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Subject: Tumor/Genetic Markers

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DESCRIPTION:

Serum tumor markers are molecules or substances shed by a tumor into the circulation where they can be detected and quantitated. Noncirculating tumor markers include those that can be detected histochemically or cytogenetically on a tissue sample.

Since serum tumor markers can also be detected in normal or benign lesions, significantly elevated circulating levels may occur with malignancy by one or more of the following mechanisms: overexpression of the antigen by malignant cells; a large tumor burden; or slower clearance of the marker. For example, since the liver clears most tumor markers, liver abnormalities (whether benign, malignant, or inflammatory) may elevate tumor marker concentrations due to impaired clearance. Because most tumor markers are not unique to malignancy, cut-off points must be established for normal versus abnormal marker levels.

The clinical applicability of tumor markers depends on how their measurements are used to influence the management of the patient and whether these management changes will result in an improvement in net health outcome.

POSITION STATEMENT:

Biochemical Markers of Alzheimer's Disease (AlzheimAlert™, AdMark®)	Measurement of cerebrospinal fluid biochemical markers of Alzheimer's disease, including but not limited to tau protein, amyloid beta peptides, or neural thread proteins, is considered **experimental or investigational** as there is insufficient clinical evidence to support the use of the measurement of cerebrospinal fluid biochemical markers of

	Alzheimer's disease for all indications. Measurement of urinary biochemical markers of Alzheimer's disease, including but not limited to neural thread proteins, is considered **experimental or investigational** as there is insufficient clinical evidence to support the use of the measurement of urinary biochemical markers of Alzheimer's disease for all indications.
Breast Tumor Markers	CA 15-3 (CA 27.29 or Truquant RIA) **meets the definition of medical necessity** for the following indications: • As an aid in the management of Stage II and Stage III breast cancer patients. Serial testing for CA 15-3 assay values should be used in conjunction with other clinical methods for monitoring breast cancer • As an aid to predict recurrent breast cancer in patients with previously treated Stage II or Stage III disease • As an aid in monitoring response to therapy in patients with Stage IV breast cancer. A partial or complete response to treatment will be confirmed by declining levels. A persistent rise of CA 27-29 levels despite therapy strongly suggests progressive disease. CA 15-3 (CA 27.29 or Truquant RIA) is considered **experimental or investigational**, as there is insufficient clinical evidence to support the use of CA 15-3 (CA 27.29 or Truquant RIA) as a screening test for breast cancer. There is a lack of clinical data to permit conclusions on efficacy and net health outcomes.
Cancer Antigen 125 (CA-125)	CA-125 testing **meets the definition of medical necessity** in individuals with symptoms suggestive of ovarian cancer; symptoms may include: • Swelling of the abdomen (ascites) • Gastrointestinal symptoms (e.g., gas, bloating, long-term stomach pain, indigestion) • Bleeding between periods or after menopause • Pelvic pain • Feeling of pressure in the pelvis • Leg pain. CA-125 testing **meets the definition of medical necessity** in individuals with other gynecologic malignancies, such as endometrial cancer, in whom baseline levels of CA-125 have been shown to be elevated. CA-125 testing in asymptomatic individuals is considered **experimental or investigational.** There is insufficient

	clinical evidence to support the use of CA-125 testing as a screening technique for ovarian cancer.
Cardiovascular Risk Panels	Cardiovascular risk panels, consisting of multiple individual biomarkers intended to assess cardiac risk (other than simple lipid panels*****), are considered **experimental or investigational**. There is a lack of evidence as to how the panels would impact management decisions, on the clinical utility beyond simple lipid measures; and how the use of the panels would improve health outcomes. (Cardiovascular risk panels may include: Applied Genetics Cardiac Panel; Boston Heart Advanced Risk Markers Panel; Cleveland HeartLab CVD Inflammatory Profile; Genetiks Genetic Diagnosis and Research Center Cardiovascular Risk Panel; Genova Diagnostics CV Health Plus Genomics™ Panel; Health Diagnostics Cardiac Risk Panel; Metametrix Cardiovascular Health Profile; Spectracell LPP™.) ***** A simple lipid panel is generally composed of the following lipid measures:Total cholesterol; LDL cholesterol; HDL cholesterol; Triglycerides. Certain calculated ratios, such as the total/HDL cholesterol may also be reported as part of a simple lipid panel. Other types of lipid testing, i.e., apolipoproteins, lipid particle number or particle size, lipoprotein (a), etc., are not considered to be components of a simple lipid profile.
Circulating Tumor DNA (Liquid Biopsy) (CancerIntercept™, CellSearch®, FoundationACT™, GeneStrat®, Oncotype SEQ™)	**EGFR Testing** Analysis of 2 types of somatic sensitizing variants within the epidermal growth factor receptor (EGFR) gene- small deletions in exon 19 and a point mutation variant in exon 21 (L858R)- using the cobas® EGFR Mutation Test v2, Guardant360 test, or OncoBEAM test with plasma specimens to detect circulating tumor DNA (ctDNA) **meets the definition of medical necessity** as an alternative to tissue biopsy to predict treatment response to an EGFR tyrosine kinase inhibitor (TKI) therapy in members with advanced stage III or IV non-small-cell lung cancer (NSCLC). The cobas test is a companion diagnostic for erlotinib and gefitinib. Analysis of other EGFR sensitizing variants within exons 18 to 24 using ctDNA for applications related to NSCLC is considered **experimental or investigational**. The evidence is insufficient to determine the effects of the technology on health outcomes.

	Analysis of EGFR T790M resistance variant for targeted therapy with osimertinib using ctDNA or for other applications related to NSCLC, is considered **experimental or investigational**. The evidence is insufficient to determine the effects of the technology on health outcomes. Analysis of 2 types of somatic mutations variants within the EGFR gene- small deletions in exon 19 and a point mutation variant in exon 21 (L858R)- using ctDNA is considered **experimental or investigational** for members with advanced NSCLC of squamous cell type. The evidence is insufficient to determine the effects of the technology on health outcomes. **ALK Testing** Analysis of somatic rearrangement variants of the ALK gene using plasma specimens to detect ctDNA or RNA is considered **experimental or investigational** as an alternative to tissue biopsy to predict treatment response to ALK inhibitor therapy (eg, crizotinib [Xalkori], ceritinib [Zykadia], alectinib [Alecensa], or brigatinib [Alunbrig]) in members with NSCLC. **BRAF V600E Testing** Analysis of the BRAF V600E variant using plasma specimens to detect ctDNA is considered **experimental or investigational** as an alternative to tissue biopsy to predict treatment response to BRAF or MEK inhibitor therapy (eg, dabrafenib [Tafinlar], trametinib [Mekinist]) in members with NSCLC. The evidence is insufficient to determine the effects of the technology on health outcomes. **ROS1 Testing** Analysis of somatic rearrangement variants of the ROS1 gene using plasma specimens to detect ctDNA or RNA is considered **experimental or investigational** as an alternative to tissue biopsy to predict treatment response to ALK inhibitor therapy (crizotinib [Xalkori]) in members with NSCLC. The evidence is insufficient to determine the effects of the technology on health outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes. **KRAS Testing** Analysis of somatic variants of the KRAS gene using plasma specimens to detect ctDNA is considered **experimental or investigational** as a technique to predict treatment

