Payer Coverage Policies of Tumor Biomarker Testing

September 2020

Commissioned By: American Cancer Society Cancer Action Network and LUNGevity Foundation

Conducted By: ADVI

Table of Contents

Overview of ADVI's Research Approach

Through secondary research efforts, ADVI evaluated payer policies and collated our findings to identify trends and opportunities for patient access to appropriate biomarker testing (also referred to as molecular testing and molecular profiling in this document) in selected tumor types, including non-small cell lung cancer, colorectal cancer, breast cancer, and prostate cancer. Also, ADVI evaluated payer policies to understand adoption and coverage of liquid biopsy (also referred to as blood-based biomarker testing, plasma cell-free/circulating tumor DNA) assays. ADVI considered how the type of test (e.g., single analyte, Next Generation Sequencing (NGS) panel, Multi-analyte assays with algorithmic analyses (MAAAs), or immunohistochemistry (IHC) impacted payer policies and clinical guidelines. ADVI focused on national commercial payers with a sampling of regional commercial payers (that have high incidence of the tumor types of interest in their populations) as well as local Medicare Administrative Contractors (MACs).

ADVI conducted a similar analysis in 2018, and this report reflects updates as of September 2020.

Executive Summary

For oncology biomarkers, commercial payers have uniformly covered companion diagnostics (historically single analytes approved in parallel with a therapeutic agent) because clinical utility is established as a component of FDA review. In a departure from this paradigm, F1CDx has not achieved uniform coverage. For other biomarkers that are not FDA reviewed, commercial payers rely upon National Comprehensive Cancer Network (NCCN) guidelines, American Society of Clinical Oncology (ASCO) guidelines, Technology Assessment organizations, and peer-reviewed published evidence. Often, evidence of clinical utility is the determinant of coverage.

The addition of new companion diagnostics is generally acted upon promptly by payers, likely a consequence of the mandated coverage of the therapeutic agent that the companion diagnostic (CDx) supports. The one exception is the very inconsistent coverage of FoundationOne CDx (F1CDx) across payers. While F1CDx has numerous CDx indications, the inclusion of multiple biomarkers in this panel that do not have established clinical utility continues to be a challenge.

Since our last review, the number of commercial payers specifically covering F1CDx has increased substantially. However, numerous payers including Aetna, United and most BCBS plans continue to consider large multi-gene panels as experimental and investigational (E&I). This is most certainly due to the number of genes included that are felt to be inactionable.

There is continued payer skepticism that large panels meet the clinical utility threshold. Depending on the tumor type, the number of recognized biomarkers with clinical utility may number fewer than five. It is difficult, therefore, to justify coverage of a panel with 50 or more genes. Consequently, payers may consider the entire test to be E&I if all genes on the panel do not have established utility. Others will cover the test but negotiate payment only for those medically necessary biomarkers. While multi-gene panels can identify patients eligible for clinical trials, the mandate to cover clinical trials does not extend to testing to determine eligibility.

Biomarker testing in solid tumors continues to be hampered by the discordance between the number of genes in multi-gene panels and the generally accepted genes that are true companion diagnostics. The continued identification of single biomarkers as companion diagnostics as well as tumor site agnostic biomarkers, particularly those not measured well except by NGS (e.g., TMB), will likely lead to positive coverage determinations, albeit slowly. Alternatively, the introduction of smaller, targeted panels would likely be embraced by payers, especially if FDA-approved. In fact, payers may even choose a panel with less than 50 genes that only has NY state accreditation[1] over a panel with over 50 genes that has FDA approval.

As the number of single genes that should be tested has increased, and as challenges with tissue adequacy has been more universally recognized, it is likely that panels will be universally covered in NSCLC, particularly those with less than 50 genes. NSCLC has an adequate number of actionable biomarkers for payers to consider coverage of NGS panels. Breast cancer, colon cancer, and prostate cancer do not have an adequate number of biomarkers with established utility to warrant coverage of large panels.

Tumor site agnostic biomarkers, including NTRK, TMB, MSI, and HRD, present a specific challenge. Although NTRK is routinely covered as a specific biomarker, in many cases, the testing is done via IHC, which is suboptimal. In general, NTRK sequencing as well as homologous recombination deficiency (HRD) are only available as a component of a multi-gene panel. Accordingly, these relatively uncommon patients are not being identified and therefore are ineligible to receive the optimal treatment for their malignancy. This is even more of an issue for immuno-oncology (IO) therapy and microsatellite instability (MSI) high and tumor mutational burden (TMB) high patients. MSI can be assessed outside of a multi-gene panel, but in general TMB cannot. Consequently, the pan-tumor approval of the IO companion therapy for these patients is difficult in practice if panels are not covered. This paradox requires action.

The coverage of proprietary "gene expression" panels is tumor site specific. In breast cancer, these panels are widely covered and are believed by payers to have significant clinical utility based on internal and peer-reviewed data. Coverage in colon cancer and prostate cancer are much less common; this is largely related to the lack of evidence supporting clinical utility.

Biomarker testing in solid tumors is considered standard of care and is critical to supporting coverage policy for therapeutic agents in oncology, particularly drugs managed by specialty pharmacy.

The maturation of the evidence base for liquid biopsy coupled with challenges of biopsy tissue stewardship has resulted in some payer coverage, particularly for CDx indications in NSCLC and breast cancer. Challenges with having adequate tissue to allow sequential biomarker testing in lung cancer (as recognized in the NCCN guidelines) has clearly impacted coverage policy for NGS panels in NSCLC. It is reasonable to expect the same logic to facilitate broader coverage of liquid biopsy.

The recent FDA approvals of Guardant360 CDx and FoundationOne Liquid CDx will expand coverage for liquid biopsy panels. The performance characteristics, especially analytic and clinical validity, of other liquid biopsy assays has historically been an issue, but concerns should be resolved by the FDA approvals.

[1] https://www.wadsworth.org/regulatory/clep/clinical-labs/obtain-permit/test-approval

Non-Small Cell Lung Cancer (NSCLC)

Key Takeaways

Most payers cover and pay for select individual biomarkers, including EGFR, ALK, ROS1, BRAF, and NTRK. Some payers also cover KRAS. Emerging biomarkers, like HER2, RET, and MET, are covered by even fewer payers.

Since our 2018 review, tissue-based multi-gene panels in NSCLC are more widely covered though there are still large gaps in coverage. There seems to be growing recognition by payers that sequential testing of individual biomarkers is not practical when patients have limited tissue available and the results of these tests can inform urgent treatment decisions. The increasing number of individual actionable analytes in NSCLC is leading to a consideration of coverage for a panel as the most expeditious and potentially most cost-effective approach.

Payers recognize the value of liquid biopsies in NSCLC in certain clinical scenarios. Most notably, if a patient is medically unfit for invasive tissue sampling of a metastatic focus or if following pathologic confirmation of a NSCLC diagnosis there is insufficient material for molecular analysis.

Clinical Guidelines

NCCN Guidelines (Version 6.2020)[2] currently support biomarker testing of PD-L1 expression, EGFR mutations, ALK rearrangements, ROS1 rearrangements, BRAF mutations, KRAS mutations, and NTRK fusions. PDL1 testing, routinely performed by IHC, is recommended though not required by the guidelines for administration of check-point inhibitor therapy. There are numerous antibodies used with varying performance characteristics to measure PDL1 expression; this precludes explicit guidance on testing details. On the other hand, the guidelines acknowledge that "although PD-L1 expression can be elevated in patients with an oncogenic driver, targeted therapy for the oncogenic driver should take precedence over treatment with an immune checkpoint inhibitor." This relates to the somewhat controversial suggestion that IO therapy is less effective in patients with driver mutations. The guidelines identify the following emerging biomarkers: HER2 mutations, MET amplifications, RET gene rearrangement, and tumor mutational burden (TMB). To conserve tissue, NCCN recommends broad biomarker testing using a validated test to assess a minimum of the following genetic variants: EGFR mutations, BRAF mutations, METex14 skipping mutations, RET rearrangements, ALK fusions, and ROS1 fusions. NCCN also recommends broad biomarker testing to identify rare driver mutations for which effective therapy may be available – NTRK gene fusions, high-level MET amplification, HER2 mutations, and TMB.

Gene	NCCN Category	Change Since 2018
PD-L1	1	
ALK	1	
EGFR	1	
ROS1	2A	
KRAS	2A	
BRAF	2A	
NTRK 1/2/3	2A	Added

[2] https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf

MET	2A	
RET	2A	
HER2	2B	
TMB	2A	Added

Liquid biopsy may be considered at progression to detect whether patients have T790M. However, the guidelines explicitly state that liquid biopsy should not be used to diagnose NSCLC. Generally, studies have shown liquid biopsy testing has high specificity but low sensitivity, with up to 30% false negative rate. Additionally, standards for analytical performance characteristics of liquid biopsy have not been established and there are no guideline recommendations regarding performance characteristics.

With respect to IHC testing, the guidelines state that IHC may be used to detect ALK fusions, ROS1 rearrangements, and NTRK fusions. However, the guidelines also note some limitations of IHC. For detection of ROS1 rearrangements, the guidelines acknowledge that IHC has low specificity and follow-up confirmatory testing is a necessary component of utilizing ROS1 IHC as a screening modality. For analysis of NTRK fusions, the guidelines recognize that IHC methods are complicated by baseline expression in some tissues.

