Kansas City

PAYMENT INTEGRITY COMPLIANCE
Serum Tumor Markers for Malignancies

POLICY INFORMATION			
Policy Number:	POL-PP- 310 AHS – G2124 – Serum Tumor Markers for Malignancies	Original Effective Date:	07/01/2025
Version Number:	001	Revision Date:	
Policy Status:	Active	Next Revision Date:	07/01/2026

Blue KC reserves the right to review and revise these policies when necessary. When there is an update, we will publish the most current policy to: https://providers.bluekc.com/ContactUs/PaymentPolicies.

PROVIDER/ENTITY IMPACTED					
☒ PROFESSIONAL	☒ FACILITY	☐ DME	☐ AMBULATORY SURGERY	☒ LAB	☐ OTHER

LINES OF BUSINESS IMPACTED						
☒ COMMERCIAL	☒ BLUE MEDICARE ADVANTAGE	☒ ACA QHP[1]	☒ SMALL GROUP ACA	☒ JAA[2]	☒ FEP[3]	☐ DENTAL

[1] ACA QHP: Affordable Care Act Qualified Health Plan for Individual/Family [2] JAA: Joint Administrative Account [3] FEP: Federal Employee Program

Disclaimer

Blue KC has developed Provider Payment Policies to provide guidance on payment methodologies as they pertain to submitted claims. These policies are written following industry standard recommendations from sources such as:

- Current Procedural Terminology
- Centers for Medicare and Medicaid
- American Medical Association
- National Correct Coding Initiative
- Other professional organizations and societies

Coverage of any service is determined by date of service, a member's eligibility and benefit limits for the service or services rendered, all terms of the Provider Service Agreement, and other standards of coding rules and guidelines.
Final payment is subject to the application of claims adjudication and edits common to the industry.

For confirmation of which services may be eligible for coverage and description of when medical services are considered medically necessary, not medically necessary or investigational, please contact:

- Blue KC Provider Hotline for Commercial lines of Business 816-395-3929
- Affordable Care Act Provider Hotline 866-859-3822
- Blue Medicare Advantage Provider Hotline 866-508-7140

In the event of a conflict between any policies, the Member's coverage document will govern.

Description/Application

Circulating tumor biomarkers are substances detected in the blood, urine, or other body fluids that are either produced by a tumor itself or in response to its presence. These biomarkers can be used to help detect, diagnose, stage, and manage some types of cancer, because their amounts are typically elevated in individuals harboring a tumor (Hottinger & Hormigo, 2011; NCI, 2023). There are currently dozens of tumor markers in common use; this laboratory policy addresses tumor markers which may be measured in an individual's serum.

Terms such as male and female are used when necessary to refer to sex assigned at birth.

The following management of serum tumor markers is built from recommendations from the National Comprehensive Cancer Network (NCCN) Biomarkers Compendium®, which contains information "designed to support decision making around the use of biomarker testing in patients with cancer. The NCCN Biomarkers Compendium® is updated in conjunction with the NCCN Guidelines on a continual basis" (NCCN, 2023).

Policy

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request.

Note: Except for where otherwise specified in the coverage criteria below, quarterly measurement of designated serum tumor markers is permitted for follow-up, monitoring, and/or surveillance

Measurement of the following serum tumor markers **may be reimbursed** for the following indications:

Serum Tumor Marker	Indication
Alkaline phosphatase (ALP)	Bone neoplasms: **workup**; **during treatment**; **surveillance** Systemic light chain amyloidosis: **initial diagnostic workup**
Alpha fetoprotein (AFP)	Hepatocellular carcinoma: **screening**; **workup** for confirmed HCC; **surveillance** (every 3-6 months for 2 years, then every 6 months) Intrahepatic cholangiocarcinoma: **workup** for isolated intrahepatic mass Occult primary: **additional workup** for localized adenocarcinoma or carcinoma not otherwise specified; liver, mediastinum, or retroperitoneal mass Ovarian cancer/fallopian tube cancer/primary peritoneal cancer: **initial workup**; **during primary chemotherapy**; **monitoring/follow-up for complete response** (as clinically indicated) Ovarian cancers (less common): – Carcinosarcoma (malignant mixed mullerian tumors): **monitoring/follow-up** – Clear cell carcinoma of the ovary: **monitoring/follow-up** – Grade 1 endometrioid carcinoma: **monitoring/follow-up** – Mucinous neoplasms of the ovary: **monitoring/follow-up** – Low-grade serous carcinoma: **monitoring/follow-up** Ovarian cancers:

Serum Tumor Marker	Indication
	– Borderline epithelial tumors: **monitoring/follow-up** (every visit if initially elevated) – Malignant germ cell tumors: **surveillance** (no more than every 2 months for the first 2 years, every 4 months in years 3-5, and then annually after year 5) – Malignant sex cord stromal tumors: **surveillance** if clinically indicated. If done, frequency based on stage (i.e., 6-12 months if early-stage, low-risk disease; 4-6 months if high-risk disease)
	Testicular cancer – nonseminoma: **post-diagnostic workup**; **risk classification**; **surveillance** (no more than every 2 months)
	Testicular cancer - pure seminoma: **initial diagnostic workup**; **post-diagnostic workup**; **risk classification**; **post-treatment surveillance** (no more than every 2 months)
	Thymomas and thymic carcinomas: **initial evaluation**, if appropriate
Beta-2 microglobulin (B2M)	B-cell lymphomas (Castleman disease; diffuse large B-cell; follicular [grade 1-2]; HIV-related; lymphoblastic; mantle cell): **workup**
	Chronic lymphocytic leukemia/small lymphocytic lymphoma: **workup**; for **prognostic** and/or **therapy determination**
	Multiple myeloma: **initial diagnostic workup**; **follow-up/surveillance** (as needed) for solitary plasmacytoma or solitary plasmacytoma with minimal marrow involvement
	Systemic light chain amyloidosis: **initial diagnostic workup**
	Waldenström macroglobulinemia / lymphoplasmacytic lymphoma: **workup**
Beta human chorionic gonadotropin (beta-HCG)	Gestational trophoblastic neoplasia: **initial workup**; **during and post treatment** (no more than weekly); **follow-up/surveillance** (no more than monthly for 12 months)
	Occult primary: **additional workup** for localized adenocarcinoma or carcinoma not otherwise specified; individuals < 65 years of age with testes presenting with retroperitoneal mass
	Ovarian cancer/fallopian tube cancer/primary peritoneal cancer: **initial workup**; **during primary chemotherapy**; **monitoring/follow-up for complete response** (as clinically indicated)
	Ovarian cancers: – Borderline epithelial tumors: **monitoring/follow-up** (every visit if initially elevated) – Malignant germ cell tumors: **surveillance** (no more than every 2 months for the first 2 years, every 4 months in years 3-5, and then annually after year 5) – Malignant sex cord stromal tumors: **surveillance** if clinically indicated. If done, frequency based on stage (i.e., 6-12 months if early-stage, low-risk disease; 4-6 months if high-risk disease)
	Testicular cancer – nonseminoma: **post-diagnostic workup**; **risk classification**; **surveillance** (no more than every 2 months)