	nonresponse to anti-EGFR therapy with tyrosine kinase inhibitors and for the use of the anti-EGFR monoclonal antibody cetuximab in NSCLC. The evidence is insufficient to determine the effects of the technology on health outcomes. **Other Genes** Analysis of alterations in the HER2, RET, and MET genes using plasma specimens to detect ctDNA for targeted therapy in members with NSCLC is considered **experimental or investigational**. The evidence is insufficient to determine the effects of the technology on health outcomes. The use of other circulating tumor DNA tests and circulating tumor cells (CTC) is considered **experimental or investigational** for all indications. The evidence is insufficient to determine the effects of the technology on health outcomes.
Cutaneous Melanoma	Gene expression testing, including but not limited to the Pigmented Lesion Assay (PLA), in the evaluation of members with suspicious pigmented lesions is considered **experimental or investigational**. Gene expression testing, including but not limited to the myPath Melanoma test, in the evaluation of members with melanocytic lesions with indeterminate histopathologic features is considered **experimental or investigational**. Gene expression testing, including but not limited to DecisionDx-Melanoma, in the evaluation of members with cutaneous melanoma is considered **experimental or investigational** for all indications. The evidence is insufficient to determine the effects of the technology on health outcomes.
Microarray-Based Gene Expression Profile Testing for Multiple Myeloma Risk Stratification (MyPRS™/MyPRS Plus™)	Microarray-based gene expression profile testing for multiple myeloma is considered **experimental or investigational** for all indications. The evidence is insufficient to determine the effects of the technology on health outcomes.
Molecular Analysis for Targeted Therapy of Non-Small-Cell Lung Cancer (NSCLC)	**EGFR Testing** Analysis of somatic variants in exons 18 through 21 (such as G719X, L858R, T790M, S678I, L861Q) within the epidermal growth factor receptor (EGFR) **meets the definition of medical necessity** to predict treatment response to an

	EGFR tyrosine kinase inhibitor (TKI) therapy (e.g. erlotinib [Tarceva®], gefitinib [Iressa®], afatinib [Gilotrif®], or osimertinib [Tagrisso]) in members with advanced lung adenocarcinoma, large cell carcinoma, advanced squamous cell NSCLC, and NSCLC not otherwise specified. Analysis of other EGFR variants within exons 22 to 24, or other applications related to NSCLC, is considered **experimental or investigational**. The evidence is insufficient to determine the effects of the technology on health outcomes. **ALK Testing** Analysis of somatic rearrangement variants of the anaplastic lymphoma kinase (ALK) gene **meets the definition of medical necessity** to predict treatment response to ALK inhibitor therapy (e.g. crizotinib [Xalkori®], ceritinib [Zykadia™]), alectinib [Alecensa®], or brigatinib [Alunbrig™] in members with advanced lung adenocarcinoma or in whom an adenocarcinoma component cannot be excluded (cases showing squamous cell histology). Analysis of somatic rearrangement variants of the ALK gene is considered **experimental or investigational** in all other situations. The evidence is insufficient to determine the effects of the technology on health outcomes.**BRAF V600E Testing** Analysis of the BRAF V600E variant **meets the definition of medical necessity** to predict treatment response to BRAF or MEK inhibitor therapy (eg, dabrafenib [Tafinlar] and trametinib [Mekinist]), in members with advanced lung adenocarcinoma or in whom an adenocarcinoma component cannot be excluded (cases showing squamous cell histology). **KRAS Testing** Analysis of somatic variants of the KRAS gene is considered **experimental or investigational** as a technique to predict treatment nonresponse to anti-EGFR therapy with tyrosine kinase inhibitors and for the use of the anti-EGFR monoclonal antibody cetuximab in NSCLC. The evidence is insufficient to determine the effects of the technology on health outcomes. **ROS1 Testing** Analysis of somatic rearrangement variants of the ROS1

	gene **meets the definition of medical necessity** to predict treatment response to ALK inhibitor therapy (crizotinib [Xalkori®]) in members with advanced lung adenocarcinoma or in whom an adenocarcinoma component cannot be excluded (cases showing squamous cell histology). **Other Genes** Analysis of genetic alterations in the genes HER2, RET, and MET for targeted therapy in members with NSCLC is considered **experimental or investigational**. The evidence is insufficient to determine the effects of the technology on health outcomes.
Molecular Markers in Fine Needle Aspirates of the Thyroid	The use of either the Afirma Genomic Sequencing Classifier or ThyroSeq v2 in fine needle aspirates of the thyroid nodules with cytologic findings (ie, Bethesda diagnostic category III [atypia/follicular lesion of undetermined significance] or Bethesda diagnostic category IV [follicular neoplasm/suspicion for a follicular neoplasm]) **meets the definition of medical necessity** in members who have the following characteristics: • Thyroid nodules without strong clinical or radiologic findings suggestive of malignancy AND • In whom surgical decision making would be affected by test results. The use of any of the following types of molecular marker testing or gene variant analysis in fine needle aspirates of thyroid nodules with indeterminate findings (Bethesda diagnostic category III [atypia/follicular lesion of undetermined significance] or Bethesda diagnostic category IV [follicular neoplasm/suspicion for a follicular neoplasm]) or suspicious findings [Bethesda diagnostic category V (suspicious for malignancy)] to rule in malignancy to guide surgical planning for initial resection rather than a 2-stage surgical biopsy followed by definitive surgery **meets the definition of medical necessity**: • ThyroSeq v3; • ThyraMIR microRNA/ThyGenX; • Afirma BRAF after Afirma Genomic Sequencing Classifier; or • Afirma MTC after Afirma Genomic Sequencing Classifier. Gene expression classifiers, genetic variant analysis, and molecular marker testing in fine needle aspirates of the

