Medical Policy

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

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Policy Number: 016
BCBSA Reference Number: 2.04.23
NCD/LCD: Local Coverage Determination (LCD): MolDX: Biomarkers in Cardiovascular Risk Assessment (L36523)

Related Policies
None

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

Measurement of plasma levels of homocysteine is considered NOT MEDICALLY NECESSARY 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.

Medicare HMO BlueSM and Medicare PPO BlueSM Members

Medical necessity criteria and coding guidance for Medicare Advantage members living in Massachusetts can be found through the link below.

Local Coverage Determination (LCD): MolDX: Biomarkers in Cardiovascular Risk Assessment (L36523)

For medical necessity criteria and coding guidance for Medicare Advantage members living outside of Massachusetts, please see the Centers for Medicare and Medicaid Services website for information regarding your specific jurisdiction at https://www.cms.gov.

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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<tr>
<td>Commercial Managed Care (HMO and POS)</td>
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<tr>
<td>Commercial PPO and Indemnity</td>
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<tr>
<td>Medicare HMO Blue&lt;sup&gt;SM&lt;/sup&gt;</td>
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<td>Medicare PPO Blue&lt;sup&gt;SM&lt;/sup&gt;</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, and Indemnity**:

**CPT Codes**

<table>
<thead>
<tr>
<th>CPT codes:</th>
<th>Code Description</th>
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<tr>
<td>83090</td>
<td>Homocysteine</td>
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**Description**

Homocysteine is a sulfur-containing amino acid that is rapidly oxidized in plasma into homocysteine and cysteine-homocysteine disulfide. Measurement of total plasma homocysteine is the sum of homocysteine and its oxidized forms.

Plasma levels of homocysteine have been actively researched as a risk factor for cardiovascular disease (CVD), initially based on the observation that patients with hereditary homocystinuria, an inborn error of metabolism associated with high plasma levels of homocysteine, had a markedly increased risk of CVD. Subsequently, prospective epidemiologic studies were conducted to determine if an elevated plasma level of homocysteine was an independent risk factor for CVD and could be used to improve current risk prediction models. Several case-control studies have also suggested that elevated homocysteine is a risk factor for venous thromboembolism (VTE; pulmonary embolism, deep vein thrombosis).

Interest in homocysteine as a potentially modifiable risk factor has been stimulated by the epidemiologic finding that levels of homocysteine inversely correlate with levels of folate. This finding has raised the possibility that treatment with folic acid might lower homocysteine levels and, in turn, reduce the risk of CVD and thrombotic events. Therefore, homocysteine has potential utility both as a risk predictor and as a target of treatment.

Determination of homocysteine concentration may be offered as a component of a comprehensive cardiovascular risk assessment that may include evaluation of small-density lipoproteins, subclassification of high-density lipoproteins, evaluation of lipoprotein (a), high-sensitivity C-reactive protein, and genotyping of apolipoprotein E. Determination of homocysteine concentration may also be offered as part of risk assessment for patients at high risk of VTE events or who have experienced idiopathic VTE, recurrent VTE, thrombosis occurring at a young age, or thrombosis at an unusual site.
Summary
Homocysteine is an amino acid that 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 homocysteine-lowering interventions and risk of CVD or thrombotic events has also been examined.

For individuals who are asymptomatic with risk of CVD or who have CVD who receive homocysteine testing, the evidence includes observational studies and randomized controlled trials (RCTs) of homocysteine-lowering interventions. Relevant outcomes are test accuracy and validity, other test performance measures, change in disease status, and morbid events. Observational evidence has generally supported the association between homocysteine levels and CVD risk, especially in patients with preexisting vascular disease. However, evidence from RCTs evaluating homocysteine-lowering interventions does not support the hypothesis that lowering homocysteine levels with folate and/or B vitamins improves cardiovascular outcomes. Numerous large RCTs and meta-analyses of these trials have consistently reported that homocysteine-lowering treatment is ineffective in reducing major cardiovascular events. One systematic review of a subgroup analysis from 3 RCTs of patients not on antiplatelets at baseline found that homocysteine-lowering treatment reduced the risk of stroke in that group. However, replication of this effect in countries with grain enriched with folic acid 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 change management that improves health outcomes. The evidence is sufficient to determine that the technology is unlikely to improve the net health outcome.

For individuals who are asymptomatic with risk of venous thromboembolism (VTE) or who have experienced VTE events who receive homocysteine testing, the evidence includes of observational studies and RCTs of homocysteine-lowering interventions. Relevant outcomes are test accuracy and validity, other test performance measures, change in disease status, and morbid events. Observational evidence has generally supported the association between homocysteine levels and VTE risk, although the association was limited to men in the largest prospective study. However, evidence from RCTs evaluating homocysteine-lower interventions does not support the hypothesis that lowering homocysteine levels with folate and/or B vitamins reduces risk of VTE. Only 1 RCT was designed to test for VTE as a primary outcome. The evidence is insufficient to determine the effects of the technology on health outcomes.

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
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<tbody>
<tr>
<td>1/2016</td>
<td>New references added from BCBSA National medical policy.</td>
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<tr>
<td>8/2015</td>
<td>Added coding language.</td>
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<tr>
<td>6/2015</td>
<td>New references added from BCBSA National medical policy.</td>
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<tr>
<td>7/2014</td>
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<tr>
<td>5/2013</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
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