PriorityHealth

MEDICAL POLICY
No. 91562-R5

TUMOR MARKERS

Effective Date: April 15, 2016	**Review Dates: 8/09, 8/10, 8/11, 2/12, 2/13, 2/14, 2/15, 2/16, 2/17**
Date Of Origin: August 12, 2009	**Status: Current**

I. 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 in Section IV) 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.

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.

Refer to Appendix II for a list of non-covered tumor markers. This list is NOT all-inclusive and any tumor marker not listed is still subject to the main policy criteria listed above.

II. MEDICAL NECESSITY REVIEW

☒ All tests performed at non-participating laboratories will require prior authorization.

III. 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. Consult individual plan documents as state mandated benefits may apply. If there is a conflict between this policy and a plan document, the provisions of the plan document will govern.***
- **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); if a coverage determination has not been adopted by CMS, this policy applies.***
- **MEDICAID/HEALTHY MICHIGAN PLAN:** ***For Medicaid/Healthy Michigan Plan members, this policy will apply. Coverage is based on medical necessity criteria being met and the appropriate code(s) from the coding section of this policy being included on the Michigan Medicaid Fee Schedule located at: http://www.michigan.gov/mdch/0,1607,7-132-2945_42542_42543_42546_42551-159815--,00.html. If there is a discrepancy between this policy and the Michigan Medicaid Provider Manual located at: http://www.michigan.gov/mdch/0,1607,7-132-2945_5100-87572--,00.html, the Michigan Medicaid Provider Manual will govern. For Medical Supplies/DME/Prosthetics and Orthotics, please refer to the Michigan Medicaid Fee Schedule to verify coverage.***

IV. 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.

V. CODING INFORMATION

ICD-10 Diagnosis Codes:
See Criteria

See also policies: *91540 Genetics Counseling, Testing and Screening*
91570 Pharmacogenomic Testing
91609 Multi-Marker Tumor Panels
91566 Chemosensitivity Assays
91583 Markers for Digestive Disorders

Unlisted Codes (*explanatory notes must accompany claim*)
81479 Unlisted molecular pathology procedure
81599 Unlisted multianalyte assay with algorithmic analysis
84999 Unlisted chemistry procedure
88299 Unlisted cytogenetic study

**PA required for In or Out of Network lab*

APPENDIX I
COVERED TESTS/MARKERS
Last Update: 2/2017

TEST/MARKER	CODE	DESCRIPTION/NOTES	APPLICATION
Afirma thyroid FNA analysis	81545	Oncology (thyroid), gene expression analysis of 142 genes, utilizing fine needle aspirate, algorithm reported as a categorical result (eg, benign or suspicious) (*Not covered for Medicaid)*	Cytologically indeterminate thyroid nodule
Alpha Fetoprotein (AFP)	82105 82107	Alpha-fetoprotein (AFP); serum Alpha-fetoprotein (AFP); AFP-L3 fraction isoform and total AFP (including ratio)	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).
Anaplastic lymphoma kinase (ALK) fusion gene	81401	Molecular pathology procedure, Level 2 (eg, 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat)	• ALK gene fusion as a molecular biomarker in non-small cell lung cancer • ALK translocations for selecting candidates for crizotinib (Xalkori) in inflammatory myofibroblastic tumor
BCR/ABL	81206 81207 81208	BCR/ABL1 (t(9;22)) (eg, chronic myelogenous leukemia) translocation analysis; major breakpoint, qualitative or quantitative BCR/ABL1 (t(9;22)) (eg, chronic myelogenous leukemia) translocation analysis; minor breakpoint, qualitative or quantitative BCR/ABL1 (t(9;22)) (eg, chronic myelogenous leukemia) translocation analysis; other breakpoint, qualitative or quantitative	BCR/ABL fluorescent in situ hybridization (FISH) for lymphoblastic lymphoma, acute myeloid leukemia, acute lymphocytic leukemia and chronic myelogenous leukemia; experimental for other indications.
Bladder tumor antigen (BTA) Stat test; or nuclear matrix protein (NMP22) test; or fibrin/fibrinogen degradation		The following procedure codes are covered **only** for the dx codes listed. **ICD-10 Codes** covered: C67.0 – C67.9 Malignant neoplasm of	Medically necessary in any of the following conditions: 1. Follow-up of treatment for bladder

