Anthem

Clinical UM Guideline

Subject: Thyroid Testing
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Description

This document addresses laboratory testing of thyroid function. Thyroid function tests include serum testing for thyroid stimulating hormone (TSH) and levels of specific thyroid hormones; including total and free thyroxine, thyroid hormone (T3 or T4) uptake, and thyroid hormone binding ratio (THBR). Thyroid gland hormones regulate the metabolic rate, affecting all body functions.

Clinical Indications

Medically Necessary:

Thyroid function testing is considered **medically necessary** for individuals who meet any of the following indications:

- For evaluation of signs or symptoms consistent with thyroid disease; **or**
- To evaluate, assess, or monitor confirmed or suspected thyroid disease; **or**
- To evaluate thyroid function when there are risk factors for thyroid disease.

Not Medically Necessary:

The use of thyroid function tests are considered **not medically necessary** when the criteria listed above are not met, including as a screening test in the absence of risk factors.

Coding

The following codes for treatments and procedures applicable to this guideline are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services are Medically Necessary:

CPT	
84436	Thyroxine; total
84439	Thyroxine; free
84443	Thyroid stimulating hormone (TSH)
84479	Thyroid hormone (T3 or T4) uptake or thyroid hormone binding ratio (THBR)

ICD-10 Diagnosis	
A15.0-A19.9	Tuberculosis
A50.01-A53.9	Syphilis
B35.0-B49	Mycoses
C00.0-C96.9	Malignant neoplasms
D00.00-D09.9	In situ neoplasms
D27.0-D27.9	Benign neoplasm of ovary
D34-D35.9	Benign neoplasm of thyroid gland, other and unspecified endocrine glands
D44.0-D44.9	Neoplasm of uncertain behavior of endocrine glands
D49.7	Neoplasm of unspecified behavior of endocrine glands and other parts of nervous system
D50.0-D53.9	Nutritional anemias
D59.0-D59.19	Drug-induced and other autoimmune hemolytic anemias
D64.89-D64.9	Other specified/unspecified anemias
D76.1-D76.3	Other specified diseases with participation of lymphoreticular and reticulohistiocytic tissue [histiocytosis]
D80.0-D89.9	Certain disorders involving the immune mechanism
E00.0-E07.9	Disorders of thyroid gland
E08.00-E13.9	Diabetes mellitus
E20.0-E35	Disorders of other endocrine glands
E43-E46	Protein-calorie malnutrition
E53.0-E53.9	Deficiency of other B group vitamins
E64.0-E64.9	Sequelae of malnutrition and other nutritional deficiencies
E66.01-E66.9	Overweight and obesity
E67.1	Hypercarotenemia
E75.26	Sulfatase deficiency
E78.00-E78.9	Disorders of lipoprotein metabolism and other lipidemias
E83.00-E83.9	Disorders of mineral metabolism
E87.0-E87.1	Hyperosmolality and hypernatremia; hypo-osmolality and hyponatremia
E88.02	Plasminogen deficiency
E89.0-E89.89	Postprocedural endocrine and metabolic complications and disorders, not elsewhere classified
F02.80-F03.C4	Dementia in other diseases classified elsewhere and unspecified
F05-F07.9	Delirium/other mental disorders/personality change and behavioral disorders due to known physiological condition
F12.10-F12.99	Cannabis related disorders

