

# MEDICAL POLICY

<b>POLICY TITLE</b>	<b>MOLECULAR MARKERS IN FINE NEEDLE ASPIRATES OF THE THYROID</b>
<b>POLICY NUMBER</b>	<b>MP 2.275</b>

<b>CLINICAL BENEFIT</b>	<input type="checkbox"/> MINIMIZE SAFETY RISK OR CONCERN. <input checked="" type="checkbox"/> MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. <input type="checkbox"/> ASSURE APPROPRIATE LEVEL OF CARE. <input type="checkbox"/> ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. <input type="checkbox"/> ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. <input type="checkbox"/> ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
<b>Effective Date:</b>	<b>4/1/2024</b>

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## I. POLICY

For individuals who have thyroid nodules without strong clinical or radiologic findings suggestive of malignancy in whom surgical decision making would be affected by test results the use of either of the following types of molecular marker testing or gene variant analysis in fine needle aspirates of thyroid nodules with indeterminate cytologic findings (ie, Bethesda diagnostic category III [atypia/follicular lesion of undetermined significance] or Bethesda diagnostic category IV [follicular neoplasm/suspicion for a follicular neoplasm]) may be considered **medically necessary**:

- Afirma® Genomic Sequencing Classifier; or
- ThyroSeq® Genomic Classifier ; or
- In lieu of the above tests:
  - BRAF V600E, RET/PTC, RAS, PAX8/PPAR

The use of any of the following types of molecular marker testing or gene variant analysis in fine needle aspirates of thyroid nodules with indeterminate findings (Bethesda diagnostic category III [atypia/follicular lesion of undetermined significance] or Bethesda diagnostic category IV [follicular neoplasm/suspicion for a follicular neoplasm]) or suspicious findings (Bethesda diagnostic category V [suspicious for malignancy]) to rule in malignancy to guide surgical planning for initial resection rather than a 2-stage surgical biopsy followed by definitive surgery may be considered **medically necessary**:

- ThyroSeq® Genomic Classifier; or
- ThyraMIR® microRNA/ThyGeNEXT®; or
- Afirma® Genomic Sequencing Classifier; or
- In lieu of the above tests:
  - BRAF V600E, RET/PTC, RAS, PAX8/PPAR

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Gene expression classifiers, genetic variant analysis, and molecular marker testing in fine needle aspirates of the thyroid not meeting criteria outlined above, including but not limited to use of RosettaGX Reveal, ThyroSeq CRC, Thyroid GuidePx, and single-gene *TERT* testing are considered **investigational** as there is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

*If coverage of a test is requested, but is not listed above, please refer to **MP 2.259 Expanded Molecular Panel Testing of Cancers to Identify Targeted Therapies** for additional guidance.*

The National Comprehensive Cancer Network (NCCN) is a nonprofit alliance of cancer centers throughout the United States. NCCN develops the Clinical Practice Guidelines in Oncology which are recommendations aimed to help health care professionals diagnose, treat and manage patients with cancer. The National Cancer Institute's PDQ (Physician Data Query) is NCI's comprehensive source of cancer information, which includes evidence-based summaries on topics that cover adult and pediatric cancer treatment. These guidelines evolve continuously as new treatments and diagnostics emerge, and may be used by Capital BlueCross when determining medical necessity according to this policy.

### Policy Guidelines

In individuals who do not undergo surgical biopsy or thyroidectomy on the basis of gene expression classifier or molecular marker results, regular active surveillance is indicated.

Use of molecular marker testing based on fine needle aspirate of a thyroid nodule to rule in malignancy prior to surgical biopsy may guide surgical planning, particularly factors such as choice of surgical facility provider to ensure that the capability is available to conduct a frozen section pathologic reading during surgical biopsy so that surgical approach may be adjusted accordingly in a single surgery.