	thyroid not meeting criteria outlined above, including but not limited to use of RosettaGX Reveal and single-gene TERT testing, are considered **experimental or investigational**. The evidence is insufficient to determine the effects of the technology on health outcomes.
Fecal Calprotectin Testing (CalPrest®,CalPrest®NG, PhiCal®)	Fecal calprotectin testing **meets the definition of medical necessity** for the evaluation of members when the differential diagnosis is inflammatory bowel disease or noninflammatory bowel disease (including irritable bowel syndrome) for which endoscopy with biopsy is being considered. Fecal calprotectin testing is considered **experimental or investigational** in the management of inflammatory bowel disease, including the management of active inflammatory bowel disease and surveillance for relapse of disease in remission. The evidence is insufficient to determine the effects of the technology on health outcomes.
Holo-Transcobalamin	Measurement of holo-transcobalamin, including but not limited to its use in the diagnosis and management of vitamin B12 deficiency, is considered **experimental or investigational.** There is insufficient clinical evidence to support the use of the measurement of holo-transcobalamin to identify early states of vitamin B12 deficiency. There are inadequate data to establish holo-TC testing as an alternative to either serum cobalamin or levels of MMA or homocysteine.
Homocysteine Testing	Measurement of plasma levels of homocysteine is considered **experimental or investigational** in the screening, evaluation, and management of members for cardiovascular disease. The technology is unlikely to change management or improve the net health outcome. Measurement of plasma levels of homocysteine is considered **experimental or investigational** in the screening, evaluation, and management of members with venous thromboembolism or risk of venous thromboembolism. The evidence is insufficient to determine the effects of the technology on health outcomes.
Long-Chain Omega-3 Fatty Acids in Red Blood Cell Membranes	Measurement of long chain omega-3 fatty acids in red blood cell membranes is considered **experimental or investigational**, as there is insufficient clinical evidence to support the use of the measurement of long chain omega-3 fatty acids as a cardiac risk factor. There is a lack of scientific evidence in the published literature regarding how measurements of red blood cell omega-3 fatty acid would

	affect management of individuals at risk for or patients with coronary artery disease (CAD).
Management of Pulmonary Nodules (REVEAL Lung Nodule Characterization)	Plasma-based proteomic screening, including but not limited to BDX-XL2 , in members with undiagnosed pulmonary nodules detected by computed tomography is considered **experimental or investigational**. The evidence is insufficient to determine the effects of the technology on health outcomes. Gene expression profiling on bronchial brushings, including but not limited to Percepta® Bronchial Genomic Classifier, in members with indeterminate bronchoscopy results from undiagnosed pulmonary nodules is considered **experimental or investigational**. The evidence is insufficient to determine the effects of the technology on health outcomes.
Measurement of Serum Levels and Antibodies to Adalimumab, Infliximab, Ustekinumab, & Vedolizumab (LabCorp® Adalimumab Concentration & Anti-Adolimumab Antibody; Prometheus® Anser™ IFX; Prometheus® Anser™ ADA; Prometheus® Anser UST; Prometheus® Anser™ VDZ)	Measurement of antibodies to adalimumab, infliximab, ustekinumab, or vedolizumab either alone or as a combination test which includes the measurement of serum adalimumab, infliximab, ustekinumab, or vedolizumab levels is considered **experimental or investigational**. There is insufficient evidence in medical literature regarding the clinical utility and impact on clinical outcomes to permit conclusions on net health outcomes.
Gene Expression-Based Assays for Cancers of Unknown Primary (CancerTYPE ID®, MiRview® Mets, PathWork® Tissue of Origin Test™, ProOnc TumorSource DX™, ResponseDX: Tissue of Origin™, RosettaGX Cancer Origin™ (formerly miRview® mets2), Tissue of Origin®)	Gene expression profiling is considered **experimental or investigational** to evaluate the site of origin of a tumor of unknown primary, or to distinguish a primary from a metastatic tumor. The evidence is insufficient to determine the effects of the technology on health outcomes.
Expanded Cancer Molecular Panels (BioSpeciFx®, FoundationOne® Heme, GeneKey, GeneTrails, Illumina TruSight, Ion AmpliSeq	The use of expanded cancer molecular panels for selecting targeting cancer treatment is considered e**xperimental or investigational**. Additional evidence is needed to demonstrate the efficacy of the technology and the impacts on health outcomes.

Panel, Ion AmpliSeq Hotspot Panel v2,, MI Profile™, MI Profile™ PLUS OncInsights™, Molecular Intelligence™ Service, OmniSeq Comprehensive, OnkoMatch, Paradigm Cancer Diagnostic (PCDx), SmartGenomics, Target Now®, TruSeq®)	
Multianalyte Assays for Chronic Liver Disease	A single FibroSURE® multianalyte assay **meets the definition of medical necessity** for the evaluation of members with chronic liver disease. FibroSURE® multianalyte assays are considered **experimental or investigational** for monitoring members with chronic liver disease.The evidence is insufficient to determine the effects of the technology on health outcomes. The use of other multianalyte assays with algorithmic analyses (e.g. FIBROSpect® II) is considered **experimental or investigational** for the evaluation or monitoring of members with chronic liver disease. The evidence is insufficient to determine the effects of the technology on health outcomes.
Multibiomarker Disease Activity Score for Rheumatoid Arthritis (Prism™ RA)	The use of a multibiomarker disease activity score for rheumatoid arthritis (eg, Vectra® DA score) is considered **experimental or investigational** in all situations. The evidence is insufficient to determine the effects of the technology on health outcomes.
Multimarker Serum Testing Related to Ovarian Cancer	All uses of the OVA1®, Overa™, and ROMA™ tests are considered **experimental or investigational**, including but not limited to: • preoperative evaluation of adnexal masses to triage for malignancy • screening for ovarian cancer • selecting members for surgery for an adnexal mass • evaluation of members with clinical or radiologic evidence of malignancy • evaluation of members with nonspecific signs or symptoms suggesting possible malignancy, or • postoperative testing and monitoring to assess surgical outcome and/or to detect recurrent malignant disease following treatment. The evidence is insufficient to determine the effects of the

	technology on health outcomes.
Pharmacogenomic and Metabolite Markers for Members Treated with Thiopurines	One-time genotypic analysis or phenotypic analysis of the enzyme TPMT gene **meets the definition of medical necessity** in members beginning therapy with azathioprine (AZA), mercaptopurine (6-MP), thioguanine, or in members on thiopurine therapy with abnormal complete blood count (CBC) results that do not respond to dose reduction. Genotypic analysis and/or phenotypic analysis of the enzyme TPMT is considered **experimental or investigational** for all other indications. There is limited clinical evidence in peer-reviewed medical literature to permit conclusions on net health outcomes. Analysis of the metabolite markers of azathioprine (AZA) and mercaptopurine (6-MP), including 6-methyl-mercaptopurine ribonucleotides (6-MMRP) and 6-thioguanine nucleotides (6-TGN), is considered **experimental or investigational.** There is insufficient evidence from prospective studies on whether metabolite markers will lead to improved outcomes (primarily improved disease control and/or less adverse drug effects).
Proteogenomic Testing for Members With Cancer	Proteogenomic testing of members with cancer (including but not limited to GPS Cancer™ test) is considered **experimental or investigational** for all indications. The evidence is insufficient to determine the effect of the technology on health outcomes.
Proteomic Testing for Advanced Non-Small Cell Lung Cancer (NSCLC)	Proteomic testing (VeriStrat®) **meets the definition of medical necessity** for members with advanced non-small cell lung cancer (NSCLC) meeting **ALL** of the following criteria: • tumor is wild-type (no mutation detected) EGFR **OR** with unknown EGFR status; • failed first-line systemic chemotherapy; **AND** • test results will determine whether to proceed with erlotinib (Tarceva®) therapy. Proteomic testing (VeriStrat) is considered **experimental or investigational** for all other indications. There is insufficient evidence to permit conclusions on clinical utility or net health outcomes.
Serum Biomarker Human Epididymis Protein 4 (Architect HE4 assay, Elecsys	Measurement of human epididymis protein 4 (HE4) is considered **experimental or investigational** for all indications. The evidence is insufficient to determine the