F22-F23	Delusional/brief psychotic disorders
F30.10-F39	Mood [affective] disorders
F41.0-F41.9	Other anxiety disorders
F50.00-F50.9	Eating disorders
F53.0-F53.1	Mental and behavioral disorder associated with the puerperium, not elsewhere classified
G12.23	Primary lateral sclerosis
G25.0-G26	Other extrapyramidal and movement disorders
G30.0-G31.9	Alzheimer's disease, other degenerative diseases of nervous system, not elsewhere classified
G35	Multiple sclerosis
G47.00-G47.9	Sleep disorders
G56.00-G59	Mononeuropathies of upper limb, lower limb, other, unspecified
G60.0-G61.9	Hereditary and idiopathic neuropathy, inflammatory polyneuropathy
G70.00-G73.7	Myasthenia gravis and other myoneural disorders, primary disorders of muscles, other and unspecified myopathies
G93.31-G93.39	Postviral and related fatigue syndromes
H02.001-H02.9	Other disorders of eyelid
H05.00-H05.9	Disorders of orbit
H10.821-H10.829	Rosacea conjunctivitis
H11.421-H11.439	Conjunctival edema, hyperemia
H49.00-H49.9	Paralytic strabismus
H53.2	Diplopia
I10-I16.9	Hypertensive diseases
I31.0-I32	Other diseases of pericardium, pericarditis
I43	Cardiomyopathy in diseases classified elsewhere
I44.0-I45.9	Atrioventricular and left bundle-branch block, other conduction disorders
I47.0-I49.9	Paroxysmal tachycardia, atrial fibrillation and flutter, other cardiac arrhythmias
I50.1-I50.9	Heart failure
I51.7	Cardiomegaly
I60.00-I60.9	Nontraumatic subarachnoid hemorrhage
I67.1	Cerebral aneurysm, nonruptured
I69.00-I69.098	Sequelae of nontraumatic subarachnoid hemorrhage
I72.0	Aneurysm of carotid artery
J90-J91.8	Pleural effusion
J96.00-J96.92	Respiratory failure, not elsewhere classified
K14.8	Other diseases of tongue
K52.0-K52.9	Other and unspecified noninfective gastroenteritis and colitis
K56.0-K56.7	Paralytic ileus and intestinal obstruction without hernia
K58.0-K59.9	Irritable bowel syndrome, other functional intestinal disorders
K90.0-K90.9	Intestinal malabsorption
L11.0	Acquired keratosis follicularis
L29.8-L29.9	Pruritus, other or unspecified
L60.0-L62	Nail disorders
L63.0-L66.9	Alopecia areata, androgenic alopecia, other nonscarring hair loss, cicatricial alopecia
L80	Vitiligo
L85.0-L87.9	Other epidermal thickening, keratoderma, transepidermal elimination disorders
M04.1-M04.9	Autoinflammatory syndromes
M05.00-M08.9A	Rheumatoid arthritis
M30.0-M36.8	Systemic connective tissue disorders [systemic lupus erythematosus, systemic sclerosis, etc.]
M60.000-M60.9	Myositis
M62.50-M63.89	Muscle wasting and atrophy, not elsewhere classified; other specified disorders of muscle
M79.0-M79.9	Other and unspecified soft tissue disorders, not elsewhere classified [myalgia, fibromyalgia]
M81.6-M81.8	Localized osteoporosis [Lequesne]; other osteoporosis without current pathological fracture
M86.00-M86.9	Osteomyelitis
N91.0-N92.6	Absent, scanty and rare menstruation/excessive, frequent and irregular menstruation
N94.4-N94.6	Dysmenorrhea, primary, secondary, unspecified
N97.0-N97.9	Female infertility
O09.00-O09.93	Supervision of high risk pregnancy
O10.011-O16.9	Edema, proteinuria and hypertensive disorders in pregnancy, childbirth and the puerperium
O20.0-O29.93	Other maternal disorders predominantly related to pregnancy
O30.001-O48.1	Maternal care related to the fetus and amniotic cavity and possible delivery problems
O85-O92.79	Complications predominantly related to the puerperium
O94-O9A.53	Other obstetric conditions, not elsewhere classified
P04.40-P04.5	Newborn affected by maternal use of drugs of addiction, nutritional chemical substances
P05.00-P07.39	Disorders of newborn related to slow fetal growth and fetal malnutrition, short gestation and low birth weight
P09.1-P09.9	Abnormal findings on neonatal screening
P28.0-P29.9	Other respiratory conditions/cardiovascular disorders originating in the perinatal period
P37.0	Congenital tuberculosis
P52.5	Subarachnoid (nontraumatic) hemorrhage of newborn
P70.0-P74.9	Transitory endocrine and metabolic disorders specific to newborn
Q38.2	Macroglossia
Q89.2	Congenital malformations of other endocrine glands
Q90.0-Q90.9	Down syndrome
Q96.0-Q96.9	Turner's syndrome
R00.0-R00.9	Abnormalities of heart beat
R06.00-R06.9	Abnormalities of breathing
R07.0	Pain in throat
R09.89	Other specified symptoms and signs involving the circulatory and respiratory systems
R13.0-R13.19	Aphagia and dysphagia

