

Emerging Tumor Markers for Diagnosis and Monitoring of Cancer



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Medical Coverage Policy

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Related Medical/Pharmacy Coverage Policies

abemaciclib (Verzenio)
[Comprehensive Molecular Profiling for Hematologic Malignancies and Solid Tumors](#)
[In Vitro Chemoresistance and Chemosensitivity Assays](#)
[Laboratory Analysis for Prostate Cancer](#)
[Liquid Biopsy](#)
[Molecular Markers in Fine Needle Aspirates of Thyroid Nodules](#)

Description

A tumor marker is a protein, antibody, antigen or hormone in the body that may indicate the presence of cancer. Generally, these markers are specific to certain types of cancer and can be detected in blood, body fluids (eg, cerebral spinal fluid [CSF]), stool, tissue and urine samples. The body may produce the marker in response to cancer or the tumor itself may produce the marker. The detection of tumor markers may be

used to determine a diagnosis or as an indicator of disease (cancer) progression. It can also be used to document clinical response to treatment.

Individual protein tumor markers include, but may not be limited to: alpha-fetoprotein (AFP), CA 15-3/CA 27.29, CA 19-9, CA 50, CA 72-4, CA 125, CA 549 and carcinoembryonic antigen (CEA). Protein tumor markers may be tested individually or used in combination with genetic or other molecular markers.

Bladder cancer-associated urine-based markers, such as proteins with increased cancer cell expression or chromosomal abnormalities in the urine, may be detected using a variety of laboratory methods to aid in the management of bladder cancer. The following markers/tests are currently available:

- Bladder tumor antigen (BTA) (eg, BTA stat and BTA TRAK)
- Nuclear matrix protein 22 (NMP22) (eg, NMP22 BladderChek and Matritech NMP22 Test)

Urine-based markers have a role in the detection of bladder cancer recurrence in an individual with a history of bladder cancer and are used adjunctively with urinary cytology. These tests have also been proposed for bladder cancer screening, diagnosis of bladder cancer in an individual who has symptoms of bladder cancer and for the evaluation of hematuria. **(Refer to Coverage Limitations section)**

Topoisomerase II alpha is a protein encoded by the *TOP2A* gene and is proposed as a predictive and prognostic marker for breast cancer. It is also proposed as an aid in predicting response to anthracycline therapy in breast cancer. **(Refer to Coverage Limitations section)**

Coverage Determination

Any state mandates for tumor markers for the diagnosis and monitoring of cancer take precedence over this medical coverage policy.

The General Criteria for Genetic Tests may be applied if specific criteria for a genetic test are not available on any medical coverage policy. For information regarding **genetic testing**, please refer to [Genetic Testing](#) Medical Coverage Policy.

Humana members may be eligible under the Plan for **tumor markers for the diagnosis and monitoring of cancer** when the following criteria are met:

Tumor Marker	Indication(s)/Criteria
Bladder tumor antigen (BTA) (eg, BTA <i>stat</i> and BTA TRAK) (86294) (Refer to Coverage Limitations section)	<ul style="list-style-type: none">• Bladder cancer – as an adjunct to urinary cytology (when urinary cytology results are equivocal) for monitoring bladder cancer recurrence in an individual previously diagnosed with bladder cancer

Tumor Marker	Indication(s)/Criteria
Ki-67 (Refer to Coverage Limitations section)	<ul style="list-style-type: none"> Breast cancer – when treatment with a cyclin-dependent kinase (CDK) 4 and 6 inhibitor (eg, abemaciclib [Verzenio]) is being considered.
Nuclear matrix protein 22 (NMP22) (eg, NMP22 BladderChek and Matritech NMP22 Test Kit) (86386) (Refer to Coverage Limitations section)	<ul style="list-style-type: none"> Bladder cancer – as an adjunct to urinary cytology (when urinary cytology results are equivocal) for monitoring bladder cancer recurrence in an individual previously diagnosed with bladder cancer
ZAP-70 (Refer to Coverage Limitations section)	<ul style="list-style-type: none"> Chronic lymphocytic leukemia/small lymphoblastic lymphoma ONLY as part of a clinical trial

Coverage Limitations

Humana members may **NOT** be eligible under the Plan for tumor markers for diagnosis and monitoring for any indications other than those listed above, including the following:

Tumor Marker	Noncovered Indication(s)
Bladder tumor antigen (BTA) (eg, BTA stat and BTA TRAK) (86294)	<ul style="list-style-type: none"> Bladder cancer detection in a symptomatic individual without prior history of bladder cancer; OR Bladder cancer screening in an asymptomatic individual with risk factors for bladder cancer; OR Evaluation of hematuria
CA 50 (86316)	Any indication including, but not limited to: <ul style="list-style-type: none"> Carcinoid tumors; OR Gastrointestinal cancer
CA 72-4 (86316)	Any indication including, but not limited to: <ul style="list-style-type: none"> Breast cancer; OR Colorectal cancer
CA 549 (86316)	Any indication including, but not limited to: <ul style="list-style-type: none"> Breast cancer; OR Carcinoid tumors
Des-gamma-carboxy prothrombin (DCP) (also known as protein induced by vitamin K absence-II or PIVKA-II) (83951)	Any indication including, but not limited to: <ul style="list-style-type: none"> Hepatocellular carcinoma (HCC)
Fibrin/fibrinogen degradation products (FDP) test (eg, DR-70 or Onko-Sure) (85362)	Any indication including, but not limited to: <ul style="list-style-type: none"> Colorectal cancer
Human epididymis protein 4 (HE4) (eg, Elecsys HE4 Assay) (86305)	Any indication including, but not limited to: <ul style="list-style-type: none"> Endometrial cancer; OR

Tumor Marker	Noncovered Indication(s)
	<ul style="list-style-type: none"> Evaluation of pelvic mass, including to assist in the determination of referral for surgery to a gynecologic oncologist or to a general surgeon; OR Ovarian cancer
Ki-67	All other indications not listed in the Coverage Determination section
Lectin-reactive alpha-fetoprotein (AFP-L3) (82107)	Any indication including, but not limited to: <ul style="list-style-type: none"> Liver cancer
Nuclear matrix protein 22 (NMP22) (eg, NMP22 BladderChek and Matritech NMP22 Test Kit) (86386)	<ul style="list-style-type: none"> Bladder cancer detection in a symptomatic individual without prior history of bladder cancer; OR Bladder cancer screening in an asymptomatic individual with risk factors for bladder cancer; OR Evaluation of hematuria
p53 protein by immunohistochemistry (IHC)	Any indication including, but not limited to: <ul style="list-style-type: none"> Breast cancer
Thymidine kinase activity (TKa) (0404U)	Any indication including, but not limited to: <ul style="list-style-type: none"> Breast cancer
Topoisomerase II (Topo II) protein expression by immunohistochemistry (IHC)	Any indication including, but not limited to: <ul style="list-style-type: none"> Breast cancer
ZAP-70	If not part of a clinical trial

These are considered experimental/investigational as they are not identified as widely used and generally accepted for the proposed uses as reported in nationally recognized peer-reviewed medical literature published in the English language.

Coding Information

Any codes listed on this policy are for informational purposes only. Do not rely on the accuracy and inclusion of specific codes. Inclusion of a code does not guarantee coverage and/or reimbursement for a service or procedure.

CPT® Code(s)	Description	Comments
81479	Unlisted molecular pathology procedure	Not Covered if used to report any test outlined in Coverage Limitations section
82107	Alpha-fetoprotein (AFP); AFP-L3 fraction isoform and total AFP (including ratio)	Not Covered
82308	Calcitonin	

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83951	Oncoprotein; des-gamma-carboxy-prothrombin (DCP)	Not Covered
84999	Unlisted chemistry procedure	Not Covered if used to report any test outlined in Coverage Limitations section
85362	Fibrin(ogen) degradation (split) products (FDP) (FSP); agglutination slide, semiquantitative	Not Covered if used to report any test outlined in Coverage Limitations section
86294	Immunoassay for tumor antigen, qualitative or semiquantitative (eg, bladder tumor antigen)	Not Covered if used to report any test outlined in Coverage Limitations section
86305	Human epididymis protein 4 (HE4)	Not Covered
86386	Nuclear Matrix Protein 22 (NMP22), qualitative	Not Covered if used to report any test outlined in Coverage Limitations section
88184	Flow cytometry, cell surface, cytoplasmic, or nuclear marker, technical component only; first marker	Not Covered if used to report any test outlined in Coverage Limitations section
88185	Flow cytometry, cell surface, cytoplasmic, or nuclear marker, technical component only; each additional marker (List separately in addition to code for first marker)	Not Covered if used to report any test outlined in Coverage Limitations section
88341	Immunohistochemistry or immunocytochemistry, per specimen; each additional single antibody stain procedure (List separately in addition to code for primary procedure)	Not Covered if used to report any test outlined in Coverage Limitations section
88342	Immunohistochemistry or immunocytochemistry, per specimen; initial single antibody stain procedure	Not Covered if used to report any test outlined in Coverage Limitations section
88360	Morphometric analysis, tumor immunohistochemistry (eg, Her-2/neu, estrogen receptor/progesterone receptor), quantitative or semiquantitative, per specimen, each single antibody stain procedure; manual	Not Covered if used to report any test outlined in Coverage Limitations section
0404U	Oncology (breast), semiquantitative measurement of thymidine kinase activity by immunoassay, serum, results reported as risk of disease progression	Not Covered New Code Effective 10/01/2023

CPT® Category III Code(s)	Description	Comments
No code(s) identified		
HCPCS Code(s)	Description	Comments
No code(s) identified		

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Change Summary

- 01/25/2024 Annual Review, No Coverage Change.