Medica Coverage Policy

<table>
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<tr>
<th>Policy Name:</th>
<th>Multivariate Biomarker Blood Testing for Predicting Malignancy in Women with Adnexal Mass</th>
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<td>Effective Date:</td>
<td>8/16/2021</td>
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**Important Information – Please Read Before Using This Policy**

These services may or may not be covered by all Medica plans. Please refer to the member’s plan document for specific coverage information. If there is a difference between this general information and the member’s plan document, the member’s plan document will be used to determine coverage. With respect to Medicare and Minnesota Health Care Programs, this policy will apply unless those programs require different coverage. Members may contact Medica Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this Medica coverage policy may call the Medica Provider Service Center toll-free at 1-800-458-5512.

Medica coverage policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care and treatment.

**Coverage Policy**

OVA1® and Risk of Ovarian Malignancy Algorithm™ (ROMA™) multivariate biomarker blood testing for predicting malignancy in women with adnexal mass is considered investigative and unproven and therefore NOT COVERED. There is insufficient reliable evidence in the form of high quality peer-reviewed medical literature to establish the safety and efficacy or effects on health care outcomes.

OVERA multivariate biomarker blood testing for predicting malignancy in women with adnexal mass is considered investigative and unproven and therefore NOT COVERED. There is insufficient reliable evidence in the form of high quality peer-reviewed medical literature to establish the efficacy or effects on health care outcomes.

**Note:** This policy is no longer scheduled for routine review of the scientific literature.

**Description**

Proteomic testing attempts to identify biomarkers for early detection, prognosis, and/or prediction of response to therapy for various diseases, using methodologies such as mass spectrometry and fluorescence microscopy protein microarrays in conjunction with computerized bioinformatics analysis. Multivariate biomarker blood testing for predicting malignancy in women with adnexal mass is an example of proteomic testing. When used in conjunction with standard pre-surgical evaluations, these tests are intended to: (1) assess the likelihood that an ovarian adnexal mass is malignant prior to surgery, (2) help identify individuals for referral to gynecologic oncologists (GOs), and (3) increase the likelihood of optimal surgery, treatment, and follow-up for those with confirmed ovarian cancer. These tests are not intended for screening or to determine if the individual should proceed with surgery.

Commercially available proteomic tests for predicting ovarian cancer in women with adnexal mass are the OVA1® (ASPIRA Labs; Vermillion, Inc), Overa (ASPIRA Labs; Vermillion, Inc), and the Risk of Ovarian Malignancy Algorithm™ (ROMA™) test (Fujirebio Diagnostics Inc.). They are purported for use in women with a pelvic mass who are considering exploratory surgery for definitive diagnosis.

The OVA1 qualitative immunoassay combines results from five biomarker tests (CA-125, transthyretin, apolipoprotein A-1, Beta2-microglobulin, transferrin) to estimate the risk that the pelvic mass is malignant. Test results and a patient’s menopausal status are incorporated into the proprietary multivariate OvaCalc software to calculate the OVA1 score, reported as a number from 0-10. The higher the reported number, the higher probability of a malignancy being present.
The Overa assay, also known as second generation OVA1 or OVA2, is a qualitative serum test that combines the results of five biomarkers (follicle stimulating hormone, transferrin, HE4, APO A1, and CA-125) from 5 immunoassays into a proprietary algorithm to calculate a single numeric risk score. As Overa included FSH assay, the patient’s menopausal status does not need to be considered in calculating the risk score.

The Risk of Ovarian Malignancy Algorithm™ (ROMA™) is a qualitative serum test that measures the levels of two blood markers, HE4 and CA125. The test results indicate whether the mass is at high or low risk of being malignant. ROMA is intended to aid in assessing whether a premenopausal or postmenopausal woman who presents with an ovarian adnexal mass is at high or low likelihood of finding malignancy on surgery.

FDA Approval
The OVA1 test (Vermillion, Inc.) was FDA cleared in July 2009 as a biomarker test intended to aid in the diagnosis of a pelvic mass in women at least 18 years of age who present with a pelvic mass and are considering exploratory surgery for definitive diagnosis.

Overa 1 Next Generation Test (Vermillion, Inc.) was FDA cleared in March 2016. It is indicated for women who are over 18 years of age, with an ovarian adnexal mass present for which surgery is planned, and not yet referred to an oncologist.

ROMA was FDA cleared in September 2011. OVA1 was used as the predicate device for FDA approval of the ROMA test. ROMA is indicated for women over at least age 18 years of age who have an ovarian adnexal mass for which surgery is planned, and who have not yet been referred to an oncologist.

Prior Authorization
Prior authorization is not applicable. Claims for this service are subject to retrospective review and denial of coverage, as investigative services are not eligible for reimbursement.

Coding Considerations
Use the current applicable CPT/HCPCS code(s). The following codes are included below for informational purposes only, and are subject to change without notice. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement.

CPT Codes

- 81500 – Oncology (ovarian) biochemical assays of two proteins (CA-125 and HE4), utilizing serum, with menopausal status, algorithm reported as a risk score (This code is for reporting the ROMA™ test)
- 81503 – Oncology (ovarian) biochemical assays of five proteins (CA-125, apolipoprotein A1, beta-2 microglobulin, transferrin and pre-albumin), utilizing serum, algorithm reported as a risk score (This code is for reporting the OVA1™ test)
- 0003U - Oncology (ovarian) biochemical assays of five proteins (apolipoprotein A-1, CA 125 II, follicle stimulating hormone, human epididymis protein 4, transferrin), utilizing serum, algorithm reported as a likelihood score (Overa)

Original Effective Date: 5/1/2015
Re-Review Date(s): 5/16/2018
2/20/2020 – administrative update; format
6/16/2021

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