R18.0-R19.8	Ascites, other symptoms and signs involving the digestive system and abdomen
R20.0-R20.9	Disturbances of skin sensation
R23.0-R23.9	Other skin changes
R25.0-R27.9	Abnormal involuntary movements, abnormalities of gait, other lack of coordination
R29.0-R29.91	Other symptoms and signs involving the nervous and musculoskeletal systems
R40.0-R41.9	Somnolence, stupor and coma/other symptoms and signs involving cognitive functions and awareness
R45.0-R45.89	Symptoms and signs involving emotional state
R47.01-R47.9	Speech disturbances, not elsewhere classified [Dysphasia, aphasia, dysarthria, anarthria, other]
R49.0-R49.9	Voice and resonance disorders
R50.2-R50.9	Fever of other and unknown origin
R52-R53.83	Pain, unspecified; malaise and fatigue
R60.0-R60.9	Edema, not elsewhere classified
R61	Generalized hyperhidrosis
R62.0-R62.59	Delayed milestone/other and unspecified lack of expected normal physiological development in childhood
R63.0-R63.8	Symptoms and signs concerning food and fluid intake
R68.0	Hypothermia, not associated with low environmental temperature
R68.81-R68.89	Other general symptoms and signs
R73.01-R73.9	Elevated blood glucose level
R90.0-R90.89	Abnormal findings on diagnostic imaging of central nervous system
R93.0-R93.9	Abnormal radiologic findings on diagnostic imaging of other body structures
R94.01-R94.8	Abnormal results of function studies
S00.00XA-S09.93XS	Injuries to the head
T66.XXXA-T66.XXXS	Radiation sickness, unspecified
U07.1	Covid-19
Z05.0-Z05.9	Encounter for observation and evaluation of newborn for suspected diseases and conditions ruled out
Z08-Z09	Encounter for follow-up examination after completed treatment for malignant neoplasms, for conditions other than malignant neoplasm
Z19.1-Z19.2	Hormone sensitivity malignancy status
Z31.7	Encounter for procreative management and counseling for gestational carrier
Z34.00-Z34.93	Encounter for supervision of normal pregnancy
Z51.11-Z51.12	Encounter for antineoplastic chemotherapy and immunotherapy
Z79.01-Z79.899	Long term (current) drug therapy
Z83.2-Z83.49	Family history of diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism, diabetes mellitus, other endocrine, nutritional and metabolic diseases
Z84.82	Family history of sudden infant death syndrome
Z85.00-Z85.9	Personal history of malignant neoplasm
Z86.000-Z87.898	Personal history of certain other diseases and conditions
Z92.21-Z92.3	Personal history of drug therapy, irradiation

When services are Not Medically Necessary:
For the procedure codes listed above, for all other diagnoses not listed.

Discussion/General Information

Background

Thyroid stimulating hormone (TSH), also known as thyrotropin, thyrotropic hormone, is produced in the pituitary gland in response to low levels of serum free thyroxine, also known as T4, or triiodothyronine, also known as T3, in the bloodstream. TSH stimulates the thyroid gland to produce and secrete T4. T4 is converted to T3 by the removal of an iodine atom. Over 99% of the T3 and T4 are bound to transport proteins in circulation and are not metabolically available. Free T3 or T4 levels consists of the amount of hormone which is not bound to transport proteins and is available for uptake and use by body tissue.

Serum TSH levels are used as the first-line test to diagnose and monitor thyroid function. They are used to detect thyroid dysfunction, both overt and subclinical, in those with intact hypothalamic and pituitary function. Serum free T4 levels can be used to detect or monitor hypothyroidism. When T4 testing is combined with TSH testing, a low free T4 level can detect primary or central hypothyroidism. Serum T4 testing is also used to monitor for hypothyroidism during hyperthyroidism treatment. Free or total T3 levels can be used to evaluate those with suspected hyperthyroidism (Esfandiari, 2017).

Thyroid Disorders

Symptoms

The most common thyroid disease is hypothyroidism. The reported rate of subclinical disease varies from 4.3% to 8.5% and approximately 0.3% to 0.4% of overt disease. In the United States, the most common cause of hypothyroidism is chronic autoimmune thyroiditis (Hashimoto's thyroiditis) (Garber, 2012). Hypothyroidism has multiple etiologies including treatment of hyperthyroidism, thyroid cancer, benign nodular thyroid disease or non-thyroid-related head and neck malignancy. The symptoms of hypothyroidism are varied and nonspecific including fatigue, cold intolerance, dry skin, constipation, myalgia, depression, edema, menstrual irregularities, hoarse or deep voice, muscle cramps, puffy eyes and weight gain. Hypothyroidism has been associated with an increased risk of developing a number of conditions, including decreased bone density, atrial fibrillation, premature atrial beats and elevated serum cholesterol levels (Canaris, 2000). Untreated congenital hypothyroidism in infants can lead to structural and intellectual impairments (Ortiga-Carvalho, 2016).

