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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

A18.81	Tuberculosis of thyroid gland
C56.1-C56.9	Malignant neoplasm of ovary
C73	Malignant neoplasm of thyroid gland
C75.8	Malignant neoplasm with pluriglandular involvement, unspecified
D09.3	Carcinoma in situ of thyroid and other endocrine glands
D27.0-D27.9	Benign neoplasm of ovary
D34	Benign neoplasm of thyroid gland
D35.2-D35.3	Benign neoplasm of pituitary gland, craniopharyngeal duct
D44.0	Neoplasm of uncertain behavior of thyroid gland
D44.2	Neoplasm of uncertain behavior of parathyroid gland
D51.0	Vitamin B12 deficiency anemia due to intrinsic factor deficiency
D53.9	Nutritional anemia, unspecified
D59.0-D59.19	Drug-induced and other autoimmune hemolytic anemias
D89.82	Autoimmune lymphoproliferative syndrome [ALPS]

D89.831-D89.839	Cytokine release syndrome
E00.0-E07.9	Disorders of thyroid gland
E08.00-E13.9	Diabetes mellitus
E20.0-E20.9	Hypoparathyroidism
E22.1	Hyperprolactinemia
E22.8-E22.9	Other/unspecified hyperfunction of pituitary gland
E23.0-E23.1	Hypopituitarism
E23.6	Other disorders of pituitary gland
E25.0-E25.9	Adrenogenital disorders
E27.1-E27.49	Adrenocortical insufficiency
E28.310-E28.39	Primary ovarian failure
E29.1	Testicular hypofunction
E31.0-E31.9	Polyglandular dysfunction
E35	Disorders of endocrine glands in diseases classified elsewhere
E43-E46	Protein-calorie malnutrition
E53.0	Riboflavin deficiency
E64.0	Sequelae of protein-calorie malnutrition
E67.1	Hypercarotenemia
E75.26	Sulfatase deficiency
E78.00-E78.2	Pure hypercholesterolemia, pure hyperglyceridemia, mixed hyperlipidemia
E78.41-E78.5	Other/unspecified hyperlipidemia
E83.50-E83.59	Disorders of calcium metabolism
E83.81	Hungry bone syndrome
E87.0-E87.1	Hyperosmolality and hypernatremia; hypo-osmolality and hyponatremia
E88.02	Plasminogen deficiency
E89.0	Postprocedural hypothyroidism
E89.2-E89.3	Postprocedural hypoparathyroidism, hypopituitarism
E89.6	Postprocedural adrenocortical (-medullary) hypofunction
F03.90-F03.91	Unspecified dementia
F05	Delirium due to known physiological condition

F06.0-F06.8	Other mental disorders due to known physiological condition
F12.23	Cannabis dependence with withdrawal
F22	Delusional disorders
F23	Brief psychotic disorder
F07.0	Personality change due to known physiological condition
F30.10-F33.9	Manic episode; bipolar disorder; depressive episode; major depressive disorder, recurrent
F34.81-F34.9	Other/unspecified persistent mood [affective] disorders
F39	Unspecified mood [affective] disorder
F41.0-F41.9	Other anxiety disorders
F50.82	Avoidant/restrictive food intake disorder
F53.0-F53.1	Mental and behavioral disorder associated with the puerperium, not elsewhere classified
F63.3	Trichotillomania
G12.23	Primary lateral sclerosis
G25.0-G25.2	Essential, drug-induced, other specified forms of tremor
G25.70-G25.79	Other and unspecified drug induced movement disorders
G25.89-G26	Other specified/unspecified extrapyramidal and movement disorders; and in diseases classified elsewhere
G30.0-G31.1	Alzheimer's disease, frontotemporal dementia, senile degeneration of brain, not elsewhere classified
G31.84	Mild cognitive impairment, so stated
G47.00-G47.09	Insomnia
G47.30-G47.39	Sleep apnea
G47.62	Sleep related leg cramps
G47.9	Sleep disorder, unspecified
G56.00-G56.93	Mononeuropathies of upper limb
G57.80-G57.93	Other/unspecified mononeuropathies of lower limbs
G60.9	Hereditary and idiopathic neuropathy, unspecified
G61.82	Multifocal motor neuropathy
G71.9	Primary disorder of muscle, unspecified
G72.9	Myopathy, unspecified