HE4, HE4 EIA Kit, HE4 immunoassay, Lumipulse G HE4 Immunoreaction)	effects of the technology on health outcomes.
Serum Biomarker Panel Testing for Systemic Lupus Erythematosus and Other Connective Tissue Diseases (Avise® CTD, Avise® Lupus, Avise® Monitor, Avise® MTX, Avise®, PG, Avise® Prognostic, Avise® SLE, Avise® SLE+)	Serum biomarker panel testing with proprietary algorithms and/or index scores for the diagnosis of systemic lupus erythematosus is considered **experimental or investigational.** The evidence is insufficient to determine the effects of the technology on health outcomes.
Serum Biomarker Tests for Multiple Sclerosis	Serum biomarker tests (e.g. gMS® Dx, gMS® Pro EDSS) for multiple sclerosis are considered **experimental or investigational** for all indications. There is insufficient evidence from prospective studies demonstrating improved health outcomes in individuals who may have multiple sclerosis and who are treated according to test results.
Uveal Melanoma	Gene expression profiling for uveal melanoma with DecisionDx-UM **meets the definition of medical necessity** for members with primary, localized uveal melanoma. Gene expression profiling for uveal melanoma that do not meet the above criteria is considered **experimental or investigational**. The evidence is insufficient to determine the effects of the technology on health outcomes.

The following tumor markers are considered **experimental or investigational** for all indications, as there is insufficient evidence in the peer reviewed medical literature to support the use of these markers for screening, diagnosing, staging, surveillance or monitoring response to treatment:

Table 1

a2-PAG	pregnancy-associated alpha-2-glycoprotein
BCM	breast cancer mucin
CA50	cancer antigen 50
CA72-4	cancer antigen 72-4
CA195	cancer antigen 195
CA242	cancer antigen 242
CA549	carbohydrate antigen/cancer antigen 594
CA-SCC	squamous cell carcinoma antigen
CAM17-1	monocolonal antimucin antibody 17-1
CAM-26	monocolonal antimucin antibody 26
CAM-29	monocolonal antimucin antibody 29
CAR-3	antigenic determinant recognized by monoclonal antibody AR-3

DU-PAN-2	sialylated carbohydrate antigen DU-PAN-2
MCA	mucin-like carcinoma-associated antigen
NSE	neuron-specific enolase
P-LAP	placental alkaline phosphatase
PNA/ELLA	peanut lectin bonding assay
SLEX	sialylated Lewis X-I antigen
SLX	sialylated SSEA-1 antigen
SPAN-1	sialylated carbohydrate antigen SPAN-1
ST-439	sialylated carbohydrate antigen ST-439
TAG12	tumor-associated glycoprotein 12
TAG72	tumor-associated glycoprotein 72
TAG72.3	tumor-associated glycoprotein 72.3
TATI	tumor-associated trypsin inhibitor
TNF-a	tumor necrosis factor alpha
TPA	tissue polypeptic antigen

Home testing (including self-testing home kits) is considered **experimental or investigational** for all indications. The clinical validity of the tests have not been established and the evidence is insufficient to determine the effects of the technology on health outcomes.

The following tests are considered experimental or investigational, as there is insufficient evidence to support the use of these tests for all indications. Although there are ongoing clinical studies the current data are inadequate to permit scientific conclusions regarding the impact on management decisions and net health outcomes.

- Academic Profile
- Avise MCV
- Cxbladder™
- FiT IQ™
- GeneSearch™ BLN
- HERmark®
- InflammaDry®
- NETest
- Ova Check™
- OvaSure™
- PathwayFit®
- PharmaRisk™
- Post-Op Px™ (previously known as ProstatePX)
- PreDx Diabetes Risk Score™
- Prostate Px+
- ResponseDX: Lung™
- ResponseDX: Colon™
- Thyroid Cancer Mutation Panel
- xTAG® Gastrointestinal Pathogen Panel (GPP).

BILLING/CODING INFORMATION:

Afirma® Genomic Sequencing Classifier

CPT Coding

81545	Oncology (thyroid), gene expression analysis of 142 genes, utilizing fine needle aspirate, algorithm reported as a categorical result (eg, benign or suspicious)

ICD-10 Diagnosis Codes That Support Medical Necessity (81545)

C73	Malignant neoplasm of thyroid gland
D44.0	Neoplasm of uncertain behavior of thyroid gland

Biochemical Markers of Alzheimer's Disease

There are no specific CPT or HCPCS codes describing measurement of biochemical markers of Alzheimer's disease.

Breast Tumor Markers

CPT Coding

86300	Immunoassay for tumor antigen, Quantitative; CA 15-3 (27.29)

ICD-10 Diagnosis Codes That Support Medical Necessity (86300)

C50.011 – C50.929	Malignant neoplasm of breast
C79.2	Secondary malignant neoplasm of skin
C79.81	Secondary malignant neoplasm of breast
G89.3	Neoplasm related pain (acute) (chronic)
R97.8	Other abnormal tumor markers
Z85.3	Personal history of malignant neoplasm of breast

Cancer Antigen 125 (CA-125)

CPT Coding

86304	Immunoassay for tumor antigen, CA-125

ICD-10 Diagnosis Codes That Support Medical Necessity (86304)

C45.1	Mesothelioma of peritoneum
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
C53.0	Malignant neoplasm of endocervix
C53.1	Malignant neoplasm of exocervix
C54.1 – C54.9	Malignant neoplasm of corpus uteri
C56.1 – C56.9	Malignant neoplasm of ovary
C57.00 – C57.9	Malignant neoplasm of other and unspecified female genital organs
C79.60	Secondary malignant neoplasm of ovary, unspecified side

C79.61	Secondary malignant neoplasm of right ovary
C79.62	Secondary malignant neoplasm of left ovary
C79.82	Secondary malignant neoplasm of genital organs
C79.89	Secondary malignant neoplasm of other specified sites
D39.0 D39.10 – D39.12 D39.7 – D39.9	Neoplasm of uncertain behavior of female genital organs
G89.3	Neoplasm related pain (acute) (chronic)
R19.00	Intra-abdominal and pelvic swelling, mass and lump, unspecified site
R19.01	Right upper quadrant abdominal swelling, mass and lump
R19.02	Left upper quadrant abdominal swelling, mass and lump
R19.03	Right lower quadrant abdominal swelling, mass and lump
R19.04	Left lower quadrant abdominal swelling, mass and lump
R19.05	Periumbilical swelling, mass or lump
R19.06	Epigastric swelling, mass or lump
R19.07	Generalized intra-abdominal and pelvic swelling, mass and lump
R19.09	Other intra-abdominal and pelvic swelling, mass and lump
R97.1	Elevated cancer antigen 125 [CA 125]
R97.8	Other abnormal tumor markers
Z85.40	Personal history of malignant neoplasm of unspecified female genital organ
Z85.41	Personal history of malignant neoplasm of cervix uteri
Z85.42	Personal history of malignant neoplasm of other parts of uterus
Z85.43	Personal history of malignant neoplasm of ovary
Z85.44	Personal history of malignant neoplasm of other female genital organs

CancerType ID®

CPT Coding

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 **(Investigational)**

Cutaneous Melanoma

0089U	Oncology (melanoma), gene expression profiling by RTqPCR, PRAME and LINC00518, superficial collection using adhesive patch(es) (**Investigational**)
0090U	0090U Oncology (cutaneous melanoma), mRNA gene expression profiling by RT-PCR of 23 genes (14 content and 9 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a categorical result (ie, benign, indeterminate, malignant) (**Investigational**)

Cxbladder™

CPT Coding

0012M	Oncology (urothelial), mRNA, gene expression profiling by real-time quantitative PCR of five genes (MDK, HOXA13, CDC2 [CDK1], IGFBP5, and XCR2), utilizing urine, algorithm reported as a risk score for having urothelial carcinoma **(Investigational)**
0013M	Oncology (urothelial), mRNA, gene expression profiling by real-time quantitative PCR of five genes (MDK, HOXA13, CDC2 [CDK1], IGFBP5, and CXCR2), utilizing urine, algorithm reported as a risk score for having recurrent urothelial carcinoma **(Investigational)**

DecisionDx-UM

CPT Coding

0081U	Oncology (uveal melanoma), mRNA, gene-expression profiling by real-time RT-PCR of 15 genes (12 content and 3 housekeeping genes), utilizing fine needle aspirate or formalin-fixed paraffin-embedded tissue, algorithm reported as risk of metastasis

Epidermal Growth Factor Receptor (EGFR) Analysis

CPT Coding

81235	EGFR (epidermal growth factor receptor) (e.g., non-small cell lung cancer) gene analysis, common variants (e.g., exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q)

Expanded Cancer Mutation Panels

CPT Coding

81445	Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, and RNA analysis when performed, 5-50 genes (eg, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, NRAS, MET, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed **(Investigational)**
81450	Targeted genomic sequence analysis panel, hematolymphoid neoplasm or disorder, DNA analysis, and RNA analysis when performed, 5-50 genes (eg, BRAF, CEBPA, DNMT3A, EZH2, FLT3, IDH1, IDH2, JAK2, KRAS, KIT, MLL, NRAS, NPM1, NOTCH1), interrogation for sequence variants, and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed **(Investigational)**
81455	Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA analysis, and RNA analysis when performed, 51 or greater genes (eg, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed **(Investigational)**

Fecal Calprotectin Testing

CPT Coding

83993	Calprotectin, fecal

ICD-10 Diagnosis Codes That Support Medical Necessity (83993)

K51.90	Ulcerative colitis, unspecified, without complications
K52.3	Indeterminate colitis
R19.8	Other specified symptoms and signs involving the digestive system and abdomen

Homocysteine Testing

CPT Coding

83090	Homocysteine **(Investigational)**

InflammaDry®

InflammaDry® may be reported with CPT code 83516-Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; qualitative or semiquantitative, multiple step method.

KRAS Testing

81275	KRAS (Kirsten rat sarcoma viral oncogene homolog) (eg, carcinoma) gene analysis; variants in exon 2 (eg, codons 12 and 13) **(Investigational)**
81276	KRAS (Kirsten rat sarcoma viral oncogene homolog) (eg, carcinoma) gene analysis; additional variant(s) (eg, codon 61, codon 146) **(Investigational)**

Long-Chain Omega-3 Fatty Acids in Red Blood Cell Membranes

CPT Coding

0111T	Long chain (C20-22) omega-3 fatty acids in red blood cell (RBC) membranes **(Investigational)**

Circulating Tumor Cells/Liquid Biopsy

CPT Coding

86152	Cell enumeration using immunologic selection and identification in fluid specimen (eg, circulating tumor cells in blood) **(Investigational)**
86153	Cell enumeration using immunologic selection and identification in fluid specimen (eg, circulating tumor cells in blood); physician interpretation and report, when required **(Investigational)**

0009U	Oncology (breast cancer), ERBB2 (HER2) copy number by FISH, tumor cells from formalin fixed paraffin embedded tissue isolated using image-based dielectrophoresis (DEP) sorting, reported as ERBB2 gene amplified or non-amplified **(Investigational)**
0091U	Oncology (colorectal) screening, cell enumeration of circulating tumor cells, utilizing whole blood, algorithm, for the presence of adenoma or cancer, reported as a positive or negative result (**Investigational**)

OVA1®

CPT Coding

81503	Oncology (ovarian), biochemical assays of five proteins (CA-125, apoliproprotein A1, beta-2 microglobulin, transferrin and pre-albumin), utilizing serum, algorithm reported as a risk score **(Investigational)**

Overa™

CPT Coding

0003U	Oncology (ovarian) biochemical assays of five proteins (apolipoprotein A-1, CA 125 II, follicle stimulating hormone, human epididymis protein 4, transferrin), utilizing serum, algorithm reported as a likelihood score **(Investigational)**

HE4 immunoassays & Kits

CPT Coding

86305	Human epididymis protein 4 (HE4) **(Investigational)**

Management of Pulmonary Nodules

0080U	Oncology (lung), mass spectrometric analysis of galectin-3-binding protein and scavenger receptor cysteine-rich type 1 protein M130, with five clinical risk factors (age, smoking status, nodule diameter, nodule-spiculation status and nodule location), utilizing plasma, algorithm reported as a categorical probability of malignancy (**Investigational**)
0092U	Oncology (lung), three protein biomarkers, immunoassay using magnetic nanosensor technology, plasma, algorithm reported as risk score for likelihood of malignancy (**Investigational**)

