Summary of Veracyte Recommendations

Code	Recommendation	2020 CLFS Rate
81XX2	Crosswalk to 81545	$3,600.00
0204U	Crosswalk to 81455	$2,919.60
0208U	Gapfill	N/A
81XX1	Submitted for ADLT, if not approved, Gapfill	N/A

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81XX2: Oncology (thyroid), mRNA, gene expression analysis of 10,196 genes, utilizing fine needle aspirate, algorithm reported as a categorical result (eg, benign or suspicious)

Public Comment	**Rationale**
Crosswalk to 81545 ($3,600)	81545 describes the original Afirma classifier; when the testing platform was updated the AMA required a new code for the Afirma GSC classifier. Test 81XX2 uses the same methodology and sample type, measures the same analyte, has the same indications for use, and reports same results as 81545. The code descriptors are identical with the exception of the gene count. 81545 has been priced on the CLFS at $3,600 since 2018 based on private payor rates submitted under Section 1834A of the Social Security Act.

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Afirma GSC

81XX2: Oncology (thyroid), mRNA, gene expression analysis of 10,196 genes, utilizing fine needle aspirate, algorithm reported as a categorical result (eg, benign or suspicious)

- **Test Purpose**: Afirma GSC is a pre-operative genomic test for thyroid tumor biopsies that have indeterminate (i.e. not clearly benign or malignant) cytopathology. The classifier has a high sensitivity and negative predictive value to aid physicians in identifying patients who may avoid a potentially costly and invasive diagnostic thyroidectomy surgery.
- **Test Methodology:** mRNA-based gene expression assay that incorporates an ensemble model of classifiers to produce a single patient specific result - ***benign*** or ***suspicious for malignancy***
- **Crosswalk Recommendation Rationale:**
  - 81XX2 represents the Afirma classifier with an updated platform, with the new code required by AMA. 81XX2 uses the same methodology and sample type, measures the same analyte, has the same indications for use, and reports same results as 81545, which described the original Afirma classifier. The code descriptors are identical with the exception of the gene count.
  - Afirma has been covered by Medicare since 2012 and since 2018 has been priced at $3,600 on the CLFS based on private payor rates submitted under Section 1834A of the Social Security Act.
  - We recommend CMS maintain the existing, market-based rate for the Afirma classifier, as the market-based rate takes into account the costs of test development and performance.

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0204U: Oncology (thyroid) mRNA gene expression analysis of 593 genes for sequence variants and rearrangements, including BRAF, RAS, RET, PAX8 and NTRK, utilizing fine needle aspirate, reported as detected/not detected

Public Comment	**Rationale**
Crosswalk to 81455 ($2,920)	0208U is consistent with the code descriptor for 81455 in that it is a genomic sequence analysis to detect variants in greater than 50 genes. The panel includes genes that have been identified as clinically relevant oncogenes and driver mutations in thyroid cancer, including common variants that are therapy targets for the treatment of thyroid cancer.

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Afirma Xpression Atlas (XA)

0204U: Oncology (thyroid) mRNA gene expression analysis of 593 genes for sequence variants and rearrangements, including BRAF, RAS, RET, PAX8 and NTRK, utilizing fine needle aspirate, reported as detected/not detected

- **Test Purpose:** Afirma XA can provide clinicians insight into tissue cellular morphology, clinical syndromes, cancer behavior (including mode of metastasis), prognosis, and facilitate the identification of potential therapy targets in the appropriate clinical setting.
- **Test Methodology:** mRNA gene expression analysis of 593 genes for sequence variants and rearrangements that have been reported to be associated with thyroid carcinoma in published studies, including the landmark TCGA CGP study of thyroid carcinoma.
- **Crosswalk Recommendation Rationale:**
  - 0204U aligns with the code descriptor for 81455 in that it is a genomic sequence analysis to detect variants in greater than 50 genes. It includes clinically relevant oncogenes and driver mutations in thyroid cancer, including common variants that are therapy targets for the treatment of thyroid cancer. 0204U includes some of the genes listed as examples in the 81455 code descriptor (BRAF, RAS, RET).
  - 81455 was established as a general code reflecting the resources required to develop and perform large targeted genomic sequencing panels like Afirma XA.
- **Alternative Crosswalk Recommendation**: 0048U ($2920) - MSK Impact Test
  - OO48U and 0204U are both NGS gene panels that interrogate a similar number of genes, 468 and 593 respectively. Their test purposes are similar in that they both help clinicians better understand genetic drivers of therapeutic targets and/or prognostic predictors.

0208U: Oncology (medullary thyroid carcinoma), mRNA, gene expression analysis of 108 genes, utilizing fine needle aspirate, algorithm reported as positive or negative for MTC

Public Comment	**Rationale**
Gapfill	There is no comparable test on the CLFS to which we would recommend crosswalk

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Afirma MTC

0208U: Oncology (medullary thyroid carcinoma), mRNA, gene expression analysis of 108 genes, utilizing fine needle aspirate, algorithm reported as positive or negative for MTC

- **Test Purpose:** Medullary thyroid cancer (MTC) accounts for only 2.2% of thyroid cancers, but is responsible for 13.5% of its mortality. The Afirma MTC classifier can preoperatively diagnose medullary thyroid cancer from the initial fine needle aspiration biopsy and is more sensitive than traditional methods of detecting MTC. A specific diagnosis of MTC is critical to planning the optimal thyroid surgery including central neck lymph-node dissection.
- **Test Methodology:** mRNA-based gene expression assay utilizing a unique algorithm to classify thyroid FNA biopsy samples as **Positive** or **Negative for MTC**.
- **Recommendation Rationale:** Recommend gapfill as there is no comparable test on the CLFS to which we would recommend crosswalk

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81XX1: Pulmonology (idiopathic pulmonary fibrosis), mRNA, gene expression analysis of 190 genes, utilizing transbronchial biopsies, diagnostic algorithm reported as positive or negative

Public Comment	**Rationale**
Submitted application for New ADLT approval	If not approved as a New ADLT, we recommend Gapfill since this test is unique and there is no comparable test on the CLFS

Envisia Genomic Classifier

81XX1: Pulmonology (idiopathic pulmonary fibrosis), mRNA, gene expression analysis of 190 genes, utilizing transbronchial biopsies, diagnostic algorithm reported as positive or negative

- **Test Purpose:** Envisia uses molecular signatures from lung tissue to help diagnose a rare disease called Idiopathic Pulmonary Fibrosis (IPF). IPF is difficult to diagnose, often requiring surgical lung biopsy to get a diagnosis. Veracyte developed Envisia to increase diagnostic accuracy and reduce the need for surgical lung biopsies in patients suspected to have IPF.
- **Test Methodology:** mRNA-based gene expression assay that utilizes a unique algorithm to classify lung transbronchial biopsy samples into a single patient specific result – ***Positive for UIP*** or ***Negative for UIP*** (Usual Interstitial Pneumonia refers to a histopathological signature that is required to be present to make an IPF Dx)
- **Crosswalk Recommendation Rationale:**
  - Veracyte has submitted an application for approval of the Envisia Genomic Classifier as a New ADLT. If the application is approved, the test will be priced at Actual List Charge and then based on private payor rates, as required under Section 1834A of the Social Security Act.
  - If not approved as a New ADLT, Envisia should be gapfilled since this test is unique and there is no comparable test on the CLFS

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