# MULTIMARKER SERUM TESTING RELATED TO OVARIAN CANCER - OVA1®, OVERA®, AND ROMA™

The purpose of this document is to assist providers enrolled in the Connecticut Medical Assistance Program (CMAP) with the information needed to support a medical necessity determination for OVA1, Overa, and the Risk of Ovarian Malignancy Algorithm (ROMA) testing. By clarifying the information needed for prior authorization of services, HUSKY Health hopes to facilitate timely review of requests so that individuals obtain the medically necessary care they need as quickly as possible.

A number of serum biomarkers have been studied for their association with ovarian cancer. Special interest has been given to tests that integrate results from multiple analytes into a risk score to predict the presence of malignancy in women with adnexal masses. Three tests based on this principle, OVA1, Overa (the second generation OVA1 test), and ROMA have been cleared by the U.S. Food and Drug Administration (FDA).

**OVA1**
The OVA1 test uses proprietary software to incorporate the values of five biomarkers into a single numerical risk score. The biomarkers are: cancer antigen 125 (CA 125), transferrin (TRF), apolipoprotein A-1 (APO A-1), beta-2 microglobulin (B2M), and prealbumin (TT).

From the FDA 510K decision summary: *The OVA1 Test is a qualitative serum test that combines the results of five immunoassays into a single numerical score. It is indicated for women who meet the following criteria: over age 18, ovarian adnexal mass present for which surgery is planned, and not yet referred to an oncologist. The OVA1 Test is an aid to further assess the likelihood that malignancy is present when the physician's independent clinical and radiological evaluation does not indicate malignancy. The test is not intended as a screening or stand-alone diagnostic assay.*

**Overa**
The Overa test uses proprietary software to incorporate the values of five biomarkers into a single numerical risk score. The biomarkers are: CA 125, TRF, APO A-1, follicle-stimulating hormone (FSH), and human epididymis protein 4 (HE4).

From the FDA 510K decision summary: *Overa (referred to as OVA1 Next Generation or Multivariate Index Assay [MIA2G]) is a qualitative serum test that combines the results of five immunoassays into a single numeric result. It is indicated for women who meet the following criteria: over age 18, ovarian adnexal mass present for which surgery is planned, and not yet referred to an oncologist. The OVA1 Next Generation test is an aid to further assess the likelihood that malignancy is present when the physician's independent clinical and radiological evaluation does not indicate malignancy. The test is not intended as a screening or stand-alone diagnostic assay.*

**ROMA**
The ROMA test is an assay that combines HE4, CA 125, and menopausal status into a numerical score.

From the FDA 510K decision summary: *The Risk of Ovarian Malignancy Algorithm (ROMA) is a qualitative serum test that combines the results of HE4 EIA, ARCHITECT CA125 II™ and menopausal status into a numerical score. 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. ROMA is indicated for women who meet the following criteria: over age 18, ovarian adnexal mass present for which surgery is planned, and not yet referred to an oncologist. ROMA must be interpreted in conjunction with an independent clinical and radiological assessment. The test is not intended as a screening or stand-alone diagnostic assay.*

**FDA Black Box Warning**
Each of the above tests have black box warnings that state the following: "*PRECAUTION: Test should not be used without an independent clinical and imaging evaluation and is not intended to be a screening test or to determine whether a patient should proceed to surgery. Incorrect use of this test carries a risk of unnecessary testing, surgery, and/or delayed diagnosis."*

**CLINICAL GUIDELINE**
Coverage guidelines for OVA1, Overa, and ROMA testing are made in accordance with the DSS definition of Medical Necessity. The following criteria are guidelines *only*. Coverage determinations are based on an individual assessment of the member and their unique clinical needs. If the guidelines conflict with the definition of Medical Necessity, the definition of Medical Necessity shall prevail. The guidelines are as follows:

OVA1, OVA1 Next Generation (Overa), and ROMA testing may be considered medically necessary, based on FDA indications, to further assess the likelihood that malignancy is present when the physician's clinical and radiological preoperative evaluations do not indicate malignancy in an individual with an ovarian (adnexal) mass when:

A. The individual is over the age of 18;
B. An ovarian adnexal mass is present, for which surgery is planned; and
C. The individual has not yet been referred to an oncologist or gynecologic oncologist and referral is being considered in the event of a positive test result.