### GENETICS NOMENCLATURE UPDATE

The Human Genome Variation Society nomenclature is used to report information on variants found in DNA and serves as an international standard in DNA diagnostics. It is being implemented for genetic testing medical evidence review updates starting in 2017 (see Table PG1). The Society's nomenclature is recommended by the Human Variome Project, the Human Genome Organization, and by the Human Genome Variation Society itself. The American College of Medical Genetics and Genomics and the Association for Molecular Pathology standards and guidelines for interpretation of sequence variants represent expert opinion from both organizations, in addition to the College of American Pathologists. These recommendations primarily apply to genetic tests used in clinical laboratories, including genotyping, single genes, panels, exomes, and genomes. Table PG2 shows the recommended standard terminology-"pathogenic," "likely pathogenic," "uncertain significance," "likely benign," and "benign"-to describe variants identified that cause Mendelian disorders.

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**Table PG1. Nomenclature to Report on Variants Found in DNA**

Previous	Updated	Definition
Mutation	Disease-associated variant	Disease-associated change in the DNA sequence
	Variant	Change in the DNA sequence
	Familial variant	Disease-associated variant identified in a proband for use in subsequent targeted genetic testing in first-degree relatives

**Table PG2. ACMG-AMP Standards and Guidelines for Variant Classification**

Variant Classification	Definition
Pathogenic	Disease-causing change in the DNA sequence
Likely pathogenic	Likely disease-causing change in the DNA sequence
Variant of uncertain significance	Change in DNA sequence with uncertain effects on disease
Likely benign	Likely benign change in the DNA sequence
Benign	Benign change in the DNA sequence

ACMG: American College of Medical Genetics and Genomics; AMP: Association for Molecular Pathology.

### GENETIC COUNSELING

Experts recommend formal genetic counseling for patients who are at risk for inherited disorders and who wish to undergo genetic testing. Interpreting the results of genetic tests and understanding risk factors can be difficult for some patients; genetic counseling helps individuals understand the impact of genetic testing, including the possible effects the test results could have on the individual or their family members. It should be noted that genetic counseling may alter the utilization of genetic testing substantially and may reduce inappropriate testing; further, genetic counseling should be performed by an individual with experience and expertise in genetic medicine and genetic testing methods.

#### ***Cross-reference:***

**MP 2.259** Molecular Panel Testing of Cancers to Identify Targeted Therapies

### II. PRODUCT VARIATIONS

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This policy is only applicable to certain programs and products administered by Capital Blue Cross and subject to benefit variations as discussed in Section VI. Please see additional information below.

FEP PPO - Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at: <https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies>

### III. DESCRIPTION/BACKGROUND

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### THYROID NODULES

Thyroid nodules are common, present in 5% to 7% of the U.S. adult population; however, most are benign, and most cases of thyroid cancer are curable surgically when detected early.

#### Diagnosis

Sampling thyroid cells by fine needle aspirate (FNA) is currently the most accurate procedure to distinguish benign thyroid lesions from malignant ones, reducing the rate of unnecessary thyroid surgery for patients with benign nodules and triaging patients with thyroid cancer to appropriate surgery.

About 60% to 70% of thyroid nodules are classified cytologically as benign, and 4% to 10% of nodules are cytologically deemed malignant. However, the remaining 20% to 30% have equivocal findings, usually due to overlapping cytologic features between benign and malignant nodules; these nodules usually require surgery for a final diagnosis. Thyroid FNA cytology is classified by Bethesda System criteria into the following groups: nondiagnostic; benign; follicular lesion of undetermined significance (FLUS) or atypia of undetermined significance (AUS); follicular neoplasm (or suspicious for follicular neoplasm); suspicious for malignancy; and malignant. Lesions with FNA cytology in the atypia of undetermined significance or follicular neoplasm of undetermined significance or follicular neoplasm categories are often considered indeterminate.

#### Management

There is some individualization of management for patients with FNA-indeterminate nodules, but many patients will require a surgical biopsy, typically thyroid lobectomy, with intraoperative pathology. Consultation would typically be the next step in diagnosis. Approximately 80% of patients with indeterminate cytology undergo surgical resection; postoperative evaluation has revealed a malignancy rate ranging from 6% to 30%, making this a clinical process with very low specificity. Thus, if analysis of FNA samples could reliably identify the risk of malignancy as low, there is potential for patients to avoid surgical biopsy.

