CLINICAL MEDICAL POLICY	
Policy Name:	Tumor Markers
Policy Number:	MP-120-MD-PA
Responsible Department(s):	Medical Management
Provider Notice/Issue Date:	08/01/2023
Effective Date:	09/01/2023
Next Annual Review:	06/2024
Revision Date:	06/21/2023
Products:	Highmark Wholecare℠ Medicaid
Application:	All participating hospitals and providers
Page Number(s):	1 of 10

Policy History

Date	Action
09/01/2023	Provider Effective date
07/21/2023	PARP Approval
06/21/2023	QI/UM Committee review
06/21/2023	Policy initially developed

Disclaimer

Highmark Wholecare℠ medical policy is intended to serve only as a general reference resource regarding coverage for the services described. This policy does not constitute medical advice and is not intended to govern or otherwise influence medical decisions.

Policy Statement

Highmark Wholecare℠ may provide coverage under the medical-surgical benefits of the Company's Medicaid products for medically necessary tumor markers.

This policy is designed to address medical necessity guidelines that are appropriate for the majority of individuals with a particular disease, illness or condition. Each person's unique clinical circumstances warrant individual consideration, based upon review of applicable medical records.

(Current applicable Pennsylvania HealthChoices Agreement Section V. Program Requirements, B. Prior Authorization of Services, 1. General Prior Authorization Requirements.)

Definitions

Prior Authorization Review Panel (PARP) – A panel of representatives from within the PA Department of Human Services who have been assigned organizational responsibility for the review, approval and denial of all PH-MCO Prior Authorization policies and procedures.

Tumor markers - substances normally produced in low quantities by cells in the body. Detection of a higher-than-normal serum level by radioimmunoassay or immunohistochemical techniques usually indicates the presence of a certain type of cancer. Currently, the main use of tumor markers is to assess a cancer's response to treatment and to check for recurrence. In some types of cancer, tumor marker levels may reflect the extent or stage of the disease and can be useful in predicting how well the disease will respond to treatment.

Procedures

1. Tumor markers may be considered medically necessary for the following tests:
    A. **Alpha-fetoprotein (AFP) serum** (CPT code 82105 or 84702) may be considered medically necessary for EITHER of the following:
        1) Serial measurements of AFP to diagnose germ cell tumors in individuals with adenocarcinoma, or carcinoma not otherwise specified, involving mediastinal nodes; or the diagnosis and monitoring of hepatocellular carcinoma, OR
        2) Serial AFP measurements are indicated for members at high-risk group (overgrowth syndromes) germ tumors such as heptoblastoma.
    B. **CA 19-9** (CPT code 86301) may be considered medically necessary when reported for monitoring response to treatment in individuals with an established diagnosis of pancreatic and biliary ductal carcinoma.
    C. **CA 27.29** or **CA 15-3** (CPT code 86300) may be considered medically necessary when reported for use in the management of individuals with breast cancer.
    D. **CA 125** (CPT code 86304) may be considered medically necessary when reported for individuals with symptoms suggestive of ovarian cancer or in those with known ovarian cancer. It may be considered medically necessary for individuals with carcinomas of the fallopian tube, endometrium, and endocervix and may be associated with the presence of a malignant mesothelioma, as well as primary peritoneal carcinoma and metastatic adenoma cancer of unknown origin in the peritoneum.
    E. **Calcitonin (CT)** (CPT code 82308) is a tumor marker essential for the diagnosis and follow-up of medullary thyroid cancer. Calcitonin serum test may be considered medically necessary for the diagnosis and management of medullary thyroid cancer.
    F. **Carcinoembryonic Antigen (CEA)** (CPT code 82378) may be considered medically necessary for ANY of the following:
        1) As a preoperative prognostic indicator with known colorectal carcinoma or mucinous appendiceal carcinoma when it will assist in staging and surgical treatment planning; OR
        2) 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); OR
        3) To monitor response to treatment for metastatic cancer.
    G. **Chromogranin A (CgA)** (CPT code 86316) may be considered medically necessary only in the evaluation of suspected or known neuroendocrine tumors, including carcinoid,

neuroblastoma and in the assessment of disease progression and treatment efficacy for these conditions. Immunoassay for tumor antigen, other antigen, quantitative (e.g., CA 50, 72-4, 549) represents immunoassays for tumor antigens other than CgA that are not designated with a specific procedure code.

2. Any requests for tumor markers approval that does not meet the guidelines listed above will require a review by a Medical Director on a case-by-case basis.

3. Contraindications
    - CA 19-9 is not indicated for diagnosing or screening technique.
    - CA 27.29 or CA 15-3 is not indicated for diagnosing or screening technique.
    - CA 125 is not indicated for diagnosing or screening technique.

