Purpose
The purpose of this News Article is to provide advance notice regarding the updated coverage position for the Company's Commercial Products for the test called Afirma Thyroid Fine-Needle Aspiration (FNA) Analysis (by Veracyte Inc.) Afirma Thyroid Fine-Needle aspiration (FNA) Analysis (by Veracyte Inc.) is already a covered service for the Company's Medicare Advantage Products when the medical necessity criteria outlined in the Molecular Diagnostics (MA06.017) Policy are met.

Policies Impacted
- Genetic Testing (06.02.35g)
- Molecular Diagnostics (MA06.017)

Background
The Afirma Thyroid Fine-Needle Aspiration (FNA) Analysis includes a standard cytopathologic evaluation of FNA specimens obtained from the thyroid nodules, and an expression analysis of 167 genes in nodules with indeterminate FNA cytopathology. However, the test may only include the gene expression analysis if the initial cytopathologic evaluation was performed elsewhere. The molecular portion of the test, which involves an analysis of ribonucleic acid (RNA) extracted from thyroid nodule aspirates, utilizes the gene expression classifier (GEC) to classify indeterminate nodules as either “benign” or suspicious." A nondiagnostic result indicates that the RNA sample was insufficient for analysis. The Afirma Thyroid FNA Analysis may be considered in adults with thyroid nodules at least 1 centimeter (cm) in size, who are being evaluated for the possibility of a thyroid malignancy.

The Afirma Thyroid FNA Analysis was designed to help distinguish benign and malignant thyroid lesions in adults with indeterminate FNA cytology. The main limitation of the analysis is that adequate sampling of the thyroid nodule is necessary for an accurate assessment, which may require multiple FNA biopsies. According to recent data, between 3% and 10% of thyroid aspirates yield RNA samples that are insufficient for analysis. The first study that examined the analytical validity of the Afirma GEC reported a test sensitivity of 92.3%, with a test specificity of 83.9%. An estimation of false-positive and false-negative rates using 30-times cross-validation yielded a
receiver operating characteristic (ROC) area under the curve (AUC) of 0.96. A more recent study showed that Afirma test performance was not significantly impacted by changes in preanalytic factors such as storage and shipping conditions, and that the test could be reliably performed with as little as 5 nanograms (ng) of input RNA. In addition, the study demonstrated that the assay could tolerate up to 83% blood content and up to 30% genomic deoxyribonucleic acid (DNA) content, without a significant effect on the number of false-negative GEC calls. Moreover, analyses of test reproducibility yielded intra-assay, interassay, interlaboratory, and intranodule concordance rates of 93.9%, 97%, 100%, and 95%, respectively.

The clinical validity of the Afirma GEC was first evaluated using 265 thyroid FNA specimens with indeterminate FNA cytology but known surgical diagnoses. This study indicated that the Afirma test had a clinical sensitivity of 92% and clinical specificity of 52%, while the negative predictive value (NPV) and positive predictive value (PPV) were 93% and 47%, respectively. A second study involving 339 adults with indeterminate thyroid nodules found that 53 of 121 (44%) nodules that were classified as suspicious and had surgical follow-up were malignant on pathological evaluation, for a false-positive rate of 56%. In addition, of 71 adults with nodules classified as benign by the GEC, who also had adequate follow-up data, 1 was found to have a malignant thyroid tumor. While this corresponds to a false-negative rate of 1.4%, the identified malignancy was smaller than 1 cm (the minimal nodule size for FNA biopsy). In a single-institution study involving 58 adults with thyroid nodules of indeterminate cytology, there were 21 confirmed malignancies in 30 adults with a suspicious GEC result and relevant follow-up data, for a false-positive rate of 30%. The false-negative rate in this population was 10%, with 2 of 20 adults having a benign GEC result and a pathologically confirmed malignancy. Calculations based on these data yielded a NPV of 89.6%.

Data regarding the clinical utility of the Afirma Thyroid FNA Analysis indicate that use of this test could lead to a significant reduction in diagnostic thyroid surgery for indeterminate thyroid nodules. In a study, 7.6% of adults with a benign GEC result underwent diagnostic surgery, compared with a historical rate of 74% for adults with indeterminate FNA results (P<0.001). In a subsequent study, follow-up surgery was recommended in 95% of adults who had Afirma results classified as suspicious, compared with only 2% of those with Afirma results classified as benign (P<0.01). Consistent with these findings, a retrospective review of 358 thyroidectomy cases revealed that the overall number of thyroidectomies performed in adults with thyroid nodules would decrease by 7.2% when the Afirma test was used in adults with indeterminate FNA cytology. Moreover, based on the data presented in the 2 most recent studies of clinical utility, use of the Afirma GEC would lead to a change in follow-up recommendations in 41.2% to 50% of adults with indeterminate thyroid nodules. Finally, a modeling study in 2010 suggested that inclusion of Afirma testing in the evaluation of adults with thyroid nodules could result in a slight increase (4.57 versus 4.50) in quality-adjusted life-years (QALY) over a period of 5 years.

Coverage Statement
Afirma Thyroid FNA Analysis is considered medically necessary and, therefore, covered for the evaluation of adults with thyroid nodules (> 1 cm), who are being evaluated for the possibility of a thyroid malignancy.

Coding

THE FOLLOWING CODES REPRESENT AFIRMA THYROID FNA ANALYSIS:

81479, 84999, 89240.

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