Preoperative planning of optimal surgical management in patients with equivocal cytologic results is challenging, because different thyroid malignancies require different surgical procedures (e.g., unilateral lobectomy vs total or subtotal thyroidectomy with or without lymph node dissection) depending on several factors, including histologic subtype and risk-stratification strategies (tumor size, patient age). If a diagnosis cannot be made intraoperatively, a lobectomy is typically performed, and, if on postoperative histology the lesion is malignant, a second surgical intervention may be necessary for completion thyroidectomy.

### THYROID CANCER

Most thyroid cancers originate from thyroid follicular cells and include well-differentiated papillary thyroid carcinoma (PTC; 80% of all thyroid cancers) and follicular carcinoma (15%). Poorly differentiated and anaplastic thyroid carcinomas are uncommon and can arise de novo or from preexisting well-differentiated papillary or follicular carcinomas. Medullary thyroid carcinoma originates from parafollicular or C cells and accounts for about 3% of all thyroid cancers.

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The diagnosis of malignancy in the case of PTC is primarily based on cytologic features. If FNA in a case of PTC is indeterminate, surgical biopsy with intraoperative pathology consultation is most often diagnostic, although its efficacy and therefore its use will vary across institutions, surgeons, and pathologists. In 2016, reclassification of encapsulated follicular-variant PTC as a noninvasive follicular tumor with papillary-like nuclei was proposed and largely adopted; this classification removes the word *carcinoma* from the diagnosis to acknowledge the indolent behavior of these tumors.

For follicular carcinoma, the presence of invasion of the tumor capsule or blood vessels is diagnostic, and cannot be determined by cytology, because tissue sampling is necessary to observe these histologic characteristics. Intraoperative diagnosis of follicular carcinoma is challenging and often not feasible because extensive sampling of the tumor and capsule is usually necessary and performed on postoperative, permanent sections.

New approaches for improving the diagnostic accuracy of thyroid FNA include variant analysis for somatic genetic alterations, to more accurately classify which patients need to proceed to surgery (and may include the extent of surgery necessary), and a gene expression classifier to identify patients who do not need surgery and can be safely followed.

### Genetic Variants Associated with Thyroid Cancer

A number of genetic variants have been discovered in thyroid cancer. The most common 4 gene variants are *BRAF* and *RAS* single nucleotide variants (SNVs) and *RET/PTC* and *PAX8/PPAR* rearrangements.

Papillary carcinomas carry SNVs of the *BRAF* and *RAS* genes, as well as *RET/PTC* and *TRK* rearrangements, all of which can activate the mitogen-activated protein kinase pathway. These mutually exclusive variants are found in more than 70% of papillary carcinomas. *BRAF* SNVs are highly specific for PTC. Follicular carcinomas harbor either *RAS* SNVs or *PAX8/PPAR* rearrangements. These variants have been identified in 70% to 75% of follicular carcinomas. Genetic alterations involving the PI3K/AKT signaling pathway also occur in thyroid tumors, although they are rare in well-differentiated thyroid cancers and have a higher prevalence in less differentiated thyroid carcinomas. Additional variants known to occur in poorly differentiated and anaplastic carcinomas involve the *TP53* and *CTNNB1* genes. Medullary carcinomas, which can be familial or sporadic, frequently possess SNVs located in the *RET* gene.

Studies have evaluated the association between various genes and cancer phenotype in individuals with diagnosed thyroid cancer.

Telomerase reverse transcriptase (*TERT*) promoter variants occur with varying frequency in different thyroid cancer subtypes. Overall, *TERT* C228T or C250T variants have been reported in approximately 15% of thyroid cancers, with higher rates in the undifferentiated and anaplastic subtypes compared with the well-differentiated subtypes. *TERT* variants are associated with several demographic and histopathologic features such as older age and advanced TNM stage. *TERT* promoter variants have been reported to be independent predictors of disease recurrence and cancer-related mortality in well-differentiated thyroid cancer. Also, the co-occurrence of *BRAF* or *RAS* variants with *TERT* or *TP53* variants may identify a subset of thyroid cancers with unfavorable outcomes.

