

Thyrogen (thyrotropin alfa)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Surgery is the primary treatment for differentiated thyroid cancer. High-risk patients may require radioactive iodine therapy to destroy any remaining thyroid tissue. TSH suppression is necessary for patients with thyroid cancer since their cancer cells are sensitive to TSH. Long-term thyroid hormone supplements are provided to patients who have undergone partial or total thyroidectomy and/or radioactive iodine treatment to maintain metabolism and suppress TSH levels.

Ongoing monitoring for recurrence and metastasis in patients with a history of thyroid cancer involves regular check-ups, thyroglobulin levels, radioiodine scans, and adequate TSH suppression. A high TSH level is required for sensitive thyroglobulin testing and radioiodine imaging to detect residual thyroid tissue or metastatic cancer. Patients need to stop taking hormone supplements for two to six weeks to raise TSH before testing, which can lead to hypothyroidism symptoms like fatigue, weight gain, constipation, mental sluggishness, tiredness, dry skin, depression, and other negative effects.

Thyrogen (thyrotropin alfa), a recombinant TSH form, is utilized as an adjunctive diagnostic tool for serum thyroglobulin testing and radioiodine imaging in well-differentiated thyroid cancer patients, preventing hypothyroidism symptoms due to hormone supplement withdrawal. The FDA approved Thyrogen based on two phase III clinical trial results, indicating that it significantly improved thyroglobulin testing sensitivity in patients on thyroid hormone therapy. However, there is still a risk of missing a thyroid cancer diagnosis or underestimating the disease extent when using Thyrogen-stimulated thyroglobulin testing.

Thyrogen also aids in radioiodine ablation of residual thyroid tissue after surgery for differentiated thyroid carcinoma, as an alternative to thyroid hormone withdrawal. Low-dose radioiodine combined with Thyrogen has proven to be as effective as high-dose radioiodine, with fewer adverse events. Thyrogen has been used to treat benign multi-nodular non-toxic goiter as well.

The Plan considers Thyrogen medically necessary in the following cases:

1. Thyroid cancer evaluation: Thyrogen is used to evaluate patients who have undergone total or near-total thyroidectomy for well-differentiated thyroid cancer, stimulating residual thyroid tissue and facilitating the detection of remaining cancer tissue via a radioactive iodine scan.
2. Radioactive iodine treatment preparation: Thyrogen prepares patients for radioactive iodine treatment for thyroid cancer, remnant thyroid tissue ablation or non-toxic multinodular goiter.
3. Thyroid cancer patient monitoring: Thyrogen is employed to monitor treatment response in thyroid cancer patients. An increase in serum thyroglobulin levels, a protein produced by the thyroid, may indicate residual or recurrent cancer.

Definitions

“Ablation” is a medical procedure that involves the removal or destruction of tissue, often to treat abnormal or diseased tissue. In the context of thyroid cancer, radioactive iodine ablation is a common treatment to destroy any remaining thyroid tissue after a thyroidectomy.

“Adjunctive” refers to something that is supplementary or complementary to the primary treatment. It is typically used in conjunction with the main therapy to enhance its effectiveness or to address additional aspects of a condition.

“Hypothyroidism” is a condition in which the thyroid gland does not produce enough thyroid hormones. This can lead to various symptoms, including fatigue, weight gain, and sensitivity to cold.

Hypothyroidism can be caused by several factors, such as iodine deficiency, autoimmune diseases, or treatments for hyperthyroidism.

“Metastatic” refers to the process by which cancer cells spread from the primary tumor site to other parts of the body through the bloodstream or lymphatic system. In the context of cancer, metastatic disease indicates that cancer has spread from its original location to one or more distant sites.

“Radioiodine imaging” is a diagnostic imaging test used to evaluate the presence, location, and extent of thyroid cancer. It involves taking a small amount of radioactive iodine by mouth, which is taken up by the thyroid gland and can be detected by a special camera.