Multianalyte Assays for Chronic Liver Disease (FibroSURE® tests)

CPT Coding

81596	Infectious disease, chronic hepatitis C virus (HCV) infection, 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
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)
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)

NETest

CPT Coding

0007M	Oncology (gastrointestinal neuroendocrine tumors), real-time PCR expression analysis of 51 genes, utilizing whole peripheral blood, algorithm reported as a nomogram of tumor disease index **(Investigational)**

Pathwork Tissue of Origin®

CPT Coding

81504	Oncology (tissue of origin), microarray gene expression profiling of > 2000 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as tissue similarity scores **(Investigational)**

PreDx Diabetes Risk Score™

CPT Coding

81506	Endocrinology (type 2 diabetes), biochemical assays of seven analytes (glucose, HbA1c, insulin, hs-CRP, adiponectin, ferritin, interleukin 2-receptor alpha), utilizing serum or plasma, algorithm reporting a risk score (Investigational)

ROMA™

CPT Coding

81500	Oncology (ovarian), biochemical assays of two proteins (CA-125 and HE4), utilizing serum, with menopausal status, algorithm reported as a risk score **(Investigational)**
86316**	Immunoassay for tumor antigen; other antigen, quantitative (e.g., CA 50, 72-4, 549), each **(Investigational)**

****May be covered when meets the definition of medical necessity when used to report the Chromogranin A (CgA) test for neuroendocrine tumors (i.e. carcinoid tumors).**

Serum Biomarker Panel Testing for Systemic Lupus Erythematosus and Other Connective Tissue Diseases

CPT Coding

0062U	Autoimmune (systemic lupus erythematosus), IgG and IgM analysis of 80 biomarkers, utilizing serum, algorithm reported with a risk score **(Investigational)**

TERT Testing

81345	TERT (telomerase reverse transcriptase) (eg, thyroid carcinoma, glioblastoma multiforme) gene analysis, targeted sequence analysis (eg, promoter region) **(Investigational)**

ThyraMIR™

CPT Coding

0018U	Oncology (thyroid), microRNA profiling by RT-PCR of 10 microRNA sequences, utilizing fine needle aspirate, algorithm reported as a positive or negative result for moderate to high risk of malignancy

ICD-10 Diagnosis Codes That Support Medical Necessity (0018U)

C73	Malignant neoplasm of thyroid gland
D44.0	Neoplasm of uncertain behavior of thyroid gland

Thyroseq®

CPT Coding

0026U	Oncology (thyroid), DNA and mRNA of 112 genes, next-generation sequencing, fine needle aspirate of thyroid nodule, algorithmic analysis reported as a categorical result ("Positive, high probability of malignancy" or "Negative, low probability of malignancy")

ICD-10 Diagnosis Codes That Support Medical Necessity (0026U)

C73	Malignant neoplasm of thyroid gland
D44.0	Neoplasm of uncertain behavior of thyroid gland

Vectra®DA

CPT Coding

81490	Autoimmune (rheumatoid arthritis), analysis of 12 biomarkers using immunoassays, utilizing serum, prognostic algorithm reported as a disease activity

	score **(Investigational)**

VeriStrat®

CPT Coding

81538	Oncology (lung), mass spectrometric 8-protein signature, including amyloid A, utilizing serum, prognostic and predictive algorithm reported as good versus poor overall survival

ICD-10 Diagnosis Codes That Support Medical Necessity (81538)

C34.00 – C34.92	Malignant neoplasm of bronchus and lung

xTAG® Gastrointestinal Pathogen Panel (GPP)

CPT Coding

87505	Infectious agent detection by nucleic acid (DNA or RNA); gastrointestinal pathogen (e.g., Clostridium difficile, E. coli, Salmonella, Shigella, norovirus, Giardia), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types or subtypes, 3-5 targets **(Investigational)**
87506	Infectious agent detection by nucleic acid (DNA or RNA); gastrointestinal pathogen (e.g., Clostridium difficile, E. coli, Salmonella, Shigella, norovirus, Giardia), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types or subtypes, 6-11 targets **(Investigational)**
87507	Infectious agent detection by nucleic acid (DNA or RNA); gastrointestinal pathogen (e.g., Clostridium difficile, E. coli, Salmonella, Shigella, norovirus, Giardia), includes multiplex reverse transcription, when performed, and Multiplex amplified probe technique, multiple types or subtypes, 12-25 targets **(Investigational)**

Tumor markers that do not have a specific CPT or HCPCS code may be reported with a nonspecific code such as CPT code 86316.

REIMBURSEMENT INFORMATION:

Breast Tumor Markers

Reimbursement for CA 15-3 (CA 27.29 or Truquant RIA) (86300) is limited to twelve (12) tumor markers within a twelve (12) month period. Additional CA 15-3 (CA 27.29 or Truquant RIA) (86300) is subject to medical review for determination of medical necessity (e.g., clinical indications indicate additional tumor markers contribute to improved health outcomes or alters treatment and/or management).

During chemotherapy, the usual frequency for monitoring CA 15-3 (CA 27.29 or Truquant RIA) is once (1) every three (3) weeks to coincide with the chemotherapy cycles (usually 6 to 12 months). If there is clinical indication(s) of progression during the course of chemotherapy, a CA 15-3 (CA 27.29 or Truquant RIA) may be performed between cycles, up to a weekly interval. Patients who have completed chemotherapy generally have a monthly test for the first three (3) months, then every three (3) months afterwards. As the patient approaches a five (5) year disease free status, the frequency is reduced to every six (6) months. Patients who are at low

risk for recurrence (Stage I and selected Stage II) may be tested at three (3) month intervals, even during the period immediately following chemotherapy.

Cancer Antigen 125 (CA-125)

Reimbursement for CA-125 (86304) is limited to twelve (12) tumor markers within a twelve (12) month period. Additional tumor markers (86304) are subject to medical review for determination of medical necessity (e.g., clinical indications indicate additional tumor markers contribute to improved health outcomes or alter treatment or management).

The following information is required documentation to support medical necessity: physician history and physical, physician progress notes, laboratory studies, treatment plan, and physician operative report (if applicable).

LOINC Codes

Documentation Table	LOINC Codes	LOINC Time Frame Modifier Code	LOINC Time Frame Modifier Codes Narrative
Physician history and physical	28626-0	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim
Attending physician progress note	18741-9	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Plan of treatment	18776-5	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Laboratory studies	26436-6	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim
Physician operative report	28573-4	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products:

The following National Coverage Determinations (NCD) located at www.cms.gov were reviewed on the last guideline reviewed date: Tumor Antigen by Immunoassay-CA 125 (190.28); Tumor Antigen by Immunoassay-CA 15-3/CA 27.29 (190.29); Tumor Antigen by Immunoassay-CA19-9 (190.30).