The American Thyroid Association (2016) defines thyrotoxicosis as "a clinical state that results from inappropriately high thyroid hormone action in tissues generally due to inappropriately high tissue thyroid hormone levels." Hyperthyroidism is the most common form of thyrotoxicosis with a prevalence in the U.S. of approximately 1.2%. The most common causes of hyperthyroidism are Graves' disease, toxic multinodular goiter, and toxic adenoma. The symptoms of hyperthyroidism can be widespread and vague including nervousness, irritability, anxiety, increased sweating, hand tremors, sleep problems, changes in menstrual cycle, thin skin, fine brittle hair or hair loss, upper extremity weakness, unexplained weight loss, frequent bowel movements, goiter, palpitations, heat

intolerance, shortness of breath, vision changes and enlarged or bulging eyes.

In some cases, thyroid disorders can present with behavioral health symptoms, including psychosis. These symptoms can mimic intoxication, drug use or a psychotic break. The possibility of a thyroid etiology should be explored in those with altered mental status (Bennett, 2021; Carroll, 2010; Cota, 2017; Desai, 2018; Mohammed, 2021; Toloza, 2021; Ueno, 2015).

Thyroid disorders may contribute to or result in a number of cardiac disorders and may exhibit in the form of cardiac arrhythmias. Hypothyroidism can cause abnormal systolic and diastolic performance (Yancy, 2013). The American College of Cardiology (ACC) /American Heart Association (AHA) and the Heart Rhythm Society (HRS) guideline on the management of atrial fibrillation (2014) notes that atrial fibrillation is the most common arrhythmia in individuals with hyperthyroidism, affecting 5% to 15% of the population. The treatment of atrial fibrillation with the long-term use amiodarone therapy has infrequently caused hyperthyroidism and thyrotoxicosis and these individuals should be monitored. The 2018 ACC/AHA/HRS guideline on the evaluation and management of bradycardia and cardiac conduction delay lists hypothyroidism as a potential reversible cause of sinus bradycardia. Both hypothyroidism and hyperthyroidism can result in an atrioventricular block. Hyperthyroidism may also play a role in the development of dilated cardiomyopathy in some cases. The 2013 ACC/AHA guideline on heart failure recommends that the diagnostic testing of individuals presenting with heart failure should include TSH levels.

In the absence of new symptoms, thyroid testing is used to monitor thyroid levels during various therapies. TSH levels are also used to monitor both thyroid hormone replacement therapy to treat primary hypothyroidism and suppressive therapy to treat follicular, papillary or Hürthle cell thyroid cancer (Esfandiari, 2017; National Comprehensive Cancer Network® [NCCN], V2.2024; Ross; 2016). For pregnant individuals who are currently being treated for hypothyroidism, thyroid levels are typically evaluated every 4 to 6 weeks, while adjusting medications (ACOG, 2020). The 2016 ATA guidelines recommend “an assessment of free T4, total T3 and TSH” within 1 to 2 months following radioactive iodine therapy for hyperthyroidism. In addition, the recommendation continues:

> Biochemical monitoring should be continued at 4- to 6-week intervals for 6 months, or until the patient becomes hypothyroid and is stable on thyroid hormone replacement. **Strong recommendation, low-quality evidence**

The hypothalamus-pituitary-thyroid axis is a hormone regulatory system which sets the baseline level thyroid hormone production. Dysregulation within the complex system can influence the function of both central and peripheral mechanisms. Hypothalamus or pituitary gland dysfunction can lead to central hypothyroidism which is associated with vague and nonspecific clinical symptoms usually milder than symptoms of primary hypothyroidism (Feldt-Rasmussen, 2021). A deficiency of thyroid hormones during the neonatal period is associated with impaired neurologic development, including decreased vascularity, dendritic and axonal growth, astrocyte proliferation and differentiation. Thyroid hormone deficiency also interferes with the normal development of cellular processes.

Conditions Associated with Increased Risk of Thyroid Disorder

There is an increased prevalence of thyroid disorders in survivors of adolescent/childhood cancers and individuals who have undergone irradiation of the thyroid region for the treatment of cancer. Hodgkin’s lymphoma survivors, who are typically treated with thyroid region irradiation, may experience thyroid disease, with the risk rising along with the radiation dose (Jensen, 2018). The pathophysiology behind this increased incidence is thought to be caused by radiation-related disturbances of the thyroid hormonal axis. These disturbances result in both secondary dysfunction (central pituitary axis) and primary dysfunction (thyroid gland) (Nome, 2021; Vogelius, 2011). The NCCN Clinical Practice Guideline (CPG) on cancer related fatigue (V2.2024) recommendation assessment of endocrine dysfunction as part of the primary evaluation due to the high incidence of thyroid dysfunction in normal individuals and those receiving thyroid medication or immunotherapy.

