I. Policy: Molecular Markers to Predict Thyroid FNA (Fine-Needle Aspiration)

II. Purpose/Objective:
To provide a policy of coverage regarding Molecular Markers to Predict Thyroid FNA (Fine-Needle Aspiration)

III. Responsibility:
A. Medical Directors
B. Medical Management

IV. Required Definitions
1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than the department requiring/authoring the policy.
3. Devised – the date the policy was implemented.
4. Revised – the date of every revision to the policy, including typographical and grammatical changes.
5. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

V. Additional Definitions
Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
b. provided for the diagnosis, and the direct care and treatment of the Member's condition, illness disease or injury;
c. in accordance with current standards of good medical treatment practiced by the general medical community.
d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient.

Medicaid Business Segment
Medical Necessity shall mean a service or benefit that is compensable under the Medical Assistance Program and if it meets any one of the following standards:

(i) The service or benefit will, or is reasonably expected to, prevent the onset of an illness, condition or disability.
(ii) The service or benefit will, or is reasonably expected to, reduce or ameliorate the physical, mental or development effects of an illness, condition, injury or disability.
(iii) The service or benefit will assist the Member to achieve or maintain maximum functional
capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for members of the same age.

**DESCRIPTION:**
Gene expression analysis and mutation analysis has been developed as a means to identify benign nodules when cytopathology of thyroid fine needle aspirate is indeterminate, thereby reducing the number of unnecessary thyroid surgeries. The testing provides provide valuable additive information that may help guide decisions on the appropriate surgery.

**INDICATIONS:**
Thyroid FNA (Fine-Needle Aspiration) Analysis (e.g., Affirma, ThyraMIR, ThyroSeq, ThyGenX, etc) is considered medically necessary when the thyroid nodule is greater than or equal to 1.0 cm and fine needle aspiration is cytologically considered to be indeterminate, atypical, or suspicious for malignancy

**LIMITATIONS:**
The use of a thyroid nodule gene expression classifier or mutation analysis is considered not medically necessary if criteria above is not met.

**Note:** A complete description of the process by which a given technology or service is evaluated and determined to be experimental, investigational or unproven is outlined in MP 15 - Experimental Investigational or Unproven Services or Treatment.

**CODING ASSOCIATED WITH:**
The following codes are included below for informational purposes and may not be all inclusive. Inclusion of a procedure or device code(s) does not constitute or imply coverage nor does it imply or guarantee provider reimbursement. Coverage is determined by the member specific benefit plan document and any applicable laws regarding coverage of specific services. Please note that per Medicare coverage rules, only specific CPT/HCPCS Codes may be covered for the Medicare Business Segment. Please consult the CMS website at www.cms.gov or the local Medicare Administrative Carrier (MAC) for more information on Medicare coverage and coding requirements.

- **81210**  
  BRAF, gene analysis V600 variant {Affirma malignancy classifier BRAF V600E testing}

- **81445**  
  Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, and RNA analysis when performed, 5-50 genes {ThyGenX}

- **81545**  
  Oncology (thyroid), gene expression analysis of 142 genes, utilizing fine needle aspirate, algorithm reported as a categorical result (eg, benign or suspicious) {Affirma Gene Expression Classifier}

- **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 {ThyraMIR}

- **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") {ThyroSeq}

- **81479**  
  Unlisted molecular pathology procedure


**LINE OF BUSINESS:**
Eligibility and contract specific benefits, limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy. For Medicare, applicable LCD’s and NCD’s will supercede this policy. For PA Medicaid Business segment, this policy applies as written.

**REFERENCES:**
Labourier E, Shifrin A, et al. Molecular Testing for miRNA, mRNA, and DNA on Fine-Needle Aspiration Improves the Preoperative Diagnosis of Thyroid Nodules With Indeterminate Cytology. JCEM 2015;100 (7).


Ohori NP, Nikiforova MN, Schoedel KE, et al. Contribution of molecular testing to thyroid fine-needle aspiration cytology of "follicular lesion of undetermined significance/atypia of undetermined significance". Cancer Cytopathol 2010; 118(1):17-23


Angell, TE, Frates, MC, Medici, M, Liu, X, Kwong, N, Cibas, ES, Kim, MI, and Marqusee, E. Afirma benign thyroid nodules show similar growth to cytologically benign nodules during follow-up. J Clin Endocrinol Metab. 2015;100(11):E1477-E1483

Brauner, E, Holmes, BJ, Krane, JF, Nishino, M, Zurakowski, D, Hennessey, JV, Faquin, WC, and Parangi, S. Performance of the Afirma gene expression classifier in Hurthle cell thyroid nodules differs from other indeterminate thyroid nodules. Thyroid. 2015;25(7):789-796


American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer, Cooper DS, Doherty GM, Haugen BR, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid. 2009; 19(11):1167-1214


Witt RL. Outcome of thyroid gene expression classifier testing in clinical practice. Laryngoscope. 2016; 126(2):524-527

Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid. 2016; 26(1):1-133

Novitas Solutions, Inc. Local Coverage Determination (LCD): Biomarkers for Oncology (L35396) 07/26/18


This policy will be revised as necessary and reviewed no less than annually.

Devised: 1/4/2016

Revised:

Reviewed: 1/17, 1/18, 1/19, 1/20