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### Molecular Diagnostic Testing

#### ***Variant Detection and Rearrangement Testing***

SNVs in specific genes, including *BRAF*, *RAS*, and *RET*, and evaluation for rearrangements associated with thyroid cancers can be accomplished with Sanger sequencing or pyrosequencing or with real-time polymerase chain reaction (PCR) of single or multiple genes or by next-generation sequencing (NGS) panels. Panel tests for genes associated with thyroid cancer, with varying compositions, are also available. For example, Quest Diagnostics offers a Thyroid Cancer Mutation Panel, which includes *BRAF* and *RAS* variant analysis and testing for *RET/PTC* and *PAX8/PPAR* rearrangements.

The ThyroSeq Genomic Classifier (Sonic Healthcare) is an NGS panel of 112 genes for four main classes of molecular alterations, including mutations, gene fusions, copy number alterations, and gene expression alterations. The results are processed by a unique genomic classifier (GC) and reported as positive or negative. ThyGeNEXT is an NGS panel that sequences 10 genes and identifies specific gene variants and translocations associated with thyroid cancer. ThyGeNEXT is intended to be used in conjunction with the ThyraMIRv2 microRNA expression test when the initial ThyGeNEXT test is negative.

#### ***Gene Expression Profiling***

Genetic alterations associated with thyroid cancer can be assessed using gene expression profiling, which refers to the analysis of messenger RNA (mRNA) expression levels of many genes simultaneously. Several gene expression profiling tests are available and stratify tissue from thyroid nodules biologically.

The Afirma Gene Expression Classifier (Afirma GSC; Veracyte) analyzes the expression of 142 different genes to determine patterns associated with benign findings on surgical biopsy. It is designed to evaluate thyroid nodules that have an “indeterminate” classification on FNA as a method to select patients (“rule out”) who are at low risk for cancer. In 2017, Veracyte migrated the Afirma GSC microarray analysis to a next-generation RNA sequencing platform and now markets the Afirma Gene Sequencing Classifier (Afirma GSC) which evaluates 10196 genes with 1115 core genes.

Other gene expression profiles have been reported in investigational settings, but have not been widely validated or used commercially (e.g., Barros-Filho et al [2015], Zheng et al [2015]); they are not addressed in this review.

ThyraMIRv2 is a microRNA expression–based classifier intended for use in thyroid nodules with indeterminate cytology on FNA following a negative result from the ThyGeNEXT Thyroid Oncogene Panel.

#### ***Algorithmic Testing***

Algorithmic testing involves the use of 2 or more tests in a prespecified sequence, with a subsequent test automatically obtained depending on results of an earlier test.

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### **Algorithmic Testing Using ThyGeNEXT and ThyraMIRv2**

The ThyGeNEXT Thyroid Oncogene Panel (Interpace Diagnostics) is an NGS panel designed to assess patients with indeterminate thyroid FNA results. It includes sequencing of 10 genes and 38 RNA fusions. ThyGeNEXT has replaced the predicate ThyGenXThyroid test.

ThyraMIRv2 (Interpace Diagnostics) is a microRNA expression–based classifier intended for use in thyroid nodules with indeterminate cytology on FNA following a negative result from the ThyGeNEXT Thyroid Oncogene Panel.

The testing strategy for combined ThyGeNEXT and ThyraMIRv2 testing is first to predict malignancy. A positive result on ThyGeNEXT would “rule in” patients for surgical resection. The specific testing results from a ThyGeNEXT positive test would be used to inform preoperative planning when positive. For a ThyGeNEXT negative result, the reflex testing involves the ThyraMIRv2 microRNA expression test to “rule out” for a surgical biopsy procedure given the high negative predictive value of the second test. Patients with a negative result from the ThyraMIRv2 test would be followed with active surveillance and avoid a surgical biopsy.

### **Recurrence**

ThyroSeq Cancer Risk Classifier (CRC) and Thyroid GuidePx are tests for recurrence. ThyroSeq CRC is to be used in FNAs from cytologically malignant (Bethesda VI) nodules and in resected thyroid cancers to predict risk of cancer recurrence. Thyroid GuidePx is used in papillary thyroid cancer and identifies a low risk group with <5% recurrence rate.

