**EFFECTIVE DATE:** 06|01|2025
**POLICY LAST REVIEWED:** 02|19|2025

## OVERVIEW
CA 125 is a high-molecular-weight serum tumor marker elevated in 80% of patients who present with epithelial ovarian carcinoma. It is also elevated in carcinomas of the fallopian tube, endometrium, and endocervix.

## MEDICAL CRITERIA
Not applicable

## PRIOR AUTHORIZATION
Not applicable

## POLICY STATEMENT
**Medicare Advantage Plans and Commercial Products**
Measurements of CA 125 may be considered medically necessary in patients with symptoms suggestive of ovarian cancer or in those with known ovarian cancer or in individual patients with other gynecologic malignancies, such as endometrial cancer, in whom baseline levels of CA 125 have been shown to be elevated.

**Note:** Laboratories are not allowed to obtain clinical authorization or participate in the authorization process on behalf of the ordering physician. Only the ordering physician shall be involved in the authorization, appeal or other administrative processes related to prior authorization/medical necessity.

In no circumstance shall a laboratory or a physician/provider use a representative of a laboratory or anyone with a relationship to a laboratory and/or a third party to obtain authorization on behalf of the ordering physician, to facilitate any portion of the authorization process or any subsequent appeal of a claim where the authorization process was not followed and/or a denial for clinical appropriateness was issued, including any element of the preparation of necessary documentation of clinical appropriateness. If a laboratory or a third party is found to be supporting any portion of the authorization process, BCBSRI will deem the action a violation of this policy and severe action will be taken up to and including termination from the BCBSRI provider network. If a laboratory provides a laboratory service that has not been authorized, the service will be denied as the financial liability of the participating laboratory and may not be billed to the member.

**Commercial Products**
Some genetic testing services are not covered and a contract exclusion for any self-funded group that has excluded the expanded coverage of biomarker testing related to the state mandate, R.I.G.L. **§27-19-81** described in the Biomarker Testing Mandate policy. For these groups, a list of which genetic testing services are covered with prior authorization, are not medically necessary or are not covered because they are a contract exclusion can be found in the Coding section of the Genetic Testing Services or Proprietary Laboratory Analyses policies. Please refer to the appropriate Benefit Booklet to determine whether the member's plan has customized benefit coverage. Please refer to the list of Related Policies for more information.

## COVERAGE
Benefits may vary between groups/contracts. Please refer to the appropriate section of the Benefit Booklet, Evidence of Coverage or Subscriber Agreement for services not medically necessary.

## BACKGROUND

CA 125 is a high-molecular-weight protein antigen that is commonly elevated in patients with known ovarian cancer. CA 125 may also be elevated in other gynecologic malignancies, such as endometrial cancer, although the association is not as consistent as that with ovarian cancer. CA 125 has been widely used as a technique to monitor patients with known ovarian cancer or other gynecologic malignancies that, in individual patients, are associated with elevated levels of CA 125. Frequently, a rising CA 125 will be the initial sign of recurrent disease.

CA 125 has also been investigated as a possible screening tool for ovarian cancer, both in the general population and in patients considered at high risk of ovarian cancer.

Levels of CA 125 may also be elevated in nonmalignant conditions, including pregnancy, endometriosis, pelvic inflammatory disease, benign ovarian masses, and without any identifiable cause.

The use of CA 125 to monitor ovarian cancer recurrence in patients with known ovarian cancer is considered standard practice and is not further discussed. In addition, other gynecologic malignancies, particularly endometrial cancer, may also be associated with CA 125 in individual cases. If so, levels of CA 125 may be similarly monitored for cancer recurrence.

CA-125 testing to monitor ovarian cancer and other gynecologic malignancies is considered standard practice. A large published randomized trial, conducted in the United States, found that screening asymptomatic women for ovarian cancer with CA-125 does not reduce ovarian cancer mortality but does result in unnecessary invasive procedures among women with false-positive test results.

A CA 125 level may be obtained as part of the initial pre-operative workup for women presenting with a suspicious pelvic mass to be used as a baseline for purposes of post-operative monitoring. Initial declines in CA 125 after initial surgery and/or chemotherapy for ovarian carcinoma are also measured by obtaining three serum levels during the first month post treatment to determine the patient's CA 125 half-life, which has significant prognostic implications.

The CA 125 levels are again obtained at the completion of chemotherapy as an index of residual disease. Surveillance CA 125 measurements are generally obtained every 3 months for 2 years, every 6 months for the next 3 years and yearly thereafter. CA 125 levels are also an important indicator of a patient's response to therapy in the presence of advanced or recurrent disease. In this setting, CA 125 levels may be obtained prior to each treatment cycle.

These services are not covered for the evaluation of patients with signs or symptoms suggestive of malignancy. The service may be ordered at times necessary to assess either the presence of recurrent disease or the patient's response to treatment with subsequent treatment cycles.

The CA 125 is specifically not covered for aiding in the differential diagnosis of patients with a pelvic mass as the sensitivity and specificity of the test is not sufficient. In general, a single "tumor marker" will suffice in following a patient with one of these malignancies.

For those with high-risk factors (eg, BRCA mutations, family history of breast or ovarian cancer), Risk-Reducing Salpingo-Oophorectomy (RRSO) is generally preferred over screening as it reduces the likelihood of breast, ovarian, fallopian tube, and primary peritoneal cancers. For those who choose to defer or decline RRSO, some physicians use CA-125 monitoring and endovaginal US. However, prospective studies in high-risk patients have also shown that screening with CA-125 and TVUS may improve the likelihood of diagnosis at an earlier stage, and may improve survival of the patients who develop ovarian cancer. As in average-risk patients, analyses of data from high-risk patients suggests that interpretation of CA-125 using risk of ovarian cancer algorithm (ROCA) rather than a single concentration threshold improves screen sensitivity and the likelihood of ovarian cancer detection at an earlier stage. In high-risk patients the appropriate CA-125 cut-point may depend on menopausal status.

Measurement of CA 125 may be considered medically necessary in asymptomatic women who are BRCA mutation carriers, as a screening technique for ovarian cancer up to twice a year.

CA 125 is used for the following indications:
Note: The following guidelines are not applicable for a simple ovarian cyst:

- In detecting suspicious gynecological cancers such as epithelial ovarian, fallopian tube, endometrium and endocervix carcinomas, or a complex ovarian cyst.
- In detecting suspicious symptoms suggestive of malignant mesothelioma or primary peritoneal carcinoma.
- In detecting a suspicious pelvic mass preoperatively and as a baseline for post-operative monitoring.
- In the management and treatment of ovarian cancer after initial surgery and/or chemotherapy.
- In monitoring advanced or recurrent disease response after therapy.
- As a screening test for ovarian cancer in women who are BRCA mutation carriers.

## CODING

**Medicare Advantage Plans and Commercial Products**
The following CPT code(s) is considered medically necessary when filed with one of the ICD-10 Diagnosis Code(s)* listed below:
**86304** Immunoassay for tumor antigen, quantitative; CA 125

***ICD-10 Diagnosis Code(s):**

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|---|---|
| C45.1 | M33.03 |
| C48.1-C48.8 | M33.13 |
| C51.8 | M33.93 |
| C53.0 | N83.201-N83.209 |
| C54.1-C54.3 | N83.291-N83.299 |
| C54.9 | R19.01-R19.04 |
| C56.1-C56.9 | R19.09 |
| C57.00-C57.02 | R97.1 |
| C57.4-C57.8 | R97.8 |
| C79.60-C79.63 | Z15.01 |
| C79.82 | Z15.02 |
| D39.0 | Z85.41-Z85.44 |
| D39.10-D39.9 | |
| G89.3 | |

## RELATED POLICIES

Biomarker Testing Mandate
Genetic Testing Services

## PUBLISHED

Provider Update, April 2025
Provider Update, April 2024
Provider Update, March/November 2023
Provider Update, June 2022
Provider Update, April 2021

## REFERENCES

1. Centers for Medicare and Medicaid Services cms.gov National Coverage Determination (NCD) for Tumor Antigen by Immunoassay - CA 125 (190.28) https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=130&ncdver=2&bc=AgAAgAAAAAAAAA%3d%3d&

2. Buys SS, Partridge E, Black A et al. for the PLCO team. Effect of screening on ovarian cancer mortality: The prostate, lung, colorectal and ovarian (PLCO) cancer screening randomized controlled trial. JAMA 2011; 305: 2295-2303.
3. Jacobs IJ, Skates SJ, MacDonald N et al. Screening of ovarian cancer: a pilot randomized controlled trial. Lancet 1999; 353(9160): 1207-10.
4. Burke W. Daly M. Garber J et al. Recommendations for follow-up care of individuals with an inherited predisposition to cancer. II. BRCA1 and BRCA2. JAMA 1997; 277(12): 997-1003.
5. United Kingdom Collaborative Trial of Ovarian Cancer Screening. Available online at: http://www.instituteforwomenshealth.ucl.ac.uk/academic_research/gynaecologicalcancer/gcrc/ukctocs Last accessed September 2011.
6. NCCN Clinical Practice Guidelines in Oncology Genetic/Familial High-Risk Assessment: Breast and Ovarian, Version 3 2019-January 18, 2019: 14
7. NCCN Clinical Practice Guidelines in Oncology Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic, Version 1.2025 2024-September 11, 2024. Retrieved January 24, 2025 from https://www.logan.org/wp-content/uploads/2024/09/genetics_bop.pdf
8. Ovarian Cancer Continue Including Fallopian Tube Cancer and Primary Peritoneal Cancer. (2024). In *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)* (Version 3.2024). National Comprehensive Cancer Network. Retrieved January 24, 2025, from https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf