The following Protocol contains medical necessity criteria that apply for this service. It is applicable to Medicare Advantage products unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Preauthorization is required.* Please note that payment for covered services is subject to eligibility and the limitations noted in the patient’s contract at the time the services are rendered.

Description

The OVA1™ test (Vermillion, Inc., Fremont, CA) is a qualitative serum test that combines immunoassay results for five 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.

Background

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. (1) 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). (2) 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. (3) To date dozens of articles and several meta-analyses or systemic reviews (2, 4, 5) 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 (4, 5) concluding improved outcomes in patients with ovarian cancer when treated by gynecologic oncologists. Data are 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 eight months (12 to 21 months). (6) 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. (5)

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. (2) 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. (7) observed that comprehensive treatment was linked not only to physician factors but also to a number of simple demographic factors including age, race, insurance status, and geographic location (urban vs. 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. (8) 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. Referral guidelines were published by the American College of Obstetricians and Gynecologists (ACOG) and the Society of Gynecologic Oncologists (SGO) for women with pelvic masses that are suspicious for ovarian cancer who are being referred to gynecologic oncologists. (9) In these guidelines, a decision to refer in postmenopausal women was based on the presence of at least one of the following indicators: elevated CA 125, ascites, a nodular or fixed pelvic mass, evidence of abdominal or distant metastasis, or a family history of one or more first-degree relatives with ovarian or breast cancer. A decision to refer in premenopausal women was based on at least one of the following: elevated CA 125, ascites, evidence of abdominal or distant metastasis, or a positive family history.

A validation study (10) has been performed on these criteria, suggesting a high negative predictive value ([NPV] 90% or more) in both premenopausal and postmenopausal patients but a much lower positive predictive value (as low as 34%).

Recent publications have appeared describing the use of CA 125 with a symptom index, (11) the use of an “ovarian crescent sign” on ultrasound, (8) the use of three-dimensional ultrasound (12) to provide increased diagnostic reliability in this decision-making process, and most recently the use of an algorithm based on use of key features identified by ACOG/SGO. (7) Since many of these studies have been performed in referral centers, it is not clear how generalizable they are to use in the general population. Further independent validation of these various approaches is needed.

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 U.S. Food and Drug Administration (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 Protocol:**

Analysis of Proteomic Patterns for Early Detection of Cancer

**Corporate Medical Guideline**

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:

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

Policy Guideline

This test is intended to be used for women who meet the following four criteria: older than age 18 years; ovarian adnexal mass present; surgery is planned for treatment of the mass; and the patient has not yet been referred to a gynecologic oncologist. The test allows additional risk assessment in patients already believed to have benign disease using routine clinical and radiological parameters to estimate the risk that there is actually an underlying malignant process.

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. Some of this Protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.

References

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.


