

## Corporate Medical Policy

# Proteomics-based Testing for the Evaluation of Ovarian (Adnexal) Masses

<b>File Name:</b>	proteomics_based_testing_for_the_evaluation_of_ovarian_adnexal_masses
<b>Origination:</b>	7/2010
<b>Last CAP Review:</b>	3/2012
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### Description of Procedure or Service

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The OVA1™ test (Vermillion, Inc., Fremont, CA) is a qualitative serum test that combines immunoassay results for 5 analytes (CA 125, prealbumin, apolipoprotein A-1, beta2 microglobulin, and transferrin) into a single numerical score. It is intended to be used in women with adnexal masses who are planning to have surgery by a non-gynecologic oncologist for disease considered benign using routine clinical and radiologic evaluation. In this patient subset, the test serves as an aid to further assess the likelihood that malignancy is present.

In 2009, it was estimated that more than 21,000 women in the U.S. were diagnosed with ovarian cancer and more than 14,000 died of this disease. The mortality rate depends on three variables: 1) characteristics of the patient; 2) the biology of the tumor (grade, stage and type); and 3) the quality of treatment (nature of staging, surgery and chemotherapy used). In particular, comprehensive staging and completeness of tumor resection appear to have a positive impact on patient outcome.

In 1997, the Society of Surgical Oncology first recommended ovarian cancer surgery and follow-up treatment be performed by physicians with ovarian cancer disease expertise. To date dozens of articles and several meta-analyses or systemic reviews have been published relevant to this recommendation looking at long-term outcomes, short-term outcomes and process measures (types of treatment such as complete staging or tumor debulking).

At least two meta-analyses have been performed concluding improved outcomes in patients with ovarian cancer when treated by gynecologic oncologists. Data is most convincing for patients with advanced stage disease. Median improvements in survival for patients treated by non-gynecologic oncologists versus gynecologic oncologists have been variable but impressive with increases recently reported to be up to 8 months (12 to 21 months). In at least some reports, important differences have also been observed showing improved survival in patients with early stage disease as well when treated by gynecologic oncologists.

A recent systematic review of 198 studies addressing the role of specialty treatment by gynecologic oncologists and evaluation of other practice related factors (type of hospital, surgical volume, etc.) was more guarded in its analysis. This review noted that not all reports confirmed these findings of improved performance based on sub-specialty. It also noted that in some reports only patients presenting with certain stages of disease (in most cases advanced stage although in some cases early stage) were studied and found to exhibit treatment differences. Nevertheless, this review also concluded that the use of sub-specialists and better education of treatment options for both primary care physicians and patients was warranted.

In an analysis of predictors of comprehensive surgical treatment (meticulous and extensive disease staging, efforts at debulking of the tumor with removal of all visible lesions, lymphadenectomy) in patients with ovarian cancer, Goff et al. observed that comprehensive treatment was linked not only to physician factors but also to a number of simple demographic factors including age, race, insurance

# Proteomics-based Testing for the Evaluation of Ovarian (Adnexal) Masses

status and geographic location (urban versus rural). Optimization of treatment for ovarian cancer may clearly be complicated by these factors.

Adult women presenting with an adnexal mass have an estimated 68% likelihood of having a benign lesion. About 6% have borderline tumors, 22% invasive lesions, and 3% metastatic disease.

Obviously a majority of patients can be treated without use of surgical oncology expertise. To date no existing diagnostic modalities have been identified to discriminate reliably between benign and malignant lesions. Recent publications have appeared describing the use of CA 125 with a symptom index, the use of an “ovarian crescent sign” on ultrasound, and the use of three-dimensional ultrasound to provide increased diagnostic reliability in this decision-making process, but all of these appear to require further validation before being considered for routine clinical use.

The OVA1 is a new proteomic test that has been developed specifically to triage patients thought to have benign adnexal masses with planned treatment by a non-gynecologic-oncologist physician. Patients with positive results should be considered candidates for referral to a gynecologic oncologist for treatment. As described above, this treatment is likely to produce improved patient outcomes.

## Regulatory Status

On July 16, 2009, the Vermillion OVA1 test was cleared for market by the FDA as a 510(k) submission. No predicate was identified and the review decision was based on the de novo (automatic classification of class III devices) 510(k) review process. The intended use carried a boxed warning: “PRECAUTION: The OVA1™ test should not be used without an independent clinical/radiological evaluation and is **not** intended to be a screening test or to determine whether a patient should proceed to surgery. Incorrect use of the OVA1™ test carries the risk of unnecessary testing, surgery, and/or delayed diagnosis.”

## Related Policies

Analysis of Proteomic Patterns for Early Detection of Cancer

**\*\*\*Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

## Policy

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**BCBSNC will cover proteomics-based testing for the evaluation of ovarian (adnexal) masses when determined to be medically necessary because the medical criteria and guidelines shown below are met.**

## Benefits Application

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This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

## When proteomics-based testing for the evaluation of ovarian (adnexal) masses is covered

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The proteomics-based OVA1™ test may be considered **medically necessary** as an aid to further assess the likelihood of ovarian cancer when the generalist gynecologist/surgeon's preoperative clinical and radiological evaluations of an ovarian (adnexal) mass are not suspicious for malignancy.

# Proteomics-based Testing for the Evaluation of Ovarian (Adnexal) Masses

## When proteomics-based testing for the evaluation of ovarian (adnexal) masses is not covered

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All other uses of the OVA1™ test are investigational including but not limited to:

- screening for ovarian cancer, or
- selecting patients for surgery for an adnexal mass, or
- evaluation of patients with clinical or radiologic evidence of malignancy, or
- evaluation of patients with nonspecific signs or symptoms suggesting possible malignancy, or
- post-operative testing and monitoring to assess surgical outcome and/or to detect recurrent malignant disease following treatment.

## Policy Guidelines

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The OVA1 test has been analytically validated and clinical performance has been established in a prospective multi-center clinical trial. The plan for this trial (although not the trial itself) has been described in the peer-reviewed literature and a brief summary of results has appeared in a single abstract.

Extensive information about the trial is available through the posting of an FDA decision summary resulting from FDA clearance of the product in 2009. Use of the OVA1 test clearly improves the diagnostic sensitivity and the preoperative detection of ovarian cancers. This increase in the identification of malignancies should result in more early referrals to gynecological oncologists with resulting improvement in clinical outcomes. Thus, use of the OVA 1 test is considered medically necessary as part of the preoperative evaluation of patients with ovarian masses by non-gynecologic oncologists whose initial evaluation does not indicate the mass is malignant.

There is insufficient evidence to support clinical utility and improved health outcomes for all other uses of this test, including use as a screening tool for ovarian cancer.

## Billing/Coding/Physician Documentation Information

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This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at [www.bcbsnc.com](http://www.bcbsnc.com). They are listed in the Category Search on the Medical Policy search page.

*Applicable service codes: no specific code*

*May be reported with unlisted CPT code 84999. It is sometimes performed with tests 83001 and 83002. The results of the following laboratory tests are used in this test: 82172, 82232, 84134, 84466, 86304*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

## Scientific Background and Reference Sources

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U.S. Food and Drug Administration. 510(k) Substantial Equivalence Determination Decision Summary. OVA1™ Test (K081754). Retrieved 7/14/10

# Proteomics-based Testing for the Evaluation of Ovarian (Adnexal) Masses

from:[http://www.accessdata.fda.gov/cdrh\\_doc/reviews/K081754.pdf](http://www.accessdata.fda.gov/cdrh_doc/reviews/K081754.pdf)

Goff BA, Matthews BJ, Larson EH, et al. Predictors of comprehensive surgical treatment in patients with ovarian cancer. *Cancer* 2007; 109(10):2031-42

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.62, 4/08/2010

Senior Medical Director review 7/22/2010

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.62, 4/14/2011

## Policy Implementation/Update Information

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- 8/17/10 New policy issued. The proteomics-based OVA1™ test may be considered **medically necessary** as an aid to further assess the likelihood that malignancy is present when the physician's (other than gynecologic oncologist) independent clinical and radiological preoperative evaluations do not indicate malignancy in a patient with an ovarian (adnexal) mass. All other uses of the OVA1™ test are investigational including but not limited to: screening for ovarian cancer; or selecting patients for surgery for an adnexal mass; or evaluation of patients with clinical or radiologic evidence of malignancy; or evaluation of patients with nonspecific signs or symptoms suggesting possible malignancy; or post-operative testing and monitoring to assess surgical outcome and/or to detect recurrent malignant disease following treatment. Notification given 8/17/10 for policy effective date of 11/23/10. (adn)
- 1/18/2011 Specialty Matched Consultant Advisory Panel review 12/16/2010. Policy accepted as written. (adn)
- 4/17/12 Related policies added. Reworded when covered section. No change to policy intent. Specialty Matched Consultant Advisory Panel review 3/21/12. (sk)

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Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.