4. When comprehensive tumor sequencing services are not considered medically necessary:
    - Comprehensive tumor sequencing not meeting the criteria as indicated in this policy is considered not medically necessary.
    - Immunoassay for tumor antigen, other antigen, quantitative, (e.g., CA 50, 72-4, 549) represents immunoassays for tumor antigens other than CgA not meeting the criteria as indicated in this policy is considered not medically necessary.
    - Human Epididymis Protein 4 (HE4) enzyme immunometric assay (EIA) (CPT code 86305) for the quantitative determination of HE4 in human serum is considered experimental/investigational and therefore, not medically necessary because the safety and/or effectiveness of this service cannot be established by the available published peer-reviewed literature.
    - Early cancer detection test (CDT)-Lung (CPT code 84999) for detection of lung cancer is considered experimental/investigational and therefore, not medically necessary because the safety and/or effectiveness of this service cannot be established by the available published peer-reviewed literature.

5. Post-payment Audit Statement
   The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by Highmark Wholecare℠ at any time pursuant to the terms of your provider agreement.

6. Place of Service
   Comprehensive tumor sequencing is typically an outpatient procedure, which is only eligible for coverage as an inpatient procedure in special circumstances, including, but not limited to, the presence of a co-morbid condition that would require monitoring in a more controlled environment such as the inpatient setting.

7. Genetic Counseling

Pre- and post-test genetic counseling is required to be performed by an independent genetic provider (not employed by a genetic testing lab) prior to genetic testing for mutations. This service is necessary in order to inform the patient being tested about the benefits and limitations of specific genetic tests. Genetic testing for mutations requires documentation of medical necessity from at least one of the following providers who has previously evaluated the patient, and intends to see the patient after genetic testing has been performed:

- Board Eligible or Board Certified Genetic Counselor
- Advanced Genetics Nurse
- Genetic Clinical Nurse
- Advanced Practice Nurse in Genetics
- Board Eligible or Board Certified Clinical Geneticist
- A physician of appropriate expertise or other obstetrical provider specializing in the care for the indication(s) for genetic testing

8. Related Policies
    - MP-017-MD-PA BCR-ABL1 Testing in Chronic Myelogenous Leukemia and Acute Lymphoblastic Leukemia
    - MP-062-MD-PA BRAF Mutation Analysis
    - MP-005-MD-PA Gene Expression Testing for Cancer Treatment (Breast, Colon, Prostate)
    - MP-065-MD-PA Molecular Markers for Fine Needle Aspirates of Thyroid Nodules
    - MP-061-MD-PA Molecular Tumor Markers for Non-Small Cell Lung Cancer (NSCLC)
    - MP-074-MD-PA Oncologic Genetic Testing Panels
    - MP-100-MD-PA Gene Expression and Biomarker Prostate Cancer Testing

Governing Bodies Approval

CLIA
Tumor marker tests are offered as laboratory-developed tests under Clinical Laboratory Improvement Amendments (CLIA) licensed laboratories. Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratories offering such tests as a clinical service must meet general regulatory standards of CLIA and must be licensed by CLIA for high complexity testing.

CMS
The Centers for Medicare and Medicaid Services (CMS) has published the following guidance:

- National Coverage Determination (NCD) Tumor Antigen by Immunoassay – CA 125 (190.28)
- National Coverage Determination (NCD) Tumor Antigen by Immunoassay - CA 15-3/CA 27.29 (190.29)
- National Coverage Determination (NCD) Tumor Antigen by Immunoassay - CA 19-9 (190.30)

Summary of Literature

A tumor marker is anything present in or produced by cancer cells or other cells of the body in response to cancer or certain benign (noncancerous) conditions that provides information about a cancer, such as how aggressive it is, what kind of treatment it may respond to, or whether it is responding to treatment. Tumor markers have traditionally been proteins or other substances that are made at higher amounts by cancer cells than normal cells. These can be found in the blood, urine, stool, tumors, or other tissues or bodily fluids of some patients with cancer. Increasingly, however, genomic markers (such as tumor gene mutations, patterns of tumor gene expression, and nongenetic changes in tumor DNA) that are found in tumors themselves and in tumor fragments shed into bodily fluids are being used. Many different tumor

markers have been characterized and are in clinical use. Some are associated with only one type of cancer, whereas others are associated with multiple different cancer types (NCI, 2021).

Listed below are tumor markers that are in common use, mainly to determine treatment or to help make a diagnosis of cancer. New tumor markers frequently become available and may not be reflected on this list.

