Medical Policy
Serum Biomarker Human Epididymis Protein 4 - HE4

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Policy Number: 290
BCBSA Reference Number: 2.04.66

Related Policies
- Tumor Markers for Diagnosis and Management of Cancer #536
- Proteomics-based Testing for the Evaluation of Ovarian (Adnexal) Masses #249

Policy
Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO BlueSM and Medicare PPO BlueSM Members

Measurement of HE4 for all indications is INVESTIGATIONAL.

Prior Authorization Information
Pre-service approval is required for all inpatient services for all products. See below for situations where prior authorization may be required or may not be required for outpatient services.
Yes indicates that prior authorization is required.
No indicates that prior authorization is not required.
N/A indicates that this service is primarily performed in an inpatient setting.

<table>
<thead>
<tr>
<th>Outpatient</th>
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<tbody>
<tr>
<td><strong>Commercial Managed Care (HMO and POS)</strong></td>
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<tr>
<td><strong>Commercial PPO and Indemnity</strong></td>
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<td><strong>Medicare HMO BlueSM</strong></td>
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<td><strong>Medicare PPO BlueSM</strong></td>
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CPT Codes / HCPCS Codes / ICD Codes
Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.
The following codes are included below for informational purposes only; this is not an all-inclusive list.

The following CPT code is considered investigational for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

CPT Codes

<table>
<thead>
<tr>
<th>CPT codes:</th>
<th>Code Description</th>
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<tr>
<td>86305</td>
<td>Human epididymis protein 4 (HE4)</td>
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**Description**

Ovarian cancer is the fifth most common cause of cancer mortality in U.S. women. Stage at diagnosis is an important predictor of survival; however, most women are not diagnosed until the disease has spread. After treatment for ovarian cancer, serial measurement of CA-125 has been used to detect early recurrence of disease. A rising CA-125 level has been found to correlate with disease recurrence; however, levels can also be elevated by benign gynecological and medical conditions, such as endometriosis, congestive heart failure, and cirrhosis. This limits the specificity for distinguishing between benign and malignant masses, and there is no reliable test to differentiate between benign or malignant pelvic masses.

Human epididymis protein 4 (HE4) is a potential new biomarker for detecting ovarian cancer early and for monitoring disease progression and recurrence. HE4 is proposed as a replacement for, or a complement to, CA-125. HE4 has been found to be overexpressed by epithelial ovarian cancer tumors and to circulate in the serum of patients with epithelial ovarian cancer. Levels of HE4 may be less likely to be elevated due to benign conditions, as is the case with CA-125.

Examples of tests for HE4 include HE4 EIA test kit and the ARCHITECT HE4. All HE4 tests are considered investigational regardless of the commercial name or the laboratory performing the test or FDA status.

**Summary**

There are limited data on the diagnostic test performance of the HE4 test used to monitor disease progression and recurrence in women diagnosed with epithelial ovarian cancer, the FDA-approved indication for the test. The only available data on diagnostic test performance are in FDA documents; the reported studies were small, retrospective, may have included duplicate data on the same women, and used different cut-offs for identifying a recurrence. In addition, no data are available from prospective studies on the clinical utility of any application of the HE4 test, and no published studies exist on use of the HE4 test to screen asymptomatic women. Thus, the HE4 test is considered investigational for all indications.

**Policy History**

<table>
<thead>
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<tr>
<td>1/2017</td>
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<tr>
<td>12/2015</td>
<td>Added coding language.</td>
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<td>5/2015</td>
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<td>12/2013</td>
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<td>No changes to policy statements.</td>
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Information Pertaining to All Blue Cross Blue Shield Medical Policies
Click on any of the following terms to access the relevant information:
Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

References


