Oscar Clinical Guideline: Thyrogen (thyrotropin alfa) (PG140, Ver. 4)

Thyrogen (thyrotropin alfa)

Summary

Surgery is the primary treatment for differentiated thyroid cancer. High-risk individuals may require radioactive iodine therapy to destroy any remaining thyroid tissue. Thyroid stimulating hormone (TSH) suppression is necessary for those with thyroid cancer since their cancer cells are sensitive to TSH. Long-term thyroid hormone supplements are provided to those 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 those with a history of thyroid cancer involves regular check-ups, thyroglobulin (Tg) levels, radioiodine scans, and adequate TSH suppression. However, a high TSH level is required for sensitive thyroglobulin testing and radioiodine imaging to detect residual thyroid tissue or metastatic cancer. There are two main methods to increasing TSH levels: thyroid hormone withdrawal or administration of recombinant human TSH (i.e., thryotropin alfa [Thryrogen]). For adequate hormone withdrawal, individuals 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. Thus, the preferred methodology is administering a recombinant human TSH (rhTSH) product.

Thyrogen (thyrotropin alfa), a rhTSH form, is utilized as an adjunctive diagnostic tool for serum thyroglobulin testing and radioiodine imaging in well-differentiated thyroid cancer, 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 those 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 is also indicated for use as an adjunctive treatment for radioiodine ablation of residual thyroid tissue after surgery for differentiated thyroid carcinoma (in those who have undergone near-total or total thyroidectomy), 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 goiters as well.

The Plan considers Thyrogen medically necessary in the following cases:

1. Thyroid cancer evaluation: Thyrogen is used to evaluate those 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 individuals for radioactive iodine treatment for thyroid cancer, remnant thyroid tissue ablation or non-toxic multinodular goiter.
3. Thyroid cancer monitoring: Thyrogen is employed to monitor treatment response in thyroid cancer. 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.

"Documentation" refers to written information, including but not limited to:

- Up-to-date chart notes, relevant test results, and/or relevant imaging reports to support diagnoses; or
- Prescription claims records, and/or prescription receipts to support prior trials of formulary alternatives.

"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 individuals.

"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.

"[s]" indicates state mandates may apply.

Clinical Indications

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Well-differentiated Thyroid Cancer or Non-toxic Multinodular Goiter

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 those with thyroid cancer; *AND*
2. The member is 18 years of age or older; *AND*
3. The member has a diagnosis of ONE (1) of the following:
    a. Well-differentiated thyroid cancer; *or*
    b. Non-toxic multinodular goiter*; AND*
4. Thyrogen (thyrotropin alfa) is being used for ONE (1) of the following:
    a. As an adjunctive diagnostic and monitoring tool for serum thyroglobulin (Tg) testing AND the member has documented evidence of BOTH of the following[s]:
        i. Have previously undergone thyroidectomy; *and*
        ii. The member has a documented inability to undergo thyroid hormone withdrawal*; or*
    b. As an adjunct 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[s]; *or*
    c. As an adjunct to radioiodine ablation for the treatment of non-toxic multi-nodular goiter; *AND*
5. Thyrogen (thyrotropin alfa) is being prescribed at a dose and frequency that is within FDA approved labeling OR is supported by compendia or evidence-based published dosing guidelines for the requested indication.

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 up to 3 months.[s]

Experimental or Investigational or Unproven / Not Medically Necessary[s]

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, unproven, or not medically necessary.

Applicable Billing Codes

Table 1	
CPT/HCPCS Codes for Well-differentiated thyroid cancer or Non-toxic multinodular goiter considered medically necessary if criteria are met:	
Code	*Description*
96372	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular
J3240	Injection, thyrotropin alpha, 0.9 mg, provided in 1.1 mg vial

Table 2	
ICD-10 diagnostic codes considered medically necessary for Well-differentiated thyroid cancer or Non-toxic multinodular goiter with Table 1 (CPT/HCPCS) codes if criteria are met:	
Code	*Description*
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

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