Name	Cancer Types	What's Analyzed	How Used
Alpha-fetoprotein (AFP)	Liver cancer and germ cell tumors	Blood	To help diagnose liver cancer and follow response to treatment; to assess stage, prognosis, and response to treatment of germ cell tumors
CA 19-9	Pancreatic, gallbladder, bile duct, and gastric cancers	Blood	To assess whether treatment is working
CA 27.29	Breast cancer	Blood	To detect metastasis or recurrence
CA 15-3	Breast cancer	Blood	To assess whether treatment is working or if the cancer has recurred
CA-125	Ovarian cancer	Blood	To help in diagnosis, assessment of response to treatment, and evaluation of recurrence
Calcitonin (CT)	Medullary thyroid cancer	Blood	To aid in diagnosis, check whether treatment is working, and assess recurrence
Carcinoembryonic antigen (CEA)	Colorectal cancer and some other cancers	Blood	To keep track of how well cancer treatments are working and check if cancer has come back or spread
Chromogranin A (CgA)	Neuroendocrine tumors	Blood	To help in diagnosis, assessment of treatment response, and evaluation of recurrence

(NCI, 2021)

Coding Requirements

Procedure Codes

CPT Code	Description
82105	Alpha-fetoprotein (AFP); serum
84702	Gonadotropin, chorionic (hCG); quantitative
86301	Immunoassay for tumor antigen, quantitative; CA 19-9
86300	Immunoassay for tumor antigen, quantitative; CA 15-3 (27.29)
86304	Immunoassay for tumor antigen, quantitative; CA 125
82308	Heterophile antibodies; screening
82378	Carcinoembryonic antigen (CEA)
86316	Immunoassay for tumor antigen, other antigen, quantitative (eg, CA 50, 72-4, 549), each
86305	Human epididymis protein 4 (HE4)

Non-covered Procedure Codes

T*his procedure code will not be reimbursed without Medical Director approval.*

CPT Code	Description
84999	Unlisted chemistry procedure
86305	Human epididymis protein 4 (HE4)

Diagnosis Codes

Diagnosis Codes for Procedure Codes **82105** and **84702:**

ICD-10 Code	Description
C22.0	Liver cell carcinoma
C22.1	Intrahepatic bile duct carcinoma
C22.2	Hepatoblastoma
C22.3	Angiosarcoma of liver
C22.4	Other sarcomas of liver
C22.7	Other specified carcinomas of liver
C22.8	Malignant neoplasm of liver, primary, unspecified as to type
C22.9	Malignant neoplasm of liver, not specified as primary or secondary
C62.01	Malignant neoplasm of undescended right testis
C62.02	Malignant neoplasm of undescended left testis
C62.11	Malignant neoplasm of descended right testis
C62.12	Malignant neoplasm of descended left testis
C62.91	Malignant neoplasm of right testis, unspecified whether descended or undescended
C62.92	Malignant neoplasm of left testis, unspecified whether descended or undescended
C77.1	Secondary and unspecified malignant neoplasm of intrathoracic lymph nodes
D07.60	Carcinoma in situ of unspecified male genital organs
D07.61	Carcinoma in situ of scrotum
D07.69	Carcinoma in situ of other male genital organs
E71.440	Ruvalcaba-Myhre-Smith syndrome

Q87.3	Congenital malformation syndromes involving early overgrowth
Q87.89	Other specified congenital malformation syndromes, not elsewhere classified
Z12.71	Encounter for screening for malignant neoplasm of testis
Z85.47	Personal history of malignant neoplasm of testis

Diagnosis Codes for Procedure Code **86301:**

ICD-10 Code	Description
C22.1	Intrahepatic bile duct carcinoma
C24.0	Malignant neoplasm of extrahepatic bile duct
C24.1	Malignant neoplasm of ampulla of Vater
C24.8	Malignant neoplasm of overlapping sites of biliary tract
C24.9	Malignant neoplasm of biliary tract, unspecified
C25.0	Malignant neoplasm of head of pancreas
C25.1	Malignant neoplasm of body of pancreas
C25.2	Malignant neoplasm of tail of pancreas
C25.3	Malignant neoplasm of pancreatic duct
C25.4	Malignant neoplasm of endocrine pancreas
C25.7	Malignant neoplasm of other parts of pancreas
C25.8	Malignant neoplasm of overlapping sites of pancreas
C25.9	Malignant neoplasm of pancreas, unspecified

Diagnosis Codes for Procedure Code **86300:**

ICD-10 Code	Description
C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.012	Malignant neoplasm of nipple and areola, left female breast
C50.021	Malignant neoplasm of nipple and areola, right male breast
C50.022	Malignant neoplasm of nipple and areola, left male breast
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
C50.221	Malignant neoplasm of upper-inner quadrant of right male breast
C50.222	Malignant neoplasm of upper-inner quadrant of left male breast
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast
C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of left female breast

