Protocol

Proteomics-based Testing Related to Ovarian Cancer

(20462)

(Formerly Proteomics-based Testing for the Evaluation of Ovarian Cancer [Adnexal] Masses)

Medical Benefit		**Effective Date**: 04/01/14	**Next Review Date**: 01/15
Preauthorization	Yes	**Review Dates**: 01/11, 01/12, 01/13, 01/14	

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

A variety of gene-based biomarkers have been studied in association with ovarian cancer. Of particular interest have been tests that integrate results from multiple analytes into a risk score to predict the presence of disease. Two tests based on this principle (Ova1™ test and ROMA™ test) have now been cleared by FDA for use in women with adnexal masses 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 recommended ovarian cancer surgery and follow-up treatment be performed by physicians with ovarian cancer disease expertise. (3) To date, dozens of articles have been published relevant to this recommendation looking at long-term outcomes, short-term outcomes, and process measures (e.g., types of treatment such as complete staging or tumor debulking). At least two meta-analyses have concluded that outcomes are better in patients with ovarian cancer when they are treated by gynecologic oncologists. (4, 5) Data have been most convincing for patients with advanced stage disease.

Adult women presenting with an adnexal mass have an estimated 68% likelihood of having a benign lesion. (6) About 6% have borderline tumors, 22%, invasive malignant lesions, and 3%, metastatic disease. Clinicians generally agree that women with masses that have a high likelihood of malignancy should undergo surgical staging by gynecologic oncologists. However, women with clearly benign masses do not require referral to a specialist. Criteria and tests that help differentiate benign from malignant pelvic masses are thus desirable.

In 2005, the American College of Obstetricians and Gynecologists (ACOG) and the Society of Gynecologic Oncologists (SGO) jointly released referral guidelines that address criteria for referring women with pelvic masses that are suspicious for ovarian cancer to gynecologic oncologists. (7) Separate criteria were developed for pre-menopausal and post-menopausal women. In premenopausal women, referral criteria included at least one of the following: elevated CA 125 (greater than 200 U/mL), ascites, evidence of abdominal or distant metastasis, or a positive family history. The referral criteria in postmenopausal women were similar, except that

a lower threshold for an elevated CA-125 test was used (35 U/ml) and nodular or fixed pelvic mass was an additional criterion.

Two proteomic tests have now been cleared by the U.S. Food and Drug Administration (FDA) with the intended use to triage patients with adnexal masses. A suggested use of the test is to identify women with a positive test who have a higher likelihood of malignant disease and may benefit from referral to a gynecologic-oncology specialist. Patients with positive results may be considered candidates for referral to a gynecologic oncologist for treatment.

Regulatory Status

On July 16, 2009, the OVA1TM test (Vermillion, Inc. Fremont, CA) was cleared for market by the U.S. Food and Drug Administration (FDA) as a 510(k) submission. On September 1, 2011, the Risk of Ovarian Malignancy Algorithm (ROMATM test, Fujirebio Diagnostics, Inc., Malvern, PA) was cleared by the U.S. Food and Drug Administration (FDA) as a 510(k) submission. Because the OVA1 test had been found to be a class II medical device by virtue of the July 2009 clearance, ROMA was found to be substantially equivalent to that predicate device.

Black Box Warning: On December 10, 2011, the FDA published an amendment to the regulation for classifying ovarian adnexal mass assessment score test systems to restrict these devices so that a prescribed warning statement that addresses off-label risks be highlighted by a black box warning. (8) The warning is intended to mitigate the risk to health associated with off-label use as a screening test, stand-alone diagnostic test, or as a test to determine whether or not to proceed with surgery.

Related Protocol

Analysis of Proteomic Patterns for Early Detection of Cancer

Policy (Formerly Corporate Medical Guideline)

All uses of the OVA1 and ROMA tests are **investigational** including but not limited to:

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

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.

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