Medicare Medical Policy

Genetic Testing for Thyroid Nodules

MEDICARE MEDICAL POLICY NUMBER: 40

Effective Date: 7/1/2024

Last Review Date: 6/2024

Next Annual Review: 10/2024

INSTRUCTIONS FOR USE: Company Medicare Medical Policies serve as guidance for the administration of plan benefits and do not constitute medical advice nor a guarantee of coverage. Company Medicare Medical Policies are reviewed annually to guide the coverage or non-coverage decision-making process for services or procedures in accordance with member benefit contracts (otherwise known as Evidence of Coverage or EOCs) and Centers of Medicare and Medicaid Services (CMS) policies, manuals, and other CMS rules and regulations. In the absence of a CMS coverage determination or specific regulation for a requested service, item or procedure, Company policy criteria or applicable utilization management vendor criteria may be applied. These are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

The Company reserves the right to determine the application of Medicare Medical Policies and make revisions to these policies at any time. Any conflict or variance between the EOC and Company Medical Policy will be resolved in favor of the EOC.

SCOPE: Providence Health Plan, Providence Health Assurance, and Providence Plan Partners as applicable (referred to individually as “Company” and collectively as “Companies”).

PRODUCT AND BENEFIT APPLICATION

☒ Medicare Only

MEDICARE COVERAGE CRITERIA

IMPORTANT NOTE: More than one Centers for Medicare and Medicaid Services (CMS) reference may apply to the same health care service, such as when more than one coverage policy is available (e.g., both an NCD and LCD exist). All references listed should be considered for coverage decision-making. The Company uses the most current version of a Medicare reference available at the time of publication; however, these websites are not maintained by the Company, so Medicare references and their corresponding hyperlinks may change at any time. If there is a conflict between the Company Medicare Medical Policy and CMS guidance, the CMS guidance will govern.

Service	Medicare Guidelines
Afirma™ Gene Expression Classifier Assay or Afirma™ Genomic Sequencing Classifer (GSC) (Veracyte, California; *CPT 81546)*	**Services performed prior to 7/28/2024:** Local Coverage Article (LCA): Billing and Coding: MolDX: Afirma™ Assay by Veracyte (A54358) **Services performed on or after 7/28/2024:** Local Coverage Determination (LCD): MolDX: Molecular Testing for Risk Stratification of Thyroid Nodules (L39682) **NOTE:** The LCD L39682 requires that the test in question successfully completes a technical assessment to ensure the test is reasonable and necessary as described by the LCD coverage requirements. The following tests are **not medically necessary** because they have been reviewed by the MolDX Program Contractor, but as of the most recent review of this policy, MolDX has determined these tests are "Not Covered," and are listed in the DEX™ Diagnostics Exchange Registry as such. • Afirma Xpression Atlas (Veracyte, California) • Afirma Medullary Thyroid Carcinoma (MTC) Classifier (Veracyte, California; CPT 81599)
Afirma Xpression Atlas (Veracyte, California*)* Afirma Medullary Thyroid Carcinoma (MTC) Classifier (Veracyte, California; *CPT 81599)*	**Services performed on or after 7/28/2024:** See row above. **Services performed prior to 7/28/2024:** These tests are considered **not medically necessary**, based on Medicare guidelines. *See "Policy Guidelines" below. These tests have been reviewed by the MolDX Program Contractor. As of the most recent review of this policy, MolDX has determined these tests are "Not*

	Covered," as listed in the DEX™ Diagnostics Exchange Registry, and as such, are considered "not medically necessary."
NRAS Single Gene Testing for Proliferative Thyroid Lesions	• Testing performed in OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY: Local Coverage Determination (LCD): MolDX: NRAS Genetic Testing (L36339) • Testing performed in CA or NV: LCD: MolDX: NRAS Genetic Testing (L36335) • For testing performed in AL, GA, TN, SC, NC, VA, or WV: LCD: MolDX: NRAS Genetic Testing (L35073)
ThyraMIR *(Interpace Diagnostics, Pittsburgh, PA; CPT 0018U)* ThyGeNEXT Thyroid Oncogene Panel test (*Interpace Diagnostics, Pittsburgh, PA; CPT 0245U*) ThyroSeq *(CBLPath, Inc. & Univ of Pittsburgh Medical Center, testing performed in Pittsburgh, PA; CPT 0026U)* ThyroSeq® CRC *(CBLPath, Inc. & Univ of Pittsburgh Medical Center, testing performed in Pittsburgh, PA; CPT 0287U)*	• LCD: Biomarkers for Oncology (L35396) • LCA: Billing and Coding: Biomarkers for Oncology (A52986) **NOTE:** For ThyroSeq® CRC (0287U), use the same criteria currently used for the original ThyroSeq test. Testing frequency, as well as medically necessary diagnoses codes for all of these thyroid nodule tests can be found in the above LCA.
Thyroid GuidePx® *(Protean BioDiagnostics and Qualisure Diagnostics; Florida; CPT 0362U)*	LCA: Billing and Coding: Genetic Testing for Oncology (A59123) *(CPT code is included in "Non-Covered CPT Codes" section)*

IMPORTANT NOTICE: While some services or items may appear medically indicated for an individual, they may also be a direct exclusion of Medicare or the member's benefit plan. Such excluded services or items by Medicare and member EOCs include, but are not limited to, services or procedures considered to be cosmetic, not medical in nature, or those considered not medically reasonable or necessary under *Title XVIII of the Social Security Act, §1862(a)(1)(A).* If there is uncertainty regarding coverage of a service or item, please review the member EOC or submit a pre-service organization determination request. Note that the Medicare Advance Beneficiary Notice of Noncoverage (ABN) form **cannot** be used for Medicare Advantage members. *(Medicare Advance Written Notices of Non-coverage. MLN006266 May 2021)*

POLICY CROSS REFERENCES

None

The full Company portfolio of Medicare Medical Policies is available online and can be accessed here.

POLICY GUIDELINES

MEDICARE AND MEDICAL NECESSITY

Laboratories performing tests in service areas which have adopted guidelines or coverage determinations made by the Medicare Molecular Diagnostics (MolDX) Program contractor are required to submit a technology assessment (TA) to establish analytical and clinical validity (AV/CV) and clinical utility (CU). Supporting LCDs regarding TA reviews include, but are not limited to, the following:

- Laboratories in CA & NV: LCD for MolDX: Molecular Diagnostic Tests (MDT) (L35160)
- Laboratories in NC, SC, GA, TN, AL, VA, & WV: LCD for MolDX: Molecular Diagnostic Tests (MDT) (L35025)
- Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, & WY: LCD for MolDX: Molecular Diagnostic Tests (MDT) (L36256)

Coverage or non-coverage determinations made by MolDX are maintained in the DEX™ Diagnostics Exchange registry catalog and are available for public viewing. Some tests are listed in the registry as being "Not covered." However, if a test does not have any coverage determination by the MolDX Program documented in the registry, then AV/CV and CU is considered to have **not** been established and the test is also considered not medically reasonable and necessary under *SSA §1862(a)(1)(A)* until a MolDX review is complete and coverage is indicated by MolDX or Noridian. Tests identified in this policy as not meeting this requirement will be denied as not medically reasonable or necessary for Medicare under *SSA §1862(a)(1)(A).*

REGULATORY STATUS

U.S. FOOD & DRUG ADMINISTRATION (FDA)

While clearance by the Food and Drug Administration (FDA) is a prerequisite for Medicare coverage, the 510(k) premarket clearance process does not in itself establish medical necessity. Medicare payment policy is determined by the interaction of numerous requirements, including but not limited to, the availability of a Medicare benefit category and other statutory requirements, coding and pricing guidelines, as well as national and local coverage determinations and clinical evidence.

BILLING GUIDELINES AND CODING

GENERAL

See related local coverage articles (LCAs) for additional coding and billing assistance.

- LCAs: Billing and Coding: MolDX: NRAS Genetic Testing (A57487, A57486, or A56962)
- LCA: Billing and Coding: Biomarkers for Oncology (A52986)

Several tests have had code changes over the years, due to new CPT and PLA codes being developed and other codes being deleted:

Table 1: Code changes over the years

Test	Code(s) and Date(s)
Afirma™ Gene Expression Classifier Assay or Afirma™ Genomic Sequencing Classifer (GSC) (Veracyte)	• Prior to 1/1/2021, CPT 81545 • As of 1/1/2021, CPT 81546

Afirma Medullary Thyroid Carcinoma (MTC) Classifier (Veracyte)	• From 10/1/2020 and 1/1/2022, CPT 0208U • As of 1/1/2022, unlisted codes (e.g., CPT 81599)
ThyGeNEXT Thyroid Oncogene Panel test (Interpace Diagnostics)	• Prior to 04/01/2021, CPT 81455 • As of 04/01/2021, CPT 0245U

CODES*		
CPT	0018U	Oncology (thyroid), microRNA profiling by RT-PCR of 10 microRNA sequences, utilizing fine needle aspirate, algorithm reported as a positive or negative result for moderate to high risk of malignancy *(For the ThyraMir, by Interpace Diagnostics)*
	0026U	Oncology (thyroid), DNA and mRNA of 112 genes, next-generation sequencing, fine needle aspirate of thyroid nodule, algorithmic analysis reported as a categorical result ("Positive, high probability of malignancy" or "Negative, low probability of malignancy") *(For the Thyroseq Genomic Classifier, by CBL Path Inc.)*
	~~0204U~~	**TERMED 6/30/2024** ~~Oncology (thyroid), mRNA, gene expression analysis of 593 genes (including BRAF, RAS, RET, PAX8, and NTRK) for sequence variants and rearrangements, utilizing fine needle aspirate, reported as detected or not detected *(For the Afirma Xpression Atlas, by Veracyte Inc.)*~~
	0245U	Oncology (thyroid), mutation analysis of 10 genes and 37 RNA fusions and expression of 4 mRNA markers using next-generation sequencing, fine needle aspirate, report includes associated risk of malignancy expressed as a percentage *(For the ThyGeNEXT® test, by Interpace Diagnostics)*
	0287U	Oncology (thyroid), DNA and mRNA, next-generation sequencing analysis of 112 genes, fine needle aspirate or formalin fixed paraffin-embedded (FFPE) tissue, algorithmic prediction of cancer recurrence, reported as a categorical risk result (low, intermediate, high) *(For the ThyroSeq® CRC, by CBL Path, Inc.)*
	0362U	Oncology (papillary thyroid cancer), gene-expression profiling via targeted hybrid capture–enrichment RNA sequencing of 82 content genes and 10 housekeeping genes, fine needle aspirate or formalin-fixed paraffin embedded (FFPE) tissue, algorithm reported as one of three molecular subtypes *(For the Thyroid GuidePx®, by Protean BioDiagnostics)*
	81210	BRAF (B-Raf proto-oncogene, serine/threonine kinase) (eg, colon cancer, melanoma), gene analysis, V600 variant(s)
	81311	NRAS (neuroblastoma RAS viral [v-ras] oncogene homolog) (eg, colorectal carcinoma), gene analysis, variants in exon 2 (eg, codons 12 and 13) and exon 3 (eg, codon 61)
	81401	Molecular Pathology Procedure Level 2
	81403	Molecular Pathology procedure, Level 4
	81404	Molecular Pathology Procedure, Level 5
	81405	Molecular Pathology Procedure, Level 6
	81406	Molecular Pathology Procedure, Level 7
	81445	Solid organ neoplasm, genomic sequence analysis panel, 5-50 genes, interrogation for sequence variants and copy number variants or rearrangements, if performed; DNA analysis or combined DNA and RNA analysis
	81449	Solid organ neoplasm, genomic sequence analysis panel, 5-50 genes, interrogation for sequence variants and copy number variants or rearrangements, if performed; RNA analysis
	81479	Unlisted molecular pathology procedure

	81546	Oncology (thyroid), mRNA, gene expression analysis of 10,196 genes utilizing fine needle aspirate, algorithm reported as a categorical result (eg, benign or suspicious) *(For the updated Afirma Genomic Sequence Classifier [GSC] test, by Veracyte)*
	81599	Unlisted multianalyte assay with algorithmic analysis
	84999	Unlisted chemistry procedure
HCPCS	None	

***Coding Notes:**

- The code list above is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit. According to Medicare, "presence of a payment amount in the MPFS and the Medicare physician fee schedule database (MPFSDB) does not imply that CMS has determined that the service may be covered by Medicare." The issuance of a CPT or HCPCS code or the provision of a payment or fee amount by Medicare does **not** make a procedure medically reasonable or necessary or a covered benefit by Medicare. *(Medicare Claims Processing Manual, Chapter 23 - Fee Schedule Administration and Coding Requirements, §30 - Services Paid Under the Medicare Physician's Fee Schedule, A. Physician's Services)*
- All unlisted codes are reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is submitted for non-covered services addressed in this policy then it will be **denied as not covered**. If an unlisted code is submitted for potentially covered services addressed in this policy, to avoid post-service denial, **prior authorization is recommended**.
- **See the non-covered and prior authorization lists on the Company Medical Policy, Reimbursement Policy, Pharmacy Policy and Provider Information website for additional information.**
- HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as "medically unlikely edits" (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.

REFERENCES

None

POLICY REVISION HISTORY

DATE	REVISION SUMMARY
1/2023	Q1 2023 code updates (converted to new format 2/2023)
8/2023	Interim update; updated CMS LCD/LCA references for the ThyroSeq® CRC and Thyroid GuidePx® tests
10/2023	Q4 2023 code updates; updated CMS LCD/LCA reference for ThyroSeq® CRC, since the anticipated new Novitas LCD/LCA were not published when previously expected
12/2023	Annual review; updated CMS LCD/LCA reference for ThyroSeq® CRC, since the anticipated new Novitas LCD/LCA were not published when previously expected
1/2024	Q1 2024 code updates
7/2024	Q3 2024 code updates; add future LCD for molecular testing for risk stratification of thyroid nodules for Afirma tests