



**TUMOR MARKERS**

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**I. DESCRIPTION**

Tumor markers are molecules or substances that are produced by the tumor itself or by the body in response to the presence of a cancerous or non-cancerous condition. These markers can be detected and measured in serum. Single measurements of serum tumor markers may be used to facilitate the diagnosis and prognosis in patients with symptoms suggestive of malignancy while serial monitoring of tumor markers may be used as a tool to monitor response to therapy, detect recurrence or predict development of cancer as a screening test. This policy addresses serum tumor markers in regards to the detection and the management of cancerous conditions.

**II. POLICY/CRITERIA**

Serum tumor markers are considered medically necessary for a specific cancer type when proven to be clinically useful in the detection and management (as described above) of that specific cancer. The utilization of a specific tumor marker must be adopted into a clinical algorithm and endorsed by a professional cancer organization, i.e. NCCN, ASCO, NCI as part of routine care. Examples of this include the following:

1. Carcinoembryonic antigen (CEA) is considered medically necessary when used to detect asymptomatic recurrence of colorectal cancer after surgical and/or medical treatment for the diagnosis of colorectal cancer but is not considered medically necessary as a screening test for colorectal cancer.
2. Bladder tumor antigen (BTA) Stat test medically necessary in any of the following conditions:
  - A. Follow-up of treatment for bladder cancer; *or*
  - B. Monitoring for eradication of bladder cancer; *or*
  - C. Recurrences after eradication.

BTA Stat test is considered experimental and investigational for screening of bladder cancer and all other indications.



III. Refer to Appendix I below for a list of covered tumor markers and their associated cancers. For tumor markers not listed, please submit request for medical review and include documentation of clinical usefulness.

IV. MEDICAL NECESSITY REVIEW

Required  Not Required  Not Applicable

V. APPLICATION TO PRODUCTS

Coverage is subject to member’s specific benefits. Group specific policy will supersede this policy when applicable.

- ❖ HMO/EPO: *This policy applies to insured HMO/EPO plans.*
- ❖ POS: *This policy applies to insured POS plans.*
- ❖ PPO: *This policy applies to insured PPO plans.*
- ❖ ASO: *For self-funded plans, consult individual plan documents. If there is a conflict between this policy and a self-funded plan document, the provisions of the plan document will govern.*
- ❖ INDIVIDUAL: *For individual policies, consult the individual insurance policy. If there is a conflict between this medical policy and the individual insurance policy document, the provisions of the individual insurance policy will govern.*
- ❖ MEDICARE: *Coverage is determined by the Centers for Medicare and Medicaid Services (CMS).*
- ❖ MEDICAID: *If there is a discrepancy between this policy and the Michigan Medicaid Provider Manual and the Michigan Medicaid Fee Schedule, the Michigan Medicaid Provider Manual and the Michigan Medicaid Fee Schedule at: [http://www.michigan.gov/mdch/0,1607,7-132-2945\\_42542\\_42543\\_42546\\_42551-159815--00.html](http://www.michigan.gov/mdch/0,1607,7-132-2945_42542_42543_42546_42551-159815--00.html) will govern.*
- ❖ MICHILD: *For MICHILD members, this policy will apply unless MICHILD certificate of coverage limits or extends coverage.*

VI. CODING INFORMATION

ICD9 Diagnosis Codes:

See Criteria

CPT/HCPCS Codes:

Estrogen receptor (ER)	84233	Receptor assay; estrogen
Progesterone receptor (PR)	84234	Receptor assay; progesterone
HER2	83950	Oncoprotein; HER-2/neu
Oncotype Dx	88360	Morphometric analysis, tumor immunohistochemistry (eg, Her-2/neu, estrogen receptor/progesterone receptor), quantitative or



	88361	semiquantitative, each antibody; manual Morphometric analysis, tumor immunohistochemistry (eg, Her-2/neu, estrogen receptor/progesterone receptor), quantitative or semiquantitative, each antibody; using computer-assisted technology
	88367	Morphometric analysis, in situ hybridization (quantitative or semi-quantitative) each probe; using
	88368	Morphometric analysis, in situ hybridization (quantitative or semi-quantitative) each probe; manual
Carcinoembryonic antigen (CEA)	82378	Carcinoembryonic antigen (CEA)
CA 15-3 and CA 27-29	86300	Immunoassay for tumor antigen, quantitative; CA 15-3 (27.29)
Cancer antigen 125 (CA 125)	86304	Immunoassay for tumor antigen, quantitative; CA 125
CA19-9	86301	Immunoassay for tumor antigen, quantitative; CA 19-9
Human Chorionic Gonadotropin (HCG)	84702	Gonadotropin, chorionic (hCG); quantitative
	84703	Gonadotropin, chorionic (hCG); qualitative
	84704	Gonadotropin, chorionic (hCG); free beta chain
Alpha Fetoprotein (AFP)	82105	Alpha-fetoprotein (AFP); serum
	82107	Alpha-fetoprotein (AFP); AFP-L3 fraction isoform and total AFP (including ratio)
K-ras(KRAS)		See policy 91540 Genetics Counseling, Testing and Screening
Placental alkaline phosphatase (PLAP)	84080	Phosphatase, alkaline; isoenzymes
Myeloperoxidase (MPO) immunostaining	83876	Myeloperoxidase (MPO)



