Harvard Pilgrim Health Care | TUFTS Health Plan

Point32Health companies

Payment Policy:

Laboratory: Serum Tumor Markers for Malignancies

Effective date: Nov. 1, 2025

Applies to:

Commercial Products

☒ Harvard Pilgrim Health Care Commercial products
☐ Tufts Health Plan Commercial products

Public Plans Products

☐ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product)
☐ Tufts Health Together – MassHealth Accountable Care Partnership Plans
☐ Tufts Health RITogether – A Rhode Island Medicaid Plan
☐ Tufts Health One Care – A dual-eligible product

Senior Products

☐ Tufts Health Plan Senior Care Options (SCO) (a dual-eligible product)
☐ Tufts Medicare Preferred HMO/PPO (Medicare Advantage products)

Policy

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. 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."

Indications and/or Limitations of Coverage

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 biomarkers is permitted for follow-up, monitoring, and/or surveillance

1. Measurement of the following serum biomarkers **MEETS COVERAGE CRITERIA** for the following indications:

Serum Biomarker	Indication
Alkaline phosphatase (ALP)	Bone neoplasms: workup for osteosarcoma
	Melanoma (uveal): workup for distant metastatic disease
	Systemic light chain amyloidosis: initial diagnostic workup to assess organ involvement for suspected SLCA
Alpha fetoprotein (AFP)	Hepatocellular carcinoma: screening for at-risk individuals due to Child-Turcotte-Pugh A or B cirrhosis or hepatitis B infection; 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 adenocarcinoma or carcinoma not otherwise specified; with a clinical presentation in the liver or mediastinum, or for individuals <65 years of age with a retroperitoneal mass
	Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer: initial workup; for

Serum Biomarker	Indication
	individuals with a suspicious mass found by palpation or imaging; monitoring prior to each cycle of chemotherapy; monitoring/follow-up for patients not receiving treatment (every 2-4 months for 2 years; every 3-6 months for 3 years; annually after year 5)
	Ovarian cancers (less common): initial workup for newly diagnosed ovarian cancer; monitoring/follow-up for recurrence Less common ovarian cancers (additional surveillance recommendations): – Malignant germ cell tumors: surveillance (every 2 months , in a year every 3 months in year 2, every 6 months in year 3; year 4 and beyond, annual testing up to year 10) – 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: initial diagnostic workup for a suspicious testicular mass; post-diagnostic workup; post-orchiectomy; follow-up for nonseminoma (no more than every 2 months); follow-up for pure seminoma (no more than every 3 months)
	Thymomas and thymic carcinomas: initial evaluation, for individuals with a mediastinal mass
Beta-2 microglobulin (B2M)	B-cell lymphomas (classic follicular, diffuse large B-cell;: HIV-related; lymphoblastic; mantle cell): additional workup for specified B-cell lymphomas
	Castleman Disease: additional workup with established diagnosis
	Chronic lymphocytic leukemia/small lymphocytic lymphoma: additional workup with established diagnosis; for prognostic and/or therapy determination
	Multiple myeloma: initial diagnostic workup;
	Systemic light chain amyloidosis: initial diagnostic workup to assess organ involvement for suspected SLCA
	Waldenström macroglobulinemia / lymphoplasmacytic lymphoma: additional workup with established diagnosis
BNP or NT-proBNP	Multiple myeloma: initial diagnostic workup Systemic light chain amyloidosis: initial diagnostic workup to assess organ involvement for suspected SLCA
Calcitonin (CALCA)	Head and neck cancer – occult primary: additional workup for squamous cell carcinoma, adenocarcinoma, and anaplastic/undifferentiated epithelial tumors of the neck
	Medullary carcinoma: additional workup; with established diagnosis; surveillance (every 6-12 months)
	Multiple endocrine neoplasia, type 2: at diagnosis (clinical evaluation) for medullary thyroid cancer
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
Cancer antigen 19-9 (CA 19-9)	Ampullary adenocarcinoma: additional workup; with established diagnosis surveillance for resected ampullary cancer (every 3-6 months for 2 years, every 6-12 months for up to 5 years as clinically indicated)
	Appendiceal adenocarcinoma: workup to establish baseline. when imaging suggests appendiceal neoplasm or cancer or when there is a confirmed appendiceal neoplasm or cancer; workup for recurrence (3-6 months after CT imaging);surveillance (every 6-12 months for 2 years; annually up to 10 years)
	Extrahepatic cholangiocarcinoma: workup to establish baseline; for individuals with abdominal pain, jaundice, abnormal liver function tests, or obstruction or abnormality on imaging
	Gallbladder cancer: workup to establish baseline;: for individuals with jaundice or a mass on imaging; post-operative workup of a suspicious mass; surveillance (as clinically indicated), post-resection
	Intrahepatic cholangiocarcinoma: workup to establish baseline; for an isolated intrahepatic mass
	Occult primary: suspected metastatic malignancy: initial workup
	Epithelial Ovarian cancer/fallopian tube cancer/primary peritoneal cancer: initial workup; for individuals with a suspicious mass found by palpation or imaging; monitoring prior to each cycle of chemotherapy; monitoring/follow-up for patients not receiving treatment (every 2-4 months for 2