Updated Molecular Testing Guideline for the Selection of Lung Cancer Patients for Treatment with Targeted Tyrosine Kinase Inhibitors[3] represents a 2018 evaluation by the College for American Pathologists (CAP), International Association for the Study of Lung Cancer (IASLC), and the Association for Molecular Pathology (AMP). This joint guideline recommends multiplexed genetic sequencing panels (e.g., NGS testing) over multiple single-gene tests to identify other treatment options beyond EGFR, ALK, and ROS1. When NGS is performed, several other genes are also recommended – BRAF, ERBB2, MET, RET, and KRAS.

ASCO Guideline (2018). Molecular Testing Guideline for the Selection of Patients with Lung Cancer for Treatment with Targeted Tyrosine Kinase Inhibitors[4] supports testing for EGFR, ALK, BRAF, and ROS1. New in 2018 were recommendations for stand-alone ROS1 testing with additional confirmation testing in all patients with advanced lung adenocarcinoma, and RET, ERBB2 (HER2), KRAS, and MET testing as part of larger panels. ASCO also recommends stand-alone BRAF testing in patients with advanced lung adenocarcinoma. The guideline also preferentially supports multiplexed genetic sequencing panels, where available, over multiple single-gene tests to identify other treatment options beyond EGFR, ALK, BRAF, and ROS1. The guideline recognizes IHC as an appropriate testing methodology for ALK and ROS1.

[3] https://www.amp.org/clinical-practice/practice-guidelines/updated-molecular-testing-guideline-for-the-selection-of-lung-cancer-patients-for-treatment-with-targeted-tyrosine-kinase-inhibitors/
[4] http://ascopubs.org/doi/full/10.1200/JCO.2017.76.7293

National Commercial Payers

Payer	Medical Policy	Covered Biomarkers/Tests	Date of Last Review	CPT Codes
Aetna	Tumor Markers (link)	ALK, EGFR, KRAS, ROS-1, BRAF V600 Targeted solid organ genomic sequencing panel (5-50 genes) VeriStrat Non-covers liquid biopsy for any indication	06/08/2020	81235, 81275, 81276, 81210 0022U, 81445 81538
	Pharmacogenetic and Pharmacodynamic Testing (link)	• Measurement of microsatellite instability and mismatch repair for persons with unresectable or metastatic solid tumors being considered for treatment with pembrolizumab • MET exon 14 skipping mutation testing (e.g., FoundationOneCDx) for persons with advanced, recurrent or metastatic NSCLC being considered for treatment with the kinase inhibitor capmatinib • FDA-approved test for the ALK fusion gene (e.g., the Vysis ALK Break Apart FISH Probe Kit; Ventana ALK (D5F3) CDx Assay) for persons who are considering crizotinib, alectinib or ceritinib for the treatment of NSCLC • BRAF gene mutations (V600E or V600K) (e.g., the THxID BRAF test, cobas 4800 BRAF V600 mutation test) for persons with recurrent or metastatic NSCLC being considered for treatment with dabrafenib, pembrolizumab, or vemurafenib • EGFR exon 19 deletions or exon 21 (L858R) substitution mutations (e.g., cobas EGFR Mutation Test, therascreen EGFR RGQ PCR Kit) for persons with NSCLC being considered for treatment with erlotinib, dacomitinib, gefitinib, or afatinib • EGFR T790 mutation (e.g., cobas EGFR Mutation Test v2) for persons with NSCLC being considered for treatment with osimertinib • PD-L1 expression (e.g., PD-L1 IHC 22C3 pharmDx) for persons with NSCLC being considered for treatment with pembrolilzumab • Testing to detect PD-L1 expression (e.g., Ventana PD-L1 (SP142) Assay) medically necessary for persons with NSCLC who are being considered for treatment with atezolizumab	07/20/2020	81301, 88341, 88342, 81210, 81235

Anthem	Whole Genome Sequencing, Whole Exome Sequencing, Gene Panels, and Molecular Profiling (link)	FoundationOne CDx MSK-IMPACT MI Cancer Seek For unresectable or metastatic solid tumors when all of the criteria below are met: • The test is used to assess tumor mutation burden and identify candidates for checkpoint inhibition immunotherapy; and • Individual has progressed following prior treatment; and • Individual has no satisfactory alternative treatment options Non-covers liquid biopsy	08/13/2020	0037U 0048U 0211U
	EGFR Testing (link)	• Analysis of mutations in EGFR as a technique to predict treatment response for individuals with nonsquamous NSCLC when treatment with EGFR TKI therapy is indicated • Use of a circulating tumor DNA test to detect mutations of the EGFR gene when the volume of formalin-fixed paraffin-embedded tumor tissue available for testing is insufficient and the individual meets criterion above	11/07/2019	81235
	BRAF Mutation Analysis (link)	BRAF V600 mutations to identify those who would benefit from treatment with an FDA-approved BRAF inhibitor	08/13/2020	81210
	Circulating Tumor DNA Testing for Cancer (Liquid Biopsy) (link)	Investigational and not medically necessary for all indications	11/07/2019	81479, 0179U
Cigna	Tumor Profiling, Gene Expression Assays and Molecular Diagnostic Testing for Hematology/Oncology Indications (link) Genetic Testing Collateral (link)	ALK rearrangements BRAF (targeted mutation analysis or sequencing) EGFR Mutation Testing HER2 (ERBB2) Mutation Testing KRAS Mutation Testing MET Amplification RET Gene Rearrangements ROS Gene Rearrangements Guardant360 (to predict response to gefitinib) Oncomine Dx Target Test VeriStrat	11/15/2019	81210, 81235, 81275, 81276, 81404, 81405, 81406, 0022U, 81538

Humana	Genetic Testing for Diagnosis and Monitoring of Cancer and Molecular Profiling (link)	Non-covers NGS-based cancer profiling tests (lists examples but may not be all inclusive)	03/25/2020	81445, 81455, 0048U, 0050U, 0171U (Non-covered)
	Pharmacogenomics and Companion Diagnostics (link)	Panels including, but may not limited to, multiple genes or multiple conditions, and in cases where a tiered approach/method is clinically available, may be covered ONLY for the number of genes or tests deemed medically necessary to establish a diagnosis • ALK – prior to initiation of Alectinib, Alunbrig or Xalkori • BRAF (FDA-approved test) • EGFR (FDA-approved test) – predict response to Gilotrif, Iressa, Tagrisso and Tarceva • ROS1 – prior to the initiation of Xalkori • Serum proteomic testing – prior to initiation of Tarceva • NTRK test – metastatic solid tumor, prior to treatment with Vitrakvi Non-covers FoundationOne CDx (except for ovarian cancer indication)	08/27/2020	81210, 81235 81538

	Liquid Biopsy (link)	cobas EGFR mutation test v2
		• Performed as a companion diagnostic to aid in the selection of targeted treatment with Tarceva, Iressa ; AND
		  ○ Metastatic nonsquamous* NSCLC; OR
		  ○ Metastatic squamous NSCLC and individual is a never smoker; OR
		• Performed as a companion diagnostic to aid in the selection of targeted treatment with Gilotrif; AND
		  ○ Metastatic nonsquamous *NSCLC; OR
		  ○ Metastatic squamous NSCLC progressing after platinum-based chemotherapy
			01/28/2020	

UHC	Molecular Oncology Testing for Cancer Diagnosis, Prognosis, and Treatment Decisions (link)	Targeted solid organ genomic sequencing panel when: • The panel selected has no more than 50 genes; and • No prior molecular profiling has been performed on the same tumor; and • Individual and treating physician have had a discussion prior to testing regarding the potential results of the test and determined to use the results to guide therapy	07/01/2020	81445

Liquid biopsy testing when:

- The test selected has no more than 50 genes; and
- No prior molecular profiling has been performed on the same tumor; and
- The individual is not medically fit for invasive biopsy; or
- Non-small cell lung cancer has been pathologically confirmed, but there is insufficient material available for molecular testing; and
- Individual and treating physician have had a discussion prior to testing regarding the potential results of the test and determined to use the results to guide therapy

Regional Commercial Payers

Payer	Medical Policy	Covered Biomarkers/Tests	Date of Last Review	CPT Codes
BCBSA	Molecular Analysis for Targeted Therapy for NSCLC (link)	EGFR (exons 18-21), ALK, BRAF V600E, ROS1, NTRK (Covered) KRAS, HER2, RET, MET, TMB (Non-Covered)	11/07/2019	81210, 81235, 81401 (Covered)
	Tumor/Genetic Markers (link)	Non-covers comprehensive genomic profiling Covers EGFR liquid biopsy testing (using EGFR Mutation Test v2, Guardant360, OncoBEAM, InVisionFirst-Lung)	12/05/2019	81235 (Covered) 81445, 81455, 0013U, 0014U, 0019U, 0048U, 0111U, 0174U (Non-covered)
Blue Cross Blue Shield Arizona - eviCore	EGFR Testing for Non-Small Cell Lung Cancer TKI Response (link)	• EGFR targeted mutation testing is indicated in individuals with metastatic NSCLC prior to initiation of treatment with erlotinib, afatinib, gefitinib, or osimertinib therapy. • For patients whose disease progresses either on or after TKI therapy, repeat EGFR testing to identify the emergence of a T790M mutation may be considered to determine whether further treatment with osimertinib would be indicated. • Liquid biopsy testing for EGFR targeted mutations will be considered medically necessary for individuals meeting the above criteria and when billed as an individual tumor marker	v2.0.2020	81235
BCBSMA	Expanded Molecular Panel Testing of Cancers to Identify Targeted Therapies (link) AIM Specialty Health (link)	Covers expanded cancer mutation panels (Stage IIIB, IV or recurrent NSCLC) • ALK, BRAF, EGFR, ROS1, ERBB2 (HER2), MET, RET, KRAS Liquid biopsy testing • Stage IIIb and above when tissue biopsy is not available/insufficient • Stage IIIb and above NSCLC having a confirmed EGFR sensitizing P/LP variant with progression on EGFR TKI therapy (excluding osimertinib) for EGFR T790M status PA via AIM Specialty Health required for commercial managed care beneficiaries	April 2019	81445, 81455, 0037U
BCBSMN	Expanded Molecular Panel Testing of Solid Tumors (link)	Expanded molecular panel testing using tumor tissue samples OR plasma genotyping (i.e., liquid biopsy) may be considered medically necessary and appropriate for selection of targeted therapy in patients with metastatic NSCLC	September 2019	0022U, 0037U, 0174U, 0179U, 81479, 81455

Blue Shield California	Circulating Tumor DNA for Management of Non-Small-Cell Lung Cancer (Liquid Biopsy) (link)	Advanced (stage III or IV) or metastatic NSCLC when an initial diagnostic biopsy sample has insufficient tissue available to complete testing (or the testing is inconclusive) • cobas EGFR Mutation Test v2 • FoundationOne Liquid • Guardant360 • OncoBEAM Lung1 • OncoBEAM Lung2 • InVision First-Lung	August 2020	81445, 81455
Blue Cross Blue Shield Kansas City	Liquid Biopsy (link)	Stage IIIB/IV NSCLC • At diagnosis: When results for EGFR SNVs and indels; ALK and ROS1 rearrangements; and PD-L1 expression (by IHC) are not available AND when tissue based comprehensive somatic genomic profiling test is infeasible (i.e., quantity not sufficient for tissue based CGP or invasive biopsy is medically contraindicated); OR • At progression: For patients progressing on or after chemotherapy or • immunotherapy who have never been tested for EGFR SNVs and indels; and ALK and ROS1 rearrangements, and for whom tissue-based CGP is infeasible (i.e., quantity not sufficient for tissue-based CGP); OR For patients progressing on EGFR TKIs.	05/01/2020	81235, 81479
Highmark	Tumor Marker Testing-Solid Tumors (link)	EGFR, ALK Multi-gene panels when: • At least five tumor markers included in the panel individually meet criteria for the member's tumor type based on one of the following: • All criteria are met from a test-specific policy if ONE is available; or • An oncology therapy FDA label requires results from the tumor marker test to effectively or safely use the therapy for the member's cancer type; or • NCCN guidelines include the tumor marker test in the management algorithm for that particular cancer type and all other requirements are met (specific pathology findings, staging, etc.); however, the tumor marker must be explicitly included in the guidelines and not simply included in a footnote as an intervention that may be considered; or • The NCCN Biomarker Compendium has a level of evidence of at least 2A for the tumor marker's application to the member's specific cancer type.	March 2018	81235, 81401, 81479, 81445, 81455

Highmark-eviCore	Liquid Biopsy Testing - Solid Tumors (link)	Guardant360 testing for NSCLC • The Guardant360 multi-gene panel will only be considered for reimbursement when billed with an appropriate panel CPT code. When multiple CPT codes are billed for components of the panel, eviCore will redirect to the appropriate panel code.	v2.0.2020	81479
Priority Health	Multi-marker tumor panels (link)	NGS testing for patients newly diagnosed with stage IV NSCLC Liquid biopsy testing • Guardant360 • FoundationOne Liquid • EGFR	May 2019	81445, 81455, 0037U
	Genetics: Counseling, Testing, Screening (link)	Prior authorization (PA) and eviCore guidelines	May 2018	81445, 81455, 0037U
Wellmark	Circulating Tumor DNA for Management ff Non-Small Cell Lung Cancer (Liquid Biopsy) (link)	EGFR: cobas EGFR Mutation Test v2, Guardant360 test, OncoBEAM Lung test ALK: Guardant360, OncoBEAM Lung test ROS1: Guardant360, OncoBEAM Lung test BRAF V600E: Guardant360, OncoBEAM Lung test NTRK: Guardant360 KRAS: Guardant360, OncoBEAM Lung test	September 2019	81235, 81210, 81479

Local Medicare Administrative Contractors (MACs)

Payer	Medical Policy	Covered Biomarkers/Tests	Date of Last Review	CPT Codes
All MACs	NGS for Medicare Beneficiaries with Advanced Cancer (link)	• Patient has: ○ either recurrent, relapsed, refractory, metastatic, or advanced stage III or IV cancer; and ○ not been previously tested with the same test using NGS for the same cancer genetic content, and ○ decided to seek further cancer treatment (e.g., therapeutic chemotherapy) • The diagnostic laboratory test using NGS must have: ○ FDA approval or clearance as a companion in vitro diagnostic; and, ○ an FDA-approved or -cleared indication for use in that patient's cancer; and, ○ results provided to the treating physician for management of the patient using a report template to specify treatment options FoundationOne CDx Oncomine Dx Target Test FoundationOne Liquid CDx Guardant360 CDx	01/27/2020	0037U 0022U 0111U
MolDX	Inivata, InVisionFirst, Liquid Biopsy for Patients with Lung Cancer (link)	InVisionFirst	03/05/2020	81479
	Plasma-Based Genomic Profiling in Solid Tumors (link)	Guardant360 • Other liquid biopsies will be covered for the same indications if they display similar performance in their intended used applications to Guardant360®	03/05/2020	81479
NGS	Genomic Sequence Analysis Panels in the Treatment of Solid Organ Neoplasm (link)	• Newly diagnosed patients with advanced (stage IIIB or IV) NSCLC, who are not treatable by resection or radiation with curative intent, and who are suitable candidates for therapy at the time of testing. • Previously diagnosed patients with advanced (stage IIIB or IV) NSCLC, who have not responded to at least one systemic therapy, or who have progressed following resection. The patient must be a candidate for treatment at the time of the testing. • Previously diagnosed patients with advanced (stage IIIB or IV) NSCLC, who have been resistant to at least one targeted therapy, are able to undergo tumor tissue biopsy for testing, and who are suitable candidates for additional treatment at the time of testing.	02/14/2019	81445, 0048U

Novitas	Biomarkers for Oncology (link)	EGFR, KRAS, BRAF Oncomine DX Target Test LungSeq	07/01/2020	81235, 81275, 81276 0022U 81445

Colorectal Cancer (CRC)

Key Takeaways

All payers cover select individual biomarkers in CRC, and these biomarkers are fairly consistent across plans. Generally, NRAS, KRAS, and BRAF are considered medically necessary. Few payers cover MSI and NTRK testing.

With rare exceptions, payers consider tissue-based multi-gene panels in CRC to be experimental and investigational. The relative lack of actionable targets makes it difficult to establish clinical utility of a panel.

Since our 2018 review, there has been little change in coverage of panels for colorectal cancer. Emerging evidence supporting the role of IO therapy earlier in the treatment of metastatic colon cancer will increase the pressure on payers to cover panels.

Clinical Guidelines

NCCN Guidelines (Version 4.2020) support biomarker testing of KRAS, NRAS, and BRAF mutations as well as HER2 amplifications in patients with metastatic CRC. Microsatellite instability (MSI) or mismatch repair (MMR) testing is also supported. The guidelines do not recommend a specific methodology but acknowledge that NGS panels have the advantage of being able to detect rare and actionable genetic alterations, like NTRK fusions. If the recommended biomarkers are tested individually, HER2 testing is not required for patients whose tumor is already known to have a KRAS/NRAS or BRAF mutation. The guidelines also limit testing for NTRK fusions to those patients with those with WT KRAS, NRAS, and BRAF.

Gene	NCCN Category	Change Since 2018
KRAS/NRAS	2A	
BRAF V600E	2A	
MSI	2A	
HER2	2A	Added
NTRK 1/2/3	2A	Added

The guidelines review several multi-gene panels for prognosis and recurrence, including Oncotype DX Colon, ColoPrint, and ColDx. The guideline states that there is insufficient data to recommend the use of multi-gene assay panels to determine adjuvant therapy in colon cancer patients.

European Society for Medical Oncology (ESMO)[5] (2016) support biomarker testing of RAS, BRAF, and MSI in patients with metastatic CRC.

> RAS testing should be carried out on all patients at the time of diagnosis of mCRC. RAS testing is mandatory before treatment with the EGFR-targeted monoclonal antibodies cetuximab and panitumumab. RAS analysis should include at least KRAS exons 2, 3 and 4 (codons 12, 13, 59, 61, 117 and 146) and NRAS exons 2, 3 and 4 (codons 12, 13, 59, 61 and 117).

[5] https://www.esmo.org/Guidelines/Gastrointestinal-Cancers/Management-of-Patients-with-Metastatic-Colorectal-Cancer

Tumor BRAF mutation status should be assessed alongside the assessment of tumor RAS mutational status for prognostic assessment (and/or potential selection for clinical trials).

MSI testing in the metastatic disease setting can assist clinicians in genetic counselling. MSI testing has strong predictive value for the use of immune check-point inhibitors in the treatment of patients with mCRC.

Combined guideline from the American Society for Clinical Pathology (ASCP), College of American Pathologists (CAP), Association for Molecular Pathology (AMP), and ASCO (Version 2017)[6]

1. Colorectal carcinoma patients being considered for anti-EGFR therapy must receive RAS mutational testing. Mutational analysis should include KRAS and NRAS codons 12, 13 of exon 2; 59, 61 of exon 3; and 117 and 146 of exon 4 ("expanded" or "extended" RAS)

   Strength of Evidence: convincing/adequate, benefits outweigh harms; Quality of Evidence: high/intermediate.

2a. BRAF p.V600 (BRAF c. 1799 (p.V600) mutational analysis should be performed in colorectal cancer tissue in patients with colorectal carcinoma for prognostic stratification

   Strength of Evidence: adequate/inadequate, balance of benefits and harms; Quality of Evidence: intermediate/low.

2b. BRAF p.V600 mutational analysis should be performed in deficient MMR tumors with loss of MLH1 to evaluate for Lynch Syndrome risk. Presence of a BRAF mutation strongly favors a sporadic pathogenesis. The absence of BRAF mutation does not exclude risk of Lynch syndrome

   Strength of Evidence: adequate/inadequate, balance of benefits and harms; Quality of Evidence: intermediate/low.

3. Clinicians should order mismatch repair status testing in patients with colorectal cancers for the identification of patients at high risk for Lynch syndrome and/or prognostic stratification

   Strength of Evidence: adequate/inadequate, balance of benefits and harms; Quality of Evidence: intermediate/low.

[6] http://ascopubs.org/doi/full/10.1200/JCO.2016.71.9807

National Commercial Payers

Payer	Medical Policy	Covered Biomarkers/Tests	Date of Last Review	CPT Codes
Aetna	Tumor Markers (link)	KRAS, NRAS, BRAF tumor tissue genotyping Mismatch repair (MSI/dMMR) (MLH1, MSH2, MSH6) tumor testing Non-covers liquid biopsy for any indication	06/08/2020	81275, 81276, 81311, 81210, 81292, 81293, 81294
	Pharmacogenetic and Pharmacodynamic Testing (link)	• Measurement of microsatellite instability and mismatch repair for persons with unresectable or metastatic solid tumors being considered for treatment with pembrolizumab • BRAF and NRAS mutations (e.g., cobas KRAS Mutation Test; therascreen KRAS RGQ PCR Kit, Dako EGFR pharmDx Kit) for persons being considered for treatment with cetuximab or panitumumab • Praxis Extended RAS Panel for persons with colorectal cancer who do not have specific mutations in RAS genes [KRAS (exons 2, 3, and 4) and NRAS (exons 2, 3, and 4)] who are being considered for treatment with panitumumab	07/20/2020	81301, 88341, 88342, 81210, 81275, 81276, 0111U
Anthem	Whole Genome Sequencing, Whole Exome Sequencing, Gene Panels, and Molecular Profiling (link)	FoundationOne CDx MSK-IMPACT MI Cancer Seek For unresectable or metastatic solid tumors when all of the criteria below are met: • The test is used to assess tumor mutation burden and identify candidates for checkpoint inhibition immunotherapy; and • Individual has progressed following prior treatment; and • Individual has no satisfactory alternative treatment options Non-covers liquid biopsy	08/13/2020	0037U 0048U 0211U
	Gene Expression Profiling for Colorectal Cancer (link)	Non-covers gene expression profiling to manage CRC, including but not limited to its use for predicting the likelihood of the	11/07/2019	81525

		development of CRC as well as the likelihood of disease recurrence in individuals with a history of CRC		
	KRAS Status (link)	KRAS, NRAS to predict treatment response to cetuximab or panitumumab	05/20/2020	81275, 81276, 81311, 0111U
	BRAF Mutation Analysis (link)	BRAF V600 mutations to identify those who would benefit from EGFR-directed therapy, or treatment with an FDA-approved BRAF inhibitor	08/13/2020	81210
	Circulating Tumor DNA Testing for Cancer (Liquid Biopsy) (link)	Investigational and not medically necessary for all indications	11/07/2019	81479, 0179U
Cigna	Tumor Profiling, Gene Expression Assays and Molecular Diagnostic Testing for Hematology/Oncology Indications (link) Genetic Testing Collateral (link)	KRAS NRAS BRAF	10/15/2019	81275, 81276 81311 81210
Humana	Genetic Testing for Diagnosis and Monitoring of Cancer and Molecular Profiling (link)	Non-covers NGS-based cancer profiling tests (lists examples but may not be all inclusive)	03/25/2020	81445, 81455, 0048U, 0050U, 0171U (Non-covered)
	Pharmacogenomics and Companion Diagnostics (link)	Panels including, but may not limited to, multiple genes or multiple conditions, and in cases where a tiered approach/ method is clinically available, may be covered ONLY for the number of genes or tests deemed medically necessary to establish a diagnosis • BRAF (FDA-approved test, therascreen BRAF V600E RGQ PCR Kit) – prior to initiation of Braftovi in combination with Erbitux • KRAS, NRAS – prior to initiation of Erbitux or Vectibix • NTRK test – metastatic solid tumor, prior to treatment with Vitrakvi	08/27/2020	81275, 81276 81311 0111U (non-covered)

		Non-covers FoundationOne CDx (except for ovarian cancer indication)		
UHC	Molecular Oncology Testing for Cancer Diagnosis, Prognosis, and Treatment Decisions (link)	Non-covers multi-gene panels for CRC (e.g., Oncotype DX Colon Cancer Assay, Colorectal Cancer DSA, GeneFx Colon, OncoDefender CRC) Non-covers liquid biopsy for CRC	7/1/2020	81445, 81455 (Non-covered)

Regional Commercial Payers

Payer	Medical Policy	Covered Biomarkers/Tests	Date of Last Review	CPT Codes
BCBSA	KRAS, NRAS, and BRAF Variant Analysis (Including Liquid Biopsy) in Metastatic Colorectal Cancer (link)	KRAS, NRAS, BRAF variant analyses Non-covers KRAS, NRAF, and BRAF variant analysis using liquid biopsy	08/22/2019	81210, 81275, 81276, 81311
	Tumor/Genetic Markers (link)	Non-covers comprehensive genomic profiling	12/05/2019	81445, 81455, 0048U
Blue Cross Blue Shield Arizona - eviCore	Sept9 Methylation Analysis for Colorectal Cancer (link)	Non-covers Epi proColon and ColoVantage testing	v2.0.2020	81327
BCBSMA	Expanded Molecular Panel Testing of Cancers to Identify Targeted Therapies (link) AIM Specialty Health (link)	Covers expanded cancer mutation panels (Stage IV or recurrent or unresectable CRC) • BRAF, KRAS, NRAS PA via AIM Specialty Health required for commercial managed care beneficiaries	April 2019	81445, 81455, 0037U
Blue Cross Blue Shield Kansas City	Liquid Biopsy (link)	Liquid biopsy panel testing of up to 50 genes is considered medically necessary for individuals diagnosed with CRC	05/01/2020	81479
Highmark	Tumor Marker Testing-Solid Tumors (link)	EGFR, ALK Multi-gene panels when: • The member has a diagnosis of NSCLC; or • At least five tumor markers included in the panel individually meet criteria for the member's tumor type based on one of the following: • All criteria are met from a test-specific policy if ONE is available; or • An oncology therapy FDA label requires results from the tumor marker test to effectively or safely use the therapy for the member's cancer type; or	March 2018	81235, 81401, 81479, 81445, 81455

		• NCCN guidelines include the tumor marker test in the management algorithm for that particular cancer type and all other requirements are met (specific pathology findings, staging, etc.); however, the tumor marker must be explicitly included in the guidelines and not simply included in a footnote as an intervention that may be considered; or • The NCCN Biomarker Compendium has a level of evidence of at least 2A for the tumor marker's application to the member's specific cancer type.		
Priority Health	Multi-marker tumor panels (link)	NGS testing for: • Patients newly diagnosed with selected stage IV rare or uncommon solid tumors for whom very limited or no systemic treatment exists in clinical care guidelines and/or pathways. • Patients newly diagnosed with selected Stage IV solid tumor types having poor prognosis, very limited benefit from standard of care chemotherapies and a high prevalence of actionable genomic alterations. • Patients with stage IV solid tumors who have exhausted the established guideline-driven systemic therapy and requisite molecular testing but who desire further treatment.	May 2019	81445, 81455, 0037U
	Genetics: Counseling, Testing, Screening (link)	Prior authorization (PA) and eviCore guidelines	May 2018	81445, 81455, 81479, 81599, 0037U

Local Medicare Administrative Contractors (MACs)