Bladder tumor antigen (BTA) Stat test; or nuclear matrix protein (NMP22) test; or fibrin/fibrinogen degradation products (Aura-Tek FDP) test; or the UroVysion fluorescent in situ hybridization (FISH) test	85362	Fibrin(ogen) degradation (split) products (FDP) (FSP); agglutination slide, semiquantitative
	85366	Fibrin(ogen) degradation (split) products (FDP) (FSP); paracoagulation
	85370	Fibrin(ogen) degradation (split) products (FDP) (FSP); quantitative
	85378	Fibrin degradation products, D-dimer; qualitative or semiquantitative
	85379	Fibrin degradation products, D-dimer; quantitative
	85380	Fibrin degradation products, D-dimer; ultrasensitive (eg, for evaluation for venous thromboembolism), qualitative or semiquantitative
	86294	Immunoassay for tumor antigen, qualitative or semiquantitative (eg, bladder tumor antigen)
	88365	In situ hybridization (eg, FISH), each probe
	88385	Array-based evaluation of multiple molecular probes; 51 through 250 probes

**VII. REFERENCES**

1. Hayes Online Technology Assessment Service:
  - a. Serum Carcinoembryonic Antigen (CEA) Assay for Diagnosis of Ovarian Cancer
  - b. Total Sialic Acid and Lipid-Associated Sialic Acid as Tumor Markers
  - c. Somatostatin Receptor Scintigraphy (SRS) for Localization of Neuroendocrine Tumors and their Metastases
  - d. Ancillary Bladder Tumor-Associated Antigen (BTA) Testing for Bladder Cancer Screening and Detection
  - e. Cancer Antigen 27.29 (CA 27.29) for Diagnosis, Staging, and Treatment Monitoring of Breast Cancer
  - f. Selected Ancillary Urine Tests for Bladder Cancer Screening and Detection
  - g. Cancer Antigen 15-3 (CA 15-3) for Breast Cancer Prognosis
  - h. PathFinderTG® Test (RedPath Integrated Pathology) for the Diagnosis of Pancreatic Cancer
  - i. In Vitro Chemosensitivity Assays in Cancer Treatment
  - j. Cancer Antigen (CA) 19-9 for Pancreatic Cancer Screening
  - k. Ancillary UroVysion™ Fluorescence In Situ Hybridization (FISH) Testing for Bladder Cancer Screening and Detection
  - l. Oncotype Dx™ (Genomic Health Inc.) Genetic Assay for Breast Cancer



- m. Cancer Antigen (CA) 19-9 for Prognosis of Pancreatic Cancer Resectability
  - n. Ancillary Nuclear Matrix Protein 22 (NMP22) Testing for Bladder Cancer Screening and Detection
  - o. Prostate-Specific Antigen Testing for Prognosis and Monitoring of Patients with Prostate Cancer
  - p. Autoantibody Testing for the Early Diagnosis of Breast Cancer
  - q. Ancillary ImmunoCyt/uCyt+ Testing for Bladder Cancer Screening and Detection
  - r. Ancillary Urinary Cytokeratin (CK) Tests for Bladder Cancer Screening and Detection
  - s. CA 125 for Ovarian Cancer Screening in Average-Risk Women
  - t. Prostate Cancer Antigen 3 (PCA3) Genetic Assay for the Diagnosis and Management of Prostate Cancer
2. Aetna online medical policy bulletin: Tumor Markers -  
[http://www.aetna.com/cpb/medical/data/300\\_399/0352.html](http://www.aetna.com/cpb/medical/data/300_399/0352.html)
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  4. American Society of Clinical Oncology 2007 Update of Recommendations for the Use of Tumor Markers in Breast Cancer. *Journal of Clinical Oncology*, Vol 25, No 33 (November 20), 2007: pp. 5287-5312 © 2007 American Society of Clinical Oncology.
  5. ASCO 2006 Update of Recommendations for the Use of Tumor Markers in Gastrointestinal Cancer. *Journal of Clinical Oncology*, Vol 24, No 33(November 20), 2006: pp.5513-5527© 2006 American Society of Clinical Oncology.
  6. NCCN Clinical Practice Guidelines in Oncology™
    - a. Bladder Cancer version 1.2009:  
[http://www.nccn.org/professionals/physician\\_gls/PDF/bladder.pdf](http://www.nccn.org/professionals/physician_gls/PDF/bladder.pdf)
    - b. Breast Cancer version 1.2009:  
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[http://www.nccn.org/professionals/physician\\_gls/PDF/gastric.pdf](http://www.nccn.org/professionals/physician_gls/PDF/gastric.pdf)
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- g. Pancreatic Cancer version 2.2009:  
[http://www.nccn.org/professionals/physician\\_gls/PDF/pancreatic.pdf](http://www.nccn.org/professionals/physician_gls/PDF/pancreatic.pdf)
- h. Prostate Cancer version 2.2009:  
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**APPENDIX I**

