LEVOTHYROXINE PRODUCTS STEP THERAPY POLICY

POLICY: Levothyroxine Products Step Therapy Policy
- Ermeza™ (levothyroxine sodium 30 mcg/mL solution – Mylan)
- Levothyroxine sodium tablets (generics)
- Tirosint®-SOL (levothyroxine sodium solution [various strengths] – IBSA Pharma)
- Thyquidity™ (levothyroxine sodium 20 mcg/mL solution – Azurity)

REVIEW DATE: 03/20/2024

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

All of the products contain levothyroxine sodium and are indicated for the following uses[1-4]:
- **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.

Labeling for all of the products additionally contains the following 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.

All of the products can be used in pediatric patients, including newborns (0 to 3 months of age).[1-4] Ermeza, Thyquidity, and Tirosint-SOL were approved under the 505(b)(2) pathway and relied on efficacy data from previously approved levothyroxine products.[5-7] No new clinical efficacy studies were undertaken with any of the products.[2-4] The labeling for Ermeza states that the product may have a different concentration from other levothyroxine oral solution products and to consider the total dosage in terms of mcg and not volume when converting between products.[2] All levothyroxine products are dosed based on the patient's weight (e.g., 1.6 mcg/kg/day for adults with hypothyroidism).[1-4] Table 1 shows the availability of each levothyroxine solution.

Table 1. Availability of Levothyroxine Solutions.[2-4]

Product	Strengths Available	Package Sizes	Dosing
Ermeza™ (levothyroxine sodium oral solution)	150 mcg/5 mL (30 mcg/mL)	90 mL or 180 mL bottles	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.
Thyquidity™ (levothyroxine sodium oral solution)	100 mcg/5 mL (20 mcg/mL)	100 mL bottle	Product labeling states the pharmacy will provide a calibrated oral syringe to accurately measure the prescribed dose.
Tirosint®-SOL (levothyroxine sodium oral solution)	13, 25, 37.5, 44, 50, 62.5, 75, 88, 100, 112, 125, 137, 150, 175, 200 mcg/mL	Box of 30 unit-dose ampules and box of 5 unit-dose ampules	Squeeze contents of one single unit-dose ampule into a glass or cup containing water. Stir and drink all immediately OR squeeze ampule directly into mouth or onto a spoon (without water).

Guidelines

The American Thyroid Association guidelines for the treatment of hypothyroidism (2014) state that levothyroxine has been considered the standard of care for this condition for many years.[8] These guidelines do not address levothyroxine solutions.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. Approval for a Step 3 Product may be authorized if the patient has tried a Step 1 Product and a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product or a Step 3 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Step 1: generic levothyroxine tablets

Step 2: Ermeza solution

Step 3: Thyquidity solution, Tirosint-SOL

Levothyroxine product(s) is(are) covered as medically necessary when the following step therapy criteria is(are) met. Any other exception is considered not medically necessary.

CRITERIA

1. If the patient has tried one Step 1 Product, approve the Step 2 Product (Ermeza solution).
Note: If the patient has tried brand Synthroid (levothyroxine sodium tablet) or another brand of levothyroxine tablets, such as Levoxyl (levothyroxine sodium tablet), this would satisfy the criterion.

2. Approve the Step 2 Product (Ermeza solution) if the patient is unable to swallow or has difficulty swallowing tablets.

3. Approve either Step 3 Products (Thyquidity Solution or Tirosint-SOL) if the patient meets BOTH of the following criteria (A and B):
A) Patient meets one of the following criteria (i or ii):
i. Patient has tried one Step 1 Product; OR
Note: If the patient has tried brand Synthroid (levothyroxine sodium tablet) or another brand of levothyroxine tablets, such as Levoxyl (levothyroxine sodium tablet), this would satisfy the criteria for the Step 1 product.
ii. Patient is unable to swallow or has difficulty swallowing tablets; AND
B) Patient has tried the Step 2 Product (Ermeza solution).

REFERENCES

1. Levothyroxine sodium tablets [prescribing information]. Bridgewater, NJ: Amneal; September 2023.
2. Ermeza™ (levothyroxine sodium solution) [prescribing information]. Morgantown, WV: Mylan Specialty; April 2022.
3. Thyquidity™ (levothyroxine sodium solution) [prescribing information]. Woburn, MA: Azurity; February 2023.
4. Tirosint®-SOL (levothyroxine sodium solution) [prescribing information]. Parsippany, NJ: IBSA Pharma; November 2023.
5. FDA. Drugs@FDA. Ermeza approval letter. May 2022. Available at: Ermeza (levothyroxine sodium) oral solution. (fda.gov). Accessed on March 11, 2024.
6. FDA. Drugs@FDA. Thyquidity approval letter. November 2020. Available at: Thyquidity (levothyroxine sodium) oral solution (fda.gov). Accessed on March 11, 2024.
7. FDA. Drugs@FDA. Tirosint-SOL approval letter. December 2016. Available at: Tirosint-SOL (levothyroxine sodium oral solution) (fda.gov). Accessed on March 11, 2024.

8. Jonklaas J, Bianco AC, Bauer AJ, et al. Guidelines for the treatment of hypothyroidism: prepared by the American Thyroid Association task force on thyroid hormone replacement. *Thyroid.* 2014;24(12):1670-751.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	03/29/2023
Annual Revision	No criteria changes.	03/20/2024