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products (Aura-Tek FDP) test,; or the UroVysion fluorescent in situ hybridization (FISH) test		the bladder D09.0 Carcinoma in situ of bladder D49.4 Neoplasm of unspecified behavior of bladder Z85.51Personal history of malignant neoplasm of bladder	cancer; *or* 2. Monitoring for eradication of bladder cancer; *or* 3. Recurrences after eradication.
UroVision	88120 88121	Cytopathology, in situ hybridization (eg, FISH), urinary tract specimen with morphometric analysis, 3-5 molecular probes, each specimen; manual Cytopathology, in situ hybridization (eg, FISH), urinary tract specimen with morphometric analysis, 3-5 molecular probes, each specimen; using computer-assisted technology	Experimental and investigational in the diagnosis of bladder cancer or for screening for bladder cancer in asymptomatic persons.
BTA Stat	86294	Immunoassay for tumor antigen, qualitative or semiquantitative (eg, bladder tumor antigen)	
NMP22	86386	Nuclear Matrix Protein 22 (NMP22), qualitative	
BRAF V600	81210	BRAF RAF proto oncognene, serine/threonine kinase (e.g., colon cancer, melanoma), gene analysis, V600 variant(s)	BRAF V600 mutation for hairy cell leukemia; gastrointestinal stromal tumors; melanoma for vemurafenib, dabrafenib, and trametinib; and colorectal cancer if KRAS nonmutated; experimental for other indications
B2M (beta2-microglobulin)	82232	Beta-2 microglobulin	Multiple myeloma
CA 15-3 and CA 27-29	86300	Immunoassay for tumor antigen, quantitative; CA 15-3 (27.29)	Metastatic Breast Cancer and / or recurrent Breast cancer for treatment monitoring. to be used in conjunction with diagnostic imaging, history and physical exam.
CA19-9	86301	Immunoassay for tumor antigen, quantitative; CA 19-9	To monitor the clinical response to therapy or detect early recurrence of disease in members with known gastric cancer, pancreatic cancer, cholangiocarcinoma or adenocarcinoma of the ampulla of Vater; to rule out cholangiocarcinoma in persons with primary sclerosing cholangitis undergoing liver transplantation; as a tumor marker for mucinous

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TEST/MARKER	**CODE**	**DESCRIPTION/NOTES**	**APPLICATION**
			appendiceal carcinoma
Cancer antigen 125 (CA 125)	86304	Immunoassay for tumor antigen, quantitative; CA 125	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; or 2. As a preoperative diagnostic aid in 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; or 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; or 4. In members with adenocarcinoma of unknown primary, to rule out ovarian cancer. 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).
Carcinoembryonic antigen (CEA)	82378	Carcinoembryonic antigen (CEA)	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); *or* 2. As a preoperative prognostic indicator in members with known colorectal carcinoma when it will assist in staging and surgical

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TEST/MARKER	**CODE**	**DESCRIPTION/NOTES**	**APPLICATION**
			treatment planning; *or* 3. To monitor response to treatment for metastatic cancer.
CD20	86356 88342	Mononuclear cell antigen, quantitative (eg, flow cytometry), not otherwise specified, each antigen Immunohistochemistry or immunocytochemistry, each separately identifiable antibody per block, cytologic preparation, or hematologic smear; first separately identifiable antibody per slide	CD20, for determining eligibility for anti-CD20 treatment (rituximab)
CD25	86356 88342	Mononuclear cell antigen, quantitative (eg, flow cytometry), not otherwise specified, each antigen Immunohistochemistry or immunocytochemistry, each separately identifiable antibody per block, cytologic preparation, or hematologic smear; first separately identifiable antibody per slide	CD25, for determining eligibility for denileukin diftitox (Ontak) treatment
CD31	88342	Immunohistochemistry or immunocytochemistry, each separately identifiable antibody per block, cytologic preparation, or hematologic smear; first separately identifiable antibody per slide	CD31 immunostaining, for diagnosis of angiosarcoma.
CD33	86356 88342	Mononuclear cell antigen, quantitative (eg, flow cytometry), not otherwise specified, each antigen Immunohistochemistry or immunocytochemistry, each separately identifiable antibody per block, cytologic preparation, or hematologic smear; first separately identifiable antibody per slide	CD33, for determining eligibility for anti-CD33 (gemtuzumab, Mylotarg) treatment
CD52	86356 88342	Mononuclear cell antigen, quantitative (eg, flow cytometry), not otherwise specified, each antigen Immunohistochemistry or immunocytochemistry, each separately identifiable antibody per block, cytologic preparation, or hematologic	CD52, for determining eligibility for anti-CD52 (alemtuzumab, Campath) treatment