Serum Biomarker	Indication
	years; every 3-6 months for 3 years; annually after year 5)
	Ovarian cancers (less common): initial workup for newly diagnosed ovarian cancer; monitoring/follow-up for recurrence Less common ovarian cancers (additional surveillance recommendations): – Malignant germ cell tumors: surveillance (every 2 months in year 1, every 3 months in year2, every 6 months in year 3; year 4 and beyond, annual testing up to year 10) – 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)
	Pancreatic adenocarcinoma: **workup** to establish baseline; **monitoring** when there is either a clinical suspicion of pancreatic cancer with suspicious imaging or evidence of dilated pancreatic and/or bile duct (stricture) and when no metastatic disease is detected; **post-operative, post-adjuvant treatment surveillance** (every 3-6 months for 2 years, then every 6-12 months as clinically indicated)as appropriate
	Small bowel adenocarcinoma: additional **workup** to establish baselinewith established diagnosis; **post-treatment surveillance** (every 3-6 months for 2 years, then every 6 months for a total of 5 years); at metastasis or recurrence **additional workup** for metastatic adenocarcinoma
Cancer antigen 125 (CA-125)	Appendiceal adenocarcinoma: workup to establish baseline when imaging suggests appendiceal neoplasm or cancer or when there is a confirmed appendiceal neoplasm or cancer; workup for recurrence (3-6 months after CT imaging); surveillance (every 6-12 months for 2 years; annually up to 10 years.
	Endometrial carcinoma: additional workup; surveillance (if initially elevated)
	Occult primary: initial workup, for suspected metastatic malignancy, additional workup for adenocarcinoma or carcinoma not otherwise specified, (in those with a uterus and/or ovaries present) with a clinical presentation in the peritoneal/ascites or inguinal nodes
	Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer: initial workup; for individuals with a suspicious mass found by palpation or imaging; monitoring prior to each cycle of chemotherapy; monitoring/follow-up for patients not receiving treatment (every 2-4 months for 2 years; every 3-6 months for 3 years; annually after year 5)
	Ovarian cancers (less common): initial workup for newly diagnosed ovarian cancer; monitoring/follow-up for recurrence Less common ovarian cancers (additional surveillance recommendations): – Malignant germ cell tumors: surveillance (every 2 months in year 1, every 3 months in year 2, every 6 months in year 3, year 4 and beyond, and then annually up to year 10) – 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)
	Uterine neoplasms: initial workup, additional workup, for known or suspected malignancy, additional workup, for serous carcinoma, clear cell carcinoma, undifferentiated/dedifferentiated carcinoma, carcinosarcoma, suspected extrauterine disease; surveillance in endometrial surveillance
Carcinoembryonic antigen (CEA)	Appendiceal adenocarcinoma: workup to establish baseline; monitoring; when imaging suggests appendiceal neoplasm or cancer or when there is a confirmed appendiceal neoplasm or cancer; workup for recurrence (3-6 months after CT imaging); surveillance (every 6-12 months for 2 years, annually up to 10 years)
	Breast cancer (invasive): Monitoring metastatic disease
	Colon cancer: workup to establish baseline; for a pedunculated or sessile polyp with invasive cancer, colon cancer appropriate for resection, and suspected or proven metastatic adenocarcinoma; surveillance (every 3-6 months for 2 years, then every 6 months for a total of 5 years)
	Extrahepatic cholangiocarcinoma: workup to establish baseline; for individuals with abdominal pain, jaundice, abnormal liver function tests, or obstruction or abnormality on imaging
	Gallbladder cancer: workup to establish baseline;: for individuals with jaundice or a mass on imaging post-operative workup of a suspicious mass; surveillance; (as clinically indicated), post-resection
	Intrahepatic cholangiocarcinoma: workup to establish baseline; for post-operative workup of a suspicious mass; d intrahepatic mass

