%]; *P* = .23), as was the proportion with markedly abnormal levels (94 [4.1%; 95% CI, 3.4%-5.0%] vs 88 [3.9%; 95% CI, 3.1%-4.7%]; *P* = .65). Among 1034 propensity score–matched patients who achieved a normal thyrotropin value within 3 months of initiation of levothyroxine, the proportion maintaining subsequent normal thyrotropin levels during the next 3 months was similar for patients receiving generic vs brand-name levothyroxine (427 [82.6%] vs 433 [83.8%]; *P* = .62).

Initiation of generic vs brand-name levothyroxine formulations was associated with similar rates of normal and stable thyrotropin levels. These results suggest that generic levothyroxine as initial therapy for mild thyroid dysfunction is as effective as brand-name levothyroxine.

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