DRUG NAME: Thyrotropin alfa

SYNONYM(S): Recombinant Human Thyroid Stimulating Hormone (rh TSH), exogenous thyrotropin

COMMON TRADE NAME(S): THYROGEN®

CLASSIFICATION: Hormonal agent, noncytotoxic

Special pediatric considerations are noted when applicable, otherwise adult provisions apply.

MECHANISM OF ACTION:

Thyrotropin alfa is used as a diagnostic tool for serum thyroglobulin (Tg) testing with or without radioiodine imaging, in the follow-up of patients with well-differentiated thyroid cancer.[1] Thyrotropin alfa is a recombinant form of thyrotropin [also called thyroid stimulating hormone (TSH)]. Thyrotropin alfa binds to TSH receptor sites stimulating iodine uptake and synthesis and secretion of Tg.

Patients with well-differentiated thyroid cancer undergo surgery, with or without ablative radiotherapy.[2] They then receive thyroid hormone therapy.[3] Thyroid hormone therapy both prevents hypothyroidism and suppresses the secretion of TSH. TSH is suppressed because it can stimulate the growth of thyroid cancers.[4] Increases in Tg or iodine uptake would indicate residual thyroid tissue or thyroid cancer.[5]

The stimulation of residual thyroid tissue by elevating TSH levels is required for Tg testing and for radioiodine scanning. One way to increase endogenous TSH is the temporary withdrawal of thyroid hormone therapy.[3] However, withdrawal of thyroid hormone therapy results in symptomatic hypothyroidism.[6] The administration of thyrotropin alfa provides an alternative to thyroid hormone withdrawal. Patients who are found to have a thyrotropin alfa-stimulated TSH of < 2 ng/mL may not require an iodine or PET scan.[7,8]

PHARMACOKINETICS:

Oral Absorption	no information found	
Distribution	no information found	
	cross blood brain barrier?	no information found
	volume of distribution	no information found
	plasma protein binding	no information found
Metabolism	no information found	
	active metabolite(s)	no information found
	inactive metabolite(s)	no information found
Excretion	hepatic and renal	
	urine	yes
	feces	yes
	terminal half life	15-35 h
	clearance	no information found

Adapted from standard reference[1] unless specified otherwise.

USES:

Primary uses:
*Thyroid cancer, diagnostic

Other uses:
Thyroid cancer, ablative radiotherapy[9]

*Health Canada approved indication

SPECIAL PRECAUTIONS:

Contraindicated: In patients with a known hypersensitivity to natural or recombinant TSH or any components of the formulation.[1] Caution should be used when thyrotropin alfa is administered to patients who have been previously treated with bovine thyroid stimulation hormone especially where there has been a hypersensitivity reaction to either ***bovine or human TSH***. Note: Bovine TSH is not currently available in Canada.[10]

False negative results[1]: There is a risk of false negative results when using thyrotropin alfa-stimulated Tg testing. Thyroid hormone withdrawal Tg testing with radioiodine imaging remains the standard diagnostic tool for detecting the presence, location, and extent of thyroid cancer.

Carcinogenicity: has not been studied.[2]

Mutagenicity: Not mutagenic in the Ames test.[11]

Fertility: has not been studied.[11]

Pregnancy: FDA Pregnancy Category C.[2] Animal studies have shown fetal risks and there are no controlled studies in women. Thyrotropin alpha should be given only if potential benefit justifies the potential risk to the fetus.

Breastfeeding: It is not known if the drug is secreted into the breast milk.[1] Caution should be used when administering thyrotropin alfa to a nursing mother.[1]

Special populations: There is a potential risk for exacerbation of existing ***cardiac disease*** caused by thyrotropin alfa-induced hyperthyroidism when there is residual thyroid tissue.[11] The hyperthyroidism is due to a transient but significant rise in the thyroid hormones triiodothyronine (T_3) and/or thyroxine (T_4) after administration.[5] Thyrotropin alfa should not be given to patients with recent ***myocardial infarction.[11]*** Thyrotropin alfa should not be given to patients with ***hypopituitarism.[11]*** Patients with ***CNS metastases*** may experience pain and/or neurological symptoms after treatment due to local edema or focal hemorrhage.[1] Pre-treatment with corticosteroids should be considered for patients for whom local tumour expansion may compromise vital anatomic structures.[1]

SIDE EFFECTS:

The table includes adverse events that presented during drug treatment but may not necessarily have a causal relationship with the drug. Because clinical trials are conducted under very specific conditions, the adverse event rates observed may not reflect the rates observed in clinical practice. Adverse events are generally included if they were reported in more than 1% of patients in the product monograph or pivotal trials, and/or determined to be clinically important [7]. When placebo-controlled trials are available, adverse events are included if the incidence is $\geq$ 5% higher in the treatment group.

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
allergy/immunology	hypersensitivity reactions (<1%) increased risk with repeated administration[11]; urticaria, pruritis, flushing, and respiratory difficulties
cardiovascular (general)	***exacerbation of existing cardiac disease; due to transient hyperthyroidism***
constitutional symptoms	asthenia (3%)
dermatology/skin	*extravasation hazard: nonvesicant*
endocrine	transient increase in TSH levels
gastrointestinal	*emetogenic potential: rare*
	nausea (11%)

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
	vomiting (2%)
neurology	dizziness (2%)
	hemiplegia, hemiparesis (7% of the patients with CNS metastases)
	paresthesia (2%)
ocular/visual	acute visual loss; associated with local edema or hemorrhage at metastatic sites[2]
pain	headache (7%)
	pain (1%)
pulmonary	laryngeal edema; associated with local edema or hemorrhage at metastatic sites[2]
syndromes	flu-like syndrome (1%); chills, fever

Adapted from standard reference[1] unless specified otherwise.

INTERACTIONS[1]: Drug interaction studies have not been done.

SUPPLY AND STORAGE:

For basic information on the current brand used at the BC Cancer Agency, see Chemotherapy Preparation and Stability Chart in Appendix.

SOLUTION PREPARATION AND COMPATIBILITY:

For basic information on the current brand used at the BC Cancer Agency, see Chemotherapy Preparation and Stability Chart in Appendix.

PARENTERAL ADMINISTRATION:

BCCA administration guideline noted in ***bold***, ***italics***

Subcutaneous	no information found
Intramuscular[1]	***into the gluteal muscle***
Direct intravenous	no information found
Intermittent infusion	no information found
Continuous infusion	no information found
Intraperitoneal	no information found
Intrapleural	no information found
Intrathecal	no information found
Intra-arterial	no information found
Intravesical	no information found

DOSAGE GUIDELINES:

Refer to protocol by which patient is being treated.

Adults:

BCCA usual dose noted in ***bold, italics***

Intramuscular:	***0.9 mg IM q24h x 2 doses***[12]
	0.9 mg IM q72 h x 3 doses[2]
	if using radioiodine scan: radioiodine 24 h following the final thyrotropin alfa injection; perform scan 48 h after radioiodine (i.e., 72 h following the final thyrotropin injection)[12]
	if using PET scan: fluorodeoxyglucose (FDG) 24 h following the final thyrotropin alfa injection; perform scan on same day as FDG[12]
	serum Tg testing 72 h following the final thyrotropin alfa injection[2,12]
Concurrent radiation:	n/a
Dosage in renal failure:	no adjustment required
Dosage in hepatic failure:	no adjustment required
Dosage in dialysis:	no information found

Children:

safety and efficacy have not been established in patients below the age of 18 years[1]

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