Serum Tumor Marker	Indication
	Testicular cancer - pure seminoma: **initial diagnostic workup**; **post-diagnostic workup**; **risk classification**; **post-treatment surveillance** (no more than every 2 months)
	Thymomas and thymic carcinomas: **initial evaluation**, if appropriate
BNP or NT-proBNP	Multiple myeloma: **initial diagnostic workup**
	Systemic light chain amyloidosis: **initial diagnostic workup**
Calcitonin (CALCA)	Adenocarcinoma, and anaplastic/undifferentiated epithelial tumors: **workup**
	Medullary carcinoma: **additional workup**; **post-surgical evaluation**; **monitoring**; **surveillance** (2-3 months postoperative, then every 6-12 months)
	Multiple endocrine neoplasia, type 2: **at diagnosis** (clinical evaluation) for medullary thyroid cancer
	Occult primary (unknown primary cancer): **workup**
Cancer antigen 15-3 and 27.29 (CA 15-3 and 27.29)	Breast cancer (invasive): **monitoring** metastatic disease
	Occult primary: suspected metastatic malignancy: **initial workup**; assessing disease **prognosis**; **monitoring/follow-up** for response
Cancer antigen 19-9 (CA 19-9)	Ampullary adenocarcinoma: **workup**; **surveillance** (every 3-6 months for 2 years, then every 6-12 months for up to 5 years as clinically indicated) for resected ampullary cancer, stage I-III
	Appendiceal adenocarcinoma: **workup** to establish baseline. Abnormal measurements should be trended
	Extrahepatic cholangiocarcinoma: **workup** to establish baseline; **monitoring**
	Gallbladder cancer: **workup** to establish baseline; **monitoring**; **surveillance** (as clinically indicated), post-resection
	Intrahepatic cholangiocarcinoma: **workup** to establish baseline; **monitoring**
	Occult primary: workup to establish baseline; assessing disease **prognosis**; **monitoring/follow-up** for response
	Ovarian cancer/fallopian tube cancer/primary peritoneal cancer: **initial workup**; **during primary chemotherapy**; **monitoring/follow-up for complete response** (as clinically indicated)
	Ovarian cancers (less common): – Carcinosarcoma (malignant mixed mullerian tumors): **workup** – Clear cell carcinoma of the ovary: **workup** – Grade 1 endometrioid carcinoma: **workup** – Low-grade serous carcinoma: **workup** – Mucinous neoplasms of the ovary: **workup**
	Ovarian cancers – Borderline epithelial tumors: **monitoring/follow-up** (every visit if initially elevated) – Malignant germ cell tumors: **surveillance** (no more than every 2 months for the first 2 years, every 4 months in years 3-5, and then annually after year 5) – Malignant sex cord stromal tumors: **surveillance** if clinically indicated.

Serum Tumor Marker	Indication
	If done, frequency based on stage (i.e., 6-12 months if early-stage, low-risk disease; 4-6 months if high-risk disease) – Mucinous carcinoma of the ovary: **additional workup** (if not previously done)
	Pancreatic adenocarcinoma: **workup** to establish baseline; **monitoring**; **post-operative**, **post-adjuvant treatment surveillance** (every 3-6 months for 2 years, then every 6-12 months as clinically indicated)
	Small bowel adenocarcinoma: **workup** to establish baseline; **post-treatment surveillance** (every 3-6 months for 2 years, then every 6 months for a total of 5 years); **at metastasis or recurrence**
Cancer antigen 125 (CA-125)	Appendiceal adenocarcinoma: **workup** to establish baseline
	Endometrial carcinoma: **additional workup**; **surveillance** (if initially elevated)
	Lynch syndrome: **surveillance**
	Occult primary: **additional workup** for adenocarcinoma or carcinoma not otherwise specified, in those with a uterus and/or ovaries present
	Ovarian cancer/fallopian tube cancer/primary peritoneal cancer: **initial workup**; **during primary chemotherapy**; **monitoring/follow-up for complete response** (as clinically indicated)
	Ovarian cancers (less common): – Carcinosarcoma (malignant mixed mullerian tumors): **monitoring/follow-up** – Clear cell carcinoma of the ovary: **monitoring/follow-up** – Mucious neoplasms of the ovary: **monitoring/follow-up** – Grade 1 endometrioid carcinoma: **monitoring/follow-up** – Low-grade serous carcinoma: **monitoring/follow-up**
	Ovarian cancers: – Borderline epithelial tumors: **monitoring/follow-up** (every visit if initially elevated) – Malignant germ cell tumors: **surveillance** (no more than every 2 months for the first 2 years, every 4 months in years 3-5, and then annually after year 5) – Malignant sex cord stromal tumors: **surveillance** if clinically indicated. If done, frequency based on stage (i.e., 6-12 months if early-stage, low-risk disease; 4-6 months if high-risk disease)
	Peritoneal mesothelioma: **initial evaluation**
	Uterine neoplasms: **initial workup**
Carcinoembryonic antigen (CEA)	Appendiceal adenocarcinoma: **workup** to establish baseline; **monitoring**; **post-treatment surveillance**
	Breast cancer (invasive): **Monitoring** metastatic disease
	Colon cancer: **workup** to establish baseline; **monitoring**; **surveillance** (every 3-6 months for 2 years, then every 6 months for a total of 5 years)
	Extrahepatic cholangiocarcinoma: **workup** to establish baseline; **monitoring**
	Gallbladder cancer: **workup** to establish baseline; **monitoring**; **surveillance;**