### **REGULATORY STATUS**

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. Thyroid variant testing and gene expression classifiers are available under the auspices of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

Table 2 provides a summary of commercially available molecular diagnostic tests for indeterminate thyroid pathology.

**Table 2. Summary of Molecular Tests for Indeterminate Thyroid Cytopathology FNA Specimens**

<b>Test</b>	<b>Predicate</b>	<b>Methodology</b>	<b>Analyte(s)</b>	<b>Report</b>
Afirma® GSC	Afirma® GEC	mRNA gene expression	167 genes	Benign/suspicious
ThyroSeq GC	ThyroSeq	Next-generation sequencing	112 genes	Specific gene variant/translocation
ThyGeNEXT®	ThyGenX®, miRInfor m® <sup>a</sup>	Next-generation sequencing	10 genes and 38 gene fusions	Specific gene variant/translocation

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ThyraMIR®v2	ThyraMIR®	microRNA expression	11 microRNAs	Negative/positive
RosettaGX™ Reveal		microRNA expression	24 microRNAs	<input type="checkbox"/> Benign <input type="checkbox"/> Suspicious for malignancy <input type="checkbox"/> High risk for medullary carcinoma

FNA: fine needle aspirate; NGS: next-generation sequencing; PCR: polymerase chain reaction.

<sup>a</sup> The miR*Inform*® test is the predicate test to ThyGenX® and is not commercially available.

### IV. RATIONALE

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#### SUMMARY OF EVIDENCE

To determine which patients need thyroid resection, many physicians will perform a cytologic examination of FNA samples from a thyroid lesion; however, this method has diagnostic limitations. As a result, assays using molecular markers have been developed to improve the accuracy of thyroid FNA biopsies.

For individuals with thyroid nodule(s) and indeterminate findings on FNA who receive FNA sample testing with molecular tests to rule out malignancy and to avoid surgical biopsy or resection, the evidence includes a prospective clinical validity study with the Afirma GSC and a chain of evidence to support clinical utility. The relevant outcomes are disease-specific survival, test accuracy and validity, morbid events, and resource utilization. In a multicenter validation study, the Afirma GSC was reported to have a high (NPV 96%; 95% C I, 90%-99%). These results are consistent with an earlier study on the Afirma GEC in the same study population. In other multicenter and single-center studies, there is suggestive evidence that rates of malignancy are low in Afirma patients who are classified as benign, but the exact NPV is unknown. The available evidence suggests that the decisions a physician makes regarding surgery are altered by Afirma GEC/GSC results; however, it should be noted that long-term follow-up of patients with thyroid nodules who avoided surgery based on GEC results is limited. A chain of evidence can be constructed to establish the potential for clinical utility with GEC testing in cytologically indeterminate lesions, but there is only a single study of the marketed test reporting a true NPV. Clinical input, obtained in 2017, supported the use of the previous version of the Afirma test in FNA of thyroid nodules with indeterminate cytologic findings to rule out malignancy and avoid surgical biopsy with an acceptably low trade-off in missed malignancy. The evidence is sufficient to determine that the technology improves the net health outcome. For individuals with thyroid nodule(s) and indeterminate findings on FNA who receive FNA sample testing with molecular markers to rule in malignancy and to guide surgical planning, the evidence includes prospective and retrospective studies of clinical validity. Relevant outcomes are disease-specific survival, test accuracy and validity, morbid events, and resource utilization. Variant analysis has the potential to improve the accuracy of an equivocal FNA of the thyroid and may play a role in preoperative risk stratification and surgical planning. Single-center studies have suggested that testing for a panel of genetic variants associated with thyroid cancer may allow for the appropriate selection of patients for surgical management for the initial resection. Prospective studies in additional populations are needed to validate these



