

MEDICAL POLICY

MEDICAL POLICY DETAILS	
Medical Policy Title	Molecular Testing of Tumor Tissue to Identify Targeted Therapies for Cancers
Policy Number	2.02.51
Category	Technology Assessment
Original Effective Date	12/21/17
Committee Approval Date	12/21/18, 10/17/19, 12/16/21, 01/19/23, 01/18/24
Current Effective Date	01/18/24
Archived Date	N/A
Archive Review Date	N/A
Product Disclaimer	<ul style="list-style-type: none"> • Services are contract dependent; if a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply. • If a commercial product (including an Essential Plan or Child Health Plus product), medical policy criteria apply to the benefit. • If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit. • If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) product) covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit. • If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service, please refer to the Medicaid Product coverage line.

POLICY STATEMENT

Colorectal Cancer

- I. Based upon our criteria and assessment of the peer-reviewed literature, including the National Comprehensive Cancer Network (NCCN) clinical guidelines, gene mutational analysis of tumor tissue to predict response to targeted therapies and to direct targeted therapy, is considered **medically appropriate** for individuals:
- In the treatment of metastatic colorectal cancer; **AND**
 - The results will be used to guide management of the patient for the following targeted gene mutations; (CPT code examples not all inclusive):
 - Kirsten rat sarcoma viral oncogene (KRAS) (CPT: 81275, 81276);
 - Neuroblastoma RAS viral oncogene (NRAS) (CPT: 81311);
 - B-Raf proto-oncogene (BRAF) (CPT: 81210);
 - HER2 amplification;
 - Neurotrophic tyrosine receptor kinase (NTRK) gene fusions (CPT: 81191-81193, or 81194);
 - MSI/MMR status (if not previously done).
 - Testing for genetic alterations, for targeted therapy in any other genes than those listed above, is considered **investigational**.

Non-Small Cell Lung Cancer

- II. Based upon our criteria and assessment of the peer-reviewed literature, including the NCCN clinical guidelines, gene mutational analysis of tumor tissue to predict response to targeted therapies and to direct targeted therapy, is considered **medically appropriate** for individuals:
- Who have previous biopsy-confirmed non-small-cell lung cancer (NSCLC) including adenocarcinoma, large cell, squamous cell, and NSCLC not otherwise specified; **AND**
 - The results will be used to guide management of the patient for the following targeted gene mutations; (CPT code examples not all inclusive):
 - Epidermal Growth Factor Receptor (EGFR) gene mutations (CPT: 81235);

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2. Anaplastic lymphoma kinase (ALK) gene rearrangement;
 3. KRAS (CPT: 81275, 81276);
 4. NTRK 1/2/3 gene fusion (CPT: 81191-81193, or 81194);
 5. ROS proto-oncogene 1 (ROS-1) gene rearrangement;
 6. BRAF point mutations (CPT: 81210);
 7. Mesenchymal-epithelial transition MET exon 14 skipping variants;
 8. High-level MET amplification;
 9. Rearranged during transfection (RET) gene rearrangements;
 10. Erb-B2 Receptor Tyrosine Kinase 2 (ERBB2)/(HER2) gene mutation.
- C. Testing for genetic alterations, for targeted therapy in any other genes than those listed above, is considered **investigational**.

Melanoma

- III. Based upon our criteria and assessment of the peer-reviewed literature, including the NCCN clinical guidelines, gene mutational analysis of tumor tissue to predict response to targeted therapies and to direct targeted therapy, is considered **medically appropriate** for individuals:
- A. with Stage III melanoma at high risk for recurrence; **OR**
 - B. with Stage IV melanoma or clinical recurrence;
- AND**
- C. The results will be used to guide management of the patient for the following targeted gene mutations; (CPT code examples not all inclusive):
1. BRAF (CPT: 81210);
 2. KIT (CPT: 81272).
- D. Testing for genetic alterations, for targeted therapy in any other genes than those listed above, is considered **investigational**.

Pancreatic Cancer

- IV. Based upon our criteria and assessment of the peer-reviewed literature, including the NCCN clinical guidelines, gene mutational analysis of tumor tissue to predict response to targeted therapies and to direct targeted therapy, is considered **medically appropriate** for individuals:
- A. who have previous biopsy-confirmed, newly diagnosed metastatic pancreatic cancer; **OR**
 - B. who have metastatic pancreatic cancer that is progressing on or after chemotherapy or immunotherapy, and have never been tested for molecular and biomarker analysis;
- AND**
- C. The results will be used to guide management of the patient for the following targeted gene mutations; (CPT code examples not all inclusive):
1. Anaplastic lymphoma kinase (ALK) gene fusions;
 2. NRG1 gene fusions;
 3. NTRK 1/2/3 gene fusion (CPT: 81191-81193, or 81194);
 4. ROS-1 gene fusion;
 5. BRAF gene mutation (CPT: 81210);
 6. BRCA 1/2 gene mutation (CPT 81162);
 7. KRAS gene mutation (CPT: 81275, 81276);
 8. PALB2 gene mutation (CPT: 81307);
 9. HER2 amplifications;
 10. FGFR2 gene fusion;
 11. RET gene fusion;
 12. MSI/MMR.
- D. Testing for genetic alterations, for targeted therapy in any other genes than those listed above, is considered **investigational**.

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Ovarian Cancer

- V. Based upon our criteria and assessment of the peer-reviewed literature, including the NCCN clinical guidelines, gene mutational analysis of tumor tissue to predict response to targeted therapies and to direct targeted therapy, is considered **medically appropriate** for individuals:
- A. with recently diagnosed or recurrent ovarian cancer; **AND**
 - B. The results will be used to guide management of the patient for the following targeted gene mutations; (CPT code examples not all inclusive):
 1. BRCA 1/2 (CPT 81162);
 2. Homologous recombination deficiency (HRD) status;
 3. MSI/MMR;
 4. TMB;
 5. NTRK (CPT: 81191-81193, or 81194);
 6. BRAF (CPT: 81210);
 7. FR α ;
 8. RET.
 - C. Testing for genetic alterations, for targeted therapy in any other genes than those listed above, is considered **investigational**.

Prostate Cancer

- VI. Based upon our criteria and assessment of the peer-reviewed literature, including the NCCN clinical guidelines, gene mutational analysis of tumor tissue to predict response to targeted therapies and to direct targeted therapy, is considered **medically appropriate** for individuals:
- A. In the treatment of metastatic prostate cancer; **AND**
 - B. The results will be used to guide management of the patient for the following targeted gene mutations; (CPT code examples not all inclusive):
 1. BRCA 1/2 (CPT 81162);
 2. ATM;
 3. PALB2 (CPT 81307);
 4. FANCA;
 5. RAD51D;
 6. CHEK2;
 7. CDK12;
 8. MSI/MMR.
 - C. Testing for genetic alterations, for targeted therapy in any other genes than those listed above, is considered **investigational**.

Breast Cancer

- VII. Based upon our criteria and assessment of the peer-reviewed literature, including the NCCN clinical guidelines, gene mutational analysis of tumor tissue to predict response to targeted therapies and to direct targeted therapy, is considered **medically appropriate** for individuals:
- A. In the treatment of breast cancer (note specific classifications by genes below); **AND**
 - B. The results will be used to guide management of the patient for the following targeted gene mutations; (CPT code examples not all inclusive):
 1. PIK3CA mutation (HR-positive/HER2-negative breast cancer) (CPT 81309);
 2. PD-L1 (for triple negative breast cancer);
 3. NTRK fusion (all breast cancers) (CPT: 81191-81193, or 81194);
 4. MSI/MMR (all breast cancers);
 5. TMB (all breast cancers).

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- C. Testing for genetic alterations, for targeted therapy in any other genes than those listed above, is considered **investigational**.

Brain Cancer

VIII. Based upon our criteria and assessment of the peer-reviewed literature, including the NCCN clinical guidelines, gene mutational analysis of tumor tissue to facilitate characterization of tumors to guide treatment decisions, is considered **medically appropriate** for individuals when:

- A. The results will be used to guide management of the patient;

AND

- B. In the treatment of *primary brain tumors* for the following targeted gene mutations (CPT code examples not all inclusive):

1. Isocitrate dehydrogenase 1 (IDH1) and IDH2 (CPT: 81120, 81121);
2. 1p19q codeletion;
3. 6 -methylguanine-DNA methyl-transferase (MGMT) (CPT: 81287);
4. ATRX;
5. Telomerase reverse transcriptase (TERT) (CPT: 81345);
6. BRAF V600 (CPT: 81210); **OR**

- C. In the treatment of *ependymomas* for the following targeted gene mutations:

1. ZFTA;
2. YAP1;
3. MYCN; **OR**

- D. In the treatment of *medulloblastoma* for the following targeted gene mutations:

1. CTNNA1;
2. GAB1;
3. YAP1;
4. TP53.

- E. Testing for genetic alterations in any other genes than those listed above is considered **investigational**.

Other Cancers

IX. Based upon our criteria and assessment of the peer-reviewed literature, including the NCCN clinical guidelines, gene mutational analysis of tumor tissue to predict response to targeted therapies and to direct targeted therapy, is considered **medically appropriate** for individuals:

- A. Who have previous biopsy-confirmed, newly diagnosed advanced stage III or IV or metastatic cancer; **OR**
- B. Advanced stage III or IV or metastatic cancer that is progressing on or after chemotherapy or immunotherapy, and who have never been tested for molecular and biomarker analysis; **AND**

- C. **ALL** of the following:

1. Testing is recommended (2A or 1) by the current NCCN Guidelines for the cancer indication;
2. Testing should include only the number of genes necessary for therapeutic decision making; **AND**
3. The results will be used to guide management of the patient.

X. Based upon our criteria and assessment of the peer-reviewed literature, tumor tissue testing to identify targeted cancer treatment with a broad molecular panel, has not been medically proven to be effective and, therefore, is considered **investigational**.

XI. Based upon our criteria and assessment of the peer-reviewed literature, programmed death receptor 1 (PD-1) or its ligand (PDL-1) expression analysis is considered **medically appropriate** as a technique to predict treatment response to drug therapy.

Refer to Corporate Medical Policy #2.02.53 JAK2, MPL, and CALR Molecular Testing for Myeloproliferative Neoplasm

Refer to Corporate Medical Policy #2.02.54 Measurable Residual Disease Assessment Testing

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Refer to Corporate Medical Policy #2.02.56 Circulating Tumor DNA for Management of Cancer (Liquid Biopsy)

Refer to Corporate Medical Policy #11.01.03 Experimental or Investigational Services

POLICY GUIDELINES

- I. The Health Plan and its employees adhere to all State and Federal laws concerning the confidentiality of genetic testing and the results of genetic testing. All records, findings and results of any genetic test performed on any person shall be deemed confidential and shall not be disclosed without the written informed consent of the person to whom such genetic test relates. This information shall not be released to any person or organization not specifically authorized by the individual subject of the test or in compliance with applicable law.
- II. Genetic testing is appropriate only when performed by a qualified laboratory certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and offered in a setting with adequately trained health care professionals who are qualified to provide appropriate pre- and post-test counseling.
- III. Genetic testing is contract dependent. Coverage only applies to members with a valid contract; coverage is not provided for family members without a valid contract.
- IV. Smaller targeted panels with actionable gene mutations and drug therapies based on the presence of a specific mutation may be approvable.
- V. A negative liquid biopsy test result should be followed by reflex testing to a formalin-fixed paraffin-embedded tissue test.
- VI. A liquid biopsy and formalin-fixed paraffin-embedded tissue test should not be tested simultaneously.
- VII. Supporting documentation required - for other cancers not listed in the policy:
The purpose of tumor tissue testing is to provide information that will assist in predicting response to targeted therapies or to direct targeted therapy. Documentation that must be submitted for review includes all of the following documentation:
 - A. The purpose of the test;
 - B. The gene mutation(s) to be tested;
 - C. The drug therapy plan based on results of the testing; and
 - D. Supportive evidence demonstrating efficacy of the proposed drug therapy for the gene mutation in patient's cancer.
- VIII. The Foundation One CDx (Cambridge MA) is a broad molecular panel that includes sequencing of more than 300 cancer-related genes and select introns from another 25 genes as well as genomic signatures including microsatellite instability (MSI) and tumor mutational burden (TMB) using DNA isolated from formalin-fixed paraffin embedded (FFPE) tumor tissue specimens. Indications for testing include solid tumors of non-small cell lung cancer (NSCLC), colorectal cancer, breast cancer, ovarian cancer, and melanoma. Typical turnaround time for testing is two weeks. The U.S. Food and Drug Administration (FDA) approved the FoundationOne CDx in November 2017.
- IX. The OmniSeq Comprehensive panel test or OmniSeq Advance panel test are next-generation broad molecular sequencing assays that tests tumor DNA and RNA, identifying somatic variants in 144 genes to guide cancer therapeutic management. The OmniSeq Advance panel test also includes MSI, PD-L1 IHC, and TMB. Test turnaround time is 10-15 days.
- X. The Comprehensive Molecular Profiling, (Caris Life Sciences, Irving, TX) panel uses multiple tumor profiling technologies to decode cancer such as whole exome sequencing (WES), whole transcriptome sequencing (WTS) of RNA, tumor mutational burden (TMB), microsatellite instability (MSI), mismatch repair proteins (MMR) by immunohistochemistry (IHC) and next-generation sequencing (NGS). Turnaround time for testing is 10-14 days.

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DESCRIPTION

According to the Precision Medicine Initiative, precision medicine is an emerging approach for disease treatment and prevention that considers individual variability in genes, environment, and lifestyle for each person. Research has been directed to understanding molecular variations in tumors from different cancer types so that drugs used to treat the tumors are “targeted” or directed to inhibit the function of the molecular alteration. The goal of precision medicine is to maximize efficiency and minimize side effects of therapy. Some success has been achieved with the use of EGFR or ALK inhibitors in specific subtypes of NSCLC and BRAF/MEK inhibitors in BRAFV600E-positive melanomas. However, the benefits have not always translated for these same molecular variations in other cancers.

Multigene Panel Testing

Broad molecular panel tests evaluate between 140-300 genes in tumor tissue for which there are only a small number of FDA-approved targeted therapy options. Large panel tests contain many genes that have no actionable gene mutations, thus no targeted therapy. Molecular panel testing has been used to determine off-label drug therapy or whether or not a patient may be eligible for a clinical trial. Of those patients tested, only a small number will experience clinical utility (have a targeted therapy identified), and an even smaller number will experience clinical benefit.

RATIONALE

The Analytic validity, Clinical validity, Clinical utility and associated Ethical, legal, and social implications (ACCE) framework is used to evaluate genetic tests. It includes collecting, evaluating, interpreting, and reporting data about DNA (and related) testing for disorders with a genetic component in a format that allows policy makers to have access to up-to-date and reliable information for decision-making. Elements of the frame include evaluation of the tests’ analytic validity, clinical validity, and clinical utility, as well as associated ethical, legal, and social implications. Studies published to evaluate the analytic validity of molecular panels for targeted therapy are lacking. However, the panels are mainly performed using next-generation sequencing (NGS), which has a high analytic validity. As described in the Guidelines section of this policy, some of the tests utilize additional testing methods (e.g., IHC, Sanger sequencing), which also have high analytical validity.

Colorectal Cancer

The Molecular Biomarkers for the Evaluation of Colorectal Cancer Guidelines from the American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and the American society of Clinical Oncology (2017) recommend RAS mutational testing for colorectal carcinoma patients being considered for anti-EGFR therapy. 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. Quality of evidence: high/intermediate). 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. Quality of evidence: intermediate/low).

The NCCN guidelines for Colon Cancer have expanded recommendations regarding biomarker testing as the role of targeted therapy for treatment of advanced or metastatic colorectal cancer (mCRC) has become increasingly prominent. Currently, determination of tumor gene status for KRAS/NRAS and BRAF mutations, as well as HER2 amplifications and MSI/MMR status (if not previously done), are recommended for patients with mCRC. The testing can be performed on formalin-fixed paraffin-embedded tissue (preferred) or blood-based assay and may be carried out for individual genes or as part of an NGS panel, although no specific methodology is recommended. NGS panels have the advantage of being able to pick up rare and actionable genetic alterations, such as neurotrophic tyrosine receptor kinase (NTRK) fusions. Based on the limited data in the colorectal cancer population, the NCCN Panel does not currently recommend TMB biomarker testing, unless measured as part of a clinical trial. Patients with known KRAS mutation (exon 2, 3, 4) or NRAS mutation (exon 2, 3, 4) should not be treated with either cetuximab or panitumumab. BRAF V600E mutation makes response to panitumumab or cetuximab highly unlikely unless given with a BRAF inhibitor. HER2-targeted therapies are now recommended as subsequent therapy options in patients with tumors that have HER2 overexpression. Testing for

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HER2 amplifications for patients with metastatic colorectal cancer is recommended. If the tumor is already known to have a KRAS/NRAS or BRAF mutation, HER2 testing is not required. However, HER2-targeted therapies are still under investigation, enrollment in a clinical trial is encouraged. Anti-HER2 therapy is only indicated in HER2-amplified tumors that are also RAS and BRAF wild type. NTRK fusions were limited to cancer that were wild type for KRAS, NRAS, and BRAF. A majority of the CRCs harboring NTRK fusions were also MMR-deficient. NTRK fusion testing may be limited to those patients with wild-type KRAS, NRAS, and BRAF. There are two targeted therapies (larotrectinib and entrectinib) that have been FDA-approved for the treatment of patients with metastatic, unresectable solid tumors that have an NTRK gene fusion and no satisfactory alternative treatment options, regardless of the location of the primary tumor. These treatment options are not appropriate for most patients due to the rarity of the NTRK fusion in CRC.

Non-Small Cell Lung Cancer

Evidence compiled from nonconcurrent-prospective studies and one-arm prospective enrichment studies is sufficient to conclude that a gain-of-function somatic mutation in the tumor-cell EGFR gene tyrosine kinase domain identifies a population subset (patients with mutation-positive tumors) with advanced NSCLC who exhibit improved objective radiologic response, progression-free survival, and overall survival when treated with erlotinib compared to the same treatment in patients with wild-type tumors or to standard chemotherapy in patients with EGFR-positive tumors.

Data are strongest for demonstrating differences in objective radiologic response: the response is less consistent, but strong, for progression-free survival, and is less consistent, but strong, for overall survival. There is growing consensus that both objective radiologic response and progression-free survival are reasonable endpoints to use for assessment of treatment response. There is a published meta-analysis suggesting objective radiologic response is strongly associated with median overall survival in patients with NSCLC treated with TKIs. There is also a growing discussion that overall survival may be a compromised endpoint for NSCLC, due to the fact that NSCLC is a particularly aggressive disease with an increasing number of treatment choices, many specifically available for cross-over use in patients demonstrating resistance to earlier therapies. These cross-over therapies are likely to make evaluation of overall survival a challenging, and perhaps impossible, study endpoint.

Recent prospective and retrospective studies have shown convincing evidence that EGFR mutations can identify disease likely to respond to erlotinib. There is growing evidence that this information affects the net health outcome by identifying patients who are likely to exhibit good outcomes with this treatment with minimal toxicity. Recent reports suggest EGFR mutations also identify patients more likely to respond to erlotinib than to alternative drug choices.

There is also growing information demonstrating that EGFR status can help physicians identify wild-type tumors in patients who are unlikely to respond to erlotinib. In these patients, alternative treatment choices should be considered. It is, therefore, prudent for physicians to evaluate patients with wild-type tumors carefully, considering the unique patient specific variables and preferences at hand, to discuss these with the patient, and to use this information to make patient-informed, collaborative, personalized treatment choices.

The NCCN guidelines for Non-Small Cell Lung Cancer (NSCLC) strongly advises broader molecular profiling with the goal of identifying rare driver mutations for which effective drugs may already be available, or to appropriately counsel patients regarding the availability of clinical trials. Broad molecular profiling is a key component of the improvement of care of patients with NSCLC. If there is insufficient tissue to allow testing for all of EGFR, ALK, ROS1, BRAF, ERBB2 (HER2), KRAS, NTRK 1/2/3, MET, and RET, repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results, and, if unknown, these patients are treated as though they do not have driver oncogenes. Erlotinib is recommended, with or without chemotherapy, as first-line therapy for advanced or metastatic NSCLC in patients with known activated EGFR mutation or gene amplification. EGFR mutations were predictive of a better response in patients receiving erlotinib (53% in patients with mutations versus 18% in those without mutations). KRAS mutations are associated with intrinsic TKI resistance and KRAS gene sequencing could be useful for the selection of patients as candidates for TKI therapy. Overlapping EGFR and KRAS mutations occur in less than 1% of patients with lung cancer. Other TKIs such as Afatinib and Osimertinib have been recommended by NCCN in patients with EGFR mutations and metastatic NSCLC. Afatinib has been recommended and FDA approved for first-line therapy in patients with metastatic non-squamous NSCLC who have sensitizing EGFR mutations. Osimertinib has

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been approved by the FDA for patients with metastatic EGFR T790M mutation-positive NSCLC, who have progressed on or after EGFR TKI therapy. NCCN recommends Osimertinib for individuals with stage IB NSCLC with EGFR exon 19 deletion or L858R. ROS1 gene rearrangements occur more frequently in younger women with adenocarcinoma who are never smokers and in those who are negative for EGFR mutations, KRAS mutations, and ALK gene rearrangements (also known as triple negative). Crizotinib is very effective for patients with ROS1 rearrangement with response rates of about 70% including complete responses. The FDA has approved crizotinib for patients with ROS1 rearrangements.

Other genetic alterations such as, BRAF V600E and HER2 mutations, MET amplification, and RET rearrangements have been associated with emerging targeted therapies. Targeted agents are available for patients with NSCLC who have these other genetic alterations, although they are FDA approved for other indications.

As a primary immunosuppressive driver, PD-L1 overexpression may be an important facilitator for tumor growth and metastasis. PD-L1 has been detected in up to 50% of human cancers, making the PD-L1 pathway a focus of cancer research. NCCN recommends IHC testing for PD-L1 expression before first-line treatment in patients with metastatic NSCLC with negative or unknown test results for EGFR mutations, ALK rearrangements, and ROS1 rearrangements. Although it is not an optimal biomarker, PD-L1 expression is currently the best available biomarker to assess whether patients are candidates for pembrolizumab. PD-L1 expression is continuously variable and dynamic; thus, a cutoff value for a positive result is artificial. Patients with PD-L1 expression levels just below and just above 50% will probably have similar responses. The definition of a positive PD-L1 test result varies depending on which biomarker assay is used. For the 2022 update, the NCCN NSCLC Panel recommends testing for ERBB2 (HER2) mutations in eligible patients with metastatic NSCLC based on clinical trial data and the FDA approval of fam-trastuzumab deruxtecan-nxki. ERBB2 (HER2) exon 20 mutations occur in approximately 3% of patients (median age, 62 years) with advanced nonsquamous NSCLC. Patients tend to be females who do not smoke cigarettes; they have a higher incidence of brain metastases than those with other actionable mutations. Emerging predictive molecular biomarkers include high-level MET amplifications. Targeted agents are available for patients with NSCLC who have high-level MET amplifications. However, there is less data to support using these agents and they may not be FDA approved for NSCLC; therefore, they are referred to as emerging biomarkers.

The College of American Pathologists (CAP), the International Association for the Study of Lung Cancer (IASLC), and the Association for Molecular Pathology (AMP) guidelines on molecular testing for the selection of patients with lung cancer for epidermal growth factor receptor (EGFR) recommend EGFR molecular testing in patients with lung adenocarcinoma and mixed lung cancers with an adenocarcinoma component regardless of clinical characteristics (e.g., younger age, smoking status) for EGFR-targeted TKI therapy. EGFR mutation testing should be ordered at the time of diagnosis for patients who present with advanced-stage disease who are suitable for therapy, or at time of recurrence or progression in patients who originally presented with lower stage disease but were not previously tested, or testing tumors at time of diagnosis for stage I, II, or III disease so that molecular information is available to an oncologist at the time of recurrence for a subset of patients who subsequently experience recurrence, although this decision is deferred to local laboratories and oncology teams. KRAS mutation testing is not recommended as a sole determinant of EGFR-targeted therapy.

Melanoma

The NCCN guidelines for Cutaneous Melanoma state emerging molecular technologies for cutaneous melanoma diagnosis and prognostication indications include that BRAF or next-generation sequencing (NGS) for resected stage I-II cutaneous melanoma is not recommended unless it will inform clinical trial participation. BRAF mutation is recommended for patients with stage III at high risk for recurrence for whom future BRAF-directed therapy may be an option. For initial presentation with stage IV disease or clinical recurrence, obtain tissue to ascertain alterations in BRAF, and in the appropriate clinical setting, KIT from either biopsy of the metastasis (preferred) or archival material if the patient is being considered for targeted therapy. Broader genomic profiling (e.g., larger NGS panels, BRAF non-V600 mutations) is recommended if feasible, especially if the test results might guide future treatment decisions or eligibility for participation in a clinical trial. If BRAF single-gene testing was the initial test performed, and is negative, clinicians should strongly consider larger NGS panels to identify other potential genetic targets (e.g., KIT, BRAF non-V600).

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BRAF and KIT mutations appear to be early genetic driver events in melanoma. Thus, repeat molecular testing upon recurrence or metastases is likely to be of low yield. Repeat testing following progression on targeted therapy (BRAF- or KIT-directed therapy) does not appear to have clinical utility, since the mechanisms of resistance are diverse and do not have prognostic or therapeutic relevance.

Pancreatic Cancer

The NCCN guidelines for Pancreatic Adenocarcinoma recommends gene profiling of tumor tissue as clinically indicated for individuals with locally advanced/metastatic disease who are candidates for anti-cancer therapy to identify uncommon mutations. Consider specifically testing for actionable somatic findings including, but not limited to fusions (ALK, NRG1, NTRK, ROS1, FGFR2, RET), mutations (BRAF, BRCA 1/2, KRAS, PALB2), amplifications (HER2), microsatellite instability (MSI), and/or mismatch repair (MMR) deficiency. Testing on tumor tissue is preferred and may be performed if recurrence after resection if not previously performed.

Ovarian Cancer

The NCCN guidelines for Ovarian Cancer/Fallopian Tube Cancer/ Primary Peritoneal Cancer state comprehensive tumor testing may not be necessary for certain patients in the upfront setting, specifically those with a germline mutation in BRCA1/2 or other homologous recombination/DNA repair pathway genes. Initially molecular analysis should include BRCA1/2 status, loss of heterozygosity, or homologous recombination status, in the absence of a germline BRCA mutation. However, some patients (such as those who lack a BRCA1/2 mutation or experience disease recurrence) may benefit from a more thorough tumor molecular analysis to inform additional targeted therapy options. In the recurrence setting, tumor molecular analysis is recommended to include, at a minimum, tests to identify potential benefit from targeted therapeutics that have tumor-specific or tumor-agnostic benefit including, but not limited to, BRCA1/2, HR status, MSI, MMR, TMB, BRAF, *FRα*, *RET*, and NTRK if prior testing did not include these markers. Additional somatic tumor testing can be considered at the physician's discretion to identify genetic alterations for which FDA-approved tumor-specific or tumor-agnostic targeted therapy options exist. These additional tests may be particularly useful for patients who recurrence therapy options are limited.

Prostate Cancer

The NCCN guidelines for Prostate Cancer state that tumor molecular and biomarker analysis may be used for treatment decision-making, including understanding eligibility for biomarker-directed treatments, genetic counseling, early use of platinum chemotherapy, and eligibility for clinical trials. Clinical trials may include established and/or candidate molecular biomarkers for eligibility. Tumor molecular profiles may change with subsequent treatments and re-evaluation may be considered at time of cancer progression for treatment decision-making. Tumor testing for alterations in homologous recombination DNA repair genes, such as BRCA1, BRCA2, ATM, PALB2, FANCA, RAD51D, CHEK2, and CDK12, is recommended for individuals with metastatic prostate cancer and can be considered in individuals with regional (N1) prostate cancer. Tumor testing for MSI-H or dMMR is also recommended in patients with metastatic castration-resistant prostate cancer and may be considered in patients with regional or castration-sensitive metastatic prostate cancer. Early studies suggest germline and somatic mutations in these genes may be predictive of the clinical benefit of poly-ADP ribose polymerase (PARP) inhibitors. At present, two PARP inhibitors are approved by the FDA for use in prostate cancer are Olaparib and Rucaparib.

Breast Cancer

The NCCN guidelines for Breast Cancer state for recurrent unresectable (local or regional) or stage IV disease, for HR-positive/HER2-negative breast cancer, assess for PIK3CA mutations with tumor tissue to identify candidates for alpelisib plus fulvestrant. (Category 1 Evidence). In triple negative breast cancer, PD-L1 can be assessed by IHC (Category 1 Evidence). In all types of breast cancer NTRK fusion and MSI/MMR can be assessed in tumor tissue and tumor mutational burden (TMB) by NGS (Category 2A Evidence). Larotrectinib and entrectinib are indicated for the treatment of solid tumors that have an NTRK gene fusion without a known acquired resistance mutation and have no satisfactory alternative treatments or that have progressed following treatment. Pembrolizumab is indicated for the treatment of patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR)

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solid tumors, or TMB-H tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options. Dostarlimab-gxly is indicated for adult patients with MSI-H/dMMR unresectable or metastatic tumors that have progressed on or following prior treatment and who have no satisfactory alternative treatment options.

Brain Cancer

The NCCN guidelines for Central Nervous System Cancers state with the use of genetic and molecular testing, histologically similar CNS neoplasms can be differentiated more accurately in terms of prognosis and response to different therapies. The fifth edition of the WHO classification of CNS tumors was published in 2021. In this newest classification, adult diffuse gliomas are subsumed within a super category of gliomas and glioneuronal tumors and are split into three subtypes: 1) IDH-mutant astrocytoma; 2) oligodendroglioma, 1p/19q-codeleted and IDH-mutant; and 3) glioblastoma, IDH wild-type. The panel recommends IDH mutation testing in patients with glioma. Testing for 1p/19q codeletion is essential for the diagnosis of oligodendroglioma. Mutation testing for ATRX and TERT promoter are also recommended, given the diagnostic value of these mutations. Grade 3–4 gliomas should undergo testing for MGMT promoter methylation, since MGMT promoter-methylated tumors typically respond better to alkylating chemotherapy, compared to unmethylated tumors. Molecular testing of glioblastomas is encouraged by the panel, as patients with a detected driver mutation (e.g., BRAF V600E mutation or NTRK fusion) may be treated with a targeted therapy on a compassionate use basis, and these tests improve diagnostic accuracy and prognostic stratification. Recurrent or progressive disease of glioblastoma patients should be enrolled in clinical trials evaluating systemic therapy options.

Ependymomas arising in the supratentorium often contain activating fusions of ZFTA. This leads to increased NF-kappa-B signaling and more aggressive behavior. This event is more common in children than in adults, and occurs only in the supratentorium, not the posterior fossa or spine. A subset of spinal cord ependymomas show MYCN amplification. Such tumors tend to behave more aggressively and are therefore now codified as SP-EPN-MYCN. As is often the case in other tumor types (e.g., medulloblastoma), MYCN amplification is strongly associated with more aggressive behavior and worse prognosis.

Medulloblastomas are WHO grade 4 tumors that predominantly arise from the cerebellum in pediatric patients but can also occur in adults. The WHO committee on CNS tumors now recommends subclassification of these tumors into four distinct groups: i) WNT-activated; ii) Sonic hedgehog (SHH)-activated and TP53-mutant; iii) SHH-activated and TP53-wild type; and iv) non-WNT/non-SHH. Differentiating between WNT-activated, SHH-activated, and non-WNT/ non-SHH tumors is best classified by expression arrays, DNA methylation arrays, or an IHC panel composed of beta-catenin, GAB1, and YAP1. Because there are a variety of hotspots in TP53, gene sequencing is recommended in SHH-activated medulloblastomas. SHH-pathway inhibitors that have been evaluated in phase II trials including adults with recurrent medulloblastoma include vismodegib296 and sonidegib.297 Patients in these trials with SHH-activated disease were more likely to respond than patients with non-SHH disease.

Multigene Panel Testing

It is difficult to determine the clinical validity of the molecular panels because of the different mutations and the large number of potential cancers for which they can be used. Testing each gene in the panel for each of the cancer types would require extensive research potentially taking many years to complete. Consequently, the evidence on clinical validity of the molecular panels is insufficient to make any recommendations.

The evidence for clinical utility of molecular panel testing to direct targeted therapies in cancer patients has been conflicting. The SHIVA study, a randomized, open-label phase 2 trial, randomized patients with any kind of metastatic solid tumor refractory to standard of care (Le Tourneau, et al (2015)) to matched molecularly targeted treatment based on one of three molecular pathways; hormone receptor, PI3K/AKT/mTOR, and RAF/MEK (the experimental group) or physician's choice treatment (the control group). At median follow-up of 11.3 months, median progression-free survival was similar for both groups. Grade 3 to 4 adverse events were slightly higher in the experimental group. The authors concluded that progression-free survival was not improved with the use of molecularly targeted agents outside their indications, compared with the physician's choice treatment in heavily pretreated patients with cancer. Off-label use of molecularly targeted agents should be encouraged in clinical trials to assess predictive biomarkers of efficacy. The

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IMPACT study (2007), a phase I study at the University of Texas, MD Anderson Cancer Center, assessed whether molecular analysis of advanced cancer and targeted therapy was associated with improved clinical outcomes. Of the 1,144 patients analyzed, 40.2% had one or more molecular aberration in their tumor. The patients with one aberration and matched therapy had a higher overall response rate (27%) compared to those patients without matched therapy (5%). Patients with matched therapy had longer time-to-treatment failure (5.2 months) and longer survival (13.4 months) compared to those patients without matched therapy (2.2 months and 9.0 months, respectively). The author reported on the IMPACT2 study (2014), a randomized study, evaluating molecular profiling and targeted agents, which includes clinical trials with immunotherapy, targeted therapy, and other therapeutic strategies designed for specific patients, and continues to recruit patients. Studies have been limited by the small number of patients that have received molecularly targeted therapy and the small number of patients that have derived benefit from it.

The NCCN guidelines do not contain recommendations for the general strategy of testing a tumor for a wide range of mutations. However, there are specific genetic testing guidelines for individual cancers, based on situations in which there is a known mutation-drug combination that has demonstrated benefits for that specific tumor type (e.g., NSCLC, ovarian cancer, colorectal cancer, and melanoma).

The American Society of Clinical Oncology (ASCO) (2022) published a clinical opinion paper regarding somatic genetic testing for metastatic or advanced solid tumor cancers. They state genomic testing should be performed when there are genomic biomarker-linked therapies approved by regulatory agencies for the type of cancer and when considering a treatment for which there is a specific genomic biomarker-based contraindication (strength of recommendation: strong). For patients with metastatic or advanced solid tumors, genomic testing using multigene genomic sequencing is preferred whenever patients are eligible for a genomic biomarker-linked therapy that a regulatory agency has approved (strength of recommendation: moderate). Multigene panel-based genomic testing should be used whenever more than one genomic biomarker is linked to a regulatory agency-approved therapy (strength of recommendation: strong). For tumors with actionable genomic alterations without approved genomic biomarker-linked targeted therapies, patient participation in clinical trials is encouraged after considering the expected efficacy of available standard-of-care options (strength of recommendation: strong). Off-label and off-study use of genomic biomarker-linked therapies approved in other diseases is not recommended when a clinical trial is available or without clinical evidence of meaningful efficacy (strength of recommendation: strong).

CODES

- *Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.*
- ***CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.***
- *Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.*
- *Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).*

CPT Codes

Code	Description
81120	IDH1 (isocitrate dehydrogenase 1 [NADP+], soluble) (e.g., glioma), common variants (e.g., R132H, R132C)
81121	IDH2 (isocitrate dehydrogenase 2 [NADP+], mitochondrial) (e.g., glioma), common variants (e.g., R140W, R172M)
81162	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis (i.e., detection of large gene rearrangements)
81191	NTRK1 (Neurotrophic Receptor Tyrosine Kinase 1) (e.g., solid tumors) translocation analysis

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Code	Description
81192	NTRK2 (Neurotrophic Receptor Tyrosine Kinase 2) (e.g., solid tumors) translocation analysis
81193	NTRK3 (Neurotrophic Receptor Tyrosine Kinase 3) (e.g., solid tumors) translocation analysis
81194	NTRK (neurotrophic receptor tyrosine kinase 1, 2, and 3) (e.g., solid tumors) translocation analysis
81210	BRAF (B-Raf proto-oncogene, serine/threonine kinase) (e.g., colon cancer, melanoma), gene analysis, V600 variant(s)
81235	EGFR (epidermal growth factor receptor) (e.g., non-small cell lung cancer) gene analysis, common variants (e.g., exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q)
81272	KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) (e.g., gastrointestinal stromal tumor [GIST], acute myeloid leukemia, melanoma), gene analysis, targeted sequence analysis (e.g., exons 8, 11, 13, 17, 18)
81275	KRAS (Kirsten rat sarcoma viral oncogene homolog) (e.g., carcinoma) gene analysis; variants in exon 2 (e.g., codons 12 and 13)
81276	KRAS (Kirsten rat sarcoma viral oncogene homolog) (e.g., carcinoma) gene analysis; additional variant(s) (e.g., codon 61, codon 146)
81287	MGMT (O-6-methylguanine-DNA methyltransferase) (e.g., glioblastoma multiforme) promoter methylation analysis
81307	PALB2 (partner and localizer of BRCA2) (e.g., breast and pancreatic cancer) gene analysis; full gene sequence
81309	PIK3CA (Phosphatidylinositol-4, 5-biphosphate 3-kinase, catalytic subunit alpha) (e.g., colorectal and breast cancer) gene analysis, targeted sequence analysis (e.g., exons 7, 9, 20)
81311	NRAS (neuroblastoma RAS viral [v-ras] oncogene homolog) (e.g., colorectal carcinoma), gene analysis, variants in exon 2 (e.g., codons 12 and 13) and exon 3 (e.g., codon 61)
81345	TERT (telomerase reverse transcriptase) (e.g., thyroid carcinoma, glioblastoma multiforme) gene analysis, targeted sequence analysis (e.g., promoter region)
81402	Molecular Pathology Procedure Level 3
81403	Molecular Pathology Procedure Level 4
81404	Molecular Pathology Procedure Level 5
81405	Molecular Pathology Procedure Level 6
81406	Molecular Pathology Procedure Level 7
81407	Molecular Pathology Procedure Level 8
81408	Molecular Pathology Procedure Level 9

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Code	Description
81445	Solid organ neoplasm, genomic sequence analysis panel, 5-50 genes, interrogation for sequence variants and copy number variants or rearrangements, if performed; DNA analysis or combined DNA and RNA analysis
81449	Solid organ neoplasm, genomic sequence analysis panel, 5-50 genes, interrogation for sequence variants and copy number variants or rearrangements, if performed; RNA analysis
81455 (E/I)	Solid organ or hematolymphoid neoplasm or disorder, 51 or greater genes, genomic sequence analysis panel, interrogation for sequence variants and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; DNA analysis or combined DNA and RNA analysis
81456 (E/I)	Solid organ or hematolymphoid neoplasm or disorder, 51 or greater genes, genomic sequence analysis panel, interrogation for sequence variants and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; RNA analysis
81457	Solid organ neoplasm, genomic analysis panel; DNA analysis, microsatellite instability (<i>effective 01/01/24</i>)
81458	Solid organ neoplasm, genomic analysis panel; DNA analysis, copy number variants and microsatellite instability (<i>effective 01/01/24</i>)
81459	Solid organ neoplasm, genomic analysis panel; DNA analysis or combined DNA and RNA analysis, copy number variants, microsatellite instability, tumor mutation burden, and rearrangements (<i>effective 01/01/24</i>)
81479	Unlisted molecular pathology procedure
88363	Examination and selection of retrieved archival (i.e., previously diagnosed) tissue(s) for molecular analysis (e.g., KRAS mutational analysis)
0037U (E/I)	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 (e.g., FoundationOne CDx (F1CDx), Foundation Medicine Inc)
0154U	Oncology (urothelial cancer), RNA, analysis by real-time RT-PCR of the FGFR3 (fibroblast growth factor receptor 3) gene analysis (i.e., p.R248C [c.742C>T], p.S249C [c.746C>G], p.G370C [c.1108G>T], p.Y373C [c.1118A>G], FGFR3-TACC3v1, and FGFR3-TACC3v3) utilizing formalin-fixed paraffin-embedded urothelial cancer tumor tissue, reported as FGFR gene alteration status (e.g.; theascreen FGFR RGQ RT-PCR Kit, QIAGEN, QIAGEN GmbH)

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Code	Description
0155U	Oncology (breast cancer), DNA, PIK3CA (phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alpha) (e.g., breast cancer) gene analysis (i.e., 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 (e.g., theascreen PIK3CA RGQ PCR Kit, QIAGEN, QIAGEN GmbH) (<i>effective 04/01/20</i>)
0172U	Oncology (solid tumor as indicated by the label), somatic mutation analysis of BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) and analysis of homologous recombination deficiency pathways, DNA, formalin-fixed paraffin-embedded tissue, algorithm quantifying tumor genomic instability score (myChoice CDx, Myriad Genetics Laboratories, Inc)
0211U (E/I)	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 NGS Analysis, Caris MPI d/b/a Caris Life Sciences)
0244U (E/I)	Oncology (solid organ), DNA, comprehensive genomic profiling, 257 genes, interrogation for single-nucleotide variants, insertions/deletions, copy number alterations, gene rearrangements, tumor-mutational burden, and microsatellite instability, utilizing formalin-fixed paraffin-embedded tumor tissue (Oncotype MAPTM Pan-Cancer Tissue Test, Paradigm Diagnostics, Inc, Paradigm Diagnostics, Inc) (<i>effective 04/01/21</i>)
0249U (E/I)	Oncology (breast), semiquantitative analysis of 32 phosphoproteins and protein analytes, includes laser capture microdissection, with algorithmic analysis and interpretative report (Theralink Reverse Phase Protein Array (RPPA), Theralink Technologies, Inc.)
0250U (E/I)	Oncology (solid organ neoplasm), targeted genomic sequence DNA analysis of 505 genes, interrogation for somatic alterations (SNVs [single nucleotide variant], small insertions and deletions, one amplification, and four translocations), microsatellite instability and tumor-mutation burden (PGDx elio tissue complete, Personal Genome Diagnostics, Inc)
0329U (E/I)	Oncology (neoplasia), exome and transcriptome sequence analysis for sequence variants, gene copy number amplifications and deletions, gene rearrangements, microsatellite instability and tumor mutational burden utilizing DNA and RNA from tumor with DNA from normal blood or saliva for subtraction, report of clinically significant mutation(s) with therapy associations (Oncomap ExTra, Exact Sciences, Inc, Genomic Health Inc)
0334U (E/I)	Oncology (solid organ), targeted genomic sequence analysis, formalin-fixed paraffin embedded (FFPE) tumor tissue, DNA analysis, 84 or more genes, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability and tumor mutational burden (Guardant360 TissueNext, Guardant Health, Inc)

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Code	Description
0379U (E/I)	Targeted genomic sequence analysis panel, solid organ neoplasm, DNA (523 genes) and RNA (55 genes) by next-generation sequencing, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability, and tumor mutational burden (Solid Tumor Expanded Panel, Quest Diagnostics) (<i>effective 04/01/23</i>)
0391U (E/I)	Oncology (solid tumor), DNA and RNA by next-generation sequencing, utilizing formalin-fixed paraffin-embedded (FFPE) tissue, 437 genes, interpretive report for single nucleotide variants, splice-site variants, insertions/deletions, copy number alterations, gene fusions, tumor mutational burden, and microsatellite instability, with algorithm quantifying immunotherapy response score (Strata Select, Strata Oncology, Inc) (<i>effective 07/01/23</i>)
0414U (E/I)	Oncology (lung), augmentative algorithmic analysis of digitized whole slide imaging for 8 genes (ALK, BRAF, EGFR, ERBB2, MET, NTRK1-3, RET, ROS1), and KRAS G12C and PD-L1, if performed, formalin-fixed paraffin-embedded (FFPE) tissue, reported as positive or negative for each biomarker (LungOI, Imagen) (<i>effective 10/01/23</i>)

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HCPCS Codes

Code	Description
No specific code(s)	

ICD10 Codes

Code	Description
C18.0-C21.8	Malignant neoplasm of colon, rectosigmoid junction, rectum, and anus and anal canal (code range)
C25.0-C25.9	Malignant neoplasm of pancreas (code range)
C34.10-C34.92	Malignant neoplasm of lobe, bronchus, or lung (code range)
C43.0-C43.9	Malignant melanoma of skin (code range)
C50.011-C50.929	Malignant neoplasm of breast (code range)
C56.1-C56.9	Malignant neoplasm of ovary (code range)
C61	Malignant neoplasm of prostate
C71.0-C71.9	Malignant neoplasm of brain (code range)
C78.5	Secondary malignant neoplasm of large intestine and rectum
C79.60-C79.63	Secondary malignant neoplasm of ovary (code range)
C79.81	Secondary malignant neoplasm of breast
D05.00-D05.02	Lobular carcinoma in situ of breast (code range)
D05.10-D05.12	Intraductal carcinoma in situ of breast (code range)
D05.80-D05.92	Carcinoma in situ of breast, specified, unspecified (code range)

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Code	Description
D07.30-D07.39	Carcinoma in situ of other and unspecified female genital organs (code range)
D40.0	Neoplasm of uncertain behavior of prostate

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*Key Article

KEY WORDS

Molecular Panel Testing, Targeted Therapy, Foundation One, Caris Life Sciences, OmniSeq, PyroSeq

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

There is currently a National Coverage Determination (NCD) for Next Generation Sequencing (NGS) (90.2). Please refer to the following NCD website for Medicare Members: <https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=372&ncdver=2&bc=AAAAIAAAAA&> accessed 12/01/23.

There is currently a Local Coverage Determination (LCD) for Molecular Pathology Procedures (L35000). Please refer to the following LCD website for Medicare Members: https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=35000&ver=138&CntrctrSelected=298*1&Cntrctr=298&s=41&DocType=All&bc=AAgAAQBIAAA& accessed 12/01/23.

There is currently a Local Coverage Article (LCA) for Billing and Coding: Molecular Pathology Procedures (A56199). Please refer to the following LCA website for Medicare Members: <https://www.cms.gov/medicare-coverage-database/view/article.aspx?articleId=56199&ver=95> accessed 12/01/23.

There is currently a Local Coverage Determination (LCD) for Genomic Sequence Analysis Panels in the Treatment of Solid Organ Neoplasms (L37810). Please refer to the following LCD website for Medicare Members: <https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdId=37810&ver=17> accessed 12/01/23.

There is currently a Local Coverage Article (LCA) for Billing and Coding: Genomic Sequence Analysis Panels in the Treatment of Solid Organ Neoplasms (A56867) Please refer to the following LCA website for Medicare Members: <https://www.cms.gov/medicare-coverage-database/view/article.aspx?articleId=56867&ver=23> accessed 12/01/23.