FEP POLICY 2.04.23 Homocysteine Testing in the Screening, Diagnosis, and Management of Cardiovascular Disease and Venous Thromboembolic Disease

Effective Date: April 15, 2017
Related Policies: None

Homocysteine Testing in the Screening, Diagnosis, and Management of Cardiovascular Disease and Venous Thromboembolic Disease

Description
Homocysteine is an amino acid which has been evaluated as a potential marker of cardiovascular disease (CVD) and increased risk of thrombosis in the general population and as a potential risk marker for people with CVD and thrombotic disorders. The association between homocystine-lowering interventions and risk of CVD or thrombotic events has also been examined.

FDA REGULATORY STATUS
Several homocysteine test systems have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process.

POLICY STATEMENT
Measurement of plasma levels of homocysteine is considered investigational in the screening, evaluation, and management of patients for cardiovascular disease.

Measurement of plasma levels of homocysteine is considered investigational in the screening, evaluation, and management of patients with venous thromboembolism or risk of venous thromboembolism.

BENEFIT APPLICATION
Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

RATIONALE
Summary of Evidence
For individuals who are asymptomatic who have risk of CVD or who have CVD who receive homocysteine testing, the evidence includes observational studies and randomized controlled trials (RCTs) of homocystine-lowering interventions. Relevant outcomes include test accuracy and validity, other test performance measures, change in disease status, and morbid events. Observational evidence generally supports the association of homocysteine levels with risk of CVD, especially in patients with preexisting vascular disease. However, evidence from RCTs evaluating homocysteine-lower interventions does not support the hypothesis that lowering homocysteine levels by treatment with folate and/or B vitamins...
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Improves cardiovascular outcomes. Numerous large RCTs and meta-analyses of these trials are consistent in reporting that homocysteine-lowering treatment is ineffective in reducing major cardiovascular events. One systematic review including only the subgroup of patients who were not on antiplatelets at baseline from 3 RCTs found that homocysteine-lowering treatment reduced the risk of stroke in that group. However, replication of this effect in countries with fortification would be needed. Given the large amount of evidence from placebo-controlled RCTs that homocysteine-lowering interventions do not improve health outcomes, it is unlikely that routine homocysteine testing has the potential to lead to changes in management that improve health outcomes. The evidence is sufficient to determine that the technology is unlikely to improve the net health outcome. For individuals who are asymptomatic who have risk of venous thromboembolism (VTE) or who have experienced previous venous thromboembolic events who receive homocysteine testing, the evidence includes of observational studies and randomized controlled trials (RCTs) of homocysteine-lowering interventions. Relevant outcomes include test accuracy and validity, other test performance measures, change in disease status, and morbid events. Observational evidence generally supports the association of homocysteine levels with risk of VTE, although the association was limited to men in the largest prospective study. However, evidence from RCTs evaluating homocysteine-lowering interventions does not support the hypothesis that lowering homocysteine levels by treatment with folate and/or B vitamins reduces risk of VTE. Only 1 of the RCTs was designed to test for VTE as a primary outcome. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

National Institute for Health and Care Excellence

In 2016, the National Institute for Health and Care Excellence updated the guidance on risk assessment and reduction of cardiovascular disease, including lipid modification. The guidance asserts that full formal risk assessments should use a combination of risk assessment tools as well as informed clinical judgement. Homocysteine testing is not mentioned.

Agency for Healthcare Research and Quality

In 2016, the Agency for Healthcare Research and Quality (AHRQ) issued guidelines for effective quality improvement on preventing hospital-associated venous thromboembolism (VTE). The VTE prevention protocol recommended involves a VTE risk assessment, a bleeding risk assessment, and a clinical decision support on prophylactic choices. Homocysteine testing was not mentioned in this guidelines.

U.S. Preventive Services Task Force Recommendations

In 2009, the U.S. Preventive Services Task Force issued a recommendation statement that the evidence is insufficient (1 statement) to assess the benefits and harms of using nontraditional risk factors to screen asymptomatic adults with no history of coronary heart disease (CHD) to prevent CHD events. Homocysteine was one of the nontraditional risk factors considered in the recommendation. The recommendation statements are currently being updated.
Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

REFERENCES

7. Park CS, Ihm SH, Yoo KD, et al. Relation between C-reactive protein, homocysteine levels, fibrinogen, and lipoprotein levels and leukocyte and platelet counts, and 10-year risk for cardiovascular disease among healthy adults in the USA. Am J Cardiol. May 1 2010;105(9):1284-1288. PMID 20403480
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POLICY HISTORY

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>December 2011</td>
<td>New Policy</td>
<td>Policy statement changed to not medically necessary, literature search, references 1, 9, 11, 12 added. Remaining references renumbered. Related policies added.</td>
</tr>
<tr>
<td>June 2012</td>
<td>Update Policy</td>
<td>Policy updated with literature review, references added, renumbered or removed. No change to policy statement.</td>
</tr>
<tr>
<td>September 2013</td>
<td>Update Policy</td>
<td>Policy updated with literature review, references added, renumbered or removed. No change to policy statement.</td>
</tr>
<tr>
<td>June 2014</td>
<td>Updated Policy</td>
<td>Policy updated with literature review through February 26, 2014; no references added; no change to policy statement. Rationale section reorganized and editorial changes made.</td>
</tr>
<tr>
<td>March 2017</td>
<td>Replace policy</td>
<td>Policy updated with literature review through October 10, 2016; references 14, 19, 31-40, and 42-44 added. Title changed to “Homocysteine Testing in the Screening, Diagnosis, and Management of Cardiovascular Disease and Venous Thromboembolic Disorders” and scope of review broadened to include venous thromboembolism. Investigational policy statement added for homocysteine measurement in the evaluation of venous thromboembolic disorders.</td>
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