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results. Although the presence of certain variants may predict more aggressive malignancies, the management changes that would occur as a result of identifying higher risk tumors, are not well established. Clinical input, obtained in 2017, considered ThyraMIR microRNA/ThyGenX, Afirma BRAF after Afirma GEC, and Afirma MTC after Afirma GEC to provide a clinically meaningful improvement for patients with cytologic findings suspicious for malignancy to guide surgical planning for the initial resection. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with thyroid nodule(s) and indeterminate findings on FNA who receive FNA sample testing with molecular markers to rule out malignancy and avoid surgical biopsy or to rule in malignancy for surgical planning, the evidence includes multiple retrospective and prospective clinical validation studies for the ThyroSeq v2 or v3 test and 2 retrospective clinical validation studies that used a predicate test 17-variant panel (miRInform) test to the current ThyGenX and ThyraMIR. The relevant outcomes are disease-specific survival, test accuracy and validity, morbid events, and resource utilization. In a retrospective validation study on FNA samples, the 17-variant panel (miRInform) test and ThyraMIR had a sensitivity of 89%, and an NPV of 94%. A prospective clinical validation study of ThyroSeq v3 reported an NPV of 97% and PPV of 68%. No studies were identified demonstrating the diagnostic characteristics of the marketed ThyGenX. No studies were identified demonstrating evidence of direct outcome improvements. A chain of evidence for the ThyroSeq v3 test and combined ThyGenX and ThyraMIR testing would rely on establishing clinical validity. Clinical input, obtained in 2017, considered ThyroSeq v2 to provide a clinically meaningful improvement for patients with indeterminate cytologic findings to rule out malignancy and avoid surgical biopsy and in patients with cytologic findings suspicious for malignancy to guide surgical planning for the initial resection. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

**V. DEFINITIONS**

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N/A

**VI. BENEFIT VARIATIONS**

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The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations should be based in all cases on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. A member's health benefit plan governs which services are covered, which are excluded, which are subject to benefit limits and which require preauthorization. There are different benefit plan designs in each product administered by Capital Blue Cross. Members and providers should consult the member's health benefit plan for information or contact Capital Blue Cross for benefit information.

**VII. DISCLAIMER**

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*Capital Blue Cross's medical policies are developed to assist in administering a member's benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit*

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information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital Blue Cross' Provider Services or Member Services. Capital Blue Cross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

### VIII. CODING INFORMATION

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**Note:** This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

**RosettaGX Reveal, Thyroseq CRC, Thyroid GuidePx and single-gene *TERT* testing are considered investigational:**

Procedure Codes							
81345	81479*	0287U	0362U				

\*Can be used to bill for RosettaGX Reveal which is INV

**BRAF V600E, RET/PTC, RAS, PAX8/PPAR, Afirma Genomic Sequencing Classifier, ThyroSeq Genomic Classifier, or ThyraMIR<sup>®</sup> microRNA/ThyGeNEXT<sup>®</sup> are covered when medically necessary:**

Procedure Codes							
0018U	0026U	0204U	0245U	81210	81275	81276	81311
81401	81403	81445	81479*	81546			

\*Can be used to bill for RET/PTC Rearrangement which may be MN

ICD-10-CM Diagnosis Codes	Description
D44.0	Neoplasm of uncertain behavior of thyroid gland

### IX. REFERENCES

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### X. POLICY HISTORY

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<b>MP 2.275</b>	<b>3/30/20 Consensus review.</b> Nomenclature updated. Gene Expression updated to replace Afirma GEC to Afirma GSC throughout policy. No change to policy statement. References reviewed and updated.
	<b>9/8/2020 Administrative update.</b> New codes added: 0204U; 02085U
	<b>12/11/2020 Administrative update.</b> Deleted code 81545. Effective 1/1/21.
	<b>2/1/2021 Administrative update.</b> Added new code 0245U as covered with criteria. Effective 4/1/2021.
	<b>11/15/2021 Minor review.</b> Wording “in patients who have the following characteristics” removed from first paragraph in policy statement. No change to criteria. Description/Background updated. References reviewed and updated.
	<b>10/19/2022 Minor review.</b> Updated investigational statement to include Thyroseq CRC Thyroid GuidePx. Reviewed and updated coding and references. Added NCCN statement.
	<b>9/22/2023 Minor review.</b> Updated names of tests to current versions. Added option for non-proprietary testing for specific mutations (BRAF V600E, RET/PTC, RAS, PAX8/PPAR). Added note within policy statement regarding MP 2.259. Updated background, coding, and references.

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