“Sensitivity” refers to the accuracy of a diagnostic test in correctly identifying individuals with a specific disease or condition. A test with high sensitivity is effective at detecting true positive cases and minimizing false negatives.

“Serum thyroglobulin (Tg) testing” is a blood test used to check the level of thyroglobulin in the blood. Thyroglobulin is a protein produced by the thyroid gland, and its level in the blood can be used to monitor thyroid cancer.

“Thyroid hormone withdrawal” is a process in which thyroid hormone supplements are temporarily discontinued in order to increase the level of thyroid stimulating hormone (TSH) in the blood, which can improve the accuracy of diagnostic tests for thyroid cancer. However, this process can be uncomfortable and can cause side effects, and is therefore not suitable for all patients.

“Thyroidectomy” is a surgical procedure in which all or part of the thyroid gland is removed. This surgery is commonly performed to treat thyroid cancer, large goiters, or hyperthyroidism.

“Well-differentiated thyroid cancer” refers to a type of thyroid cancer that has a more favorable prognosis and is usually less aggressive than other forms. The cancer cells in well-differentiated thyroid cancer closely resemble normal thyroid cells. The two most common types are papillary and follicular thyroid cancer.

Medical Necessity Criteria for Authorization

The Plan considers Thyrogen (thyrotropin alfa) medically necessary when **ALL** of the following criteria are met:

1. Prescribed by or in consultation with an endocrinologist, thyroid surgeon, radiation oncologist, nuclear medicine physician or provider knowledgeable in the management of patients with thyroid cancer; **AND**
2. The member is 18 years of age or older; **AND**
3. The member has a diagnosis of well-differentiated thyroid cancer; **AND**
4. Thyrogen (thyrotropin alfa) is being used for **ONE** of the following:
 - a. as an adjunctive diagnostic tool for serum thyroglobulin (Tg) testing **AND** the member has documented evidence of **BOTH** of the following:
 - i. have previously undergone thyroidectomy; **and**
 - ii. Inability to undergo thyroid hormone withdrawal due to **ANY** of the following reasons:
 1. history of severe hypothyroid symptoms or complications during previous thyroid hormone withdrawal, putting the member at risk for significant morbidity if withdrawal is repeated; **or**
 2. comorbidities, such as cardiovascular disease, that would increase the risk of complications during thyroid hormone withdrawal; **or**
 3. member has demonstrated an inability to achieve adequate TSH elevation during previous thyroid hormone withdrawal attempts, leading to suboptimal diagnostic sensitivity; **or**
 4. psychiatric or cognitive conditions that could be exacerbated by thyroid hormone withdrawal, potentially causing significant distress or harm; **or**
 5. the provider considers the use of a less sensitive test acceptable because the member is unwilling to undergo thyroid hormone withdrawal testing or will only undergo a serum Tg test without hormone supplement withdrawal; **or**
 - b. as an adjunctive treatment for radioiodine ablation of thyroid tissue remnants **AND** the member has documented evidence of **BOTH** of the following:
 - i. local neck and/or distal metastatic thyroid cancer; **and**
 - ii. have undergone a near-total or total thyroidectomy; **or**
 - c. as an adjunct to radioiodine ablation for the treatment of non-toxic multi-nodular goiter; **AND**
5. Prescribed dose of Thyrogen does not exceed an initial 0.9 mg intramuscular (IM) injection, followed by a second 0.9 mg IM injection 24 hours later.

If the above prior authorization criteria is met, Thyrogen (thyrotropin alfa) will be approved for up to 2 injections (i.e., one carton, or two 0.9 mg single-dose vials) for 3 months.

Experimental or Investigational / Not Medically Necessary

Thyrogen (thyrotropin alfa) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven.