The following decision memo located at cms.gov was reviewed on the last guideline reviewed date: Decision Memo for Next Generation Sequencing (NGS) for Medicare Beneficiaries with Advanced Cancer (CAG-00450N).

The following Local Coverage Determination (LCD) located at www.fcso.com was reviewed on the last guideline reviewed date:Noncovered Services (L33777).

The following were reviewed on the last guideline reviewed date: MolDX LCDs located at palmettogba.com.

DEFINITIONS:

A2-PAG: pregnancy-associated alpha-2 glycoprotein (a chemical made by some cancers, consisting of a combination of protein and sugars).

BCM: breast cancer mucin; a marker made by some breast cancers.

CAM17-1, CAM26, CAM29: also known as monoclonal anti-mucin antibody markers, are markers noted in certain cancers.

CAR-3: a marker that reacts with a special test using a specific protein testing substance called "monoclonal antibody AR-3".

Carbohydrate cancer antigens: CA 19-9, CA-125, CA 15-3/CA27-23, CA 242, CA 50, CA 72-4, CA 195, CA 549, M26, M29: these and other markers are a way to test for special markers on tumors, that are made of carbohydrates (a chemical that resembles a type of sugar).

CgA: a major protein of the granin family that has been described as a potential marker for neuroendrocrine tumors.

CellSearch®: a serum-based test that measures circulating tumor cells.

DU-PAN-2: a chemical (sialylated carbohydrate antigen) that may be found with some cancers.

FibroSpect II: serum marker panels for the diagnosis or clinical management of liver disease.

FibroSure: serum marker panels for the diagnosis or clinical management of liver disease.

GeneSearch BLN: an assay for the detection of greater than 0.2mm metastases in nodal tissue removed from sentinel lymph node biopsies of breast cancer patients.

HE4: an enzyme immunoassay for the quantitative determination of Human Epididymis Protein 4 (HE4) antigen in ovarian cancer.

LPA: lysophosphatidic acid; a chemical that has bee suggested as a possible test for ovarian cancer, body levels may be high in other cancers as well.

MCA: a chemical (Mucin-like Carcinoma-associated Antigen) that may be found in breast cancers.

MSA: a chemical (Mammary Serum Antigen) that may be found in breast cancers.

NSE: Neuron-Specific Enolase, a chemical made in the presence of some cancers.

Ova Check™: a serum-based test for the early detection of epithelial ovarian cancer.

OvaSure™: ovarian cancer-screening test that may be able to assess the presence of early stage ovarian cancer in high-risk woman.

Pathwork Tissue of Origin: a diagnostic test that may aid in the diagnosis of tumors with uncertain origins.

P-LAP: placental alkaline phosphatase, a chemical made in the presence of some cancers.

PNA/ELLA: peanut lectin bonding assay, a test for a certain tumor marker.

Proteogenomic Testing: involves the integration of proteomic, transcriptomic, and genomic information.

Proteomic Testing: the measurement of protein products *alone*, without integration of genomic and transcriptomic information.

SLEX, SLX: sialylated Lewis X-I antigen and sialylated SSEA-1 antigen.

SPAN-1: a sialylated carbohydrate antigen.

ST-439: a sialylated carbohydrate antigen.

TAG12, TAG 72, TAG 72.3: tumor associated glycoproteins; chemicals made by some cancers, consisting of a combination of protein and sugars.

TATI: tumor-associated trypsin inhibitor, a chemical made by the body, in the presence of some cancers.

TNF-a: tumor necrosis factor alpha, a chemical made by the immune system in the presence of some cancers.

TPA: tissue polypeptide antigen is a marker that may be present on some cancers.

RELATED GUIDELINES:

Assays of Genetic Expression in Tumor Tissue as a Technique to Determine Prognosis in Patients with Breast Cancer, 05-86000-26
Genetic Testing, 05-82000-28
KRAS, NRAS, and BRAF Variant Analysis in Metastatic Colorectal Cancer, 05-86000-28
Molecular Testing for the Management of Pancreatic Cysts, Barrett Esophagus, and Solid Pancreatic Lesions, 05-86000-27

OTHER:

None applicable.

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9. Blue Cross Blue Shield Association Medical Policy, 2.04.10 Identification of Microorganisms Using Nucleic Acid Probes, 01/19.

10. Blue Cross Blue Shield Association Medical Policy, 2.04.14, Cerebrospinal Fluid and Urinary Biomarkers of Alzheimer Disease, 01/19.

11. Blue Cross Blue Shield Association Medical Policy, 2.04.19 Pharmacogenomic and Metabolite Markers for Patients Treated With Thiopurines, 11/18.

12. Blue Cross Blue Shield Association Medical Policy, 2.04.23, Homocysteine Testing in the Screening, Diagnosis, and Management of Cardiovascular Disease and Venous Thromboembolic Disease, 01/19.

13. Blue Cross Blue Shield Association Medical Policy, 2.04.41 Noninvasive Techniques for the Evaluation and Monitoring of Patients with Chronic Liver Disease, 11/18.

14. Blue Cross Blue Shield Association Medical Policy, 2.04.45 Molecular Analysis for Targeted Therapy of Non-Small-Cell Lung Cancer, 10/18.

15. Blue Cross Blue Shield Association Medical Policy, 2.04.54 Gene Expression–Based Assays for Cancers of Unknown Primary, 04/19.

16. Blue Cross Blue Shield Association Medical Policy, 2.04.62, Multimarker Serum Testing Related to Ovarian Cancer, 01/19.

17. Blue Cross Blue Shield Association Medical Policy,2.04.66 Serum Biomarker Human Epididymis Protein 4, 01/19.

18. Blue Cross Blue Shield Association Medical Policy, 2.04.69 Fecal Calprotectin Testing, 01/19.

19. Blue Cross Blue Shield Association Medical Policy, 2.04.78 Molecular Markersin Fine Needle Aspirates of the Thyroid, 08/19.

20. Blue Cross Blue Shield Association Medical Policy, 2.04.84 Measurement of Serum Antibodies to Infliximab and Adalimumab , 11/18.

21. Blue Cross Blue Shield Association Medical Policy, 2.04.97 Microarray-Based Gene Expression Profile Testing for Multiple Myeloma Risk Stratification, 10/18.

22. Blue Cross Blue Shield Association Medical Policy, 2.04.100, Cardiovascular Risk Panels, 01/19.

23. Blue Cross Blue Shield Association Medical Policy, 2.04.115 Expanded Molecular Panel Testing of Cancers to Identify Targeted Therapies, 10/18.

24. Blue Cross Blue Shield Association Medical Policy, 2.04.119 Multibiomarker Disease Activity Blood Test for Rheumatoid Arthritis, 6/18.