**Not Medically Necessary:**
Based on current, peer-reviewed literature, and FDA indications, the following are considered investigational and therefore not medically necessary:

- As screening for ovarian cancer
- As a method for selecting patients for surgery for an adnexal mass
- As an evaluation of patients with clinical or radiologic evidence of malignancy
- OvaWatch testing

NOTE: EPSDT Special Provision
Early and Periodic Screening, Diagnosis, and Treatment (EPSDT) is a federal Medicaid requirement that requires the Connecticut Medical Assistance Program (CMAP) to cover services, products, or procedures for Medicaid enrollees under 21 years of age where the service or good is medically necessary health care to correct or ameliorate a defect, physical or mental illness, or a condition identified through a screening examination. The applicable definition of medical necessity is set forth in Conn. Gen. Stat. Section 17b-259b (2011) [ref. CMAP Provider Bulletin PB 2011-36].

**PROCEDURE**
Prior authorization of OVA1, Overa, and ROMA testing is required. Requests for coverage of OVA1**,** Overa, and ROMA testing will be reviewed in accordance with procedures in place for reviewing requests for genetic testing. Coverage determinations will be based upon a review of requested and/or submitted case-specific information.

**The following information is needed to review requests for OVA1, Overa, and ROMA testing:**

1. Fully completed authorization request via on-line web portal;
2. Clinical information supporting the medical necessity of the requested testing; and
3. Other information as requested by CHNCT.

**EFFECTIVE DATE**
This Policy is effective for prior authorization requests for OVA1**,** Overa, and ROMA testing for individuals covered under the HUSKY Health Program on or after November 1, 2022.

**LIMITATIONS**
Not Applicable

**CODE:**

| Code | Description |
|---|---|
| 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 ***Note: this code is not currently fee'd by the CT Department of Social Services*** |
| 81500 | Oncology (ovarian), biochemical assays of two proteins (CA-125 and HE4), utilizing serum, with menopausal status, algorithm reported as a risk score |
| 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 |

**DEFINITIONS**

1. **Current Procedural Terminology (CPT):** The most recent edition of a listing, published by the American Medical Association, of descriptive terms and identifying codes for reporting medical services performed by providers.
2. **HUSKY A**: Connecticut children and their parents or a relative caregiver; and pregnant women may qualify for HUSKY A (also known as Medicaid). Income limits apply.
3. **HUSKY B**: Uninsured children under the age of 19 in higher income households may be eligible for HUSKY B (also known as the Children's Health Insurance Program) depending on their family income level. Family cost-sharing may apply.
4. **HUSKY C**: Connecticut residents who are age 65 or older or residents who are ages 18-64 and who are blind, or have another disability, may qualify for Medicaid coverage under HUSKY C (this includes Medicaid for Employees with Disabilities (MED-Connect), if working). Income and asset limits apply.
5. **HUSKY D**: Connecticut residents who are ages 19-64 without dependent children and who: (1) do not qualify for HUSKY A; (2) do not receive Medicare; and (3) are not pregnant, may qualify for HUSKY D (also known as Medicaid for the Lowest-Income populations).