Serum Biomarker	Indication
	Medullary carcinoma: additional workup; with established diagnosis; surveillance (every 6-12 months)
	Multiple endocrine neoplasia, type 2: at diagnosis (clinical evaluation) to assess risk for medullary thyroid cancer
	Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer: initial workup; for individuals with a suspicious mass found by palpation or imaging; monitoring prior to each cycle of chemotherapy; monitoring/follow-up for patients not receiving treatment (every 2-4 months for 2 years; every 3-6 months for 3 years; annually after year 5)
	Ovarian cancers (less common): initial workup for newly diagnosed ovarian cancer; monitoring/follow-up for recurrence – Less common ovarian cancers (additional surveillance recommendations): – – Malignant germ cell tumors: surveillance (every 2 months in a year, every 3 months in year 2, every 6 months in year 3; year 4 and beyond, annual testing up to year 10)) – 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) –
	Rectal cancer: workup to establish baseline;: for diagnosed rectal cancer or for a pedunculated or sessile polyp with invasive cancer; surveillance (every 3-6 months for 2 years, then every 6 months for a total of 5 years)
	Small bowel adenocarcinoma: additional workup with established diagnosis; post-treatment surveillance (every 3-6 months for 2 years, then every 6 months for a total of 5 years) additional workup for metastatic adenocarcinoma
Chorionic gonadotropin beta polypeptide (CGB3)	Gestational trophoblastic neoplasia (GTN): initial workup for suspected GTN; during and post treatment (no more than weekly); follow-up/surveillance (no more than monthly for 12 months)
	Occult primary: additional workup for adenocarcinoma or carcinoma not otherwise specified; with a clinical presentation in the mediastinum or for individuals < 65 years of age with a retroperitoneal mass
	Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer: initial workup; for individuals with a suspicious mass found by palpation or imaging; monitoring prior to each cycle of chemotherapy; monitoring/follow-up for not receiving treatment (every 2-4 months for 2 years; every 3-6 months for 3 years; annually after year 5)
	Ovarian cancers (less common): initial workup for newly diagnosed ovarian cancer; monitoring/follow-up for recurrence – Less common ovarian cancers (additional surveillance recommendations): – Malignant germ cell tumors: surveillance (every 2 months in year 1, every 3 months in year 2, every 6 months in year 3; year 4 and beyond, annual testing up to year 10) – 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: initial diagnostic workup for a suspicious testicular mass; post-diagnostic workup; post-orchiectomy; follow-up for nonseminoma (no more than every 2 months) follow-up for pure seminoma (no more than every 3 months)
	Thymomas and thymic carcinomas: initial evaluation, for individuals with a mediastinal mass
Human epididymis protein 4 (HE4)	Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer: initial workup; for individuals with a suspicious mass found by palpation or imaging; monitoring prior to each cycle of chemotherapy; monitoring/follow-up for not receiving treatment (every 2-4 months for 2 years; every 3-6 months for 3 years; annually after year 5)
	Ovarian cancers (less common): initial workup for newly diagnosed ovarian cancer; monitoring/follow-up for recurrence Less common ovarian cancers (additional surveillance recommendations):