25. Blue Cross Blue Shield Association Medical Policy, 2.04.120, Gene Expression Profiling for Uveal Melanoma, 03/19.

26. Blue Cross Blue Shield Association Medical Policy, 2.04.121, Miscellaneous Genetic and Molecular Diagnostic Tests, 07/18.

27. Blue Cross Blue Shield Association Medical Policy, 2.04.123, Serum Biomarker Panel Testing for Systemic Lupus Erythematosus and Other Connective Tissue Diseases, 06/18.

28. Blue Cross Blue Shield Association Medical Policy, 2.04.125 Proteomic Testing for Systemic Therapy in Non-Small-Cell Lung Cancer, 11/18.

29. Blue Cross Blue Shield Association Medical Policy, 2.04.140, Proteogenomic Testing for Patients With Cancer, 06/18.

30. Blue Cross Blue Shield Association Medical Policy, 2.04.141, Circulating Tumor DNA and Circulating Tumor Cells for Cancer Management (Liquid Biopsy), 08/19.

31. Blue Cross Blue Shield Association Medical Policy 2.04.142, Molecular Testing in the Management of Pulmonary Nodules, 06/19.

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33. Blue Cross Blue Shield Association Medical Policy, 2.04.146 Gene Expression Profiling for Cutaneous Melanoma, 06/19.

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Medical Policy & Coverage Committee on 07/25/19.

GUIDELINE UPDATE INFORMATION:

02/15/04	Developed separate guideline for non-covered tumor markers from the Tumor Markers guideline. Added program exception and added diagnoses [155.1, 156.1, 156.8, 156.9, 157.0 – 157.9, 197.8, 235.3, 235.5, V10.09] for 86301 for Medicare & More.
02/15/05	Deleted CA 19-9 from the investigational statement. Deleted Medicare program exception. Deleted the following from the when services are covered section of the MCG (per MPCC recommendation): Non-covered/investigational serum tumor markers may be covered if the individual subscriber has a benefit to cover non-covered/investigational services (refer to contract benefits). Updated related guidelines section.
08/15/07	Review, investigational status maintained, guideline reformatted, references updated.
09/15/08	Annual review: Position statements maintained. Description section and references updated.
08/15/09	Annual review: Guideline title changed, position statements updated, position statements from other tumor marker guidelines incorporated, description section, coding and references updated.
12/15/09	Updated the list of experimental/investigational tests.
01/01/10	Annual HCPCS coding update: added code 86305.
04/15/10	Updated the list of experimental/investigational tests and the Medicare Advantage program exception.
11/15/10	Revision; updated the list of experimental/investigational tests and added related ICD-10 codes.
08/15/11	Revision; Medicare Advantage and references updated; formatting changes.
01/01/12	Annual HCPCS update. Added CPT codes 0279T, 0280T.
04/01/12	Quarterly HCPCS update. Deleted HCPCS code S3711.
08/24/12	Reimbursement section updated.
10/15/12	Serum Antibodies for the Diagnosis of Inflammatory Bowel Disease position statement removed and added to the Genetic Testing guideline; reimbursement section updated.
11/15/12	List of experimental/investigational tests updated.
01/01/13	Annual HCPCS update. Added codes 81500, 81503, 81506, 86152, 86153, 0001M-0003M; deleted codes 0279T & 0280T.Updated position statement section and references.
02/15/13	Revision; position statement section and references updated.
03/15/13	Revision; position statement section including the list of investigational tests and references updated; title change.
05/15/13	Revision; position statement, billing/coding, program exception, and reference sections updated.
09/15/13	Revision; position statement section and references updated.
01/01/14	Annual HCPCS update. Added code 81504.
02/15/14	Revision; position statement section, Medicare program exception, and references updated.
06/15/14	Revision; position statement section, Coding, Medicare program exception, and references updated.
07/01/14	Quarterly HCPCS update. Added code 0007M.
10/15/14	Revision;Update the position statement and coding sections, program exception, and references.
01/01/15	Annual HCPCS/CPT update. Added codes 87505-87507.
06/15/15	Revision; position statement section, billing/coding, and references updated.
11/01/15	Revision: ICD-9 Codes deleted.
11/15/15	Revision; program exception and references updated.
01/01/16	Annual HCPCS/CPT update; codes 81490, 81538, 81540, 81545 added, code 0103T deleted.
01/01/16	Annual HCPCS/CPT update; codes 81490, 81538, 81540, 81545 added, code 0103T deleted.
03/15/16	Revision; position statement section, codeing and references updated.
09/15/16	Revision; position statement section, program exception, and references updated.

11/15/16	Revision; position statement section and references updated.
12/15/16	Revision; position statement, coding, and references updated.
02/01/17	Coding Update; new code 0003U added; investigational test list updated.
02/15/17	Revision; position statements, coding, and references updated.
03/15/17	Revision; Multianalyte assays for chronic liver disease position statements revised; coding and references updated.
04/15/17	Revision; Uveal Melanoma position statement added and references updated.
06/15/17	Revision; test names added to Biochemical Markers of Alzheimer's Disease & Circulating Tumor DNA position statements section; investigational test list updated.
07/15/17	Revision; Investigational test list updated.
08/01/17	Coding update; Added code 0009U.
12/15/17	Revision; Position statement section updated including the addition of ROS1 coverage statement; program exception and references updated.
01/01/18	Annual CPT/HCPCS update. Added code 0026U.
02/15/18	Revision; Circulating tumor DNA position statement added; OVA1, Overa, and ROMA tests position statement added and references updated.
04/01/18	Quarterly HCPCS/CPT update. Added codes 0012M and 0013M.
05/15/18	Revision; position statements, coding, and references updated.
09/15/18	Revision; position statements and references updated.
10/01/18	Quarterly HCPCS/CPT update. Added code 0062U.
12/15/18	Revision; Guardant360 test and OncoBEAM test added to the circulating tumor DNA for management of NSCLC position statement; investigational statement for microarray-based gene expression profile testing for multiple myeloma added; molecular analysis for targeted therapy of NSCLC position statements updated; coding, and references updated.
01/01/19	Annual CPT/HCPCS coding update. Added codes 81345, 81596; deleted code 0001M.
02/15/18	Revision; Fecal calprotectin testing position revised; coding and references updated.
05/15/19	Revision; Serum Biomarker Human Epididymis Protein 4 position statement added; references updated.
06/15/19	Revision; Xpresys test deleted (test no longer on the market).
07/01/19	Quarterly CPT/HCPCS update; Added codes 0089U-0092U. Revision; Gene expression profiling for cutaneous melanoma & molecular testing in the management of pulmonary nodules position statements added; OVA1 status maintained; coding and references updated.
08/15/19	Revision; Afirma test name updated.