Payer	Medical Policy	Covered Biomarkers/Tests	Date of Last Review	CPT Codes
All MACs	NGS for Medicare Beneficiaries with Advanced Cancer (link)	• Patient has: ○ either recurrent, relapsed, refractory, metastatic, or advanced stage III or IV cancer; and ○ not been previously tested with the same test using NGS for the same cancer genetic content, and ○ decided to seek further cancer treatment (e.g., therapeutic chemotherapy) • The diagnostic laboratory test using NGS must have: ○ FDA approval or clearance as a companion in vitro diagnostic; and, ○ an FDA-approved or -cleared indication for use in that patient's cancer; and, ○ results provided to the treating physician for management of the patient using a report template to specify treatment options FoundationOne CDx Praxis Extended RAS Panel Guardant360 CDx	01/27/2020	0037U 0022U 0111U
MolDX	Plasma-Based Genomic Profiling in Solid Tumors (link)	Guardant360 • Other liquid biopsies will be covered for the same indications if they display similar performance in their intended used applications to Guardant360®	03/05/2020	81479
	NRAS Genetic Testing (link)	NRAS testing for metastatic colorectal cancer per NCCN guidelines	11/07/2019	81311
	Minimal Residual Disease Testing for Colorectal Cancer (link)	ctDNA tests that detect minimum residual disease (MRD) in patients with a personal history of colorectal cancer (e.g., Signatera)	10/18/2020	81479
NGS	Genomic Sequence Analysis Panels in the Treatment of Solid Organ Neoplasm (link)	The patient has: • metastatic CRC; and • is a candidate for intensive chemotherapy with an anti-EGFR biologic agent; and • has not had prior RAS/BRAF testing (except after initiation of anti-EGFR therapy with evidence of acquired resistance).	02/14/2019	81445, 0048U
Novitas	Biomarkers for Oncology (link)	• KRAS (12/13) - PRED of resistance to an anti-EGFR agent • KRAS codon 61 - PRED of resistance to an anti-EGFR agent • KRAS codon 146 - PRED of resistance to an anti-EGFR agent • NRAS - PRED of resistance to an anti-EGFR agent • BRAF - PRED of resistance to an anti-EGFR agent + DX (sporadic vs. Lynch)	07/01/2020	81275, 81276, 81311, 81210,

	• PIK3CA - PRED of resistance to an anti-EGFR agent + PROG for local recurrence • MSI by PCR - PRED of 5-FU resistance + DX • MLH1 promoter hypermethylation - PRED of 5-FU resistance + DX • mRNA (oncotype-Colon) – PRED for the recurrence risk for patients with Stage II colon cancer • Sept9 • ColonSeq®	81288, 81301, 81309, 81327, 81525

Breast Cancer

Key Takeaways

Biomarkers indicated in breast cancer, including ER, PR, HER2, and PD-L1 that are detected using IHC or in situ hybridization (ISH) are widely covered. Worth noting for Medicare payment, both IHC and ISH are paid on the Physician Fee Schedule (PFS) as compared to NGS, which is paid on the Clinical Laboratory Fee Schedule (CLFS).

Biomarker testing for BRCA1, BRCA2, and PIK3CA are also widely covered. Detection of BRCA1 and BRCA2 mutations are detected by sequencing of tumor tissue specimens. PIK3CA mutations may be detected by tumor or liquid biopsy either using PCR or molecular panel testing.

Since our 2018 review, there has been little change in coverage of panels for breast cancer. While some payers cover panels to detect the NTRK biomarker, policies vary, in part, because of variability in testing modalities (e.g., NGS, PCR, FISH, IHC).

Testing for PIK3CA via tumor tissue and liquid biopsy is widely covered for its FDA-approved companion indication. Testing for NTRK fusions and mismatch repair (MSI/dMMR) is covered sparingly.

Well-established prognostic breast cancer gene expression assays are covered by most payers. Consistent with NCCN guidelines, some payers preferentially cover Oncotype DX Breast. Although, the majority of payers cover Oncotype DX Breast at parity with Mammaprint, Prosigna, EndoPredict, and Breast Cancer Index.

Clinical Guidelines

NCCN Guidelines (Version 5.2020) support biomarker testing of ER, PR, and HER2. The guidelines support germline testing of BRCA1 and BRCA2 in all patients with recurrent or metastatic breast cancer to identify candidates for PARP inhibitor therapy. PIK3CA mutation testing (for HR-positive/HER2-negative patients) can be done on tumor tissue or liquid biopsy to identify candidates for treatment with alpelisib plus fulvestrant. The guidelines support PD-L1 testing for triple negative breast cancer patients to identify candidates for treatment with atezolizumab plus albumin-bound paclitaxel. Testing for NTRK fusions (by FISH, NGS, or PCR) is supported in certain circumstances to identify candidates for treatment with larotrectinib or entrectinib (i.e., patients without a known acquired resistance mutation and have no satisfactory alternative treatments or that have progressed following treatment). The guidelines support testing for mismatch repair (by IHC or PCR) for patients who have progressed following prior treatment and who have no satisfactory alternative treatment options.

The guidelines also support gene expression assays, including Oncotype DX Breast (preferred), Mammaprint, Prosigna (PAM 50), EndoPredict, and Breast Cancer Index in certain subgroups of breast cancer patients.

Gene/Test	NCCN Category	Change Since 2018
ER	2A	
PR	2A	
HER2	2A	
BRCA1	1	Added
BRCA2	1	Added

NTRK 1/2/3	2A	Added
MLH1, MSH2, MSH6 or PMS2	2A	
MSI	2A	Added
PIK3CA	1	Added
PD-L1	2A	Added
Oncotype DX Breast	1	
Mammaprint	2A	
PAM 50	2A	
EndoPredict	2A	
Breast Cancer Index	2A	

2019 ASCO Clinical Practice Guideline Update—Integration of Results from TAILORx: Use of Biomarkers to Guide Decisions on Adjuvant Systemic Therapy for Women with Early-Stage Invasive Breast Cancer[7]

2019 Update of the ASCO Endorsement of the Cancer Care Ontario Guideline Role of Patient and Disease Factors in Adjuvant Systemic Therapy Decision Making for Early-Stage, Operable Breast Cancer[8]

The guidelines found sufficient evidence of clinical utility for the biomarker assays Oncotype DX Breast, EndoPredict, Prosigna, Breast Cancer Index, and Mammaprint (updated for 2017) in specific subgroups of breast cancer. No biomarker except for estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) was found to guide choices of specific treatment regimens. Treatment decisions should also consider disease stage, comorbidities, and patient preferences.

[7] http://ascopubs.org/doi/full/10.1200/JCO.19.00945
[8] http://ascopubs.org/doi/full/10.1200/JCO.19.00948

National Commercial Payers

Payer	Medical Policy	Covered Biomarkers/Tests	Date of Last Review	CPT Codes
Aetna	Tumor Markers (link)	Breast Cancer Index, EndoPredict, Prosigna, Mammaprint, Oncotype DX Breast	06/08/2020	81518, 81522, 81520, 81521, 81519
	Pharmacogenetic and Pharmacodynamic Testing (link)	• Measurement of microsatellite instability and mismatch repair for persons with unresectable or metastatic solid tumors being considered for treatment with pembrolizumab • PIK3CA mutation testing (e.g., therascreen PIK3CA RGQ PCR Kit) for persons with breast cancer being considered for treatment with alpelizib. ○ Aetna considers FoundationOne CDx testing panel not medically necessary for assessing candidacy of persons with breast cancer for treatment with alpelisib because there is no proven advantage of the FoundationOne CDx panel over targeted PIK3CA mutation testing for this indication • Women with hormone receptor (HR)-positive metastatic breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine treatment. Somatic (tumor) BRCA testing is considered medically necessary for this indication instead of germline testing or when germline testing is negative	07/20/2020	81301, 88341, 88342, 81309, 0037U
Anthem	Whole Genome Sequencing, Whole Exome Sequencing, Gene Panels, and Molecular Profiling (link)	FoundationOne CDx MSK-IMPACT MI Cancer Seek For unresectable or metastatic solid tumors when all of the criteria below are met: • The test is used to assess tumor mutation burden and identify candidates for checkpoint inhibition immunotherapy; and • Individual has progressed following prior treatment; and • Individual has no satisfactory alternative treatment options	08/13/2020	0037U 0048U 0211U

		Non-covers liquid biopsy		
	PIK3CA Mutation Testing for Malignant Conditions (link)	PIK3CA (tumor tissue or liquid) in individuals being considered for treatment with a PIK3CA inhibitor (e.g., alpelisib)	11/07/2019	81309, 0155U, 0177U
	Circulating Tumor DNA Testing for Cancer (Liquid Biopsy) (link)	Investigational and not medically necessary for all indications	11/07/2019	81479, 0179U
	Gene Expression Profiling for Managing Breast Cancer Treatment (link)	Oncotype DX Breast, EndoPredict, Prosigna, Breast Cancer Index, MammaPrint	02/20/2020	81518, 81521, 81519, 81520, 81522
Cigna	Tumor Profiling, Gene Expression Assays and Molecular Diagnostic Testing for Hematology/Oncology Indications (link) Genetic Testing Collateral (link)	ER, PR by IHC HER2 by IHC, FISH Breast Cancer Index Mammaprint Oncotype DX Breast Prosigna EndoPredict	10/15/2019	88360 88377 81518 81521 81519 81520 81522
Humana	Pharmacogenomics and Companion Diagnostics (link)	Panels including, but may not limited to, multiple genes or multiple conditions, and in cases where a tiered approach/ method is clinically available, may be covered ONLY for the number of genes or tests deemed medically necessary to establish a diagnosis • BRCA companion diagnostic testing (HER2-negative metastatic breast cancer) – prior to initiation of treatment with Lynparza or Talzenna • HER2 – testing must be performed by IHC. If IHC is not conclusive, consider ISH • PIK3CA (FDA-approved test, Therascreen PIK3CA RGQ PCR Kit) – prior to initiation of Piqray • NTRK test – metastatic solid tumor, prior to treatment with Vitrakvi Non-covers FoundationOne CDx (except for ovarian cancer indication)	08/27/2020	88360, 88377

UHC	Molecular Oncology Testing for Cancer Diagnosis, Prognosis, and Treatment Decisions (link)	Mammaprint, Oncotype DX Breast, Prosigna, Breast Cancer Index, EndoPredict Non-covers liquid biopsy for breast cancer	7/1/2020	81518, 81521, 81519, 81520, 81522

Regional Commercial Payers

Payer	Medical Policy	Covered Biomarkers/Tests	Date of Last Review	CPT Codes
Arkansas BlueCross BlueShield	Genetic Test: HER2 Testing (link)	HER2 (newly diagnosed invasive breast cancer or recurrent invasive breast cancer)	April 2020	88360
BCBS eviCore	Oncotype DX for Breast Cancer Prognosis (link)	Oncotype DX Breast	07/01/2020	81519
BCBSMA	Expanded Molecular Panel Testing of Cancers to Identify Targeted Therapies (link) AIM Specialty Health (link)	Covers expanded cancer mutation panels (Stage IV or recurrent or unresectable breast cancer) • PIK3CA • Oncotype DX Breast • MammaPrint • Prosigna PA via AIM Specialty Health required for commercial managed care beneficiaries	April 2019	81309 81519 81521 81520
BCBSMI	Genetic Testing-Assays of Genetic Expression in Tumor Tissue as a Technique to Determine Prognosis in Patients with Breast Cancer (link)	Mammaprint, Oncotype DX Breast, Prosigna, Breast Cancer Index, EndoPredict	07/01/2020	81518, 81521, 81519, 81520, 81522
Blue Cross Blue Shield Kansas City	Liquid Biopsy (link)	Liquid biopsy panel testing of up to 50 genes is considered medically necessary for individuals diagnosed with breast cancer Liquid biopsy testing for PIK3CA mutation is considered medically necessary for individuals diagnosed with breast cancer that is HR-positive, HER2 negative, and if therapy with alpelisib is being considered	05/01/2020	81309
Highmark	Tumor Marker Testing-Solid Tumors (link)	EGFR, ALK Multi-gene panels when:	March 2018	81235, 81401, 81479, 81445, 81455

		• At least five tumor markers included in the panel individually meet criteria for the member's tumor type based on one of the following: • All criteria are met from a test-specific policy if ONE is available; or • An oncology therapy FDA label requires results from the tumor marker test to effectively or safely use the therapy for the member's cancer type; or • NCCN guidelines include the tumor marker test in the management algorithm for that particular cancer type and all other requirements are met (specific pathology findings, staging, etc.); however, the tumor marker must be explicitly included in the guidelines and not simply included in a footnote as an intervention that may be considered; or • The NCCN Biomarker Compendium has a level of evidence of at least 2A for the tumor marker's application to the member's specific cancer type.		
Priority Health	Genetics: Counseling, Testing, Screening (link)	Oncotype DX Breast (No PA required) Prosigna, MammaPrint (PA required)	May 2018	81519 81520, 81521

Local Medicare Administrative Contractors (MACs)

Payer	Medical Policy	Covered Biomarkers/Tests	Date of Last Review	CPT Codes
All MACs	NGS for Medicare Beneficiaries with Advanced Cancer (link)	• Patient has: ○ either recurrent, relapsed, refractory, metastatic, or advanced stage III or IV cancer; and ○ not been previously tested with the same test using NGS for the same cancer genetic content, and ○ decided to seek further cancer treatment (e.g., therapeutic chemotherapy) • The diagnostic laboratory test using NGS must have: ○ FDA approval or clearance as a companion in vitro diagnostic; and, ○ an FDA-approved or -cleared indication for use in that patient's cancer; and, ○ results provided to the treating physician for management of the patient using a report template to specify treatment options FoundationOne CDx Guardant360 CDx	01/27/2020	0037U
MolDX	Plasma-Based Genomic Profiling in Solid Tumors (link)	Guardant360 • Other liquid biopsies will be covered for the same indications if they display similar performance in their intended used applications to Guardant360®	03/05/2020	81479
	Breast Cancer Index (BCI) Gene Expression Test (link)	Breast Cancer Index	10/31/2019	81518
	Breast Cancer Assay: Prosigna (link)	Prosigna	11/21/2019	81520
	EndoPredict Breast Cancer Gene Expression Test (link)	EndoPredict	11/07/2019	81522
Noridian, Palmetto, WPS	Lab: Special Histochemical Stains and Immunohistochemical Stains (link)	ER, PR, HER2 by IHC	10/31/2019	
Novitas	Biomarkers for Oncology (link)	Prosigna	07/01/2020	81520

Prostate Cancer

Key Takeaways

Inconsistent coverage of prognostic prostate cancer biomarkers, including AR-V7, and tumor-based molecular assays, including Decipher, OncotypeDx Prostate, Prolaris, and Promark, across payers.

Although there is a new companion diagnostic paradigm for BRCA testing in prostate cancer, many payers have yet to update policies. BRACAnalysis CDx and FoundationOne CDx are indicated for metastatic castration-resistant prostate cancer (mCRPC) patients who may benefit from treatment with Lynparza. FoundationOne Liquid CDx is indicated for mCRPC patients who may benefit from treatment with Rubraca.

Given the rapid expansion in knowledge of the significance of biomarkers in prostate cancer, it is likely prostate cancer will be an area of increased clinical focus for panel testing.

Clinical Guidelines

NCCN Guidelines (Version 2.2020) support multi-gene molecular testing (Decipher, Oncotype DX Prostate, Prolaris, ProMark) during initial risk stratification for men with low or favorable intermediate disease. Additionally, the Decipher molecular assay can be considered during workup for radical prostatectomy PSA persistence or recurrence (category 2B). Testing for AR-V7 can be considered to help guide selection of therapy in the post-abiraterone/enzalutamide mCRPC setting.

Tumor testing for MSI-H or dMMR can be considered in patients with regional or castration-naïve metastatic prostate cancer and is recommended in patients with mCRPC. The guidelines specifically acknowledge that DNA analysis for MSI and IHC for MMR are different assays measuring the same biological effect. If MSI is used, testing using an NGS assay validated for prostate cancer is preferred.

Gene/Test	NCCN Category
CHEK2, PALB2, RAD51D, ATM, BRCA1, BRCA2, FANCA, CDK12	2A
AR-V7	2A
MLH1, MSH2, MSH6, PMS2	2A
MSI	2A
Decipher Prostate	2A
Oncotype DX Prostate	2A
Prolaris	2A
ProMark	2A

The guidelines recommend consideration of tumor testing for somatic homologous recombination gene mutations (e.g., BRCA1, BRCA2, ATM, PALB2, FANCA, RAD51D, CHEK2) in patients with regional or metastatic prostate cancer. Early studies suggest germline and somatic mutations in homologous recombination repair genes may be predictive of the clinical benefit of PARP inhibitors, olaparib in particular. While FDA-approved targeted therapies are available for ovarian cancer, at present, no PARP inhibitor is approved for use in prostate cancer. Metastatic CRPC patients can be considered for germline and tumor testing to check for mutations in homologous recombination genes (i.e., BRCA1, BRCA2, ATM, PALB2, FANCA). The information may be used for genetic counseling, early use of platinum chemotherapy, or eligibility for clinical trials (e.g., PARP inhibitors).

ASCO Guideline (2019). Molecular Biomarkers in Localized Prostate Cancer[9] recognizes that Oncotype Dx Prostate, Prolaris, Decipher, and ProMark may improve risk stratification when added to standard clinical parameters. However, the guideline recommends their use only in situations in which the assay results, when considered as a whole with routine clinical factors, are likely to affect a clinical decision. These assays are not recommended for routine use as they have not been prospectively tested or shown to improve long-term outcomes.

[9] http://ascopubs.org/doi/full/10.1200/JCO.2017.76.7293

National Commercial Payers

Payer	Medical Policy	Covered Biomarkers/Tests	Date of Last Review	CPT Codes
Aetna	Tumor Markers (link)	AR-V7 in mCRPC after progression on abiraterone or enzalutamide Mismatch repair (MSI/dMMR) (MLH1, MSH2, MSH6) tumor testing Decipher Oncotype DX Prostate Prolaris ProMark	06/08/2020	81479 81542 0047U 81541
	Pharmacogenetic and Pharmacodynamic Testing (link)	• Measurement of microsatellite instability and mismatch repair for persons with unresectable or metastatic solid tumors being considered for treatment with pembrolizumab • BRCA testing (e.g., BRACAnalysis CDx) medically necessary for men with advanced, recurrent or metastatic prostate cancer who have been treated with androgen-receptor directed therapy and are being considered for treatment with olaparib • Somatic/tumor BRCA testing (e.g., FoundationOne CDx) medically necessary for men with advanced, recurrent or metastatic prostate cancer who have been treated with androgen-receptor directed therapy and a taxane-based chemotherapy and are being considered for trreatment with rucaparib	07/20/2020	81301, 88341, 88342, 0037U
Anthem	Whole Genome Sequencing, Whole Exome Sequencing, Gene Panels, and Molecular Profiling (link)	FoundationOne CDx MSK-IMPACT MI Cancer Seek For unresectable or metastatic solid tumors when all of the criteria below are met: • The test is used to assess tumor mutation burden and identify candidates for checkpoint inhibition immunotherapy; and • Individual has progressed following prior treatment; and • Individual has no satisfactory alternative treatment options	08/13/2020	0037U 0048U 0211U

		Non-covers liquid biopsy		
	Circulating Tumor DNA Testing for Cancer (Liquid Biopsy) (link)	Investigational and not medically necessary for all indications	11/07/2019	81479, 0179U
	Protein Biomarkers for the Screening, Detection and Management of Prostate Cancer (link)	Non-covers protein biomarker tests, including 4Kscore and AR-V7	05/14/2020	81479, 81539
	Gene-Based Tests for Screening, Detection and Management of Prostate Cancer (link)	Non-covers Decipher, Oncotype DX Prostate, Prolaris, ProMark	02/20/2020	81542, 0047U, 81541
Cigna	Tumor Profiling, Gene Expression Assays and Molecular Diagnostic Testing for Hematology/Oncology Indications (link) Genetic Testing Collateral (link)	• AR-V7 testing from circulating tumor cells is considered medically necessary for a male with mCRPC considering second line therapy when BOTH of the following criteria are met: ○ progression on androgen receptor–signaling inhibitor (ARSi) therapy (i.e., enzalutamide (Xtandi), abiraterone (Zytiga)) ○ nuclear expression of AR-V7 will be assessed to guide subsequent therapeutic decision making • 4K score test, Prostate Health Index, ConfirmMDx for Prostate Cancer, Progensa PCA3 Assay • Decipher, Oncotype DX Prostate, Prolaris, ProMark	10/15/2019	81479 81539, 81551, 81313 81541, 0047U
Humana	Genetic Testing for Diagnosis and Monitoring of Cancer and Molecular Profiling (link)	Non-covers NGS-based cancer profiling tests	03/25/2020	81445, 81455, 0048U, 0050U, 0171U (Non-covered)
	Pharmacogenomics and Companion Diagnostics (link)	Panels including, but may not limited to, multiple genes or multiple conditions, and in cases where a tiered approach/ method is clinically available, may be covered ONLY for the number of genes or tests deemed medically necessary to establish a diagnosis • NTRK test – metastatic solid tumor, prior to treatment with Vitrakvi	08/27/2020	

		Non-covers FoundationOne CDx (except for ovarian cancer indication)		
UHC	Molecular Oncology Testing for Cancer Diagnosis, Prognosis, and Treatment Decisions (link)	Non-covers multi-gene cancer panels for prostate cancer (e.g., Oncotype DX Prostate Cancer Assay, TMPRSS2 fusion gene, Prolaris Prostate Cancer Test, Decipher Prostate Cancer Classifer) Non-covers liquid biopsy for prostate cancer	7/1/2020	81445, 81455, 81479, 81541, 81542, 81551, 81599

Regional Commercial Payers

Payer	Medical Policy	Covered Biomarkers/Tests	Date of Last Review	CPT Codes
BCBS eviCore	Investigational and Experimental Molecular and Genomic Testing (link)	Non-covers ExoDx Prostate (IntelliScore), MiPS (Mi-Prostate Score), Prostate Cancer Risk Panel (Mayo), +RNAinsight for ProstateNext	07/01/2020	0005U
BCBSMA	Expanded Molecular Panel Testing of Cancers to Identify Targeted Therapies (link) AIM Specialty Health (link)	Covers expanded cancer mutation panels (metastatic castration-resistant prostate cancer) • ConfirmMDx • ExoDx • PCA3 PA via AIM Specialty Health required for commercial managed care beneficiaries	April 2019	81551 0005U
Blue Shield California	Gene Expression Profiling and Protein Biomarkers for Prostate Cancer Management (link)	Oncotype DX Prostate Prolaris	04/01/2020	81541, 0047U
Florida Blue	Genetic Testing (link)	Non-covers 4Kscore, Confirm MDx, ExosomeDx Prostate (IntelliScore), MiPS (MiProstate Score), Decipher, Oncotype DX Prostate, Prolaris, ProMark	07/01/2020	81539, 0005U, 81542, 0047U, 81541
Highmark	Tumor Marker Testing-Solid Tumors (link)	EGFR, ALK Multi-gene panels when: • The member has a diagnosis of NSCLC; or • At least five tumor markers included in the panel individually meet criteria for the member's tumor type based on one of the following: • All criteria are met from a test-specific policy if ONE is available; or • An oncology therapy FDA label requires results from the tumor marker test to effectively or safely use the therapy for the member's cancer type; or • NCCN guidelines include the tumor marker test in the management algorithm for that particular cancer type and all other requirements are met (specific pathology	March 2018	81235, 81401, 81479, 81445, 81455

		findings, staging, etc.); however, the tumor marker must be explicitly included in the guidelines and not simply included in a footnote as an intervention that may be considered; or • The NCCN Biomarker Compendium has a level of evidence of at least 2A for the tumor marker's application to the member's specific cancer type.		
Priority Health	Genetics: Counseling, Testing, Screening (link)	Subject to PA: PCA3, ConfirmMDx for Prostate Cancer, Oncotype DX Prostate Non-covered: 4Kscore test, Prolaris, NeoLAB Prostate Liquid Biopsy, ExoDx Prostate (IntelliScore), Prostate Cancer Risk Panel (Mayo), MiPS (MiProstate Score)	May 2018	81551, 0047U 81539, 0005U
Wellmark	Genetic and Protein Biomarkers for the Diagnosis and Cancer Risk Assessment of Prostate Cancer (link)	Progensa PCA3 assay, 4kscore test, Prostate Health Index, ExoDx Prostate (IntelliScore), ConfirmMDx Non-covers expanded gene panels and SNV testing for cancer risk assessment of prostate cancer	June 2020	81539, 0005U, 81551

Local Medicare Administrative Contractors (MACs)

Payer	Medical Policy	Covered Biomarkers/Tests	Date of Last Review	CPT Codes
All MACs	NGS for Medicare Beneficiaries with Advanced Cancer (link)	• Patient has: ○ either recurrent, relapsed, refractory, metastatic, or advanced stage III or IV cancer; and ○ not been previously tested with the same test using NGS for the same cancer genetic content, and ○ decided to seek further cancer treatment (e.g., therapeutic chemotherapy) • The diagnostic laboratory test using NGS must have: ○ FDA approval or clearance as a companion in vitro diagnostic; and, ○ an FDA-approved or -cleared indication for use in that patient's cancer; and, ○ results provided to the treating physician for management of the patient using a report template to specify treatment options FoundationOne CDx Guardant360 CDx	01/27/2020	0037U
MolDX	Plasma-Based Genomic Profiling in Solid Tumors (link)	Guardant360 • Other liquid biopsies will be covered for the same indications if they display similar performance in their intended used applications to Guardant360®	03/05/2020	81479
	4Kscore Assay (link)	Non-covers 4Kscore	10/31/2019	81539
	BRCA1 and BRCA2 Genetic Testing (link)	BRCA 1 and BRCA 2	12/04/2019	
	ConfirmMDx Epigenetic Molecular Assay (link)	To reduce unnecessary repeat prostate biopsies	10/31/2019	81551
	Decipher Biopsy Prostate Cancer Classifier Assay for Men with Intermediate Risk Disease (link)		11/15/2019	81542
	Decipher Biopsy Prostate Cancer Classifier Assay for Men with Very Low and Low Risk Disease (link)		11/14/2019	81542

	Decipher Prostate Cancer Classifier Assay (link)	To determine which patients traditionally considered high risk of recurrence after radical prostectomy may be closely followed rather than receive post-operative radiation therapy	11/07/2019	81542
	Genomic Health Oncotype DX Prostate Cancer Assay (link)	To help determine which patients with early stage, needle biopsy proven prostate cancer, can be conservatively managed rather than treated with definitive surgery or radiation therapy	10/31/2019	0047U
	Oncotype DX Genomic Prostate Score for Men with Favorable Intermediate Risk Prostate Cancer (link)	To help determine which patients with favorable intermediate-risk, needle biopsy proven prostate cancer, can be conservatively managed rather than treated with definitive surgery or radiation therapy.	10/31/2019	0047U
	Oncotype DX AR-V7 Nucleus Detect for Men with Metastatic Castrate Resistant Prostate Cancer (link)	To help determine which patients with metastatic castrate resistant prostate cancer may benefit from androgen receptor signaling inhibitor therapy and which may benefit from chemotherapy.	11/21/2019	81479
	Prolaris Prostate Cancer Genomic Assay (link)	To help determine which patients with early stage, needle biopsy proven prostate cancer, can be conservatively managed rather than treated with definitive surgery or radiation therapy	10/31/2019	81541
	Prolaris Prostate Cancer Genomic Assay for Men with Favorable Intermediate Risk Disease (link)	To help determine which patients with favorable intermediate risk, needle biopsy proven prostate cancer (as defined below), can be conservatively managed rather than treated with definitive surgery or radiation therapy.	10/31/2019	81541
	ProMark Risk Score (link)	To help determine which patients with early stage, needle biopsy proven prostate cancer can be conservatively managed rather than treated with definitive surgery or radiation therapy.	11/07/2019	81479
NGS	Biomarker Testing (Prior to Initial Biopsy) for Prostate Cancer Diagnosis (link)	• % free PSA • Prostate Health Index • 4Kscore • ExosomeDx Prostate (IntelliScore)	12/01/2019	81539 0005U
Novitas	Biomarkers for Oncology (link)	• The PROGENSA PCA3 Assay (PRED) is an FDA-approved, automated molecular test (assay) that helps physicians determine the need for repeat prostate biopsies in men who have had a previous negative biopsy • PTEN – PROG and THER • RB1 – DX and PROG • TP53 - PROG	07/01/2020	
	4Kscore Test Algorithm (link)	4Kscore	12/30/2019	81539

Acknowledgements

Exact Sciences

Guardant Health

Funders of LUNGevity's policy activities

Appendix A: CPT Codes

CPT Code	Descriptor	2020 Rate
81210	BRAF (B-Raf proto-oncogene, serine/threonine kinase) (eg, colon cancer, melanoma), gene analysis, V600 variant(s)	$175.40
81235	EGFR (epidermal growth factor receptor) (eg, non-small cell lung cancer) gene analysis, common variants (eg, exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q)	$324.58
81275	KRAS (Kirsten rat sarcoma viral oncogene homolog) (eg, carcinoma) gene analysis; variants in exon 2 (eg, codons 12 and 13)	$193.25
81276	KRAS (Kirsten rat sarcoma viral oncogene homolog) (eg, carcinoma) gene analysis; additional variant(s) (eg, codon 61, codon 146)	$193.25
81288	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; promoter methylation	$192.32
81292	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis	$675.40
81293	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants	$331.00
81294	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants	$202.40
81301	Microsatellite instability analysis (eg, hereditary nonpolyposis colorectal cancer, Lynch syndrome) of markers for mismatch repair deficiency (eg, BAT25, BAT26), includes comparison of neoplastic and normal tissue, if performed	$348.56
81309	PIK3CA (phosphatidylinositol-4, 5-biphosphate 3-kinase, catalytic subunit alpha) (eg, colorectal and breast cancer) gene analysis, targeted sequence analysis (eg, exons 7, 9, 20)	$274.83
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)	$295.79
81313	PCA3/KLK3 (prostate cancer antigen 3 [non-protein coding]/kallikrein-related peptidase 3 [prostate specific antigen]) ratio (eg, prostate cancer)	$255.05
81327	SEPT9 (Septin9) (eg, colorectal cancer) methylation analysis	$192.00
81445	Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, and RNA analysis when performed, 5-50 genes (eg, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, NRAS, MET, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed	$597.91
81455	Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA analysis, and RNA analysis when performed, 51 or greater genes (eg, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed	$2,919.60
81479	Unlisted molecular pathology procedure	
81518	Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 11 genes (7 content and 4 housekeeping), utilizing formalin-fixed paraffin embedded tissue, algorithms reported as percentage risk for metastatic recurrence and likelihood of benefit from extended endocrine therapy Breast Cancer Index; Biotheranostics	$3,873.00

81519	Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 21 genes, utilizing formalin fixed paraffin-embedded tissue, algorithm reported as recurrence score Oncotype DX, Genomic Health	$3,873.00
81520	Oncology (breast), mRNA gene expression profiling by hybrid capture of 58 genes (50 content and 8 housekeeping), utilizing formalin-fixed paraffin embedded tissue, algorithm reported as a recurrence risk score Prosigna Breast Cancer Assay, NanoString Technologies, Inc	$2,510.21
81521	Oncology (breast), mRNA, microarray gene expression profiling of 70 content genes and 465 housekeeping genes, utilizing fresh frozen or formalin-fixed paraffin-embedded tissue, algorithm reported as index related to risk of distant metastasis MammaPrint, Agendia, Inc.	$3,873.00
81522	Oncology (breast), mRNA, gene expression profiling by RT-PCR of 12 genes (8 content and 4 housekeeping), utilizing formalin-fixed paraffin embedded tissue, algorithm reported as recurrence risk score EndoPredict; Myriad	$3,873.00
81525	Oncology (colon), mRNA, gene expression profiling by real-time RT-PCR of 12 genes (7 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a recurrence score Oncotype DX Colon Cancer Assay, Genomic Health	$3,116.00
81538	Oncology (lung), mass spectrometric 8-protein signature, including amyloid A, utilizing serum, prognostic and predictive algorithm reported as good versus poor overall survival VeriStrat; Biodesix	$2,871.00
81539	Oncology (high-grade prostate cancer), biochemical assay of four proteins (Total PSA, Free PSA, Intact PSA and human kallikrein-2 [hK2]), utilizing plasma or serum, prognostic algorithm reported as a probability score 4Kscore test; OPKO Health	$760.00
81541	Oncology (prostate), mRNA gene expression profiling by real-time RT-PCR of 46 genes (31 content and 15 housekeeping), utilizing formalin-fixed paraffin embedded tissue, algorithm reported as a disease specific mortality risk score Prolaris; Myriad	$3,873.00
81542	Oncology (prostate) mRNA, microarray gene expression profiling of 22 content genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as metastasis risk score Decipher Prostate; Decipher Biosciences	Undergoing gapfill
81551	Oncology (prostate), promoter methylation profiling by real-time PCR of 3 genes (GSTP1, APC, RASSF1), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a likelihood of prostate cancer detection on repeat biopsy ConfirmMDx for Prostate Cancer, MDxHealth	$2,030.00
81599	Unlisted multianalyte assay with algorithmic analysis	

0022U	Targeted genomic sequence analysis panel, non-small cell lung neoplasia, DNA and RNA analysis, 23 genes, interrogation for sequence variants and rearrangements, reported as presence/absence of variants and associated therapy(ies) to consider Oncomine Dx Target Test, Thermo Fisher Scientific	$1,950.00
0037U	Targeted genomic sequence analysis, solid organ neoplasm, DNA analysis of 324 genes, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability and tumor mutational burden FoundationOne CDx; Foundation Medicine, Inc.	$3,500.00
0048U	Oncology (solid organ neoplasia), DNA, targeted sequencing of protein-coding exons of 468 cancer-associated genes, including interrogation for somatic mutations and microsatellite instability, matched with normal specimens, utilizing formalin-fixed paraffin-embedded tumor tissue, report of clinically significant mutation(s) MSK-IMPACT; Memorial Sloan Kettering Cancer Center	$2,919.60
0111U	Oncology (colon cancer), targeted KRAS (codons 12, 13, and 61) and NRAS (codons 12, 13, and 61) gene analysis, utilizing formalin-fixed paraffin embedded tissue Praxis Extended RAS Panel; Illumina	$682.29
0155U	Oncology (breast cancer), DNA, PIK3CA (phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alpha) (eg, breast cancer) gene analysis (ie, p.C420R, p.E542K, p.E545A, p.E545D [g.1635G>T only], p.E545G, p.E545K, p.Q546E, p.Q546R, p.H1047L, p.H1047R, p.H1047Y), utilizing formalin-fixed paraffin-embedded breast tumor tissue, reported as PIK3CA gene mutation status therascreen PIK3CA RGQ PCR Kit, QIAGEN,	Undergoing gapfill
0174U	Oncology (solid tumor), mass spectrometric 30 protein targets, formalin-fixed paraffin-embedded tissue, prognostic and predictive algorithm reported as likely, unlikely, or uncertain benefit of 39 chemotherapy and targeted therapeutic oncology agents LC-MS/MS Targeted Proteomic Assay; OncoOmicDx	Undergoing gapfill
0177U	Oncology (breast cancer), DNA, PIK3CA (phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha) gene analysis of 11 gene variants utilizing plasma, reported as PIK3CA gene mutation status therascreen PIK3CA RGQ PCR Kit, QIAGEN	Undergoing gapfill
0179U	Oncology (non-small cell lung cancer), cell-free DNA, targeted sequence analysis of 23 genes (single nucleotide variations, insertions and deletions, fusions without prior knowledge of partner/breakpoint, copy number variations), with report of significant mutation(s) Resolution ctDx Lung, Resolution Bioscience	Undergoing gapfill
0211U	Oncology (pan-tumor), DNA and RNA by next-generation sequencing, utilizing formalin-fixed paraffin-embedded tissue, interpretative report for single nucleotide variants, copy number alterations, tumor mutational burden, and microsatellite instability, with therapy association MI Cancer Seek; Caris Life Sciences	Undergoing gapfill
88341	Immunohistochemistry or immunocytochemistry, per specimen; each additional single antibody stain procedure	$94.19

88342	Immunohistochemistry or immunocytochemistry, per specimen; initial single antibody stain procedure	$107.19
88360	Morphometric analysis, tumor immunohistochemistry (eg, Her-2/neu, estrogen receptor/progesterone receptor), quantitative or semiquantitative, per specimen, each single antibody stain procedure; manual	$127.40
88361	Morphometric analysis, tumor immunohistochemistry (eg, Her-2/neu, estrogen receptor/progesterone receptor), quantitative or semiquantitative, per specimen, each single antibody stain procedure; using computer-assisted technology	$129.20
88377	Morphometric analysis, in situ hybridization (quantitative or semi-quantitative), manual, per specimen; each multiplex probe stain procedure	$411.78