Medical Policy
Homocysteine Testing in the Screening, Diagnosis, and Management of Cardiovascular Disease

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Policy Number: 016
BCBSA Reference Number: 2.04.23

Related Policies
- Gene Expression Testing to Predict Coronary Artery Disease, #349
- Genetic Testing for Lipoprotein-a Variants as a Decision Aid for Aspirin Treatment, #339
- Genotyping for 9p21 Single Nucleotide Polymorphisms to Predict Risk of Cardiovascular Disease or Aneurysm, #340
- KIF6 Genotyping for Predicting Cardiovascular Risk and or Effectiveness of Statin Therapy, #129
- Measurement of Lipoprotein-Associated Phospholipase A2 (Lp-PLA2) in the Assessment of Cardiovascular Risk, #558
- Novel Lipid Risk Factors in Risk Assessment and Management of Cardiovascular Disease, #283

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

The measurement of plasma levels of homocysteine, in the screening, evaluation, and management of patients for cardiovascular disease 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.

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<tr>
<th></th>
<th>Outpatient</th>
<th>Inpatient</th>
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<tbody>
<tr>
<td>Commercial Managed Care</td>
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<td>(HMO and POS)</td>
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<td>Commercial PPO and</td>
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<td>Indemnity</td>
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<tr>
<td>Medicare HMO BlueSM</td>
<td>This is not a covered service.</td>
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CPT Codes / HCPCS Codes / ICD-9 Codes
The following codes are included below for informational purposes. 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.

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. The laboratory test is referred to as either homocysteine or homocyst(e)ine.

Plasma levels of homocysteine have been actively researched as a risk factor for cardiovascular disease (CVD), 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 cardiovascular disease.

Interest in homocysteine as a potentially modifiable risk factor has been stimulated by the epidemiologic finding that levels of homocysteine are inversely correlated 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 cardiovascular disease. Therefore, homocysteine has potential utility both as a risk predictor and as a target of treatment.

Determination of homocysteine may be offered as a component of a comprehensive cardiovascular risk assessment.

Summary
Observational evidence generally supports the association of homocysteine levels with risk of cardiovascular disease, especially in patients with pre-existing vascular disease. However, evidence from randomized controlled trials does not support the hypothesis that lowering homocysteine levels by treatment with folate and/or B vitamins improves cardiovascular outcomes. Numerous large, randomized controlled trials and meta-analyses of these trials are consistent in reporting that treatment with folic acid is ineffective in reducing cardiac events. For the outcome of stroke, the evidence is less conclusive. One meta-analysis of the effect of treatment on prevention of stroke suggests that there may be an overall benefit but that this benefit is concentrated within populations in whom fortification of grain with folate is not present. Other, more recent meta-analyses of randomized trials did not find that homocysteine supplementation resulted in a significant reduction in stroke.

Due to the large amount of evidence of no benefit for cardiac health and lack of uncertainty around stroke, routine testing for homocysteine and intervention for patients with hyperhomocysteinemia is considered investigational.

Policy History

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<tr>
<th>Date</th>
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<tr>
<td>7/2014</td>
<td>New references added from BCBSA National medical policy.</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
1. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). C-reactive protein as a cardiac risk marker (special report). TEC Assessments 2002; 17 Tab 23.
8. 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 2010; 105(9):1284-88.