If a conflict arises between a Clinical Payment and Coding Policy ("CPCP") and any plan document under which a member is entitled to Covered Services, the plan document will govern. If a conflict arises between a CPCP and any provider contract pursuant to which a provider participates in and/or provides Covered Services to eligible member(s) and/or plans, the provider contract will govern. "Plan documents" include, but are not limited to, Certificates of Health Care Benefits, benefit booklets, Summary Plan Descriptions, and other coverage documents. BCBSOK may use reasonable discretion interpreting and applying this policy to services being delivered in a particular case. BCBSOK has full and final discretionary authority for their interpretation and application to the extent provided under any applicable plan documents.

Providers are responsible for submission of accurate documentation of services performed. Providers are expected to submit claims for services rendered using valid code combinations from Health Insurance Portability and Accountability Act ("HIPAA") approved code sets. Claims should be coded appropriately according to industry standard coding guidelines including, but not limited to: Uniform Billing ("UB") Editor, American Medical Association ("AMA"), Current Procedural Terminology ("CPT®"), CPT® Assistant, Healthcare Common Procedure Coding System ("HCPCS"), ICD-10 CM and PCS, National Drug Codes ("NDC"), Diagnosis Related Group ("DRG") guidelines, Centers for Medicare and Medicaid Services ("CMS") National Correct Coding Initiative ("NCCI") Policy Manual, CCI table edits and other CMS guidelines.

Claims are subject to the code edit protocols for services/procedures billed. Claim submissions are subject to claim review including but not limited to, any terms of benefit coverage, provider contract language, medical policies, clinical payment and coding policies as well as coding software logic. Upon request, the provider is urged to submit any additional documentation.

Serum Tumor Markers for Malignancies

Policy Number: CPCPLAB037

Version 1.0

Enterprise Clinical Payment and Coding Policy Committee Approval Date: July 17, 2023

Plan Effective Date November 1, 2023

Description

BCBSOK has implemented certain lab management reimbursement criteria. Not all requirements apply to each product. Providers are urged to review Plan documents for eligible coverage for services rendered.

Reimbursement Information:

1) Measurement of the following serum tumor markers **may be reimbursable** for the following indications:

a) Acute lymphoblastic leukemia (ALL) and pediatric acute lymphoblastic leukemia (PED-ALL)
    i) **Lactate dehydrogenase (LDH)**: initial diagnostic evaluation
b) Acute myeloid leukemia (AML)
    i) **Lactate dehydrogenase (LDH)**: initial diagnostic evaluation
c) B-cell lymphoma
    i) **Beta-2 microglobulin (B2M)**: initial diagnostic evaluation
    ii) **Serum light chains** (Castleman disease only): initial diagnostic evaluation
    iii) **Lactate dehydrogenase (LDH)**: initial diagnostic evaluation
d) Bone neoplasms (metastatic and primary)
    i) **Alkaline Phosphatase (ALP)**: initial diagnostic evaluation
    ii) **Lactate dehydrogenase (LDH)**: initial diagnostic evaluation
e) Breast cancer (metastatic)
    i) **Cancer Antigen 15-3 and 27.29 (CA 15-3 and 27.29)**: monitoring
    ii) **Carcinoembryonic Antigen (CEA)**: monitoring
f) Breast implant-associated anaplastic large cell lymphoma (ALCL)
    i) **Lactate dehydrogenase (LDH)**: initial diagnostic evaluation and staging
g) Chronic lymphocytic leukemia/small lymphocytic lymphoma
    i) **Beta-2 microglobulin (B2M)**: initial diagnostic evaluation
    ii) **Lactate dehydrogenase (LDH)**: initial diagnostic evaluation
h) Colon cancer
    i) **Carcinoembryonic Antigen (CEA)**: initial diagnostic evaluation and post-treatment surveillance every 3-6 months for 2 years, then every 6 months for a total of 5 years
i) Endometrial cancer
    i) **Cancer Antigen 125 (CA-125)**: additional diagnostic evaluation and/or surveillance
j) Epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer:
    i) initial diagnostic evaluation, during primary chemotherapy, and/or monitoring for complete response:
        (a) **Alpha fetoprotein (AFP)**
        (b) **Beta human chorionic gonadotropin (beta-hCG)**
        (c) **Cancer Antigen 19-9 (CA 19-9)**
        (d) **Cancer Antigen 125 (CA-125)**
        (e) **Carcinoembryonic Antigen (CEA)**
        (f) **Inhibin (INHA) expression**
        (g) **Lactate dehydrogenase (LDH)**
k) Extrahepatic cholangiocarcinoma
    i) **Cancer Antigen 19-9 (CA 19-9)**: initial diagnostic evaluation
    ii) **Carcinoembryonic Antigen (CEA)**: initial diagnostic evaluation
l) Gallbladder cancer

i) **Cancer Antigen 19-9 (CA 19-9)**: initial or postoperative diagnostic evaluation and/or surveillance
ii) **Carcinoembryonic Antigen (CEA)**: initial or postoperative diagnostic evaluation and/or surveillance

m) Hairy cell leukemia
i) **Lactate dehydrogenase (LDH)**: initial diagnostic evaluation

n) Hepatocellular carcinoma
i) **Alpha fetoprotein (AFP)**: initial diagnostic evaluation and screening and/or surveillance (every 3-6 months for 2 years, then every 6 months up to 5 years)
ii) **Cancer Antigen 19-9 (CA 19-9)**: initial diagnostic evaluation

o) Hodgkin lymphoma
i) **Lactate dehydrogenase (LDH)**: initial diagnostic evaluation

p) Intrahepatic cholangiocarcinoma
i) **Alpha fetoprotein (AFP)**: initial diagnostic evaluation
ii) **Cancer Antigen 19-9 (CA 19-9)**: initial diagnostic evaluation
iii) **Carcinoembryonic Antigen (CEA)**: initial diagnostic evaluation

q) Kidney cancer
i) **Lactate dehydrogenase (LDH)**: initial diagnostic evaluation

r) Less common ovarian cancers
i) Mucinous Carcinoma of the Ovary: initial diagnostic and (if necessary) additional evaluations
(a) **Cancer Antigen 19-9 (CA 19-9)**
(b) **Carcinoembryonic Antigen (CEA)**
ii) Ovarian low malignant potential tumors (borderline ovarian epithelial tumors): monitoring/follow-up every 3–6 months for up to 5 years, then annually
(a) **Alpha fetoprotein (AFP)**
(b) **Beta human chorionic gonadotropin (beta-hCG)**
(c) **Cancer Antigen 19-9 (CA 19-9)**
(d) **Cancer Antigen 125 (CA-125)**
(e) **Carcinoembryonic Antigen (CEA)**
(f) **Inhibin (INHA) expression**
(g) **Lactate dehydrogenase (LDH)**
iii) 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
(a) **Alpha fetoprotein (AFP)**
(b) **Beta human chorionic gonadotropin (beta-hCG)**
(c) **Cancer Antigen 19-9 (CA 19-9)**
(d) **Cancer Antigen 125 (CA-125)**
(e) **Carcinoembryonic Antigen (CEA)**
(f) **Inhibin (INHA) expression**
(g) **Lactate dehydrogenase (LDH)**

iv) Malignant sex cord stromal tumors: surveillance based on stage (i.e., 6-12 months if early-stage, low-risk disease; 4-6 months if high-risk disease)
    (a) **Alpha fetoprotein (AFP)**
    (b) **Beta human chorionic gonadotropin (beta-hCG)**
    (c) **Cancer Antigen 19-9 (CA 19-9)**
    (d) **Cancer Antigen 125 (CA-125)**
    (e) **Carcinoembryonic Antigen (CEA)**
    (f) **Inhibin (INHA) expression**
    (g) **Lactate dehydrogenase (LDH)**

s) Medullary carcinoma
    i) **Calcitonin (CALCA) expression**: initial diagnostic evaluation, monitoring, and/or surveillance 2-3 months postoperative, then every 6-12 months
    ii) **Carcinoembryonic Antigen (CEA)**: initial diagnostic evaluation and surveillance 2-3 months postoperative, then every 6-12 months

t) Melanoma (cutaneous)
    i) **Lactate dehydrogenase (LDH)**: initial diagnostic evaluation for metastatic or recurrent disease

u) Melanoma (uveal)
    i) **Alkaline phosphatase (ALP)**: initial diagnostic evaluation for metastatic or recurrent disease
    ii) **Lactate dehydrogenase (LDH)**: initial diagnostic evaluation for metastatic or recurrent disease

v) Multiple myeloma
    i) **Beta-2 microglobulin (B2M)**: initial diagnostic evaluation, staging, and/or follow-up/surveillance as needed
    ii) **Serum free light chain**: initial diagnostic evaluation and/or surveillance as needed
    iii) **Lactate dehydrogenase (LDH)**: initial diagnostic evaluation, staging, and/or follow-up/surveillance as needed

w) Myelodysplastic syndromes
    i) **Lactate dehydrogenase (LDH)**: initial diagnostic evaluation

x) Myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase fusion genes
    i) **Tryptase**: initial diagnostic evaluation

y) Myeloproliferative neoplasms
    i) **Lactate dehydrogenase (LDH)**: initial diagnostic evaluation and/or monitoring while on and after therapy

z) Neuroendocrine and adrenal tumors - multiple endocrine neoplasia, type 2
    i) **Calcitonin (CALCA) expression**: initial diagnostic evaluation
    ii) **Carcinoembryonic Antigen (CEA)**: initial diagnostic evaluation

aa) Occult primary mass of the liver, mediastinum, or retroperitoneum
    i) **Alpha fetoprotein (AFP)**: initial diagnostic evaluation

bb) Occult primary mass of the mediastinum or retroperitoneum
    i) **Alpha fetoprotein (AFP)**: additional diagnostic evaluation
    ii) **Beta human chorionic gonadotropin (beta-hCG)**: initial diagnostic evaluation

cc) Occult primary adenocarcinoma or carcinoma not otherwise specified
    i) **Cancer Antigen 125 (CA-125)**: additional diagnostic evaluation (in those with a uterus and/or ovaries present)
dd) Pancreatic adenocarcinoma
    i) **Cancer Antigen 19-9 (CA 19-9)**: initial diagnostic evaluation, risk classification, monitoring, and/or surveillance (every 3-6 months for 2 years, then every 6-12 months as clinically indicated)
ee) Pediatric aggressive mature B-cell lymphomas
    i) **Lactate dehydrogenase (LDH)**: initial diagnostic evaluation
ff) Peritoneal mesothelioma (malignant)
    i) **Cancer Antigen 125 (CA-125)**: initial diagnostic evaluation
gg) Primary cutaneous lymphomas
    i) **Lactate dehydrogenase (LDH)**: initial diagnostic evaluation
hh) Rectal cancer
    i) **Carcinoembryonic Antigen (CEA)**: initial diagnostic evaluation, monitoring, and/or surveillance every 3-6 months for 2 years, then every 6 months for a total of 5 years
ii) Richter's syndrome
    i) **Lactate dehydrogenase (LDH)**: initial diagnostic evaluation
jj) Saccrococcygeal teratoma
    i) **Alpha fetoprotein (AFP)**: initial diagnostic evaluation and surveillance for up to 3 years
    ii) **Beta human chorionic gonadotropin (beta-hCG)**: initial diagnostic evaluation
kk) Small bowel adenocarcinoma
    i) **Cancer Antigen 19-9 (CA 19-9)**: initial diagnostic evaluation and/or surveillance (every 3-6 months for 2 years, then every 6 months for a total of 5 years)
    ii) **Carcinoembryonic Antigen (CEA)**: initial diagnostic evaluation and/or surveillance (every 3-6 months for 2 years, then every 6 months for a total of 5 years)
ll) Small cell lung cancer
    i) **Lactate dehydrogenase (LDH)**: prognosis
mm) Systemic light chain amyloidosis
    i) **Alkaline Phosphatase (ALP)**: initial diagnostic evaluation
    ii) **B-type natriuretic peptide (BNP) or N-terminal fragment of B-type natriuretic peptide (NT-proBNP)**: initial diagnostic evaluation and staging
    iii) **Beta-2 microglobulin (B2M)**: initial diagnostic evaluation
    iv) **Serum free light chain**: initial diagnostic evaluation
    v) **Lactate dehydrogenase (LDH)**: initial diagnostic evaluation
    vi) **Troponin T**: initial diagnostic evaluation and staging
nn) Systemic mastocytosis
    i) **Tryptase**: initial diagnostic evaluation, monitoring response to therapy, and/or risk classification
oo) T-cell lymphomas

i) **Lactate dehydrogenase (LDH)**: initial diagnostic evaluation

pp) Testicular cancer (nonseminoma and pure seminoma):

i) Initial and post diagnostic evaluation, staging, risk classification, post-treatment follow-up, and surveillance:

(a) **Alpha fetoprotein (AFP)**

(b) **Beta human chorionic gonadotropin (beta-hCG)**

(c) **Lactate dehydrogenase (LDH)**

qq) Thymomas and thymic carcinomas

i) **Alpha fetoprotein (AFP)**: initial diagnostic evaluation

ii) **Beta human chorionic gonadotropin (beta-hCG)**: initial diagnostic evaluation

rr) Undiagnosed pelvic mass

i) **Inhibin (INHA) expression**: initial diagnostic evaluation for clinical indication to assess for LCOC (Less Common Ovarian Cancers) and pregnancy

ss) Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma

i) **Beta-2 microglobulin (B2M)**: initial diagnostic evaluation and prognostication at the time of first-line treatment initiation

ii) **Serum free light chain**: initial diagnostic evaluation

iii) **Lactate dehydrogenase (LDH)**: initial diagnostic evaluation

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

3) All other serum tumor markers not addressed above (alone or in a panel of serum tumor markers) **are not reimbursable.**

4) For the screening and detection of cancer, analysis of proteomic patterns in serum **are not reimbursable**.

Procedure Codes

The following is not an all-encompassing code list. The inclusion of a code does not guarantee it is a covered service or eligible for reimbursement.

Codes
81500, 81503, 81538, 81599, 82105, 82107, 82232, 82308, 82378, 83520, 83615, 83789, 83880, 83950, 83951, 84075, 84078, 84080, 84484, 84702, 84703, 84704, 84999, , 86300, 86301, 86304, 86305, 86316, 86336, 0003U, , 0092U, 0163U, G0327

References:

AASLD. (2018). *Diagnosis, Staging, and Management of Hepatocellular Carcinoma: 2018 Practice Guidance by the American Association for the Study of Liver Diseases*. https://pubmed.ncbi.nlm.nih.gov/29624699/

ACR. (2019). *American College of Radiology ACR Appropriateness Criteria® Chronic Liver Disease* https://acsearch.acr.org/docs/3098416/Narrative/

ACS. (2018a). *What Is Multiple Myeloma?* https://www.cancer.org/cancer/multiple-myeloma/about/what-is-multiple-myeloma.html

ACS. (2018b). *What Is Waldenstrom Macroglobulinemia?* https://www.cancer.org/cancer/waldenstrom-macroglobulinemia/about/what-is-wm.html

Akar, H., Seldin, D. C., Magnani, B., O'Hara, C., Berk, J. L., Schoonmaker, C., Cabral, H., Dember, L. M., Sanchorawala, V., Connors, L. H., Falk, R. H., & Skinner, M. (2005). Quantitative serum free light chain assay in the diagnostic evaluation of AL amyloidosis. *Amyloid*, *12*(4), 210-215. https://doi.org/10.1080/13506120500352339

Allison, K. H., Hammond, M. E. H., Dowsett, M., McKernin, S. E., Carey, L. A., Fitzgibbons, P. L., Hayes, D. F., Lakhani, S. R., Chavez-MacGregor, M., Perlmutter, J., Perou, C. M., Regan, M. M., Rimm, D. L., Symmans, W. F., Torlakovic, E. E., Varella, L., Viale, G., Weisberg, T. F., McShane, L. M., & Wolff, A. C. (2020). Estrogen and Progesterone Receptor Testing in Breast Cancer: ASCO/CAP Guideline Update. *Journal of Clinical Oncology*, JCO.19.02309. https://doi.org/10.1200/JCO.19.02309

ASPIRE. (2023). OVA1 Products. https://aspirawh.com/ova-products/

Berrebi, A., Shvidel, L., Arditti, F. D., Bassous, L., Haran, M., & Shtalrid, M. (2009). The Significance of Elevated Beta 2-Microglobulin (b2-m) in B-CLL: Evidence of in Vitro b2-m Secretion Following Activation of B-CLL Cells. *Blood*, *114*(22), 4380. http://www.bloodjournal.org/content/114/22/4380.abstract

BeScreened. (2023). BeScreened. https://bescreened.com/

Bhole, M. V., Sadler, R., & Ramasamy, K. (2014). Serum-free light-chain assay: clinical utility and limitations. *Ann Clin Biochem*, *51*(Pt 5), 528-542. https://doi.org/10.1177/0004563213518758

Bind, M. K., Mishra, R. R., Kumar, V., Misra, V., & Singh, P. A. (2021). Serum CA 19-9 and CA 125 as a diagnostic marker in carcinoma of gallbladder. *Indian J Pathol Microbiol*, *64*(1), 65-68. https://pubmed.ncbi.nlm.nih.gov/33433411/

Cautha, S., Gupta, S., Hanif, A., Moirangthem, V., & Jain, K. (2022). Lymphoplasmacytic Lymphoma with Only Lambda Light Chain Monoclonal Paraprotein Expression. *Eur J Case Rep Intern Med*, *9*(2), 003106. https://doi.org/10.12890/2022_003106

Caviglia, G. P., Abate, M. L., Petrini, E., Gaia, S., Rizzetto, M., & Smedile, A. (2016). Highly sensitive alpha-fetoprotein, Lens culinaris agglutinin-reactive fraction of alpha-fetoprotein and des-gamma-carboxyprothrombin for hepatocellular carcinoma detection. *Hepatol Res*, *46*(3), E130-135. https://doi.org/10.1111/hepr.12544

Chappuis, P. O., Dieterich, B., Sciretta, V., Lohse, C., Bonnefoi, H., Remadi, S., & Sappino, A. P. (2001). Functional evaluation of plasmin formation in primary breast cancer. *J Clin Oncol*, *19*(10), 2731-2738. https://doi.org/10.1200/jco.2001.19.10.2731

Chen, F., Shen, J., Wang, J., Cai, P., & Huang, Y. (2018). Clinical analysis of four serum tumor markers in 458 patients with ovarian tumors: diagnostic value of the combined use of HE4, CA125, CA19-9, and CEA in ovarian tumors. *Cancer Manag Res*, *10*, 1313-1318. https://doi.org/10.2147/cmar.S155693

Chen, Y., Xie, Y., Xu, L., Zhan, S., Xiao, Y., Gao, Y., Wu, B., & Ge, W. (2017). Protein content and functional characteristics of serum-purified exosomes from patients with colorectal cancer revealed by quantitative proteomics. *Int J Cancer*, *140*(4), 900-913. https://doi.org/10.1002/ijc.30496

Cheng, J., Wang, W., Zhang, Y., Liu, X., Li, M., Wu, Z., Liu, Z., Lv, Y., & Wang, B. (2014). Prognostic role of pre-treatment serum AFP-L3% in hepatocellular carcinoma: systematic review and meta-analysis. *PLoS One*, *9*(1), e87011. https://doi.org/10.1371/journal.pone.0087011

Detterbeck, F. C., Mazzone, P. J., Naidich, D. P., & Bach, P. B. (2013). Screening for lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*, *143*(5 Suppl), e78S-e92S. https://doi.org/10.1378/chest.12-2350

Dispenzieri, A. (2023). *Clinical presentation, laboratory manifestations, and diagnosis of immunoglobulin light chain (AL) amyloidosis*. https://www.uptodate.com/contents/clinical-presentation-laboratory-manifestations-and-diagnosis-of-immunoglobulin-light-chain-al-amyloidosis

Dorigo, O., & Berek, J. S. (2011). Personalizing CA125 levels for ovarian cancer screening. *Cancer Prev Res (Phila)*, *4*(9), 1356-1359. https://doi.org/10.1158/1940-6207.Capr-11-0378

Duffy, M. J. (2001). Carcinoembryonic Antigen as a Marker for Colorectal Cancer: Is It Clinically Useful? *Clinical Chemistry*, *47*(4), 624. http://clinchem.aaccjnls.org/content/47/4/624.abstract

EASL. (2018). EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. https://doi.org/10.1016/j.jhep.2018.03.019

Farkkila, A., Koskela, S., Bryk, S., Alfthan, H., Butzow, R., Leminen, A., Puistola, U., Tapanainen, J. S., Heikinheimo, M., Anttonen, M., & Unkila-Kallio, L. (2015). The clinical utility of serum anti-Mullerian hormone in the follow-up of ovarian adult-type granulosa cell tumors--A comparative study with inhibin B. *Int J Cancer*, *137*(7), 1661-1671. https://doi.org/10.1002/ijc.29532

Febbo, P. G., Ladanyi, M., Aldape, K. D., De Marzo, A. M., Hammond, M. E., Hayes, D. F., Iafrate, A. J., Kelley, R. K., Marcucci, G., Ogino, S., Pao, W., Sgroi, D. C., & Birkeland, M. L. (2011). NCCN Task Force report: Evaluating the clinical utility of tumor markers in oncology. *J Natl Compr Canc Netw*, *9 Suppl 5*, S1-32; quiz S33. https://pubmed.ncbi.nlm.nih.gov/22138009/

Feng, F., Tian, Y., Xu, G., Liu, Z., Liu, S., Zheng, G., Guo, M., Lian, X., Fan, D., & Zhang, H. (2017). Diagnostic and prognostic value of CEA, CA19-9, AFP and CA125 for early gastric cancer. *BMC Cancer*, *17*(1), 737. https://doi.org/10.1186/s12885-017-3738-y

Foekens, J. A., Peters, H. A., Look, M. P., Portengen, H., Schmitt, M., Kramer, M. D., Brunner, N., Janicke, F., Meijer-van Gelder, M. E., Henzen-Logmans, S. C., van Putten, W. L., & Klijn, J. G. (2000). The urokinase

system of plasminogen activation and prognosis in 2780 breast cancer patients. *Cancer Res*, *60*(3), 636-643. https://pubmed.ncbi.nlm.nih.gov/10676647/

Gershenson, D. (2023, 03/30/2022). *Sex cord-stromal tumors of the ovary: Epidemiology, clinical features, and diagnosis in adults*. https://www.uptodate.com/contents/sex-cord-stromal-tumors-of-the-ovary-epidemiology-clinical-features-and-diagnosis-in-adults

Gilligan, T. D., Seidenfeld, J., Basch, E. M., Einhorn, L. H., Fancher, T., Smith, D. C., Stephenson, A. J., Vaughn, D. J., Cosby, R., & Hayes, D. F. (2010). American Society of Clinical Oncology Clinical Practice Guideline on uses of serum tumor markers in adult males with germ cell tumors. *J Clin Oncol*, *28*(20), 3388-3404. https://doi.org/10.1200/jco.2009.26.4481

Halfdanarson, T. R., Strosberg, J. R., Tang, L., Bellizzi, A. M., Bergsland, E. K., O'Dorisio, T. M., Halperin, D. M., Fishbein, L., Eads, J., Hope, T. A., Singh, S., Salem, R., Metz, D. C., Naraev, B. G., Reidy-Lagunes, D. L., Howe, J. R., Pommier, R. F., Menda, Y., & Chan, J. A. (2020). The North American Neuroendocrine Tumor Society Consensus Guidelines for Surveillance and Medical Management of Pancreatic Neuroendocrine Tumors. *Pancreas*, *49*(7), 863-881. https://doi.org/10.1097/mpa.0000000000001597

Harris, L. N., Ismaila, N., McShane, L. M., Andre, F., Collyar, D. E., Gonzalez-Angulo, A. M., Hammond, E. H., Kuderer, N. M., Liu, M. C., Mennel, R. G., Van Poznak, C., Bast, R. C., & Hayes, D. F. (2016). Use of Biomarkers to Guide Decisions on Adjuvant Systemic Therapy for Women With Early-Stage Invasive Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline. *J Clin Oncol*, *34*(10), 1134-1150. https://doi.org/10.1200/jco.2015.65.2289

Harris, L. N., Ismaila, N., McShane, L. M., Andre, F., Collyar, D. E., Gonzalez-Angulo, A. M., Hammond, E. H., Kuderer, N. M., Liu, M. C., Mennel, R. G., Van Poznak, C., Bast, R. C., & Hayes, D. F. (2016). Use of Biomarkers to Guide Decisions on Adjuvant Systemic Therapy for Women With Early-Stage Invasive Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline. *Journal of Clinical Oncology*, *34*(10), 1134-1150. https://doi.org/10.1200/JCO.2015.65.2289

Harvey, R. A. (2023, 06/07/2022). *Human chorionic gonadotropin: Biochemistry and measurement in pregnancy and disease*. https://www.uptodate.com/contents/human-chorionic-gonadotropin-testing-in-pregnancy-and-gestational-trophoblastic-disease-and-causes-of-low-persistent-levels

Haugen, B. R., Alexander, E. K., Bible, K. C., Doherty, G. M., Mandel, S. J., Nikiforov, Y. E., Pacini, F., Randolph, G. W., Sawka, A. M., Schlumberger, M., Schuff, K. G., Sherman, S. I., Sosa, J. A., Steward, D. L., Tuttle, R. M., & Wartofsky, L. (2016). 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid*, *26*(1), 1-133. https://doi.org/10.1089/thy.2015.0020

Hotakainen, K., Ljungberg, B., Paju, A., Rasmuson, T., Alfthan, H., & Stenman, U. H. (2002). The free beta-subunit of human chorionic gonadotropin as a prognostic factor in renal cell carcinoma. *Br J Cancer*, *86*(2), 185-189. https://doi.org/10.1038/sj.bjc.6600050

Hottinger, A., & Hormigo, A. (2011). Serum Biomarkers. In *Encyclopedia of Cancer* (pp. 3390-3394). Springer Berlin Heidelberg. https://doi.org/10.1007/978-3-642-16483-5_5269

Husain, A. N., Colby, T. V., Ordonez, N. G., Allen, T. C., Attanoos, R. L., Beasley, M. B., Butnor, K. J., Chirieac, L. R., Churg, A. M., Dacic, S., Galateau-Salle, F., Gibbs, A., Gown, A. M., Krausz, T., Litzky, L. A., Marchevsky, A., Nicholson, A. G., Roggli, V. L., Sharma, A. K., . . . Wick, M. R. (2018). Guidelines for Pathologic Diagnosis of Malignant Mesothelioma 2017 Update of the Consensus Statement From the International Mesothelioma Interest Group. *Arch Pathol Lab Med*, *142*(1), 89-108. https://doi.org/10.5858/arpa.2017-0124-RA

Immunovia. (2023). The IMMray® PanCan-d test. https://immunoviainc.com/the-immray-pancan-d-test/

Isaksson, S., Jönsson, P., Monsef, N., Brunnström, H., Bendahl, P. O., Jönsson, M., Staaf, J., & Planck, M. (2017). CA 19-9 and CA 125 as potential predictors of disease recurrence in resectable lung adenocarcinoma. *PLoS One*, *12*(10), e0186284. https://doi.org/10.1371/journal.pone.0186284

Katou, H., Kanno, T., Hoshino, M., Hagihara, Y., Tanaka, H., Kawai, T., Hasegawa, K., Naiki, H., & Goto, Y. (2002). The role of disulfide bond in the amyloidogenic state of beta(2)-microglobulin studied by heteronuclear NMR. *Protein Sci*, *11*(9), 2218-2229. https://doi.org/10.1110/ps.0213202

Katzmann, J. A., Clark, R. J., Abraham, R. S., Bryant, S., Lymp, J. F., Bradwell, A. R., & Kyle, R. A. (2002). Serum reference intervals and diagnostic ranges for free kappa and free lambda immunoglobulin light chains: relative sensitivity for detection of monoclonal light chains. *Clin Chem*, *48*(9), 1437-1444. https://www.ncbi.nlm.nih.gov/pubmed/12194920

Kim, N. H., Lee, M. Y., Park, J. H., Park, D. I., Sohn, C. I., Choi, K., & Jung, Y. S. (2017). Serum CEA and CA 19-9 Levels are Associated with the Presence and Severity of Colorectal Neoplasia. *Yonsei Med J*, *58*(5), 918-924. https://doi.org/10.3349/ymj.2017.58.5.918

Kindler, H. L., Ismaila, N., Armato, S. G., Bueno, R., Hesdorffer, M., Jahan, T., Jones, C. M., Miettinen, M., Pass, H., Rimner, A., Rusch, V., Sterman, D., Thomas, A., & Hassan, R. (2018). Treatment of Malignant Pleural Mesothelioma: American Society of Clinical Oncology Clinical Practice Guideline. *Journal of Clinical Oncology*, *36*(13), 1343-1373. https://doi.org/10.1200/JCO.2017.76.6394

Krop, I., Ismaila, N., Andre, F., Bast, R. C., Barlow, W., Collyar, D. E., Hammond, M. E., Kuderer, N. M., Liu, M. C., Mennel, R. G., Van Poznak, C., Wolff, A. C., & Stearns, V. (2017). Use of Biomarkers to Guide Decisions on Adjuvant Systemic Therapy for Women With Early-Stage Invasive Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline Focused Update. *J Clin Oncol*, Jco2017740472. https://doi.org/10.1200/jco.2017.74.0472

Kumar, S., Dispenzieri, A., Katzmann, J. A., Larson, D. R., Colby, C. L., Lacy, M. Q., Hayman, S. R., Buadi, F. K., Leung, N., Zeldenrust, S. R., Ramirez-Alvarado, M., Clark, R. J., Kyle, R. A., Rajkumar, S. V., & Gertz, M. A. (2010). Serum immunoglobulin free light-chain measurement in primary amyloidosis: prognostic value and correlations with clinical features. *Blood*, *116*(24), 5126-5129. https://doi.org/10.1182/blood-2010-06-290668

Kyrtsonis MC, K. E., Bartzis V, Pessah I, Nikolaou E, Karalis V, Maltezas D, Panayiotidis P, Harding S. (2012). Monoclonal Immunoglobulin. In *Multiple Myeloma - A Quick Reflection on the Fast Progress*. https://doi.org/10.5772/55855

Li, J., Yin, M., Song, W., Cui, F., Wang, W., Wang, S., & Zhu, H. (2018). B Subunit of Human Chorionic Gonadotropin Promotes Tumor Invasion and Predicts Poor Prognosis of Early-Stage Colorectal Cancer. *Cell Physiol Biochem*, *45*(1), 237-249. https://doi.org/10.1159/000486770

Liu, R., Cao, J., Gao, X., Zhang, J., Wang, L., Wang, B., Guo, L., Hu, X., & Wang, Z. (2016). Overall survival of cancer patients with serum lactate dehydrogenase greater than 1000 IU/L. *Tumour Biol*, *37*(10), 14083-14088. https://doi.org/10.1007/s13277-016-5228-2

Lucarelli, G., Ditonno, P., Bettocchi, C., Vavallo, A., Rutigliano, M., Galleggiante, V., Larocca, A. M., Castellano, G., Gesualdo, L., Grandaliano, G., Selvaggi, F. P., & Battaglia, M. (2014). Diagnostic and prognostic role of preoperative circulating CA 15-3, CA 125, and beta-2 microglobulin in renal cell carcinoma. *Dis Markers*, *2014*, 689795. https://doi.org/10.1155/2014/689795

MagArray. (2023). REVEAL. https://magarray.com/reveal/#

Magnani, J. L. (2004). The discovery, biology, and drug development of sialyl Lea and sialyl Lex. *Archives of Biochemistry and Biophysics*, *426*(2), 122-131. https://doi.org/10.1016/j.abb.2004.04.008

Malmstrom, P., Bendahl, P. O., Boiesen, P., Brunner, N., Idvall, I., & Ferno, M. (2001). S-phase fraction and urokinase plasminogen activator are better markers for distant recurrences than Nottingham Prognostic Index and histologic grade in a prospective study of premenopausal lymph node-negative breast cancer. *J Clin Oncol*, *19*(7), 2010-2019. https://doi.org/10.1200/jco.2001.19.7.2010

Marcillac, I., Troalen, F., Bidart, J.-M., Ghillani, P., Ribrag, V., Escudier, B., Malassagne, B., Droz, J.-P., Lhommé, C., Rougier, P., Duvillard, P., Prade, M., Lugagne, P.-M., Richard, F., Poynard, T., Bohuon, C., Wands, J., & Bellet, D. (1992). Free Human Chorionic Gonadotropin β Subunit in Gonadal and Nongonadal Neoplasms. *Cancer Research*, *52*(14), 3901. http://cancerres.aacrjournals.org/content/52/14/3901.abstract

Marcinko, T. M., Dong, J., LeBlanc, R., Daborowski, K. V., & Vachet, R. W. (2017). Small molecule-mediated inhibition of β-2-microglobulin-based amyloid fibril formation. *J Biol Chem*, *292*(25), 10630-10638. https://doi.org/10.1074/jbc.M116.774083

Merlini, G., Wechalekar, A. D., & Palladini, G. (2013). Systemic light chain amyloidosis: an update for treating physicians. *Blood*, *121*(26), 5124-5130. https://doi.org/10.1182/blood-2013-01-453001

Moreau AS, L. X., Manning R, Coiteux V, Darre S, Hatjiharisi E, Hunter Z, Jia X, Ngo H, O'Sullivan G, Santos D, Treon S, Facon T, Anderson K, Ghobrial I. (2006). Serum Free Light Chain in Waldenstrom Macroglobulinemia. https://doi.org/10.1182/blood.V108.11.2420.2420

NANETS. (2017). *The North American Neuroendocrine Tumor Society Consensus Guidelines for Surveillance and Medical Management of Midgut Neuroendocrine Tumors*. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5642985/

NCCN. (2022a). Acute Lymphoblastic Leukemia Version 1.2022. https://www.nccn.org/professionals/physician_gls/pdf/all.pdf

NCCN. (2022b). *Genetic/Familial High-Risk Assessment: Colorectal*. https://www.nccn.org/professionals/physician_gls/pdf/genetics_colon.pdf#Page=32

NCCN. (2023a). B-Cell Lymphomas V3.2023. https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf

NCCN. (2023b). Bone Cancer Version 3.2023. https://www.nccn.org/professionals/physician_gls/pdf/bone.pdf

NCCN. (2023c). Breast Cancer. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf

NCCN. (2023d). *Cervical Cancer*. https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf

NCCN. (2023e). Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf

NCCN. (2023f). Colon Cancer. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf

NCCN. (2023g). Cutaneous Melanoma Version 2.2023. https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf

NCCN. (2023h). Genetic/Familial High-Risk Assessment: Breast and Ovarian. https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf#Page=39

NCCN. (2023i). Hairy Cell Leukemia Version 1.2023. https://www.nccn.org/professionals/physician_gls/pdf/hairy_cell.pdf

NCCN. (2023j). *Head and Neck Cancers*. https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf#Page=71

NCCN. (2023k). *Hepatocellular Carcinoma*. https://www.nccn.org/professionals/physician_gls/pdf/hcc.pdf

NCCN. (2023l). Hodgkin Lymphoma. https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf

NCCN. (2023m). Merkel Cell Carcinoma. https://www.nccn.org/professionals/physician_gls/pdf/mcc.pdf

NCCN. (2023n). *Mesothelioma: Peritoneal* https://www.nccn.org/professionals/physician_gls/pdf/meso_peritoneal.pdf

NCCN. (2023o). *Mesothelioma: Pleural*. https://www.nccn.org/professionals/physician_gls/pdf/meso_pleural.pdf

NCCN. (2023p). Multiple Myeloma, Version 3.2023. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf

NCCN. (2023q). Myelodysplastic Syndromes https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf

NCCN. (2023r). *Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes*. https://www.nccn.org/professionals/physician_gls/pdf/mlne.pdf

NCCN. (2023s). Myeloproliferative Neoplasms Version 1.2023. https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf

NCCN. (2023t). *NCCN Clinical Practice Guidelines in Oncology*. https://www.nccn.org/professionals/physician_gls/default.aspx

NCCN. (2023u). *Neuroendocrine and Adrenal Tumors*. https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf

NCCN. (2023v). *Non-Small Cell Lung Cancer*. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf

NCCN. (2023w). Occult Primary, V.3.2023. https://www.nccn.org/professionals/physician_gls/pdf/occult.pdf

NCCN. (2023x). Ovarian Cancer, V.1.2023. https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf

NCCN. (2023y). Pancreatic Adenocarcinoma, V.1.2023. https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf

NCCN. (2023z). Pediatric Acute Lymphoblastic Leukemia Version 2.2023. https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf

NCCN. (2023aa). Primary Cutaneous Lymphomas Version 1.2023. https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf

NCCN. (2023ab). Rectal Cancer. https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf

NCCN. (2023ac). Small Bowel Adenocarcinoma. https://www.nccn.org/professionals/physician_gls/pdf/small_bowel.pdf

NCCN. (2023ad). Small Cell Lung Cancer Version 3.2023. https://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf

NCCN. (2023ae). Systemic light chain amyloidosis, V.2.2023. https://www.nccn.org/professionals/physician_gls/pdf/amyloidosis.pdf

NCCN. (2023af). Systemic Mastocytosis Version 1.2023. https://www.nccn.org/professionals/physician_gls/pdf/mastocytosis.pdf

NCCN. (2023ag). *T-Cell Lymphomas*. https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf

NCCN. (2023ah). *Testicular Cancer, V.1.2023*. https://www.nccn.org/professionals/physician_gls/pdf/testicular.pdf

NCCN. (2023ai). Thymomas and Thymic Carcinomas, V.1.2023. https://www.nccn.org/professionals/physician_gls/pdf/thymic.pdf

NCCN. (2023aj). Thyroid Carcinoma, V.2.2023. https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf

NCCN. (2023ak). Uterine Neoplasms, V.2.2023. https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf

NCCN. (2023al). Waldenström's Macroglobulinemia / Lymphoplasmacytic Lymphoma V.1.2023. https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf

NICE. (2011). *Ovarian cancer: recognition and initial management*. https://www.nice.org.uk/guidance/cg122/chapter/1-Guidance

NICE. (2018). Myeloma: diagnosis and management. https://www.nice.org.uk/guidance/ng35/chapter/Recommendations

Oyaert, M., Boone, E., De Ceuninck, L., Moreau, E., Van Dorpe, J., Vanpoucke, H., & Deeren, D. (2014). Clonal multicentric Castleman's disease with increased free Kappa light chains in a patient with systemic lupus erythematosus. *Ann Hematol*, *93*(7), 1255-1257. https://doi.org/10.1007/s00277-013-1962-3

Park, S. J., Jang, J. Y., Jeong, S. W., Cho, Y. K., Lee, S. H., Kim, S. G., Cha, S. W., Kim, Y. S., Cho, Y. D., Kim, H. S., Kim, B. S., Park, S., & Bang, H. I. (2017). Usefulness of AFP, AFP-L3, and PIVKA-II, and their combinations in diagnosing hepatocellular carcinoma. *Medicine (Baltimore)*, *96*(11), e5811. https://doi.org/10.1097/md.0000000000005811

Pinzani, P., D'Argenio, V., Del Re, M., Pellegrini, C., Cucchiara, F., Salvianti, F., & Galbiati, S. (2021). Updates on liquid biopsy: current trends and future perspectives for clinical application in solid tumors. *Clin Chem Lab Med*, *59*(7), 1181-1200. https://doi.org/10.1515/cclm-2020-1685

Pucino, V., Bombardieri, M., Pitzalis, C., & Mauro, C. (2017). Lactate at the crossroads of metabolism, inflammation, and autoimmunity. *European Journal of Immunology*, *47*(1), 14-21. https://doi.org/10.1002/eji.201646477

Qin, J., Yang, Q., Ye, H., Wang, K., Zhang, M., Zhu, J., Wang, X., Dai, L., Wang, P., & Zhang, J. (2020). Using Serological Proteome Analysis to Identify and Evaluate Anti-GRP78 Autoantibody as Biomarker in the Detection of Gastric Cancer. *J Oncol*, *2020*, 9430737. https://doi.org/10.1155/2020/9430737

Raby, B. (2023, 06/09/2021). *Personalized medicine*. https://www.uptodate.com/contents/personalized-medicine

Ryu, T., Takami, Y., Wada, Y., Tateishi, M., Matsushima, H., Mikagi, K., & Saitsu, H. (2017). Double- and Triple-Positive Tumor Markers Predict Early Recurrence and Poor Survival in Patients with Hepatocellular Carcinoma within the Milan Criteria and Child-Pugh Class A. *J Gastrointest Surg*, *21*(6), 957-966. https://doi.org/10.1007/s11605-017-3394-1

Santos Schraiber, L. d., de Mattos, A. A., Zanotelli, M. L., Cantisani, G. P., Brandao, A. B., Marroni, C. A., Kiss, G., Ernani, L., & Santos Marcon, P. d. (2016). Alpha-fetoprotein Level Predicts Recurrence After Transplantation in Hepatocellular Carcinoma. *Medicine (Baltimore)*, *95*(3), e2478. https://doi.org/10.1097/md.0000000000002478

Schefer, H., Mattmann, S., & Joss, R. A. (1998). Hereditary persistence of α-fetoproteinCase report and review of the literature. *Annals of Oncology*, *9*(6), 667-672. https://doi.org/10.1023/A:1008243311122

Seo, S., Hong, J. Y., Yoon, S., Yoo, C., Park, J. H., Lee, J. B., Park, C. S., Huh, J., Lee, Y., Kim, K. W., Ryu, J. S., Kim, S. J., Kim, W. S., Yoon, D. H., & Suh, C. (2016). Prognostic significance of serum beta-2 microglobulin in patients with diffuse large B-cell lymphoma in the rituximab era. *Oncotarget*, *7*(47), 76934-76943. https://doi.org/10.18632/oncotarget.12734

Sepulveda, A. R., Hamilton, S. R., Allegra, C. J., Grody, W., Cushman-Vokoun, A. M., Funkhouser, W. K., Kopetz, S. E., Lieu, C., Lindor, N. M., Minsky, B. D., Monzon, F. A., Sargent, D. J., Singh, V. M., Willis, J., Clark, J., Colasacco, C., Rumble, R. B., Temple-Smolkin, R., Ventura, C. B., & Nowak, J. A. (2017). Molecular Biomarkers for the Evaluation of Colorectal Cancer: Guideline From the American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and the American Society of Clinical Oncology. *Journal of Clinical Oncology*, *35*(13), 1453-1486. https://doi.org/10.1200/JCO.2016.71.9807

Stankowski-Drengler, T., Gertz, M. A., Katzmann, J. A., Lacy, M. Q., Kumar, S., Leung, N., Hayman, S. R., Buadi, F., Kyle, R. A., Rajkumar, S. V., & Dispenzieri, A. (2010). Serum immunoglobulin free light chain measurements and heavy chain isotype usage provide insight into disease biology in patients with POEMS syndrome. *Am J Hematol*, *85*(6), 431-434. https://doi.org/10.1002/ajh.21707

Stephens, R. W., Brunner, N., Janicke, F., & Schmitt, M. (1998). The urokinase plasminogen activator system as a target for prognostic studies in breast cancer. *Breast Cancer Res Treat*, *52*(1-3), 99-111. https://doi.org/10.1007/978-1-4615-5195-9_15

Stoffel, E. M., McKernin, S. E., Brand, R., Canto, M., Goggins, M., Moravek, C., Nagarajan, A., Petersen, G. M., Simeone, D. M., Yurgelun, M., & Khorana, A. A. (2018). Evaluating Susceptibility to Pancreatic Cancer: ASCO Provisional Clinical Opinion. *Journal of Clinical Oncology*, *37*(2), 153-164. https://doi.org/10.1200/JCO.18.01489

Strosberg, J. (2023, 04/20/2022). *Diagnosis of carcinoid syndrome and tumor localization*. https://www.uptodate.com/contents/diagnosis-of-the-carcinoid-syndrome-and-tumor-localization

Sturgeon, C. M., Duffy, M. J., Hofmann, B. R., Lamerz, R., Fritsche, H. A., Gaarenstroom, K., Bonfrer, J., Ecke, T. H., Grossman, H. B., Hayes, P., Hoffmann, R. T., Lerner, S. P., Lohe, F., Louhimo, J., Sawczuk, I., Taketa, K., & Diamandis, E. P. (2010). National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines for use of tumor markers in liver, bladder, cervical, and gastric cancers. *Clin Chem*, *56*(6), e1-48. https://doi.org/10.1373/clinchem.2009.133124

Sturgeon, C. M., Duffy, M. J., Stenman, U. H., Lilja, H., Brunner, N., Chan, D. W., Babaian, R., Bast, R. C., Jr., Dowell, B., Esteva, F. J., Haglund, C., Harbeck, N., Hayes, D. F., Holten-Andersen, M., Klee, G. G., Lamerz, R., Looijenga, L. H., Molina, R., Nielsen, H. J., . . . Diamandis, E. P. (2008). National Academy of Clinical Biochemistry laboratory medicine practice guidelines for use of tumor markers in testicular, prostate, colorectal, breast, and ovarian cancers. *Clin Chem*, *54*(12), e11-79. https://doi.org/10.1373/clinchem.2008.105601

Sturgeon, C. M., Hoffman, B. R., Chan, D. W., Ch, ng, S.-L., Hammond, E., Hayes, D. F., Liotta, L. A., Petricoin, E. F., Schmitt, M., Semmes, O. J., Söletormos, G., van der Merwe, E., & Diamandis, E. P. (2008). National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines for Use of Tumor Markers in Clinical Practice: Quality Requirements. *Clinical Chemistry*, *54*(8), e1. https://doi.org/10.1373/clinchem.2007.094144

Theodoros, F., & Bergh, J. (2023). Prognostic and predictive factors in early, nonmetastatic breast cancer - UpToDate. In D. Hayes (Ed.), *UpToDate*. https://www.uptodate.com/contents/prognostic-and-predictive-factors-in-early-non-metastatic-breast-cancer

Tian, T., Gao, J., Li, N., Li, Y., Lu, M., Li, Z., Lu, Z., Li, J., & Shen, L. (2016). Circulating Chromogranin A as A Marker for Monitoring Clinical Response in Advanced Gastroenteropancreatic Neuroendocrine Tumors. *PLoS One*, *11*(5), e0154679. https://doi.org/10.1371/journal.pone.0154679

Tormey, W. P., Byrne, B., Hill, A. D., Sherlock, M., & Thompson, C. J. (2017). Should serum calcitonin be routinely measured in patients presenting with thyroid nodule? *Minerva Endocrinol*, *42*(4), 306-310. https://doi.org/10.23736/s0391-1977.17.02566-4

Tosi, P., Tomassetti, S., Merli, A., & Polli, V. (2013). Serum free light-chain assay for the detection and monitoring of multiple myeloma and related conditions. *Ther Adv Hematol*, *4*(1), 37-41. https://doi.org/10.1177/2040620712466863

Tuttle, R. M. (2023, 08/29/2022). *Medullary thyroid cancer: Clinical manifestations, diagnosis, and staging*. https://www.uptodate.com/contents/medullary-thyroid-cancer-clinical-manifestations-diagnosis-and-staging

Ueland, F. R., Li, Andrew John. (2023, 09/22/2022). *Serum biomarkers for evaluation of an adnexal mass for epithelial carcinoma of the ovary, fallopian tube, or peritoneum*. https://www.uptodate.com/contents/serum-biomarkers-for-evaluation-of-an-adnexal-mass-for-epithelial-carcinoma-of-the-ovary-fallopian-tube-or-peritoneum

Van Poznak, C., Somerfield, M. R., Bast, R. C., Cristofanilli, M., Goetz, M. P., Gonzalez-Angulo, A. M., Hicks, D. G., Hill, E. G., Liu, M. C., Lucas, W., Mayer, I. A., Mennel, R. G., Symmans, W. F., Hayes, D. F., & Harris, L. N. (2015). Use of Biomarkers to Guide Decisions on Systemic Therapy for Women With Metastatic Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline. *J Clin Oncol*, *33*(24), 2695-2704. https://doi.org/10.1200/jco.2015.61.1459

Walentowicz, P., Krintus, M., Sadlecki, P., Grabiec, M., Mankowska-Cyl, A., Sokup, A., & Walentowicz-Sadlecka, M. (2014). Serum inhibin A and inhibin B levels in epithelial ovarian cancer patients. *PLoS One*, *9*(3), e90575. https://doi.org/10.1371/journal.pone.0090575

Wells, S. A., Jr., Asa, S. L., Dralle, H., Elisei, R., Evans, D. B., Gagel, R. F., Lee, N., Machens, A., Moley, J. F., Pacini, F., Raue, F., Frank-Raue, K., Robinson, B., Rosenthal, M. S., Santoro, M., Schlumberger, M., Shah, M., & Waguespack, S. G. (2015). Revised American Thyroid Association guidelines for the management of medullary thyroid carcinoma. *Thyroid*, *25*(6), 567-610. https://doi.org/10.1089/thy.2014.0335

Wu, D., Lim, M. S., & Jaffe, E. S. (2018). Pathology of Castleman Disease. *Hematol Oncol Clin North Am*, *32*(1), 37-52. https://doi.org/10.1016/j.hoc.2017.09.004

Wu, M., Liu, H., Liu, Z., Liu, C., Zhang, A., & Li, N. (2018). Analysis of serum alpha-fetoprotein (AFP) and AFP-L3 levels by protein microarray. *J Int Med Res*, *46*(10), 4297-4305. https://doi.org/10.1177/0300060518789304

Yang, X., Yang, Y., Li, Z., Cheng, C., Yang, T., Wang, C., Liu, L., & Liu, S. (2015). Diagnostic value of circulating chromogranin a for neuroendocrine tumors: a systematic review and meta-analysis. *PLoS One*, *10*(4), e0124884. https://doi.org/10.1371/journal.pone.0124884

Policy Update History:

7/17/2023	Document updated with literature review. The following changes were made to Reimbursement Information: Reorganized #1 such that the focus is the cancer and then the appropriate biomarkers. In #1, removed CEA and inhibin for occult primary adenocarcinoma or carcinoma not otherwise specified; calcitonin expression testing for cervical cancer; CEA for NSCLC; calcitonin expression testing for occult primary adenocarcinoma or anaplastic/undifferentiated tumors of the head and neck, or otherwise unspecified; CEA for peritoneal mesothelioma; CEA for pleural mesothelioma; and inhibin expression testing for uterine sarcoma. Removed "The use of urokinase plasminogen activator (uPA) and plasminogen activator inhibitor type 1 (PAI 1) as serum tumor markers is not reimbursable. Remainder of reimbursement information revised for clarity. References revised.
11/1/2022	New policy