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		smear; first separately identifiable antibody per slide	
CD117	88342	Immunohistochemistry or immunocytochemistry, each separately identifiable antibody per block, cytologic preparation, or hematologic smear; first separately identifiable antibody per slide	CD117 (c-kit), for determining eligibility for treatment with imatinib mesylate (Gleevec).
ConfirmMDx		*See* Unlisted Codes	PSA-positive patients with negative biopsies for prostate cancer
Cyclin D1	88342	Immunohistochemistry or immunocytochemistry, each separately identifiable antibody per block, cytologic preparation, or hematologic smear; first separately identifiable antibody per slide	Cyclin D1, for diagnosis and predicting disease recurrence of mantle cell lymphoma
CgA (chromogranin A)	86316	Immunoassay for tumor antigen, other antigen, quantitative (eg, CA 50, 72-4, 549), each	Neuroendocrine tumors
Epidermal growth factor receptor (EGFR)	81235	EGFR (epidermal growth factor receptor) (eg, non-small cell lung cancer) gene analysis, common variants (eg, exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q)	For tyrosine kinase inhibitors (erlotinib (Tarceva), gefitinib (Iressa), afatinib (Gilotrif)) in non-small cell lung cancer
Estrogen receptor (ER)	84233	Receptor assay; estrogen	Invasive Breast Cancer including metastatic- help predict response to hormone therapy after surgery
Progesterone receptor (PR)	84234	Receptor assay; progesterone	
HER2	83950 88360 88361	Oncoprotein; HER-2/neu Morphometric analysis, tumor immunohistochemistry (eg, Her-2/neu, estrogen receptor/progesterone receptor), quantitative or 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	Invasive Breast Cancer including metastatic and recurrent- help predict response to trastuzumab and other anti-HER2 treatments and some types of chemotherapy

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Human Chorionic Gonadotropin (HCG)	84702	Gonadotropin, chorionic (hCG); quantitative	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.
IGH@	81261 81262 81263	IGH@ (Immunoglobulin heavy chain locus) (eg, leukemias and lymphomas, B-cell), gene rearrangement analysis to detect abnormal clonal population(s); amplified methodology (eg, polymerase chain reaction) IGH@ (Immunoglobulin heavy chain locus) (eg, leukemias and lymphomas, B-cell), gene rearrangement analysis to detect abnormal clonal population(s); direct probe methodology (eg, Southern blot) GH@ (Immunoglobulin heavy chain locus) (eg, leukemia and lymphoma, B-cell), variable region somatic mutation analysis	IGH@ (Immunoglobulin heavy chain locus), gene rearrangement analysis to detect abnormal clonal population(s) in non-Hodgkin's lymphomas, hairy cell leukemia, and post-transplant lymphoproliferative disorder.
IGK@	81264	IGK@ (Immunoglobulin kappa light chain locus) (eg, leukemia and lymphoma, B-cell), gene rearrangement analysis, evaluation to detect abnormal clonal population(s)	IGK@ (Immunoglobulin kappa light chain locus), gene rearrangement analysis, evaluation to detect abnormal clonal population(s) for non-Hodgkin's lymphoma, systemic light chain amyloidosis
IDH	81403	Molecular pathology procedure, Level 4 (eg, analysis of single exon by DNA sequence analysis, analysis of > 10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons)	IDH mutation for glioma
Janus Kinase 2 (JAK2)	81270	JAK2 (Janus kinase 2) (eg, myeloproliferative disorder) gene analysis, p.Val617Phe (V617F) variant	Testing for JAK2 mutations in persons with chronic myeloproliferative disorders

