Reference number(s)
4795-A

STANDARD MEDICARE PART B MANAGEMENT

THYROGEN (thyrotropin alfa injection)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Thyrogen is indicated for use as an adjunctive diagnostic tool for serum thyroglobulin (Tg) testing with or without radioiodine imaging in the follow-up of patients with well-differentiated thyroid cancer who have previously undergone thyroidectomy.
2. Thyrogen is indicated for use as an adjunctive treatment for radioiodine ablation of thyroid tissue remnants in patients who have undergone a near-total or total thyroidectomy for well-differentiated thyroid cancer and who do not have evidence of distant metastatic thyroid cancer.

B. Compendial Uses
1. Adjunct treatment for multinodular goiter
2. Adjunct treatment for thyroid cancer
3. Adjunct treatment for brain metastases

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. CRITERIA FOR INITIAL APPROVAL

A. Adjunctive diagnostic tool for well-differentiated thyroid cancer
Authorization of 1 month may be granted for use as an adjunctive diagnostic tool for serum thyroglobulin (Tg) testing when ALL of the following criteria are met:
1. Member is receiving follow-up for well-differentiated thyroid cancer
2. Member has previously undergone a thyroidectomy

B. Adjunct treatment for thyroid remnant ablation
Authorization of 1 month may be granted as an adjunctive treatment for radioiodine ablation of thyroid tissue remnants when ALL of the following criteria are met:
1. Member has received a near-total or total thyroidectomy for well-differentiated thyroid cancer
2. Member does not show evidence of distant metastatic thyroid cancer

C. Adjunct treatment for multinodular goiter
Authorization of 1 month may be granted when used for adjunct treatment prior to radioiodine treatment of large multinodular goiters.

D. Adjunct treatment for thyroid cancer
Authorization of 1 month may be granted when used as adjunct treatment for the stimulation of radioiodine uptake in the treatment of patients with differentiated thyroid carcinoma.

E. Adjunct treatment for brain metastases
Authorization of 1 month may be granted when used as adjunct treatment for the stimulation of radioiodine uptake for the treatment of brain metastases from thyroid cancer.

III. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:
1. The prescribing information for Thyrogen.
2. The available compendium
    a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    b. Micromedex DrugDex
    c. American Hospital Formulary Service- Drug Information (AHFS-DI)
    d. Lexi-Drugs
    e. Clinical Pharmacology
3. NCCN Guideline: Thyroid carcinoma

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Thyrogen are covered in addition to the following:
1. Adjunct treatment for multinodular goiter
2. Adjunct treatment for differentiated thyroid carcinoma
3. Adjunct treatment for brain metastases

IV. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using Thyrogen prior to radioiodine treatment of large multinodular goiters can be found in a prospective, controlled trial by Silva et al. The administration of recombinant human thyrotropin (rhTSH) prior to radioiodine therapy in patients with large, multinodular goiters has increased the efficacy of radioiodine uptake resulting in larger reductions in goiter volume as compared with radioiodine therapy alone. In a prospective, controlled trial (n=34), patients with very large, multinodular goiters (mean initial volume, 210 to 281 mL; range, 80 to 728 mL) with low or suppressed serum TSH levels received radioiodine treatment alone (mean iodine-131 dose, 3337 to 3552 megabecquerel) or were given a single intramuscular dose of rhTSH (0.45 mg) 24 hours prior to radioiodine treatment. All patients were also placed on a low-iodine diet. Serum thyroglobulin levels rose to significantly higher levels in patients pretreated with rhTSH as compared with patients who received radioiodine therapy only (p less than 0.05 at 24, 48, and 72 hours). Thyroid volume was significantly reduced in both treatment groups, however, a significantly greater mean individual reduction of thyroid volume was observed at 1 year in patients who received adjunctive rhTSH as compared with patients who received radioiodine therapy alone (57.8% vs 39.7%, respectively; p less than 0.05).

Support for using Thyrogen as adjunct treatment for differentiated thyroid carcinoma can be found in a case report by Rudavsky et al. Intramuscular administration of 0.9 mg daily for two days, followed by a large oral dose of 131-iodine (515 mCi), led to significant uptake in multiple metastatic lesions and clinical remission. With this treatment, it may be possible to continue thyroid suppression therapy and thereby avoid associated hypothyroid morbidity. The NCCN Guideline for thyroid carcinoma also supports using Thyrogen in elderly patients for whom prolonged hypothyroidism may be risky.

Support for using Thyrogen as adjunct treatment for brain metastases can be found in a case report by Chiu et al. Recombinant human thyrotropin safely stimulated radioiodine uptake for treatment of brain metastases from thyroid carcinoma. However, survival benefit was not obtained. Clinical studies are needed to further define the role of recombinant human TSH in treatment.

V. REFERENCES

1. Thyrogen [package insert]. Cambridge, MA: Genzyme Corporation; March 2020.
2. IBM Micromedex® DRUGDEX ® (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at https://www.micromedexsolutions.com. (Accessed: August 9, 2022)
3. Silva MNC, Rubio IGS, Romao R, et al: Administration of a single dose of recombinant human thyrotropin enhances the efficacy of radioiodine treatment of large compressive multinodular goiter. Clin Endocrinol 2004; 60:300-308.
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Thyroid Carcinoma. Version 3.2023. Accessed August 3, 2023. https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf
5. Rudavsky AZ & Freeman LM: Treatment of scan-negative, thyroglobulin-positive metastatic thyroid cancer using radioiodine 131-I and recombinant human thyroid stimulation hormone. J Clin Endocrinol Metabolism 1997; 82:11-14.
6. Chiu AC, Delpassand ES, & Sherman SI: Prognosis and treatment of brain metastases in thyroid carcinoma. J Clin Endocrinol Metab 1997; 82(11):3637-3642.