6. **HUSKY Health Program**: The HUSKY A, HUSKY B, HUSKY C, HUSKY D and HUSKY Limited Benefit programs, collectively.
7. **HUSKY Limited Benefit Program or HUSKY, LBP**: Connecticut's implementation of limited health insurance coverage under Medicaid for individuals with tuberculosis or for family planning purposes and such coverage is substantially less than the full Medicaid coverage.
8. **Medically Necessary or Medical Necessity**: (as defined in Connecticut General Statutes § 17b-259b) Those health services required to prevent, identify, diagnose, treat, rehabilitate or ameliorate an individual's medical condition, including mental illness, or its effects, in order to attain or maintain the individual's achievable health and independent functioning provided such services are: (1) Consistent with generally-accepted standards of medical practice that are defined as standards that are based on (A) credible scientific evidence published in peer-reviewed medical literature that is generally recognized by the relevant medical community, (B) recommendations of a physician-specialty society, (C) the views of physicians practicing in relevant clinical areas, and (D) any other relevant factors; (2) clinically appropriate in terms of type, frequency, timing, site, extent and duration and considered effective for the individual's illness, injury or disease; (3) not primarily for the convenience of the individual, the individual's health care provider or other health care providers; (4) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the individual's illness, injury or disease; and (5) based on an assessment of the individual and his or her medical condition.
9. **Prior authorization**: A process for approving covered services prior to the delivery of the service or initiation of the plan of care based on a determination by CHNCT as to whether the requested service is medically necessary.

**ADDITIONAL RESOURCES AND REFERENCES:**


- American College of Obstetrics and Gynecology Committee on Practice B-G. Practice Bulletin No. 174: Evaluation and Management of Adnexal Masses. Obstet Gynecol. 2016;128(5):e210-e226.
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ovary, fallopian tube, or peritoneum. Andrew John Li M.D. Topic last updated March 13, 2024. Literature review current through May 2024. Available at: https://www.uptodate.com/contents/-adnexal-mass-role-of-serum-biomarkers-in-diagnosing-epithelial-carcinoma-of-the-ovary-fallopian-tube-or-peritoneum?search=biomarker%20adnexal%20mass%20ovary&source=search_result&selectedTitle=1%7E150&usage_type=default&display_rank=1. . Accessed on June 11, 2024.
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- Kumari S. Serum Biomarker Based Algorithms in Diagnosis of Ovarian Cancer: A Review. *Indian J Clin Biochem*. 2018;33(4):382-386. doi:10.1007/s12291-018-0786-2. Accessed on June 10, 2024.
- U.S. Food and Drug Administration. 510(k) Substantial Equivalence Determination Decision Summary: OVA1™ Test (K081754). Available at: https://www.accessdata.fda.gov/cdrh_docs/reviews/K081754.pdf. Accessed on June 7, 2022.
- U.S. Food and Drug Administration. 510(k) Substantial Equivalence Determination Decision Summary: OVA1 Next Generation™ Test (K150588). Available at: https://www.accessdata.fda.gov/cdrh_docs/reviews/k150588.pdf. Accessed on June 7, 2022.
- U.S. Food and Drug Administration. 510(k) Substantial Equivalence Determination Decision Summary: ROMA™ Test (K103358). Available at: https://www.accessdata.fda.gov/cdrh_docs/reviews/k103358.pdf. Accessed on June 7, 2022.

**PUBLICATION HISTORY**

| Status | Date | Action Taken |
|---|---|---|
| Original publication | September 2022 | Approved at the July 13, 2022 CHNCT Medical Reviewer meeting. Approved by the CHNCT Clinical Quality Subcommittee on September 19, 2022. Approved by DSS on September 28, 2022. |
| Updated | September 2023 | Update to reference section. Change approved at the July 12, 2023, CHNCT Medical Reviewer meeting. Change approved by the CHNCT Clinical Quality Subcommittee on September 18, 2023. Change approved by DSS on October 2, 2023. |
| Updated | July 2024 | Clinical Guideline updated to align criteria with FDA indications and address indications for which testing would be considered not medically necessary. Update to Procedure to include prior authorization request received via the web portal. Updates to reference section. Changes approved at the July 10, 2024 CHNCT Medical Reviewer meeting. Changes approved by the CHNCT Clinical Quality Subcommittee on September 16, 2024. Changes approved by DSS on September 27, 2024. |