Serum Tumor Marker	Indication
	monitoring of adjuvant treatment (as clinically indicated), **post-resection**
	Intrahepatic cholangiocarcinoma: **workup** to establish baseline; **monitoring**
	Medullary carcinoma: **diagnosis and additional workup**; **monitoring**; **post-surgical surveillance** (2-3 months postoperative, then every 6-12 months)
	Multiple endocrine neoplasia, type 2: **at diagnosis** (clinical evaluation) for medullary thyroid cancer
	Ovarian cancer/fallopian tube cancer/primary peritoneal cancer: **initial workup**; **during primary chemotherapy**; **monitoring/follow-up for complete response** (as clinically indicated)
	Ovarian cancers (less common): – Carcinosarcoma (malignant mixed mullerian tumors: **monitoring/follow-up** – Clear cell carcinoma of the ovary: **monitoring/follow-up** – Grade 1 endometrioid carcinoma: **monitoring/follow-up** – Low-grade serous carcinoma: **monitoring/follow-up** – Mucinous neoplasms of the ovary: **monitoring/follow-up**
	Ovarian cancers : – Borderline epithelial tumors: **monitoring/follow-up** (every visit if initially elevated); **post-adjuvant treatment** – Malignant germ cell tumors: **surveillance** (no more than every 2 months for the first 2 years, every 4 months in years 3-5, and then annually after year 5) – Malignant sex cord stromal tumors: **surveillance** if clinically indicated. If done, frequency based on stage (i.e., 6-12 months if early-stage, low-risk disease; 4-6 months if high-risk disease) – Mucinous carcinoma of the ovary: **additional workup** (if not previously done)
	Rectal cancer: **workup** to establish baseline; **monitoring**; **surveillance** (every 3-6 months for 2 years, then every 6 months for a total of 5 years)
	Small bowel adenocarcinoma: **workup** to establish baseline; **post-treatment surveillance** (every 3-6 months for 2 years, then every 6 months for a total of 5 years)
Inhibin (INHA)	Adrenocortical carcinoma: **workup**
	Ovarian cancer/fallopian tube cancer/primary peritoneal cancer: **initial workup**; **during primary chemotherapy**; **monitoring/follow-up for complete response** (as clinically indicated)
	Ovarian cancers (less common): – Carcinosarcoma (malignant mixed mullerian tumors: **monitoring/follow-up** – Clear cell carcinoma of the ovary: **monitoring/follow-up** – Grade 1 endometrioid carcinoma: **monitoring/follow-up** – Low-grade serous carcinoma: **monitoring/follow-up** – Mucinous neoplasms of the ovary: **monitoring/follow-up**