G73.3-G73.7	Myasthenic syndromes/myopathy in diseases classified elsewhere
G93.3	Postviral fatigue syndrome
H02.531-H02.539	Eyelid retraction
H02.841-H02.849	Edema of eyelid
H02.881-H02.889	Meibomian gland dysfunction of eyelid
H05.20	Unspecified exophthalmos
H05.221-H05.229	Edema of orbit
H05.241-H05.269	Exophthalmos; constant, intermittent, pulsating
H05.89	Other disorders of orbit
H10.821-H10.829	Rosacea conjunctivitis
H11.421-H11.439	Conjunctival edema, hyperemia
H49.00-H49.23	Nerve palsy; third [oculomotor], fourth [trochlear], sixth [abducent]
H49.40-H49.43	Progressive external ophthalmoplegia
H49.881-H49.9	Other/unspecified paralytic strabismus
H53.2	Diplopia
I10	Essential (primary) hypertension
I12.0-I13.2	Hypertensive chronic kidney disease, heart and chronic kidney disease
I16.0-I16.9	Hypertensive crisis
I31.3	Pericardial effusion (noninflammatory)
I31.9	Disease of pericardium, unspecified
I43	Cardiomyopathy in diseases classified elsewhere
I47.1	Supraventricular tachycardia
I47.9	Paroxysmal tachycardia, unspecified
I48.0-I48.21	Paroxysmal atrial fibrillation, persistent/chronic atrial fibrillation
I48.91	Unspecified atrial fibrillation
I49.2	Junctional premature depolarization
I49.8-I49.9	Other specified/unspecified cardiac arrhythmia
I50.1-I50.9	Heart failure
I51.7	Cardiomegaly
J91.8	Pleural effusion in other conditions classified elsewhere

J96.00-J96.02	Acute respiratory failure
J96.90-J96.92	Respiratory failure, unspecified
K14.8	Other diseases of tongue
K52.21-K52.29	Allergic and dietetic gastroenteritis and colitis
K52.89	Other specified noninfective gastroenteritis and colitis
K56.0	Paralytic ileus
K56.7	Ileus, unspecified
K58.1-K58.8	Irritable bowel syndrome with constipation, mixed or other irritable bowel syndrome
K59.00-K59.09	Constipation
K59.39	Other megacolon
L11.0	Acquired keratosis follicularis
L29.9	Pruritus, unspecified
L60.1-L60.8	Nail disorders
L62	Nail disorders in diseases classified elsewhere
L63.0-L65.9	Alopecia areata, androgenic alopecia, other nonscarring hair loss
L66.0	Pseudopelade
L66.2	Folliculitis decalvans
L66.8-L66.9	Other/unspecified cicatricial alopecia
L80	Vitiligo
L85.0-L85.2	Acquired ichthyosis; keratosis [keratoderma], keratosis punctata (palmaris et plantaris)
L86	Keratoderma in diseases classified elsewhere
L87.0	Keratosis follicularis et parafollicularis in cutem penetrans
L87.2	Elastosis perforans serpiginosa
M04.1-M04.9	Autoinflammatory syndromes
M32.0-M32.9	Systemic lupus erythematosus (SLE)
M33.00-M34.9	Dermatopolymyositis; systemic sclerosis [scleroderma]
M35.00-M35.1	Sjögren syndrome; other overlap syndromes
M35.5	Multifocal fibrosclerosis
M35.81-M35.9	Multisystem inflammatory syndrome; systemic involvement of connective tissue unspecified

