IMPORTANT PRESCRIBING INFORMATION FOR THYROGEN® (thyrotropin alfa for injection)

Subject: Potential for exposure to trace amounts of vancomycin HCl in Thyrogen.

Dear Health Care Provider,

Genzyme Corporation is issuing an important safety information letter to alert Health Care Providers (HCPs) to the potential for exposure to trace amounts of vancomycin hydrochloride (HCl) in patients administered Thyrogen.

Background: Vancomycin HCl is filled at the same third party manufacturing facility where Thyrogen is filled. An investigation by Genzyme identified the presence of vancomycin HCl in some lots. Analytical testing revealed the presence of trace amounts of vancomycin HCl in some of the Thyrogen lots from lot numbers E1089 to E4023. The amount of vancomycin HCl is estimated to represent less than 1/100,000 of the vancomycin HCl therapeutic dose.

Safety risk: While it is not known if the trace levels of vancomycin HCl can cause an allergic reaction among patients with a known hypersensitivity to the antibiotic vancomycin HCl, Thyrogen should not be administered to these patients.

Guidance for Prescriber: Patients should be questioned about known hypersensitivity to vancomycin HCl. Thyrogen should not be administered if a history of hypersensitivity to vancomycin HCl is identified. Thyroxine withdrawal is an alternative method for preparing patients for diagnostic radioiodine imaging or treatment.

HCPs and patients are encouraged to report adverse events in patients administered Thyrogen or quality problems with the product to Genzyme 1-800-745-4447 (option 2).

Adverse reactions or quality problems experienced with the use of this product may be reported to the FDA’s MedWatch Adverse Event Reporting program online, by regular mail, or by fax.

- Online: [www.fda.gov/medwatch/report.htm](http://www.fda.gov/medwatch/report.htm)

Please see accompanying full Prescribing Information.

THY-US-P468-1214
• **Regular Mail**: Use postage-paid, pre-addressed Form FDA 3500 available at: [www.fda.gov/MedWatch/getforms.htm](http://www.fda.gov/MedWatch/getforms.htm). Mail to the address provided on the pre-addressed form.

• **Fax**: 1-800-FDA-0178

This letter is being issued with the knowledge of the U.S. Food and Drug Administration.

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US Medical Affairs

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Please see accompanying full Prescribing Information.
FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Adjunctive Diagnostic Tool for Serum Thyroglobulin Testing in Well Differentiated Thyroid Cancer

Thyrotron® is indicated for an adjunctive diagnostic tool for serum thyrotropin (TSH) testing in patients who have undergone thyroidectomy and who have residual or recurrent thyroid disease with serum thyroglobulin (Tg) levels >2 ng/mL and who have had treatment with radioactive iodine (RAI).

1.2 Ablation: Pretreatment with glucocorticoids should be considered for patients in whom tumor expansion may compromise the organ(s) of TSH clearance in man have not been identified, but studies of pituitary-derived TSH suggest the involvement of multiple hypothalamic-pituitary axis.

1.3 Imaging in the Follow-up of Patients with Well-Differentiated Thyroid Cancer

In clinical trials, patients who had undergone near-total thyroidectomy and had a mean age of 48.1 years. In 1.2 and 1.3, thyroid cancer outcomes would be equivalent after use of THYROGEN or use of thyroid hormone withdrawal and subsequent remnant ablation.

1.4 Calcium Administration

1.5 Pregnancy

1.6 Nursing Mothers

In clinical trials of THYROGEN, three patients experienced symptoms after receiving THYROGEN doses higher than those recommended. Two patients had nausea after a 2.7 mg IM dose (3 times the recommended dose), which resulted in prolonged elevation of TSH levels.

1.7 Children

Two prospective, randomized phase 3 clinical trials were conducted in patients with well-differentiated thyroid cancer (AJCC/TNM Stage I 50%, Stage II 20%, Stage III 20%, Stage IV 9%). The amount of Thyroglobulin was monitored in the majority of patients. In studies with functional sensitivity of 2.5 ng/mL. Patients who were included in the Tg analysis were those who had <1% uptake in the thyroid bed and...
In anti-Tg antibody negative patients with thyroid remnant or cancer (as defined by a withdrawal Tg ≥ 2.5 ng/mL or a positive scan [after thyroid hormone withdrawal or after radioiodine therapy]), the THYROGEN Tg was determined. Patients in the THYROGEN group received THYROGEN 0.9 mg IM daily on 2 consecutive days and radioiodine was withheld until they became hypothyroid. Patients in both groups received 100 mCi 131I ± 20%. The mean radiation dose to blood was 360±105 MBq in the THYROGEN group and 303±75 MBq in the thyroid hormone withdrawal group. Radioiodine residence time in remnant tissue was 0.9±1.3 hours in the THYROGEN group and 1.4±1.1 hours in the thyroid hormone withdrawal group. It is unknown whether this difference in residence time would be of clinical benefit.

Patients who completed were followed up for a median duration of 3.7 years (range 3.4 to 4.4 years) following radioiodine administration. 图1展示了2组的阳性扫描结果。The major objective of the follow-up was to evaluate the status of the remnant gland (as assessed by using THYROGEN-simulated neck imaging). In the 105-day patients who completed, eighty patients received THYROGEN for remnant neck/whole body imaging and/or thyroidectomy. Only 43 patients had imaging. Patients were still considered to be successfully ablated if there was no visible thyroid bed uptake on THYROGEN or, if sc, or radia was < 0.1%. All patients from both original treatment groups who had scans found to be still to be alive at the 105-day. Patients who were very antibody negative, 16% (9/56) of patients in the former thyroid hormone withdrawal group and 16% (9/56) of patients in the latter THYROGEN group were successfully ablated as determined by neck imaging at 24 hours.

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