Serum Tumor Marker	Indication
	Ovarian cancers: – Borderline epithelial tumors: **monitoring/follow-up** (every visit if initially elevated) – Malignant Germ cell tumors: **surveillance** (no more than every 2 months for the first 2 years, every 4 months in years 3-5, and then annually after year 5) – Malignant sex cord stromal tumors: **surveillance** if clinically indicated. If done, frequency based on stage (i.e., 6-12 months if early-stage, low-risk disease; 4-6 months if high-risk disease)
Lactate dehydrogenase (LDH)	B-cell lymphomas (Burkitt; Castleman disease; diffuse large B-cell; extranodal marginal zone lymphoma of nongastric sites [noncutaneous] and of the stomach; follicular [grade 1-2]; HIV-related; lymphoblastic; mantle cell; nodal marginal zone;pediatric aggressive mature; post-transplant lymphoproliferative disorders; primary cutaneous; splenic marginal zone): **workup**
	Bone neoplasms: **workup**
	Chronic lymphocytic leukemia/small lymphocytic lymphoma: **workup**, and at transformation or histologic progression (if applicable)
	Hairy cell leukemia: **workup**
	Kidney cancer: **initial workup**
	Melanoma (cutaneous and uveal): **workup** for metastatic or recurrent disease
	Multiple myeloma: **initial workup**; **surveillance** (as needed) post primary treatment for solitary plasmacytoma or solitary plasmacytoma with minimal marrow involvement
	Ovarian cancer/fallopian tube cancer/primary peritoneal cancer: **initial workup**; **during primary chemotherapy**, **monitoring/follow-up for complete response** (as clinically indicated)
	Ovarian cancers (less common): – Carcinosarcoma (malignant mixed mullerian tumors: **monitoring/follow-up** – Clear cell carcinoma of the ovary: **monitoring/follow-up** – Grade 1 endometrioid carcinoma: **monitoring/follow-up** – Low-grade serous carcinoma: **monitoring/follow-up** – Mucinous neoplasms of the ovary: **monitoring/follow-up**
	Ovarian cancers: – Borderline epithelial tumors: **monitoring/follow-up** (every visit if initially elevated) – Malignant germ cell tumors: **surveillance** (no more than every 2 months for the first 2 years, every 4 months in years 3-5, and then annually after year 5) – Malignant sex cord stromal tumors: **surveillance** if clinically indicated. If done, frequency based on stage (i.e., 6-12 months if early-stage, low-risk disease; 4-6 months if high-risk disease)
	Primary cutaneous lymphomas (mycosis fungoides/Sezary syndrome; primary

Serum Tumor Marker	Indication
	cutaneous CD30+ T-cell lymphoproliferative disorders): **workup**
	Systemic light chain amyloidosis: **initial diagnostic workup**
	Systemic mastocytosis: **initial diagnostic workup**
	T-cell lymphomas (adult T-cell; breast implant-associated ALCL; extranodal NK/T-cell; hepatosplenic; peripheral; T-cell prolymphocytic leukemia): **workup**; **staging** (breast implant-associated ALCL only)
	Testicular cancer – nonseminoma: **post-diagnostic workup**; **risk classification**; **surveillance** (no more than every 2 months)
	Testicular cancer – pure seminoma: **initial diagnostic workup**; **post-diagnostic workup**; **risk classification**; **post-treatment surveillance** (no more than every 2 months)
	Waldenström macroglobulinemia / lymphoplasmacytic lymphoma: **workup**
Serum free light chain	Multiple myeloma: **initial diagnostic workup**; **surveillance** (up to once per month)
	Systemic light chain amyloidosis: **initial diagnostic workup**
Troponin T	Systemic light chain amyloidosis: **initial diagnostic workup**
Tryptase	Systemic mastocytosis: **initial diagnosis**

The following does not meet coverage criteria due to a lack of available published scientific literature confirming that the test(s) is/are required and beneficial for the diagnosis and treatment of an individual's illness.

