Medical Coverage Policy | Serum Biomarker Human Epididymis Protein 4

EFFECTIVE DATE: 09|26|2003
POLICY LAST UPDATED: 11|03|2015

OVERVIEW
Human epididymis protein 4 (HE4) is a novel biomarker that has been cleared by the U.S. Food and Drug Administration (FDA) for monitoring patients with epithelial ovarian cancer. HE4 is proposed as a replacement for or a complement to carbohydrate antigen 125 (CA-125) for monitoring disease progression and recurrence. HE4 has also been proposed as a test to evaluate women with ovarian masses and to screen for ovarian cancer in asymptomatic women.

MEDICAL CRITERIA
Not applicable

PRIOR AUTHORIZATION
Not applicable

POLICY STATEMENT
BlueCHiP for Medicare and Commercial Products
Measurement of HE4 is not medically necessary for all indications as there is insufficient peer reviewed scientific literature that demonstrates that the service is effective.

COVERAGE
Benefits may vary between groups/contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage, or Subscriber Agreement for limitations of benefits/coverage when services are not medically necessary.

BACKGROUND
Human epididymis protein 4 is a novel biomarker that has been cleared by the FDA for monitoring patients with epithelial ovarian cancer. HE4 is proposed as a replacement for or a complement to carbohydrate antigen 125 (CA-125) for monitoring disease progression and recurrence. HE4 has also been proposed as a test to evaluate women with ovarian masses and to screen for ovarian cancer in asymptomatic women.

Another serum biomarker, cleared by the FDA for monitoring patients with epithelial ovarian cancer, is HE4. HE4 is made up of 2 whey acidic proteins with a 4 disulfide core domain. It 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, which would make HE4 a candidate to replace or complement CA-125. Tests for HE4 are FDA-approved for monitoring women known to have epithelial ovarian cancer. Another possible application of HE4 testing is screening asymptomatic women for ovarian cancer; screening is not an accepted use of the CA-125 test.

There is limited data on the diagnostic test performance of the HE4 test used to monitor disease progression and recurrence in women after initial treatment for epithelial ovarian cancer. There is no established cutoff for determining when an HE4 test is positive, when used for identifying disease progression or recurrence. Moreover, a survival advantage of early detection of ovarian cancer recurrence using HE4 levels or other biomarkers has not been established. A number of studies and meta-analyses of these studies have been published on HE4 for diagnosing ovarian cancer (although this is not an FDA-approved indication of the HE4 test). The evidence is insufficient to conclude that HE4 alone or in combination with CA-125 has

significantly better diagnostic performance than CA-125 alone. Meta-analyses have generally found that HE4 and CA-125 have similar overall diagnostic accuracy (i.e., sensitivity and specificity) and several found that HE4 has significantly higher specificity than CA-125 but not sensitivity. Two meta-analyses had mixed findings on whether the combination of HE4 and CA-125 is superior to CA-125 alone for the initial diagnosis of ovarian cancer. The number of studies evaluating the combined test is relatively low and publication bias in studies of HE4 has been identified. No published studies were identified evaluating use of the HE4 test to screen asymptomatic women for ovarian cancer. Thus, the HE4 test is not medically necessary for all indications as there is insufficient peer reviewed literature that demonstrates that the service is effective.

CODING

BlueCHiP for Medicare and Commercial Products

The following CPT code is considered not medically necessary:

86305

RELATED POLICIES

Proteomics-Based Testing Related to Ovarian Cancer
CA-125

PUBLISHED

Provider Update, January 2016
Provider Update, December 2014
Provider Update, July 2013
Provider Update, February 2012
Provider Update, April 2011
Provider Update, October 2009
Policy Update, July 2008

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