M36.0	Dermato(poly)myositis in neoplastic disease
M36.8	Systemic disorders of connective tissue in other diseases classified elsewhere
M60.80-M60.9	Other/unspecified myositis
M62.50-M62.59	Muscle wasting and atrophy, not elsewhere classified
M62.81	Muscle weakness (generalized)
M62.9	Disorder of muscle, unspecified
M63.80-M63.89	Disorders of muscle in diseases classified elsewhere
M79.10-M79.11	Myalgia
M79.7	Fibromyalgia
M81.6-M81.8	Localized osteoporosis [Lequesne]; other osteoporosis without current pathological fracture
M86.9	Osteomyelitis, unspecified
N91.0-N91.5	Absent, scanty and rare menstruation
N92.0	Excessive and frequent menstruation with regular cycle
N92.5-N92.6	Other specified/unspecified irregular menstruation
N94.4-N94.6	Dysmenorrhea, primary, secondary, unspecified
N97.0-N97.9	Female infertility
O09.00-O09.03	Supervision of pregnancy with history of infertility
O09.211-O09.219	Supervision of pregnancy with history of pre-term labor
O09.511-O09.529	Supervision of elderly primigravida and multigravida
O12.00-O12.25	Gestational edema, proteinuria, edema with proteinuria
O13.1-O13.9	Gestational [pregnancy-induced] hypertension without significant proteinuria
O14.00-O14.95	Pre-eclampsia
O16.1-O16.5	Unspecified maternal hypertension
O24.011-O24.93	Diabetes mellitus in pregnancy, childbirth and the puerperium
O26.20-O26.23	Pregnancy care for patient with recurrent pregnancy loss
O36.8310-O36.8399	Maternal care for abnormalities of the fetal heart rate or rhythm
O44.20-O44.53	Partial placenta previa, low lying placenta
O90.5	Postpartum thyroiditis
O92.29	Other disorders of breast associated with pregnancy and the puerperium

O99.210-O99.215	Obesity complicating pregnancy, childbirth, and the puerperium
O99.280-O99.285	Other endocrine, nutritional and metabolic diseases complicating pregnancy, childbirth and the puerperium
P04.40-P04.49	Newborn affected by maternal use of unspecified drugs of addiction, cocaine, hallucinogens, other
P05.09	Newborn light for gestational age, 2500 grams and over
Q38.2	Macroglossia
Q89.2	Congenital malformations of other endocrine glands
R00.0-R00.9	Abnormalities of heart beat
R06.00-R06.1	Dyspnea, stridor
R06.83-R06.89	Snoring, other 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-R18.8	Ascites
R19.4	Change in bowel habit
R19.7-R19.8	Diarrhea, unspecified; other specified symptoms and signs involving the digestive system and abdomen
R20.0-R20.9	Disturbances of skin sensation
R23.4-R23.9	Changes in skin texture; other/unspecified skin changes
R25.0-R25.9	Abnormal involuntary movements
R27.0-R27.9	Other lack of coordination
R29.2	Abnormal reflex
R40.0-R40.1	Somnolence, stupor
R40.4	Transient alteration of awareness
R41.0-R41.3	Disorientation, amnesia
R41.82	Altered mental status, unspecified
R41.9	Unspecified symptoms and signs involving cognitive functions and awareness
R45.0-R45.1	Nervousness, restlessness and agitation
R45.3-R45.4	Demoralization and apathy, irritability and anger

R53.81-R53.83	Other malaise and fatigue
R63.4	Abnormal weight loss
R63.5	Abnormal weight gain
Z85.850	Personal history of malignant neoplasm of thyroid
Z85.858	Personal history of malignant neoplasm of other endocrine glands

When services may be Medically Necessary when criteria are met:
For the procedure codes listed above for the following diagnoses

ICD-10 Diagnosis	
C79.89	Secondary malignant neoplasm of other specified sites
C79.9	Secondary malignant neoplasm of unspecified site
D09.8	Carcinoma in situ of other specified sites
D44.9	Neoplasm of uncertain behavior of unspecified endocrine gland
D49.7	Neoplasm of unspecified behavior of endocrine glands and other parts of nervous system
D64.89-D64.9	Other specified/unspecified anemias
D89.89	Other specified disorders involving the immune mechanism, not elsewhere classified

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 cell-derived thyroid cancer (Esfandiari, 2017; Ross; 2016). Pregnant individuals who are currently being treated for hypothyroidism. In this population, thyroid levels are typically evaluated every 4 to 6 weeks, while adjusting medications (ACOG, 2020). The 2016 ATA guidelines recommends "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 the 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 National Comprehensive Cancer Network® (NCCN) Clinical Practice Guideline (CPG) on cancer related fatigue (V2.2022) 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 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
New	02/17/2022	Medical Policy & Technology Assessment Committee (MPTAC) review. Initial document development.