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	81403	Molecular pathology procedure, Level 4 (eg, analysis of single exon by DNA sequence analysis, analysis of > 10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons)	(CMPDs) is considered medically necessary for the following indications: 1) qualitative assessment of JAK2-V617F sequence variant using methods with detection thresholds of up to 5% for initial diagnostic assessment of adult patients presenting with symptoms of CMPD; 2) diagnostic assessment of polycythemia vera in adults; and 3) differential diagnosis of essential thrombocytosis and primary myelofibrosis from reactive conditions in adults
K-ras (KRAS)	81275 81276 81405	KRAS (v-Ki-ras2 Kirsten rat sarcoma viral oncogene) (eg, carcinoma) gene analysis, variants in codons 12 and 13 KRAS (Kirsten rat sarcoma viral oncogene homolog) (eg, carcinoma) gene analysis additional variant(s) (eg, codon 61, codon 146) PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons)Molecular pathology procedure, Level 6 (eg, analysis of 6-10 exons by DNA sequence analysis, mutation	1. Mutation analysis to predict non-response to cetuximab (Erbitux) and panitumumab (Vectibix) in the treatment of metastatic colorectal cancer 2. To predict non-response to erlotinib (Tarceva) in the treatment of non-small cell lung cancer
Mammaprint		*See* Unlisted Codes	Invasive Breast cancer – stage I or II; and node negative; and ER/PR positive; and HER2 negative or HER2 positive BUT tumor <1cm
Myeloperoxidase (MPO) immunostaining /NPM1/FLT3_ITD/CEBPA	83876 81310 81245 81246	Myeloperoxidase (MPO) NPM1 (nucleophosmin) (eg, acute myeloid leukemia) gene analysis, exon 12 variants FLT3 (fms-related tyrosine kinase 3) (eg, acute myeloid leukemia), gene analysis, internal tandem duplication (ITD) variants (ie, exons 14, 15) FLT3 (fms-related tyrosine kinase 3) (eg, acute myeloid leukemia), gene analysis; tyrosine kinase domain (TKD) variants (eg, D835, I836)	Diagnosis of acute myeloid leukemia

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Oncotype Dx	81519	Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 21 genes, utilizing formalin-fixed paraffin embedded tissue, algorithm reported as recurrence score	Invasive Breast cancer – stage I or II; and node negative; and ER/PR positive; and HER2 negative or HER2 positive BUT tumor <1cm
OVA 1	81503	Oncology (ovarian), biochemical assays of five proteins (CA-125, apolipoprotein A1, beta-2 microglobulin, transferrin, and pre-albumin), utilizing serum, algorithm reported as a risk score	Ovarian Cancer
Placental alkaline phosphatase (PLAP)	88342	Immunohistochemistry (including tissue immunoperoxidase), each antibody	To diagnose germ cell seminoma and non-seminoma germ cell tumors in unknown primary cancers
VeriStrat	91538	Oncology (lung), mass spectrometric 8-protein signature, including amyloid A, utilizing serum, prognostic and predictive algorithm reported as good versus poor overall survival	Non-small cell lung cancer; and either EGFR-sensitizing mutation negative or EGFR status unknown

APPENDIX II
NON-COVERED TESTS/MARKERS
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TEST/MARKER	CODE	DESCRIPTION	APPLICATION
18q-LOH/DCC	81402	Molecular pathology procedure, Level 3 (eg, > 10 SNPs, 2-10 methylated variants, or 2-10 somatic variants [typically using non-sequencing target variant analysis], immunoglobulin and T-cell receptor gene rearrangements, duplication/deletion variants 1 exon), loss of heterozygosity [LOH], uniparenteal sisomy [UPD])	Assaying for loss of heterozygosity (LOH) on the long arm of chromosome 18 (18q) or deleted in colon cancer (DCC) protein (18q-LOH/DCC) for colorectal cancer.
Alpha-Fetoprotein (AFP)	82105	Alpha-fetoprotein (AFP); serum	For the diagnosis of trophoblastic tumors and other oncologic indications
HCV FibroSure™ FibroTest®- ActiTest®;	0001M	Infectious disease, HCV, six biochemical assays (ALT, A2-macroglobulin, apolipoprotein A-1, total bilirubin, GGT, and haptoglobin) utilizing serum, prognostic algorithm reported as scores for fibrosis and necroinflammatory activity in liver	Serum marker panels for the diagnosis or management of liver disease, including hepatitis C.
ASH FibroSURE™ ;FibroMAX™; ;;	0002M	Liver disease, ten biochemical assays (ALT, A2-macroglobulin, apolipoprotein A-1, total bilirubin, GGT, haptoglobin, AST, glucose, total cholesterol and triglycerides) utilizing serum, prognostic algorithm reported as quantitative scores for fibrosis, steatosis and alcoholic steatohepatitis (ASH)	
NASH FibroSURE™ FIBROSpect II® ;	0003M	Liver disease, ten biochemical assays (ALT, A2-macroglobulin, apolipoprotein A-1, total bilirubin, GGT, haptoglobin, AST, glucose, total cholesterol and triglycerides) utilizing serum, prognostic algorithm reported as quantitative scores for fibrosis, steatosis and nonalcoholic steatohepatitis (NASH)	
HepaScore™	82172 82247 82977 83010	Apolipoprotein, each Bilirubin; total Glutamyltransferase, gamma (GGT) Haptoglobin; quantitative	