Endocrine complications are one of the most common late effects in childhood cancer survivors, particularly thyroid disorders. Approximately 7.5% to 9.2% of childhood survivors of brain tumors and those exposed to HP radiotherapy are later diagnosed with TSH deficiency. Risk increases with time and with the presence of other central endocrinopathies (Chemaitilly, 2018). The Childhood Oncology group recommendations regarding long-term follow-up guidelines for survivors of childhood, adolescent and young adult cancers recommend testing thyroid function in several situations including individuals with:

- Any cancer experience who report fatigue or sleep problems
- Head or brain radiation history who report poor growth
- Head, brain, neck or spine radiation history in individuals attempting pregnancy and periodically throughout pregnancy
- Head, brain, neck or spine radiation history with thyroid nodules

Central hypothyroidism is categorized as congenital or acquired. Feldt-Rasmussen and associates (2016) noted that acquired central hypothyroidism can be associated with:

- Invasive and/or compressive lesions of the pituitary sella region, such as pituitary macroadenomas, craniopharyngiomas, meningiomas, gliomas, Rathke cleft cysts, metastatic seeding or carotid aneurysm
- Iatrogenic causes, such as cranial surgery or irradiation or drugs
- Injuries, such as head traumas or traumatic delivery
- Vascular accidents, such as pituitary infarction, Sheehan syndrome or subarachnoid hemorrhage
- Autoimmune diseases/immunologic lesions, such as postpartum hypophysitis, lymphocytic hypophysitis, IgG4-related hypophysitis, treatment with anti-CTLA4 antibodies and treatment of anti-PIT1 antibody
- Infiltrative lesions, such as iron overload, sarcoidosis and histiocytosis X
- Infective diseases, such as tuberculosis, mycoses and syphilis

While obesity is often associated with thyroid dysfunction, the exact mechanism of action is unknown. It has been theorized that obesity has an impact on the hypothalamic-pituitary-thyroid axis which may result in thyroid dysfunction (Garber, 2012; Laurberg, 2012; Walczak, 2021). In individuals with thyroid cancer, the presence of obesity may be associated with a more aggressive type of cancer (Laurberg, 2012). Thyroid hormones regulate the energy balance aid in the control of energy expenditure and nutrient metabolism, including cholesterol synthesis (Ortiga-Carvalho, 2016).

Autoimmune thyroid diseases (AITDs) are characterized by infiltration of the thyroid by sensitized T lymphocytes and thyroid auto-antibodies, resulting in either an abnormal regulation of the immune response or in an alteration of presenting antigen in the thyroid (Garber, 2012). Autoimmune diseases are associated with a higher incidence of thyroid disorders and are the most common form of thyroid failure (Garber, 2012). Other disorders, such as type 1 diabetes, Addison’s disease, Down’s or Turner’s Syndrome, rheumatoid arthritis, pernicious anemia, myasthenia gravis, celiac disease and systemic lupus erythematosus are associated with an increased frequency of hypothyroidism. (ACOG, 2019; Garber, 2012; Huang, 2022).

Thyroid disease has been implicated as a cause of ovulatory dysfunction. The American College of Obstetricians and Gynecologists (ACOG) and the American Society for Reproductive Medicine (ASRM) committee opinion regarding an infertility workup (2020) recommend measuring TSH levels in individuals with ovulatory dysfunction, infertility or with signs of thyroid disease. Thyroid function

abnormalities, either hypothyroidism or hyperthyroidism, are associated with increased risk of pregnancy induced hypertensive disorders (Toloza, 2022). Thyroid testing should be performed in pregnant individuals for several indications including: a personal or family history of thyroid disease, a diagnosis of type 1diabetes mellitus, clinical suspicion of thyroid disease or an increased risk of overt hypothyroidism (ACOG, 2020).

Thyroid Disorder Screening

The United States Preventive Services Task Force (USPSTF) concluded that there is insufficient evidence to recommend screening for thyroid dysfunction in nonpregnant, asymptomatic adults.

Definitions

Central hypothyroidism: Hypothyroidism caused by damage to the hypothalamus or pituitary gland which result in low TSH, T3 and T4 levels.

Graves' disease: Overproduction of thyroid hormone by the entire thyroid gland.

Primary hypothyroidism: Hypothyroidism caused by a damaged or absent thyroid gland which results in a high TSH level and low T3 and T4 levels.

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History

Status	Date	Action
Reviewed	02/15/2024	Medical Policy & Technology Assessment Committee (MPTAC) review. Updated Discussion and References sections.
Reviewed	02/16/2023	MPTAC review. Updated Discussion and References sections. Updated Coding section with additional diagnosis codes.
	04/21/2022	Corrected typographical error in one diagnosis code in the Coding section.
New	02/17/2022	MPTAC review. Initial document development.