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Medicare Advantage Policy Manual

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Multimarker and Proteomics-based Serum Testing Related to Ovarian Cancer

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IMPORTANT REMINDER

The Medicare Advantage Medical Policy manual is not intended to override the member Evidence of Coverage (EOC), which defines the insured's benefits, nor is it intended to dictate how providers are to practice medicine. Physicians and other health care providers are expected to exercise their medical judgment in providing the most appropriate care for the individual member.

The Medicare Advantage Medical Policies are designed to provide guidance regarding the decision-making process for the coverage or non-coverage of services or procedures in accordance with the member EOC and the Centers of Medicare and Medicaid Services (CMS) policies, when available. In the event of a conflict, applicable CMS policy or EOC language will take precedence over the Medicare Advantage Medical Policy. In the absence of CMS guidance for a requested service or procedure, the health plan may apply their Medical Policy Manual or MCG™ criteria, both of which are developed with an objective, evidence-based process using scientific evidence, current generally accepted standards of medical practice, and authoritative clinical practice guidelines.

Medicare and EOCs exclude from coverage, among other things, services or procedures considered to be investigational, cosmetic, or not medically necessary, and in some cases, providers may bill members for these non-covered services or procedures. Providers are encouraged to inform members in advance when they may be financially responsible for the cost of non-covered or excluded services.

DESCRIPTION

Multimarker serum tests have been proposed as a method for identifying patients likely to have malignant or benign adnexal masses, prior to surgery. A suggested use of the tests is the identification of patients with a higher likelihood of malignant disease, who may benefit from referral to a gynecologic-oncology specialist. These tests are combinations of several separate lab tests known as multi-analyte assays with algorithmic analyses (MAAA) and are performed on a blood sample by a reference laboratory, using a proprietary algorithm.

MEDICARE ADVANTAGE POLICY CRITERIA

Note: While testing addressed by this policy may include CA-125 testing, this policy does not address tumor antigen CA-125 testing alone (CPT 86304), which may be considered medically reasonable and necessary under NCD 190.28.^[1]

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| CMS Coverage Manuals* | None |
| National Coverage Determinations (NCDs)* | None |
| Noridian Healthcare Solutions (Noridian) Local Coverage Determinations (LCDs) and Articles* | <p>For the <i>Risk of Ovarian Malignancy Algorithm (ROMA™)</i> test (<i>CPT code 81500</i>):</p> <p>Note: According to the Fujirebio Diagnostics, Inc. website, “Any lab running CA125 can also perform HE4 and calculate the ROMA score.” ARUP Laboratories is listed as a resource if local laboratory is not available.^[2] Medicare guidelines state jurisdiction for coverage determinations for diagnostic laboratory services is by the contractor assigned jurisdiction over the service area in which the tests are performed.^[3,4] Therefore, the Medicare reference listed below is applicable to all laboratories in the health plan’s service area, as well as California. Other Medicare guidance may be available when the rendering laboratory is located in a different geographical area.</p> <ul style="list-style-type: none"> ✓ MolDX: Molecular Diagnostic Tests (L36256) (For laboratories in the health plan’s service area) and (L35160) (in California/Nevada). These require that molecular diagnostic tests undergo a technology assessment (TA) through the MolDX program. While this test is listed in the DEX™ Registry, it does not have a coverage determination at this time, and therefore would be considered not medically reasonable or necessary until it has completed a TA. ✓ Multimarker Serum Tests Related to Ovarian Cancer Testing (L38371) (The companion article is A57020, which can be accessed directly from the LCD) (For testing performed in laboratories in IL, MN, WI, CT, NY, ME, MA, NH, RI, VT) ✓ Biomarkers for Oncology (L35396) (For testing performed in laboratories in CO, NM, OK, TX, AR, LA, MS, DE, MD, NJ, PA) (Search for ROMA, LCD is used for coverage criteria) |
| Non-Noridian Healthcare Solutions LCDs and Articles* | For the <i>Ova-1® and Overa (OVA1 Next Generation), and OVA1Plus®</i> tests (<i>CPT codes 81503 and 0003U</i>): |

Note: The Ova1® Overa™, and Ova1PLus® tests are performed by Aspira Labs, Inc., a Vermillion Company (Texas). Medicare guidelines state jurisdiction for coverage determinations for diagnostic laboratory services is by the contractor assigned jurisdiction over the service area in which the tests are performed.^[3,4] Therefore, the applicable Medicare contractor for Texas is Novitas Solutions, Inc.

- ✓ Biomarkers for Oncology ([L35396](#)) (*According to the LCD coverage is allowed when performed according to the Food and Drug Administration [FDA] label. Apply the same rationale to the Overa™ test, since it is this test's FDA approval summary cited and used for the OVA1® test within the LCD. For coding, see companion article A52986, which can be accessed directly from the LCD.*)
- ✓ Multimarker Serum Tests Related to Ovarian Cancer Testing ([L38371](#)) (*The companion article is A57020, which can be accessed directly from the LCD*) (For testing performed in laboratories in IL, MN, WI, CT, NY, ME, MA, NH, RI, VT)

**Scroll to the "Public Version(s)" section at the bottom of the LCD for links to prior versions if necessary.

POLICY GUIDELINES

REQUIRED DOCUMENTATION

The information below **must** be submitted for review to determine whether policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome:

- Clinical documentation of the member's age, the existence of an ovarian mass, and treatment plan, which includes applicable surgery;
- Specific test requested (ROMA™, Ova1® or Overa™).

REGULATORY STATUS

The OVA1® test algorithm uses five serum biomarkers, CA-125, prealbumin, apolipoprotein A-1, beta 2 microglobulin, and transferrin. A second-generation test called Overa™ replaces

prealbumin and beta 2 microglobulin with human epididymis secretory protein 4 and follicle stimulating hormone.

The Risk of Ovarian Malignancy Algorithm (ROMA™) test combines 2 biomarkers, human epididymis secretory protein 4 (HE4) and CA-125, along with menopausal status.

The Ova1Plus® test combines two existing FDA-approved tests, Ova1® and Overa™, into a reflex test.

The OvaWatchSM test uses seven serum biomarkers; CA 125, prealbumin, apolipoprotein A-1, beta 2 microglobulin, transferrin, human epididymis protein 4 (HE4) and follicle stimulating hormone (FSH), along with patient age and menopausal status to predict the risk of malignancy in adnexal masses that are deemed benign or indeterminate on clinical assessment. According to the [company website](#), the test has not been cleared for marketing by the FDA.

FDA-approved indications for each test can be found by searching by 510(k) number (found in the table below) in the FDA [510\(k\) Premarket Notification Database](#) (for Overa™ and ROMA™ tests) or the [De Novo Database](#) (for OVA1®) and viewing the Summary.

Of note, each of these tests includes a black box warning that they should not be used without an independent clinical and imaging evaluation and are not intended to be used as screening tests or to determine whether a patient should proceed to surgery. In addition, incorrect use of these tests carries the risk of unnecessary testing, surgery, and/or delayed diagnosis.

| TEST NAME | LABORATORY/MANUFACTURER | FDA APPROVAL / NUMBER |
|------------------------------|---|---------------------------|
| Overa™ test | Aspira, Austin, TX | March 2016 / K150588 |
| OVA1® test | Aspira, Austin, TX | July 2009 / K081754 |
| ROMA™ test | Fujirebio Diagnostics, Inc. (Test is ordered through Quest Diagnostics and LabCorp) | September 2011 / K103358 |
| Ova1Plus® | Aspira, Austin, TX | Combination of Ova1/Overa |
| OvaWatchSM | Aspira, Austin, TX | |

CROSS REFERENCES

None

REFERENCES

1. NCD for Tumor Antigen by Immunoassay - CA 125 (190.28) [Last Cited 1/3/2024] (*This reference can be found on the [Medicare Coverage Database](#) website*)
2. Fujirebio Diagnostics, Inc. website: <https://www.he4test.com/en-US/providers>
3. Medicare Managed Care Manual, Pub. #100-16, Chapter 4 - Benefits and Beneficiary Protections, [§90.4.1 – MACS with Exclusive Jurisdiction over a Medicare Item or Service](#)
4. Medicare Claims Processing Manual, Chapter 1 - General Billing Requirements, [§10.1.5.4 - Independent Laboratories](#)
5. [Aspira Women’s Health website: https://aspirawh.com/](https://aspirawh.com/)

CODING

| Codes | Number | Description |
|-------|--------|---|
| CPT | 81500 | Oncology (ovarian), biochemical assays of two proteins (CA-125 and HE4), utilizing serum, with menopausal status, algorithm reported as a risk score (<i>This code is used for reporting the ROMA™ test</i>) |
| | 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 (<i>This code is used for reporting the OVA1® test</i>) |
| | 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 (<i>This code is used for reporting the Overa™ test</i>) |

HCPCS None

***IMPORTANT NOTE:** Medicare Advantage medical policies use the most current Medicare references available at the time the policy was developed. Links to Medicare references will take viewers to external websites outside of the health plan's web control as these sites are not maintained by the health plan.