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	83883 84460	Nephelometry, each analyte not elsewhere specified Transferase; alanine amino (ALT) (SGPT)	
Autoantibody detection i.e. (EarlyCDT)-Lung test, as a screening test for the early detection of lung cancer	83520	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; quantitative, not otherwise specified	Screening test for the early detection of lung cancer
BluePrint		*See* Unlisted Codes	Molecular subtyping profile for breast cancer
BRAF	81210	BRAF (v-raf murine sarcoma viral oncogene homolog B1) (e.g., colon cancer), gene analysis, V600E variant	Mutation analysis in thyroid cancer
Breast Cancer Gene Expression Ratio		*See* Unlisted Codes	HOXB13:IL17BR for breast cancer
CA125	86304	Immunoassay for tumor antigen, quantitative; CA 125	For all other indications including use as a screening test for colorectal cancer or ovarian cancer (other than as indicated above) or for differential diagnosis of members with symptoms of colonic disease for all other indications including use as a screening test for colorectal cancer or ovarian cancer (other than as indicated above) or for differential diagnosis of members with symptoms of colonic disease.
CancerNext	81201 81211*	APC (adenomatous polyposis coli) (eg, familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; full gene sequence BRCA1, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and common duplication/deletion variants in BRCA1 (ie, exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-20 del 26kb, exon 22 del 510bp, exon 8-9	Cancer tumor panel

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		del 7.1kb)	
	81213*	BRCA1, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; uncommon duplication/deletion variants	
	81294	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants	
	81295	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis	
	82197	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants	
	81298	MSH6 (mutS homolog 6 [E. coli]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis	
	81300	MSH6 (mutS homolog 6 [E. coli]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants	
	81317	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis	
	81319	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants	

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CancerType ID	81540	Oncology (tumor of unknown origin), mRNA, gene expression profiling by real-time RT-PCR of 92 genes (87 content and 5 housekeeping) to classify tumor into main cancer type and subtype, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a probability of a predicted main cancer type and subtype	
Carcinoembryonic antigen cell adhesion molecule 6 (CEACAM6)		*See* Unlisted Codes	For predicting the risk of breast cancer
Carcinoembryonic antigen cellular adhesion molecule-7 (CEACAM-7) expression		*See* Unlisted Codes	Predictive marker for rectal cancer recurrence
CEA	82378	Carcinoembryonic antigen (CEA)	NOT covered for any of the following: 1. As a screening test for colorectal cancer; or 2. As a sole determinant to treat a colorectal cancer member with adjuvant therapy or systemic therapy for presumed metastatic disease; or 3. For diagnosis, prognosis, or monitoring of treatment in members with lung cancer; or 4. For diagnosis of esophageal carcinoma; or 5. For routine use of CEA alone for monitoring response to treatment of colorectal when there are other simple tests available to indicate a response; or 6. For screening, diagnosis, staging or routine surveillance of breast cancer.