Applicable Billing Codes (HCPCS/CPT Codes)

Service(s) name	
CPT/HCPCS Codes considered medically necessary if criteria are met:	
<i>Code</i>	<i>Description</i>
78012	Thyroid uptake, single or multiple quantitative measurement(s) (including stimulation, suppression, or discharge, when performed)
78013	Thyroid imaging (including vascular flow, when performed);
78014	Thyroid imaging (including vascular flow, when performed); with single or multiple uptake(s) quantitative measurement(s) (including stimulation, suppression, or discharge, when performed)
78015	Thyroid carcinoma metastases imaging; limited area (eg, neck and chest only)
78016	Thyroid carcinoma metastases imaging; with additional studies (eg, urinary recovery)
78018	Thyroid carcinoma metastases imaging; whole body
78020	Thyroid carcinoma metastases uptake (List separately in addition to code for primary procedure)
80418	Combined rapid anterior pituitary evaluation panel
80438	Thyrotropin releasing hormone (TRH) stimulation panel; 1 hour
80439	Thyrotropin releasing hormone (TRH) stimulation panel; 2 hour
84432	Thyroglobulin
84443	Thyroid stimulating hormone (TSH)
96372	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular
J3240	Injection, thyrotropin alfa, 0.9 mg, provided in 1.1 mg vial
ICD-10 codes considered medically necessary if criteria are met:	

<i>Code</i>	<i>Description</i>
C73	Malignant neoplasm of the thyroid gland
E04.2	Nontoxic multinodular goiter [adjunct to radioiodine ablation]
Z85.850	Personal history of malignant neoplasm of thyroid

References

1. Bonnema SJ, Nielsen VE, Boel-Jørgensen H, et al. Improvement of goiter volume reduction after 0.3 mg recombinant human thyrotropin-stimulated radioiodine therapy in patients with a very large goiter: a double-blinded, randomized trial. *J Clin Endocrinol Metab* 2007; 92:3424.
2. Bonnema SJ, Nielsen VE, Boel-Jørgensen H, et al. Recombinant human thyrotropin-stimulated radioiodine therapy of large nodular goiters facilitates tracheal decompression and improves inspiration. *J Clin Endocrinol Metab* 2008; 93:3981.
3. Fast S, Hegedüs L, Grupe P, et al. Recombinant human thyrotropin-stimulated radioiodine therapy of nodular goiter allows major reduction of the radiation burden with retained efficacy. *J Clin Endocrinol Metab* 2010; 95:3719.
4. Fast S, Nielsen VE, Grupe P, et al. Prestimulation with recombinant human thyrotropin (rhTSH) improves the long-term outcome of radioiodine therapy for multinodular nontoxic goiter. *J Clin Endocrinol Metab* 2012; 97:2653.
5. Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association guidelines task force on thyroid nodules and differentiated thyroid cancer. *Thyroid*. 2016;26(1):1-133. doi:10.1089/thy.2015.0020
6. Lee YY, Tam KW, Lin YM, et al. Recombinant human thyrotropin before (131)I therapy in patients with nodular goitre: a meta-analysis of randomized controlled trials. *Clin Endocrinol (Oxf)* 2015; 83:702.
7. Mallick U, Harmer C, Yap B, et al, "Ablation With Low-Dose Radioiodine and Thyrotropin Alfa in Thyroid Cancer," *N Engl J Med*, 2012, 366(18):1674-85.
8. Pacini F, Ladenson PW, Schlumberger M, et al, "Radioiodine Ablation of Thyroid Remnants After Preparation With Recombinant Human Thyrotropin in Differentiated Thyroid Carcinoma: Results of an International, Randomized, Controlled Study," *J Clin Endocrinol Metab*, 2006, 91(3):926-32.
9. Schlumberger M, Catargi B, Borget I, et a, "Strategies of Radioiodine Ablation In Patients With Low-Risk Thyroid Cancer," *N Engl J Med*, 2012, 366(18):1663-73.
10. Thyrogen (thyrotropin alfa) [prescribing information]. Cambridge, MA: Genzyme Corporation; March 2020.

Clinical Guideline Revision / History Information

Original Date: 06/01/2023

Reviewed/Revised: