Genetic testing: oncology - circulating tumor DNA and circulating tumor cells (liquid biopsy)

These services may or may not be covered by your HealthPartners plan. Please see your plan documents for your specific coverage information. If there is a difference between this general information and your plan documents, your plan documents will be used to determine your coverage.

Administrative Process

Prior authorization is required for the following services:

- Molecular Profiling Panel Tests via Circulating Tumor DNA (ctDNA)
- *EGFR* Variant Analysis via ctDNA
- *BRAF* Variant Analysis via ctDNA
- *KRAS* Variant Analysis via ctDNA
- *AR-V7* Circulating Tumor Cells (CTCs) Analysis
- Testing that is associated with a procedure code listed in “Box A”, below.

Prior authorization is not required for *PIK3CA* Variant Analysis via ctDNA

The following genetic tests are considered investigational/experimental and, therefore, not covered:

- Circulating Tumor Cell (CTC) Enumeration

Tests that require prior authorization will be reviewed for medical necessity of the testing as a whole. That is, a single coverage decision will apply to all of the tests, services, and/or procedure codes associated with the genetic test, whether they are requested/billed together or separately.

Box A: Genetic testing procedure codes that require prior authorization
Molecular pathology procedures, Tier 2 or unlisted (CPT 81400-81408, 81479)
Unlisted multianalyte assays (CPT 81599)
Any other listed or unlisted laboratory/pathology CPT code when it is used in association with a genetic test.

Policy Reference Table

If available, codes are listed below for informational purposes only, and do not guarantee member coverage or provider reimbursement. The list may not be all-inclusive.

Coverage Criteria Sections	Example Tests, Labs	Common CPT Codes	Common ICD Codes
Molecular Profiling Panel Tests via Circulating Tumor DNA (ctDNA)			
Broad Molecular Profiling Panel Tests via Circulating Tumor DNA (ctDNA)	FoundationOne Liquid CDx (Foundation Medicine)	0239U	C15, C16, C18, C25, C34, C61
	Guardant360 CDx (Guardant Health)	0242U	
	Guardant360 83+ genes (Guardant Health)	0326U	
	NeoLAB Solid Tumor Liquid Biopsy (NeoGenomics Laboratories)	81445, 81455, 81462, 81463, 81464	
	Tempus xF: Liquid Biopsy Panel of 105 Genes (Tempus)		
	LiquidHALLMARK (Lucence Health)	0409U	
	Caris Assure (Caris Life Sciences)	0485U	
	Northstar Select (BillionToOne)	0487U	
	OptiSeq Dual Cancer Panel Kit (DiaCarta, Inc)	0499U	
	Resolution ctDx Lung (Labcorp)	0179U	C34

Lung Cancer Focused Panel Tests via Circulating Tumor DNA (ctDNA)	OncoBEAM Lung2: EGFR, KRAS, BRAF (Sysmex Inostics, Inc.)	81210, 81235, 81275, 81479	
	InVisionFirst-Lung Liquid Biopsy (NeoGenomics)	0388U	
	GeneStrat NGS (Biodesix)	81462	
Single Gene Molecular Profiling Tests via Circulating Tumor DNA (ctDNA)			
EGFR Variant Analysis via ctDNA	EGFR T790M Mutation Detection, Blood (University of Washington Medical Center – Laboratory Medicine – Genetics Laboratory)	81235	C34
BRAF Variant Analysis via ctDNA	Cell-Free DNA BRAF V600, Blood (Mayo Medical Laboratories)	81210	C18-C21, C43
	BRAF V6000E Mutation Detection in Circulating Cell-Free DNA by Digital Droplet PCR (ARUP Laboratories)		
KRAS Variant Analysis via ctDNA	Cell-Free DNA KRAS 12, 13, 61, 146 Blood (Mayo Medical Laboratories)	81275, 81276	C18-C20
PIK3CA Variant Analysis via ctDNA	therascreen PIK3CA RGQ PCR Kit (QIAGEN)	0177U	C50
	Cell-Free DNA PIK3CA Test, Blood (Mayo Medical Laboratories)	81309	
Circulating Tumor Cell (CTC) Tests			
AR-V7 Circulating Tumor Cells (CTC) Analysis	AR-V7 (Epic Sciences)	81479	C61
Circulating Tumor Cell (CTC) Enumeration	CELLSEARCH Circulating Tumor Cell (CTC) Test (CELLSEARCH)	86152	C00.0-C96.9
	CELLSEARCH Circulating Melanoma Cell (CMC) Test (Menarini Silicon)	0490U	
	CELLSEARCH ER Circulating Tumor Cell (CTC-ER) Test (Menarini Silicon)	0491U	
	CELLSEARCH PD-L1 Circulating Tumor Cell (CTC-PDL1) Test (Menarini Silicon)	0492U	

Coverage

Molecular Profiling Panel Tests via Circulating Tumor DNA (ctDNA)

Broad Molecular Profiling Panel Tests via Circulating Tumor DNA (ctDNA)

1. Broad molecular profiling panel tests via circulating tumor DNA (liquid biopsy) are considered **medically necessary** when:
   - A. The member has a diagnosis, progression, or recurrence of one of the following:
     - i. Stage IV or metastatic lung adenocarcinoma, **or**
     - ii. Stage IV or metastatic large cell lung carcinoma, **or**
     - iii. Stage IV or metastatic squamous cell lung carcinoma, **or**
     - iv. Stage IV or metastatic non-small cell lung cancer (NSCLC) not otherwise specified (NOS), **or**
     - v. Locally advanced / metastatic pancreatic adenocarcinoma, **or**
     - vi. Metastatic or advanced gastric cancer, **or**
     - vii. Metastatic or advanced esophageal or esophagogastric junction cancer, **or**
     - viii. Metastatic prostate cancer, **or**
     - ix. Stage III or higher cutaneous melanoma, **or**
     - x. Metastatic colorectal cancer, **or**
     - xi. Locally advanced or metastatic ampullary adenocarcinoma, **or**
     - xii. Persistent or recurrent cervical cancer, **or**

xiii. Unresectable or metastatic biliary tract cancer, **or**
xiv. Suspected or confirmed histiocytic neoplasm, **or**
xv. Locoregional unresectable or metastatic extrapulmonary poorly differentiated neuroendocrine carcinoma, **or**
xvi. Locoregional unresectable or metastatic extrapulmonary poorly large or small carcinoma, **or**
xvii. Locoregional unresectable or metastatic extrapulmonary poorly mixed neuroendocrine-non-neuroendocrine neoplasm, **or**
xviii. Suspected metastatic malignancy of unknown primary with initial determination of histology, **or**
xix. Recurrent ovarian, fallopian tube or primary peritoneal cancer, **or**
xx. Recurrent or stage IV breast cancer**, and**
a) If a broad molecular profiling panel test via circulating tumor DNA is being performed simultaneously with solid tumor tissue testing, the member must have one of the following diagnoses:
(a) Lung adenocarcinoma, **or**
(b) Large cell lung carcinoma, **or**
(c) Squamous cell lung carcinoma, **or**
(d) Non-small cell lung cancer (NSCLC) not otherwise specified (NOS)

2. Broad molecular profiling panel tests via circulating tumor DNA (liquid biopsy) are considered **investigational** for all other indications, including being performed simultaneously with solid tumor tissue for tumor types other than those described above.

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Lung Cancer Focused Panel Tests via Circulating Tumor DNA (ctDNA)

1. Lung cancer focused panel tests via circulating tumor DNA (ctDNA) are considered **medically necessary** when:
A. The member has a diagnosis or progression of any of the following:
i. Advanced or metastatic lung adenocarcinoma, **or**
ii. Advanced or metastatic large cell lung carcinoma, **or**
iii. Advanced or metastatic squamous cell lung carcinoma, **or**
iv. Advanced or metastatic non-small cell lung cancer (NSCLC) not otherwise specified (NOS)**.**
2. Lung cancer focused panel tests via circulating tumor DNA (ctDNA) are considered **investigational** for all other indications.

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Single Gene Molecular Profiling Panel Tests via Circulating Tumor (ctDNA)

***EGFR* Variant Analysis via ctDNA**

1. *EGFR* variant analysis via circulating tumor DNA (ctDNA) is considered **medically necessary** when:
A. The member has a diagnosis of any of the following:
i. Advanced or metastatic lung adenocarcinoma, **or**
ii. Advanced or metastatic large cell lung carcinoma, **or**
iii. Advanced or metastatic squamous cell lung carcinoma, **or**
iv. Advanced or metastatic non-small cell lung cancer (NSCLC) not otherwise specified (NOS), **and**
B. Treatment with an *EGFR* tyrosine kinase inhibitor therapy (e.g., erlotinib [Tarceva], gefitinib [Iressa], afatinib [Gilotrif], or osimertinib [Tagrisso]) is being considered**.**
2. *EGFR* variant analysis via circulating tumor DNA (ctDNA), as a stand-alone test, is considered **investigational** for all other indications.

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***BRAF* Variant Analysis via ctDNA**

1. *BRAF* variant analysis via circulating tumor DNA (ctDNA) is considered **medically necessary** when:
A. The member meets one of the following:
i. The member has metastatic colorectal cancer, **and**
a) Testing for *NRAS* and *KRAS* is also being performed, either as separate tests or as part of a panel, **or**
ii. The member has stage III or higher cutaneous melanoma, **and**
a) Is being considered for adjuvant or other systemic therapy, **or**
iii. The member has locally advanced or metastatic pancreatic adenocarcinoma, **and**

a) Is being considered for anticancer therapy**.**

2. *BRAF* variant analysis via circulating tumor DNA (ctDNA) is considered **investigational** for all other indications.

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***KRAS* Variant Analysis via ctDNA**

1. *KRAS* variant analysis via circulating tumor DNA (ctDNA) is considered **medically necessary** when:
   - A. The member has metastatic colorectal cancer, **and**
     - i. Testing for *NRAS* and *BRAF* is also being performed, either as separate tests or as part of an NGS panel, **or**
   - B. The member has locally advanced or metastatic pancreatic adenocarcinoma, **and**
     - i. Is being considered for anticancer therapy**.**
2. *KRAS* variant analysis via circulating tumor DNA (ctDNA) is considered **investigational** for all other indications.

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***PIK3CA* Variant Analysis via ctDNA**

1. *PIK3CA* variant analysis via circulating tumor DNA (ctDNA) is considered **medically necessary** when:
   - A. The member has recurrent, unresectable, or stage IV hormone receptor-positive/HER2-negative breast cancer, **and**
   - B. The member is considering treatment with alpelisib plus fulvestrant, or capivasertib plus fulvestrant, **and**
   - C. The member has had progression on at least one line of therapy.
2. *PIK3CA* variant analysis via circulating tumor DNA (ctDNA) is considered **investigational** for all other indications.

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Circulating Tumor Cell Tests

***AR-V7* Circulating Tumor Cells (CTC) Analysis**

1. *AR-V7* circulating tumor cells (CTC) analysis is considered **medically necessary** when:
   - A. The member has a diagnosis of metastatic castration-resistant prostate cancer, **and**
   - B. Tissue-based testing is not feasible for the member, **and**
   - C. The test is ordered only once during the current cancer diagnosis, **and**
   - D. The member has at least one of the following:
     - i. Newly metastatic cancer, **or**
     - ii. Signs of clinical, radiological, or pathologic disease progression
2. *AR-V7* circulating tumor cells (CTC) analysis is considered **investigational** for all other indications.

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Circulating Tumor Cell (CTC) Enumeration

1. Circulating Tumor Cell (CTC) enumeration is considered **investigational**.

Definitions

Circulating tumor DNA (ctDNA): Fragmented, tumor-derived DNA circulating in the bloodstream that is not being carried in a cell. ctDNA derives either directly from the tumor or from circulating tumor cells.

Circulating Tumor Cells (CTCs): Intact cells that have shed into the bloodstream or lymphatic system from a primary tumor or a metastasis site and are carried around the body by blood circulation.

Products

This information is for most, but not all, HealthPartners plans. Please read your plan documents to see if your plan has limits or will not cover some items. If there is a difference between this general information and your plan documents, your plan documents will be used to determine your coverage. These coverage criteria do not apply to Medicare Products. For more information regarding Medicare coverage criteria or for a copy of a Medicare coverage policy, contact Member Services at 952-883-7272 or 1-877-778-8384.

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