C50.521	Malignant neoplasm of lower-outer quadrant of right male breast
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast
D05.00	Lobular carcinoma in situ of unspecified breast
D05.01	Lobular carcinoma in situ of right breast
D05.02	Lobular carcinoma in situ of left breast
D05.11	Intraductal carcinoma in situ of right breast
D05.12	Intraductal carcinoma in situ of left breast
D05.81	Other specified type of carcinoma in situ of right breast
D05.82	Other specified type of carcinoma in situ of left breast
D05.91	Unspecified type of carcinoma in situ of right breast
D05.92	Unspecified type of carcinoma in situ of left breast
Z85.3	Personal history of malignant neoplasm of breast

Diagnosis Codes for Procedure Code **86304:**

ICD-10 Code	Description
C45.0	Mesothelioma of pleura
C45.1	Mesothelioma of peritoneum
C45.2	Mesothelioma of pericardium
C45.7	Mesothelioma of other sites
C45.9	Mesothelioma, unspecified
C48.0	Malignant neoplasm of retroperitoneum
C48.1	Malignant neoplasm of specified parts of peritoneum
C48.2	Malignant neoplasm of peritoneum, unspecified
C48.8	Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C51.8	Malignant neoplasm of overlapping sites of vulva
C53.0	Malignant neoplasm of endocervix
C54.1	Malignant neoplasm of endometrium
C54.2	Malignant neoplasm of myometrium
C54.3	Malignant neoplasm of fundus uteri
C54.9	Malignant neoplasm of corpus uteri, unspecified
C56.1	Malignant neoplasm of right ovary
C56.2	Malignant neoplasm of left ovary
C56.3	Malignant neoplasm of bilateral ovaries
C57.01	Malignant neoplasm of right fallopian tube
C57.02	Malignant neoplasm of left fallopian tube

C57.4	Malignant neoplasm of uterine adnexa, unspecified
C57.7	Malignant neoplasm of other specified female genital organs
C57.8	Malignant neoplasm of overlapping sites of female genital organs
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C79.61	Secondary malignant neoplasm of right ovary
C79.62	Secondary malignant neoplasm of left ovary
C79.63	Secondary malignant neoplasm of bilateral ovaries
C79.82	Secondary malignant neoplasm of genital organs
D07.30	Carcinoma in situ of unspecified female genital organs
D07.39	Carcinoma in situ of other female genital organs
D39.0	Neoplasm of uncertain behavior of uterus
D39.11	Neoplasm of uncertain behavior of right ovary
D39.12	Neoplasm of uncertain behavior of left ovary
D39.2	Neoplasm of uncertain behavior of placenta
D39.8	Neoplasm of uncertain behavior of other specified female genital organs
D39.9	Neoplasm of uncertain behavior of female genital organ, unspecified
Z85.42	Personal history of malignant neoplasm of other parts of uterus
Z85.43	Personal history of malignant neoplasm of ovary

Diagnosis Codes for Procedure Codes **82308:**

ICD-10 Code	Description
C73	Malignant neoplasm of thyroid gland
C76.0	Malignant neoplasm of head, face and neck
Z85.850	Personal history of malignant neoplasm of thyroid

Diagnosis Codes for Procedure Code **82378:**

ICD-10 Code	Description
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of colon
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
D01.0	Carcinoma in situ of colon
D01.1	Carcinoma in situ of rectosigmoid junction
D01.2	Carcinoma in situ of rectum
D01.3	Carcinoma in situ of anus and anal canal
D01.40	Carcinoma in situ of unspecified part of intestine
D01.49	Carcinoma in situ of other parts of intestine
D01.5	Carcinoma in situ of liver, gallbladder and bile ducts
R97.0	Elevated carcinoembryonic antigen [CEA]

Z85.030	Personal history of malignant carcinoid tumor of large intestine
Z85.038	Personal history of other malignant neoplasm of large intestine
Z85.040	Personal history of malignant carcinoid tumor of rectum

Diagnosis Codes for Procedure Code **86316:**

ICD-10 Code	Description
C7A.1	Malignant poorly differentiated neuroendocrine tumors
C7A.8	Other malignant neuroendocrine tumors
C7B.8	Other secondary neuroendocrine tumors
C7B.01	Secondary carcinoid tumors of distant lymph nodes
C7B.02	Secondary carcinoid tumors of liver
C7B.03	Secondary carcinoid tumors of bone
C7B.04	Secondary carcinoid tumors of peritoneum
C7B.09	Secondary carcinoid tumors of other sites
D3A.8	Other benign neuroendocrine tumors
D3A.00	Benign carcinoid tumor of unspecified site
E34.0	Carcinoid syndrome

Reimbursement

Participating facilities will be reimbursed per their Highmark Wholecare℠ contract.

Reference Sources

Centers for Medicare and Medicaid Services (CMS). National Coverage Determination (NCD) Tumor Antigen by Immunoassay - CA 125 (190.28). Effective date January 1, 2016. Implementation date January 1, 2006. Accessed on May 24, 2023.

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