<b>Marker</b>	<b>Application</b>
<b>Estrogen receptor (ER)</b>	Invasive Breast Cancer including metastatic- help predict response to hormone therapy after surgery
<b>Progesterone receptor (PR)</b>	Invasive Breast Cancer including metastatic- help predict response to hormone therapy after surgery
<b>HER2</b>	Invasive Breast Cancer including metastatic and recurrent- help predict response to trastuzumab and other anti-HER2 treatments and some types of chemotherapy
<b>Oncotype Dx</b>	Invasive Breast cancer – stage I or II; and node negative; and ER/PR positive; and HER2 negative or HER2 positive BUT tumor <1cm
<b>CA 15-3 and CA 27-29</b>	Metastatic Breast Cancer and / or recurrent Breast cancer for treatment monitoring. to be used in conjunction with diagnostic imaging, history and physical exam.
<b>Carcinoembryonic antigen (CEA)</b>	<ol style="list-style-type: none"> <li>1. To detect asymptomatic recurrence of colorectal cancer after surgical and/or medical treatment for the diagnosis of colorectal cancer (not as a screening test for colorectal cancer); <i>or</i></li> <li>2. As a preoperative prognostic indicator in members with known colorectal carcinoma when it will assist in staging and surgical treatment planning; <i>or</i></li> <li>3. To monitor response to treatment for metastatic cancer.</li> </ol>
<b>Cancer antigen 125 (CA 125)</b>	<ol style="list-style-type: none"> <li>1. Diagnosis of ovarian cancer in women with new symptoms (bloating, pelvic or abdominal pain, difficulty eating or feeling full quickly, or urinary frequency and urgency) that have persisted for three or more weeks, where the clinician has performed a pelvic and rectal examination and suspects ovarian cancer; <i>or</i></li> <li>2. As a preoperative diagnostic aid in</li> </ol>



	<p>women with ovarian masses that are suspected to be malignant, such that arrangements can be made for intraoperative availability of a gynecological oncologist if the CA 125 is increased; <i>or</i></p> <ol style="list-style-type: none"> <li>3. In members with known ovarian cancer, as an aid in the monitoring of disease, response to treatment, detection of recurrent disease, or assessing value of performing second-look surgery; <i>or</i></li> <li>4. In members with adenocarcinoma of unknown primary, to rule out ovarian cancer.</li> <li>5. As a screening test for ovarian cancer when there is a history of hereditary cancer syndrome (a pattern of clusters of ovarian cancer within two or more generations).</li> </ol>
<b>CA19-9</b>	To monitor the clinical response to therapy or detect early recurrence of disease in members with known <b>gastric cancer, pancreatic cancer, cholangiocarcinoma or adenocarcinoma of the ampulla of Vater.</b>
<b>Human Chorionic Gonadotropin (HCG)</b>	To diagnose germ cell tumors in members with adenocarcinoma, or carcinoma not otherwise specified, involving mediastinal nodes, or to monitor treatment in members with known trophoblastic tumors (invasive hydatidiform moles and choriocarcinomas) and germinal cell tumors (teratocarcinoma and embryonal cell carcinoma) of the ovaries or testes, or to monitor for relapse after remission is achieved.
<b>Alpha Fetoprotein (AFP)</b>	To diagnose germ cell tumors in members with adenocarcinoma, or carcinoma not otherwise specified, involving mediastinal nodes; or the diagnosis and monitoring of hepatocellular carcinoma (e.g., before considering liver transplantation).
<b>K-ras(KRAS)</b>	Mutation analysis to predict non-response to cetuximab (Erbix) and panitumumab (Vectibix) in the treatment of metastatic colorectal cancer.
<b>Placental alkaline phosphatase (PLAP)</b>	To diagnose germ cell seminoma and non-seminoma germ cell tumors in unknown primary cancers
<b>Myeloperoxidase (MPO)</b>	diagnosis of acute myeloid leukemia



<b>immunostaining</b>	
<b>Bladder tumor antigen (BTA) Stat test; or nuclear matrix protein (NMP22) test; or fibrin/fibrinogen degradation products (Aura-Tek FDP) test; or the UroVysion fluorescent in situ hybridization (FISH) test</b>	<p>Medically necessary in any of the following conditions:</p> <ol style="list-style-type: none"> <li>1. Follow-up of treatment for bladder cancer; <i>or</i></li> <li>2. Monitoring for eradication of bladder cancer; <i>or</i></li> <li>3. Recurrences after eradication.</li> </ol>

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