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CellSearch assay	86152 86153	Cell enumeration using immunologic selection and identification in fluid specimen (eg, circulating tumor cells in blood); Cell enumeration using immunologic selection and identification in fluid specimen (eg, circulating tumor cells in blood); physician interpretation and report, when required	For all cancers
CK5, CK14, p63, Racemase P504S (PIN-4)	88342 88344	Immunohistochemistry or immunocytochemistry, each separately identifiable antibody per block, cytologic preparation, or hematologic smear; first separately identifiable antibody per slide Immunohistochemistry or immunocytochemistry, per specimen; each multiplex antibody stain procedure	For Prostate Cancer
c-Met expression	88271 88275 88342	Molecular cytogenetics; DNA probe, each (eg, FISH) Molecular cytogenetics; interphase in situ hybridization, analyze 100-300 cells Immunohistochemistry or immunocytochemistry, each separately identifiable antibody per block, cytologic preparation, or hematologic smear; first separately identifiable antibody per slide *See* Unlisted Codes	For predicting prognosis in persons with advanced NSCLC and colorectal cancer, and other indications
Cofilin (CFL1)		*See* Unlisted Codes	Prognostic and drug resistance marker in non-small cell lung cancer
ColonSentry		*See* Unlisted Codes	Colorectal cancer screening
ColoPrint, CIMP, LINE-1 hypomethylation, and Immune cells		*See* Unlisted Codes	For colon cancer
CxBladder		*See* Unlisted Codes	For bladder cancer

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Cyclin D1F	88342	Immunohistochemistry or immunocytochemistry, each separately identifiable antibody per block, cytologic preparation, or hematologic smear; first separately identifiable antibody per slide	Head and neck squamous cell carcinoma
Decipher test		*See* Unlisted Codes	For prostate cancer
DecisionDX-G-CIMP		*See* Unlisted Codes	Methylation analysis of DNA for determining tumor grade (e.g., DecisionDX-G-CIMP) microarray analysis for measuring the degree of similarity in undifferentiated tumor types (e.g., Pathwork® Tissue of Origin)
Des-gamma-carboxy prothrombin (DCP)	83951	Oncoprotein; des-gamma-carboxy-prothrombin (DCP)	For diagnosing and monitoring hepatocellular carcinoma and other indications (also known as "prothrombin produced by vitamin K absence or antagonism II" [PIVKA II])
FADD (Fas-associated protein with death domain)		*See* Unlisted Codes	
Fibrin/fibrinogen degradation products (FDP) testing, i.e., Onko-Sure™ blood test	85379	Fibrin degradation products, D-dimer; quantitative	
Galectin-3	82777	Galectin-3	Prostate Cancer
Gene Hypermethylation Glutathione-S transferase P1 (GSTP1)		*See* Unlisted Codes	Prostate Cancer
GeneKey		*See* Unlisted Codes	
GeneSearch™ Breast Lymph Node (BLN) assay.		*See* Unlisted Codes	

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Guanylyl cyclase c (GCC or GUCY2C), i.e., Previstage™ GCC Colorectal Cancer Stage Test		*See* Unlisted Codes	
HERmark		*See* Unlisted Codes	Testing for breast cancer and other indications
Human epididymis protein 4 (HE4)	86305	Human epididymis protein 4 (HE4)	To monitor recurrence of ovarian cancer
Insight®Dx Mammostrat® test for predicting recurrence of breast cancer		*See* Unlisted Codes	Used for predicting recurrence of breast cancer
Lectin-reactive alpha-fetoprotein (AFP-L3)	82107	Alpha-fetoprotein (AFP); AFP-L3 fraction isoform and total AFP (including ratio)	
Mucin 4 expression	88342	Immunohistochemistry or immunocytochemistry, each separately identifiable antibody per block, cytologic preparation, or hematologic smear; first separately identifiable antibody per slide	Used as a predictor of survival in colorectal cancer
MyPRS		*See* Unlisted Codes	Microarray-based gene expression profile for multiple myeloma
Onclnsights		*See* Unlisted Codes	Multi-gene tumor profile
ROMA	81500	Oncology (ovarian), biochemical assays of two proteins (CA-125 and HE4), utilizing serum, with menopausal status, algorithm reported as a risk score	Ovarian cancer screening
Panexia	81406 81216	Molecular pathology procedure, Level 7 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia) BRCA2 (breast cancer 2) (eg,	

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		hereditary breast and ovarian cancer) gene analysis; full sequence analysis	
	81217	BRCA2 (breast cancer 2) (eg, hereditary breast and ovarian cancer) gene analysis; known familial variant	
		See Unlisted Codes	
Pathwork Tissue of origin	81504	Oncology (tissue of origin), microarray gene expression profiling of > 2000 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as tissue similarity score	Cancer of unknown origin
Post-Op Px™ *previously known as Prostate PX®;* Prostate Cancer Antigen 3 (PCA3)	88305	Level IV - Surgical pathology, gross and microscopic examination	Genetic Assay for the Diagnosis and Management of Prostate Cancer
	88313	Special stain including interpretation and report; Group II, all other (eg, iron, trichrome), except stain for microorganisms, stains for enzyme constituents, or immunocytochemistry and immunohistochemistry	
	88323	Consultation and report on referred material requiring preparation of slides	
	88347	Immunofluorescent study, each antibody; indirect method	
		See unlisted codes	
PreOvar test for KRAS variant to determine ovarian cancer risk		*See* Unlisted Codes	To determine ovarian cancer risk
Progensa PCA3 Assay	81313	PCA3/KLK3 (prostate cancer antigen 3 [non-protein coding]/kallikrein-related peptidase 3 [prostate specific antigen]) ratio (eg, prostate cancer)	Performed when negative prostate biopsy
Prolaris		*See* Unlisted Codes	Prognostic assessment of prostate CA

APPENDIX II NON-COVERED TESTS/MARKERS This list is not all inclusive – any test not listed is still subject to medical necessity review Last Update: 2/2017			
TEST/MARKER	**CODE**	**DESCRIPTION**	**APPLICATION**
ProOnc TumorSourceDx		*See* Unlisted Codes	To identify tissue or origin for metastatic tumors
ResponseDx Colon		*See* Unlisted Codes	Colon cancer
Septin 9 (SEPT9) DNA methylation assay for the early detection of colorectal cancer, i.e., Epi *pro*Colon or ColoVantage™	81327	SEPT9 (Septin9) (eg, colorectal cancer) methylation analysis Molecular pathology procedure, Level 2 (eg, 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat)	Early detection of colorectal cancer
Serum amyloid A recurrence and response to therapy	88342	Immunohistochemistry or immunocytochemistry, each separately identifiable antibody per block, cytologic preparation, or hematologic smear; first separately identifiable antibody per slide	Biomarker for endometrial endometrioid carcinoma to monitor disease
Target Now Molecular Profiling Test (Caris)		*See* Unlisted Codes	
Theros Breast Cancer Index		*See* Unlisted Codes	
Topographic genotyping, such as PathFinderTG®		*See* Unlisted Codes	For any indication including breast cancer and pancreatic cancer
Topoisonmerase II alpha (TOP2A) gene amplification or deletion, i.e., TOP2A FISH pharmDx™ Assay	88365 88368	In situ hybridization (eg, FISH), each probe Morphometric analysis, in situ hybridization (quantitative or semi-quantitative) each probe; manual	

VI. 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
3. Cigna online medical policy bulletin: Tumor Markers for Diagnosis and Management of Cancer - http://www.cigna.com/customer_care/healthcare_professional/coverage_positions/medical/mm_0172_coveragepositioncriteria_tumor_markers_for_diagnosis_mgmt_cancer.pdf
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

b. Breast Cancer version
1.2009: http://www.nccn.org/professionals/physician_gls/PDF/breast.pdf
http://www.nccn.org/professionals/physician_gls/PDF/breast-screening.pdf
c. Colon Cancer version
2.2009: http://www.nccn.org/professionals/physician_gls/PDF/colon.pdf http://www.nccn.org/professionals/physician_gls/PDF/colorectal_screening.pdf
d. Gastric Cancer version
2.2009: http://www.nccn.org/professionals/physician_gls/PDF/gastric.pdf
e. Kidney Cancer version
2.2009: http://www.nccn.org/professionals/physician_gls/PDF/kidney.pdf
f. Ovarian Cancer version
2.2009: http://www.nccn.org/professionals/physician_gls/PDF/ovarian.pdf
g. Pancreatic Cancer version
2.2009: http://www.nccn.org/professionals/physician_gls/PDF/pancreatic.pdf
h. Prostate Cancer version
2.2009: http://www.nccn.org/professionals/physician_gls/PDF/prostate.pdf http://www.nccn.org/professionals/physician_gls/PDF/prostate_detection.pdf

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