



## Medical Policy

# Serum Tumor Markers for Breast and Gastrointestinal Malignancies

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### Policy Number: 538

BCBSA Reference Number: 2.03.02A

NCD/LCD: National Coverage Determination (NCD) for Carcinoembryonic Antigen (190.26)

### Related Policies

Non-BRCA Breast Cancer Risk Assessment (eg, OncoVue) #[188](#)

Tumor Markers for Diagnosis and Management of Cancer #[167](#)

### Policy<sup>1</sup>

#### Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue<sup>SM</sup> and Medicare PPO Blue<sup>SM</sup> Members

**CA 15-3** (also known as CA 27-29, Truquant BR RIA®) This testing is used to monitor women for breast cancer. Experts disagree about whether this test gives valuable information to breast cancer patients. Therefore, we have chosen to let doctors and patients make their own informed decisions about this test.

**CA 19-9** testing for patients with an established diagnosis of pancreatic cancer or gastric cancer may be considered **MEDICALLY NECESSARY** when used to monitor the clinical response to therapy in order to either discontinue ineffective therapy or to detect early recurrence of disease.

**CA 19-9** testing for the diagnosis, following, or prognosis of colorectal, liver or breast cancer is considered **INVESTIGATIONAL**.

**CEA** testing for the diagnosis and follow-up of metastatic breast cancer and for gastrointestinal malignancies may be considered **MEDICALLY NECESSARY**.

**CEA** testing for the diagnosis, following, or prognosis of lung cancer is considered **INVESTIGATIONAL**.

**CEA** testing for routine cancer screening is considered **INVESTIGATIONAL**.

#### Medicare HMO Blue<sup>SM</sup> and Medicare PPO Blue<sup>SM</sup> Members

Medical necessity criteria and coding guidance can be found through the link(s) below.

[National Coverage Determinations \(NCDs\)](#)

National Coverage Determination (NCD) for Carcinoembryonic Antigen (190.26)

**Note:** To review the specific NCD, please remember to click “accept” on the CMS licensing agreement at the bottom of the CMS webpage.

## Prior Authorization Information

### Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

### Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is <b>required</b> .
Commercial PPO and Indemnity	Prior authorization is <b>required</b> .
Medicare HMO Blue <sup>SM</sup>	Prior authorization is <b>required</b> .
Medicare PPO Blue <sup>SM</sup>	Prior authorization is <b>required</b> .

## CPT Codes / HCPCS Codes / ICD Codes

*Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.*

*Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.*

*The following codes are included below for informational purposes only; this is not an all-inclusive list.*

The above **medical necessity criteria MUST** be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity:

### CPT Codes

CPT codes:	Code Description
82378	Carcinoembryonic antigen (CEA)

The following ICD Diagnosis Codes are considered medically necessary when submitted with the CPT code above if **medical necessity criteria** are met:

### ICD-10 Diagnosis Codes

ICD-10-CM diagnosis codes:	Code Description
C15.3	Malignant neoplasm of upper third of esophagus
C15.4	Malignant neoplasm of middle third of esophagus
C15.5	Malignant neoplasm of lower third of esophagus
C15.8	Malignant neoplasm of overlapping sites of esophagus
C15.9	Malignant neoplasm of esophagus, unspecified
C16.0	Malignant neoplasm of cardia
C16.1	Malignant neoplasm of fundus of stomach
C16.2	Malignant neoplasm of body of stomach
C16.3	Malignant neoplasm of pyloric antrum
C16.4	Malignant neoplasm of pylorus
C16.5	Malignant neoplasm of lesser curvature of stomach, unspecified
C16.6	Malignant neoplasm of greater curvature of stomach, unspecified

C16.8	Malignant neoplasm of overlapping sites of stomach
C16.9	Malignant neoplasm of stomach, unspecified
C17.0	Malignant neoplasm of duodenum
C17.1	Malignant neoplasm of jejunum
C17.2	Malignant neoplasm of ileum
C17.3	Meckel's diverticulum, malignant
C17.8	Malignant neoplasm of overlapping sites of small intestine
C17.9	Malignant neoplasm of small intestine, unspecified
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of colon
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.0	Malignant neoplasm of anus, unspecified
C21.1	Malignant neoplasm of anal canal
C21.2	Malignant neoplasm of cloacogenic zone
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C26.0	Malignant neoplasm of intestinal tract, part unspecified
C26.9	Malignant neoplasm of ill-defined sites within the digestive system
C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.012	Malignant neoplasm of nipple and areola, left female breast
C50.019	Malignant neoplasm of nipple and areola, unspecified female breast
C50.021	Malignant neoplasm of nipple and areola, right male breast
C50.022	Malignant neoplasm of nipple and areola, left male breast
C50.029	Malignant neoplasm of nipple and areola, unspecified male breast
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.119	Malignant neoplasm of central portion of unspecified female breast
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.129	Malignant neoplasm of central portion of unspecified male breast
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
C50.219	Malignant neoplasm of central portion of unspecified male breast
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.319	Malignant neoplasm of lower-inner quadrant of unspecified female breast
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast
C50.329	Malignant neoplasm of lower-inner quadrant of unspecified male breast
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
C50.419	Malignant neoplasm of upper-outer quadrant of unspecified female breast
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast
C50.429	Malignant neoplasm of upper-outer quadrant of unspecified male breast

C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of left female breast
C50.519	Malignant neoplasm of lower-outer quadrant of unspecified female breast
C50.521	Malignant neoplasm of lower-outer quadrant of right male breast
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast
C50.529	Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.619	Malignant neoplasm of axillary tail of unspecified female breast
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.629	Malignant neoplasm of axillary tail of unspecified male breast
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.819	Malignant neoplasm of overlapping sites of unspecified female breast
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.829	Malignant neoplasm of overlapping sites of unspecified male breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.919	Malignant neoplasm of unspecified site of unspecified female breast
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast
C50.929	Malignant neoplasm of unspecified site of unspecified male breast
C78.4	Secondary malignant neoplasm of small intestine
C78.5	Secondary malignant neoplasm of large intestine and rectum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
C78.89	Secondary malignant neoplasm of other digestive organs
C79.2	Secondary malignant neoplasm of skin
C79.81	Secondary malignant neoplasm of breast
D01.0	Carcinoma in situ of colon
D01.1	Carcinoma in situ of rectosigmoid junction
D01.2	Carcinoma in situ of rectum
D05.90	Unspecified type of carcinoma in situ of unspecified breast
D05.91	Unspecified type of carcinoma in situ of right breast
D05.92	Unspecified type of carcinoma in situ of left breast
D37.1	Neoplasm of uncertain behavior of stomach
D37.2	Neoplasm of uncertain behavior of small intestine
D37.4	Neoplasm of uncertain behavior of colon
D37.5	Neoplasm of uncertain behavior of rectum
D48.60	Neoplasm of uncertain behavior of unspecified breast
D48.61	Neoplasm of uncertain behavior of right breast
D48.62	Neoplasm of uncertain behavior of left breast
D49.3	Neoplasm of unspecified behavior of bladder
Z85.028	Neoplasm of unspecified behavior of bladder
Z85.038	Personal history of other malignant neoplasm of large intestine
Z85.048	Personal history of other malignant neoplasm of rectum, rectosigmoid junction, and anus

The above medical necessity criteria **MUST** be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity:

### CPT Codes

CPT codes:	Code Description
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86301	Immunoassay for tumor antigen, quantitative; CA 19-9
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The following ICD Diagnosis Codes are considered medically necessary when submitted with the CPT code above if medical necessity criteria are met:

### ICD-10 Diagnosis Codes

ICD-10-CM diagnosis codes:	Code Description
C16.0	Malignant Neoplasm of Cardia
C16.1	Malignant Neoplasm of Fundus of Stomach
C16.2	Malignant Neoplasm of Body of Stomach
C16.3	Malignant Neoplasm of Pyloric Antrum
C16.4	Malignant Neoplasm of Pylorus
C16.5	Malignant Neoplasm of Lesser Curvature of Stomach, Unspecified
C16.6	Malignant Neoplasm of Greater Curvature of Stomach, Unspecified
C16.8	Malignant Neoplasm of Overlapping Sites of Stomach
C16.9	Malignant Neoplasm of Stomach, Unspecified
C25.0	Malignant Neoplasm of Head of Pancreas
C25.1	Malignant Neoplasm of Body of Pancreas
C25.2	Malignant Neoplasm of Tail of Pancreas
C25.3	Malignant Neoplasm of Pancreatic Duct
C25.7	Malignant Neoplasm of Other Parts Of Pancreas
C25.8	Malignant Neoplasm of Overlapping Sites of Pancreas
C25.9	Malignant Neoplasm of Pancreas, Unspecified
C78.7	Secondary Malignant Neoplasm of Liver and Intrahepatic Bile Duct
C78.80	Secondary Malignant Neoplasm of Unspecified Digestive Organ
C78.89	Secondary Malignant Neoplasm of Other Digestive Organs
D00.2	Carcinoma in Situ of Stomach
D01.7	Carcinoma in Situ of Other Specified Digestive Organs
D01.9	Carcinoma in Situ of Digestive Organ, Unspecified

The above medical necessity criteria **MUST** be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity:

### CPT Codes

CPT codes:	Code Description
86300	Immunoassay for tumor antigen, quantitative; CA 15-3 (27.29)

### Description

Serum tumor markers are molecules or substances shed by a tumor into the circulation where they can be detected and quantitated. Noncirculating tumor markers include those that can be detected histochemically or cytogenetically on a tissue sample. Examples of the latter include the HER2 oncoprotein, detected by immunohistochemistry on a subset of breast cancers, and the Philadelphia chromosome, which is a cytogenetic marker for chronic myelogenous leukemia.

Serum tumor markers have been investigated in many malignancies, including most prominently myeloma (ie,  $\kappa$ 2-microglobulin), germ cell tumors (ie, alpha fetoprotein, human chorionic gonadotropin), and prostate cancer (ie, PSA). The HER2 oncoprotein extracellular domain has been studied as a serum tumor marker in breast and other malignancies. Carcinoembryonic antigen (CEA) has also been widely investigated in gastrointestinal malignancies. This policy focuses on specific tumor markers for breast and gastrointestinal malignancies.

For breast cancer, the most extensively investigated serum tumor markers besides HER2 are those associated with the MUC-1 gene. For gastrointestinal cancer, including gastric, pancreatic, and colorectal cancer, the most extensively studied tumor markers, other than CEA, are those related to mucinous glycoproteins. The MUC-1

gene encodes a cell-associated mucin-like antigen, and different antibodies may be used to detect different epitopes. CA 15-3 and CA 27.29 are 2 related monoclonal antibodies that detect epitopes encoded by the MUC-1 gene. While much of the literature has focused on the use of CA 15-3, it has been largely replaced by CA 27.29, which is reportedly more sensitive. The mucinous glycoproteins of the gastrointestinal tract include CA 19-9, and CA 72-4, depending on which antibody is used.

Since serum tumor markers can also be detected in normal or benign lesions, significantly elevated circulating levels may occur with malignancy by one or more of the following mechanisms: (1) overexpression of the antigen by malignant cells; (2) a large tumor burden; and/or (3) slower clearance of the marker. For example, since most tumor markers are cleared by the liver, liver abnormalities (whether benign, malignant, or inflammatory) may elevate tumor marker concentrations due to impaired clearance. Because most tumor markers are not unique to malignancy, cut-off points must be established for normal versus abnormal marker levels. In contrast, serial monitoring of serum tumor markers in a setting of established malignancy may not require such cutoff points. Various clinical applications of serum tumor markers can be broadly divided into 2 categories, those involving a single measurement and those involving serial measurements.

## Policy History

Date	Action
2/2016	Clarified coding information.
11/2015	Ongoing medically necessary and investigational statements transferred from medical policy #167 Tumor Markers for Diagnosis and Management of Cancer. 11/1/2015
1/2015	Clarified coding information.
6/2014	Updated coding section with ICD10 procedure and diagnosis codes, effective 10/2015.
4/2014	Clarified coding information.
6/2012	Updated with additional references based on BCBSA national policy reviewed 10/2011.

## Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

[Medical Policy Terms of Use](#)

[Managed Care Guidelines](#)

[Indemnity/PPO Guidelines](#)

[Clinical Exception Process](#)

[Medical Technology Assessment Guidelines](#)

## References

- 1995 TEC Assessments; Tab 19: Serum tumor markers for the diagnosis and monitoring of breast cancer.
- 1996 TEC Assessments; Tab 23: Serum tumor markers for the diagnosis and monitoring of gastrointestinal cancer.
- 1996 TEC Assessments; Tab 24: Serum tumor markers (CA 15-3, CA 27.29 and CA 549) for the monitoring of breast cancer recurrence.
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19. Berger AC, Garcia Jr M, Hoffman JP, et al. Postresection CA 19-9 predicts overall survival in patients with pancreatic cancer treated with adjuvant chemoradiation: A prospective validation by RTOG 9704. *J Clin Oncol* 2008; 26:5918-22.
20. Hess V, Glimelius B, Grawe P, et al. CA 19-9 tumour-marker response to chemotherapy in patients with advanced pancreatic cancer enrolled in a randomized controlled trial. *Lancet Oncol* 2008; 9(2):132-8.

## Endnotes

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<sup>1</sup> Based on expert opinion and MPRM 2.03.02A