Medical Policy

**Section**

Prescription Drug

**Original Policy Date**

12:2013

**Last Review Status/Date**

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**Issue**

12:2013

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**Description**

Surgery is the cornerstone of management of patients with differentiated thyroid cancer. As an adjunct to this treatment, some high-risk patients may need to undergo radioactive iodine treatment, further destroying normal thyroid tissue. All patients with tumors arising from follicular epithelium require TSH suppression since differentiated thyroid cancers contain membrane receptors responsive to TSH. Long-term thyroid hormone supplements are used to maintain metabolism in patients who have had partial or total thyroidectomy and/or radioactive iodine treatment and to suppress endogenous levels of TSH.

Management of patients with a history of thyroid carcinoma requires continuing evaluation to monitor cancer recurrence and metastatic disease by periodic physical examinations, thyroglobulin levels, radiiodine scans, and assurance of appropriate TSH suppression. A high level of TSH in a patient's bloodstream is necessary to achieve optimal sensitivity of serum thyroglobulin testing and in order for radiiodine imaging to detect remnant thyroid tissue or metastatic disease. In order to accomplish this, patients must stop taking their hormone supplements for two to six weeks prior to testing. This thyroid hormone withdrawal causes patients to experience symptoms of hypothyroidism -- fatigue, weight gain, constipation, mental dullness, lethargy, depression, and other adverse reactions.

On December 1, 1998, the FDA granted marketing approval for Thyrogen (thyrotropin alfa) for use as 'an adjunctive diagnostic tool for serum thyroglobulin testing with or without radiiodine imaging in the follow-up of patients with well-differentiated thyroid cancer.' Thyrogen, a recombinant form of TSH, provides an external source of TSH and allows thyroid cancer patients to avoid hormone withdrawal and its debilitating effects while undergoing diagnostic testing.

The FDA made its decision based on review of two phase III clinical trials which were conducted on 358 patients with well-differentiated thyroid cancer to compare 48-hour radiiodine whole body scans obtained after Thyrogen to whole body scans after thyroid hormone withdrawal. One of these trials also compared thyroglobulin levels obtained after Thyrogen to those on thyroid hormone suppression therapy, and to those after thyroid hormone withdrawal. Across the two clinical studies, Thyrogen was shown to significantly enhance the sensitivity of thyroglobulin testing in patients maintained on thyroid hormone therapy. The combination of a Thyrogen-stimulated scan and a serum thyroglobulin test did detect all patients with metastatic disease, although not as sensitive as combination testing performed after patients were...
withdrawn from thyroid hormone supplements. The Thyrogen-stimulated scan failed to detect remnant and/or cancer localized to the thyroid bed in 16% (20/124) of patients in whom it was detected by a scan after thyroid hormone withdrawal. In addition, the Thyrogen scan failed to detect metastatic disease in 24% (9/38) of patients in whom it was detected by a scan after thyroid hormone withdrawal. Based on these studies, one can conclude that even when Thyrogen-stimulated thyroglobulin testing is performed in combination with radioiodine imaging, there remains a meaningful risk of missing a diagnosis of thyroid cancer or of underestimating the extent of disease.

Recombinant human thyrotropin has also been demonstrated to be useful to facilitate radioiodine ablation of remnant thyroid tissue after surgery for differentiated thyroid carcinoma, as an alternative to thyroid hormone withdrawal. After surgery for differentiated thyroid carcinoma, many patients are treated with radioiodine to ablate remnant thyroid tissue. This procedure is most commonly performed with the patient in the hypothyroid state to promote endogenous TSH stimulation to optimize radioiodine uptake by remnant thyroid tissue. However, thyroid hormone withdrawal is associated with hypothyroid symptoms and impaired quality of life. Pacini, et al. (2006) reported the results of a randomized controlled clinical trial to compare recombinant human thyrotropin to prepare patients on thyroid hormone therapy to ablate remnant thyroid tissue with radioiodine, compared with conventional remnant ablation preformed in the hypothyroid state. The investigators found comparable remnant ablation rates by administering recombinant human thyrotropin or by withholding thyroid hormone. Successful thyroid remnant ablation was achieved by 23 of 24 patients (96 percent) treated with recombinant human thyrotropin, compared to 18 of 21 (86 percent) patients treated in the hypothyroid state (p = 0.23). The investigators reported that subjects treated with recombinant human thyrotropin had a significantly higher quality of life during treatment than subjects treated in the hypothyroid state. The investigators reported that subjects treated with recombinant human thyrotropin also had a significantly lower radiation exposure to the blood than patients treated in the hypothyroid state.

Policy

Thyrogen (thyrotropin alfa) is considered medically necessary for the following patients with a history of differentiated thyroid carcinoma:

- For thyroglobulin (Tg) testing and radioiodine imaging in place of thyroid hormone withdrawal for any of the following:
  - Patients who would otherwise be examined solely with a serum thyroglobulin test without undergoing hormone supplement withdrawal; or
  - Patients with an undetectable Tg on thyroid hormone suppressive therapy to exclude the diagnosis of residual or recurrent thyroid cancer; or
  - Patients requiring serum Tg testing and radioiodine imaging who are unwilling to undergo thyroid hormone withdrawal testing and whose treating physician believes that use of a less sensitive test is justified; or
  - Patients who are either unable to mount an adequate endogenous thyroid stimulating hormone (TSH) response to thyroid hormone withdrawal; or
  - Patients in whom withdrawal from hormone supplement is contraindicated for medical reasons.
To facilitate radioiodine ablation of remnant thyroid tissue after surgery for differentiated thyroid carcinoma, as an alternative to thyroid hormone withdrawal.

Thyrogen is considered **investigational** for all other indications.

Note: Periodic thyroid hormone withdrawal Tg testing, with or without radioiodine imaging, still remains the standard diagnostic modality to assess the presence, location and extent of thyroid cancer in persons who have undergone surgery or radioactive iodine treatment.

References:


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<th>Codes</th>
<th>Number</th>
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<tbody>
<tr>
<td>HCPCS</td>
<td>J3240</td>
<td>Injection, thyrotrpoin alpha, 0.9 mg, provided in 1.1 mg vial</td>
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