For all other cancer indications not discussed above, use of the above biomarkers (alone or in a panel of serum tumor markers) **may not be reimbursed.**

All other serum tumor markers not addressed above (alone or in a panel of serum tumor markers) **may not be reimbursed.**

The screening and detection of cancer, analysis of proteomic patterns in serum **may not be reimbursed.**

Coding

CPT	Code Description
81479	Unlisted molecular pathology procedure
81500	Oncology (ovarian), biochemical assays of two proteins (CA-125 and HE4), utilizing serum, with menopausal status, algorithm reported as a risk score Proprietary test: Risk of Ovarian Malignancy Algorithm (ROMA)™ Lab/manufacturer: Fujirebio Diagnostics
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 Proprietary test: OVA1™ Lab/manufacturer: Vermillion, Inc
81538	Oncology (lung), mass spectrometric 8-protein signature, including amyloid A, utilizing serum, prognostic and predictive algorithm reported as good versus poor overall survival

CPT	Code Description
	Proprietary test: VeriStrat® Lab/manufacturer: Biodesix, Inc
81599	Unlisted multianalyte assay with algorithmic analysis
82105	Alpha-fetoprotein (AFP); serum
82107	Alpha-fetoprotein (AFP); AFP-L3 fraction isoform and total AFP (including ratio)
82232	Beta-2 microglobulin
82308	Calcitonin
82378	Carcinoembryonic antigen (CEA)
83520	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; quantitative, not otherwise specified
83521	Immunoglobulin light chains (i.e., kappa, lambda), free, each
83615	Lactate dehydrogenase (LD), (LDH);
83789	Mass spectrometry and tandem mass spectrometry (e.g., MS, MS/MS, MALDI, MS-TOF, QTOF), non-drug analyte(s) not elsewhere specified, qualitative or quantitative, each specimen
83880	Natriuretic peptide
83950	Oncoprotein; HER-2/neu
83951	Oncoprotein; des-gamma-carboxy-prothrombin (DCP)
84075	Phosphatase, alkaline
84078	Phosphatase, alkaline; heat stable (total not included)
84080	Phosphatase, alkaline; isoenzymes
84484	Troponin, quantitative
84702	Gonadotropin, chorionic (hCG); quantitative
84703	Gonadotropin, chorionic (hCG); qualitative
84704	Gonadotropin, chorionic (hCG); free beta chain
84999	Unlisted chemistry procedure
86300	Immunoassay for tumor antigen, quantitative; CA 15-3 (27.29)
86301	Immunoassay for tumor antigen, quantitative; CA 19-9
86304	Immunoassay for tumor antigen, quantitative; CA 125
86305	Human epididymis protein 4 (HE4)
86316	Immunoassay for tumor antigen, other antigen, quantitative (eg, CA 50, 72-4, 549), each
86336	Inhibin A
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 Proprietary test: Overa™ (OVA1 Next Generation) Lab/manufacturer: Aspira Labs, Inc, Vermillion, Inc
0092U	Oncology (lung), three protein biomarkers, immunoassay using magnetic nanosensor technology, CPTsma, algorithm reported as risk score for likelihood of malignancy Proprietary test: REVEAL Lung Nodule Characterization Lab/Manufacturer: MagArray, Inc
0163U	Oncology (colorectal) screening, biochemical enzyme-linked immunosorbent assay (ELISA) of 3 plasma or serum proteins (teratocarcinoma derived growth factor-1 [TDGF-1, Cripto-1], carcinoembryonic antigen [CEA], extracellular matrix protein [ECM]), with demographic data (age, gender, CRC-screening compliance) using a

CPT	Code Description
	proprietary algorithm and reported as likelihood of CRC or advanced adenomas Proprietary test: BeScreened™-CRC Lab/Manufacturer: Beacon Biomedical Inc
0404U	Oncology (breast), semiquantitative measurement of thymidine kinase activity by immunoassay, serum, results reported as risk of disease progression Proprietary test: Divitum®Tka Lab/Manufacturer: Biovica Inc
G0327	Colorectal cancer screening; blood-based biomarker

References and Resources

Policy Number	Policy Title
	Not applicable

Related Documents

Avalon Medical Policy AHS – G2124 – Serum Tumor Markers for Malignancies

Revision History

Version	Date	Summary of Revisions
001	06/01/2025	Initial version