Serum Biomarker	Indication
	– Malignant germ cell tumors: surveillance (every 2 months in year 1, every 3 months in year 2, every 6 months in year 3; year 4 and beyond, annual testing up to year 10)) – 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)
Inhibin (INHA)	Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer: initial workup; for individuals with a suspicious mass found by palpation or imaging; monitoring prior to each cycle of chemotherapy; monitoring/follow-up for patients not receiving treatment (every 2-4 months for 2 years; every 3-6 months for 3 years; annually after year 5)
	Ovarian cancers (less common): initial workup for newly diagnosed ovarian cancer; monitoring/ follow-up for recurrence Less common ovarian cancers (additional surveillance recommendations): – Malignant germ cell tumors: surveillance (every 2 months in year 1, every 3 months in year 2, every 6 months in year 3; year 4 and beyond, annual testing up to year 10) – 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)
Serum free light chains	Castleman disease: workup for established diagnosis
	Multiple myeloma: initial diagnostic workup for multiple myeloma and polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes (POEMS); follow-up/surveillance for solitary plasmacytoma (every 3-6 months), asymptomatic smoldering myeloma (every 3-6 months), symptomatic multiple myeloma
	Systemic light chain amyloidosis: initial diagnostic workup
Troponin T	Systemic light chain amyloidosis: initial diagnostic workup to assess organ involvement for suspected SLCA
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.

2. For all other cancer indications not discussed above, use of the above biomarkers (alone or in a panel of serum tumor markers) **DOES NOT MEET COVERAGE CRITERIA**.
3. All other serum tumor markers not addressed above (alone or in a panel of serum tumor markers) **DO NOT MEET COVERAGE CRITERIA**.
4. For the screening and detection of cancer, analysis of proteomic patterns in serum **DOES NOT MEET COVERAGE CRITERIA**.

Applicable CPT/HCPCS Procedure Codes

Procedure codes appearing in policy documents are included only as a general reference tool for each policy. They may not be all-inclusive.

Coding

Code	Description
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 Proprietary test: VeriStrat® Lab/manufacturer: Biodesix, Inc
82105	Alpha-fetoprotein (AFP); serum

Code	Description
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
83880	Natriuretic peptide
83950	Oncoprotein; HER-2/neu
83951	Oncoprotein; des-gamma-carboxy-prothrombin (DCP)
84075	Phosphatase, alkaline
84484	Troponin, quantitative
84702	Gonadotropin, chorionic (hCG); quantitative
84704	Gonadotropin, chorionic (hCG); free beta chain
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 (e.g., 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 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.
0558U	Oncology (colorectal), quantitative enzyme-linked immunosorbent assay (ELISA) for secreted colorectal cancer protein marker (BF7 antigen), using serum, result reported as indicative of response/no response to therapy or disease progression/regression Proprietary test: IGoCheckTM (Blood-Based Colorectal Cancer Test) Lab/Manufacturer: Milagen, Inc.
0559U	Oncology (breast), quantitative enzyme-linked immunosorbent assay (ELISA) for secreted breast cancer protein marker (BF9 antigen), serum, result reported as indicative of response/no response to therapy or disease progression/regression Proprietary test: Haystack MRDTM Baseline Lab/Manufacturer: Quest Diagnostics®
G0327	Colorectal cancer screening; blood-based biomarker

Evidence-based Scientific References

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Publication History

08/01/2026:	Annual policy review: administrative edits; removed CPT codes 81479, 81599, 83789, 84078, 84080, 84703, and 84999
09/01/2025:	Policy created to support coverage guidelines, effective for dates of service beginning Nov. 1, 2025

Background and Disclaimer Information

This policy applies to the products of Harvard Pilgrim Health Care and Tufts Health Plan and their affiliates, as identified in the check boxes on the first page for services performed by contracted providers.

Payment is based on member benefits and eligibility on the date of service, medical necessity review, where applicable, and the provider's network participation agreement with the Plan. As every claim is unique, this policy is neither a guarantee of payment, nor a final indication of how specific claim(s) will be adjudicated. Claims payment is subject to member eligibility and benefits on the date of service, coordination of benefits, referral/authorization, and utilization management requirements (when applicable), adherence to Plan policies and procedures, and claims editing logic. An authorization is not a guarantee of payment.

Point32Health reserves the right to amend a payment policy at its discretion. CPT and HCPCS codes are updated as applicable; please adhere to the most recent CPT and HCPCS coding guidelines.

We reserve the right to conduct audits on any provider and/or facility to ensure accuracy and compliance with the guidelines stated in this payment policy. If such an audit determines that a provider/facility did not comply with this payment policy, Harvard Pilgrim Health Care and Tufts Health Plan will expect the provider/facility to refund all payments related to noncompliance.