



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): MoIDX: 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(s) below.

[Local Coverage Determination \(LCDs\) for Palmetto GBA on Molecular Diagnostic Tests](#)

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

Note: To review the specific LCD, please remember to click “accept” on the CMS licensing agreement at the bottom of the CMS webpage.

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 at <https://www.cms.gov> for information regarding your specific jurisdiction.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	This is not a covered service.
Commercial PPO and Indemnity	This is not a covered service.
Medicare HMO BlueSM	Prior authorization is not required .
Medicare PPO BlueSM	Prior authorization is not required .

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

CPT codes:	Code Description
83090	Homocysteine

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 as a potential risk marker for people with CVD and thrombotic disorders; the presence of this amino acid raises one’s risk of developing a blood clot. The association between homocysteine-lowering interventions and risk of CVD or thrombotic events has been examined.

For individuals who are asymptomatic with risk of CVD or individuals with CVD who receive homocysteine testing, the evidence includes observational studies and randomized controlled trials (RCTs) of homocysteine-lowering interventions. Relevant outcomes are test 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-lower 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, with a subgroup analysis of patients from 3 RCTs who were not on antiplatelet therapy 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 randomized trials 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 individuals who have experienced VTE events who receive homocysteine testing, the evidence includes observational studies and RCTs of homocysteine-lowering interventions. Relevant outcomes are test 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 specific 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 the risk of VTE. Only a single 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

Date	Action
2/2019	BCBSA National medical policy review. Description, summary and references updated. Policy statements unchanged.
5/2017	BCBSA National medical policy review. New not medically necessary and investigational indications described. Title changed. New references added. Effective 5/1/2017.
2/2017	Coverage for Medicare Advantage members clarified based on Local Coverage Determination (LCD): MoIDX: Biomarkers in Cardiovascular Risk Assessment (L36523). 2/2017
1/2016	New references added from BCBSA National medical policy.
8/2015	Added coding language.
6/2015	New references added from BCBSA National medical policy.
7/2014	New references added from BCBSA National medical policy.
5/2013	New references from BCBSA National medical policy.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.

4/2011	Reviewed - Medical Policy Group – Cardiology and Pulmonology. No changes to policy statements.
4/2010	Reviewed - Medical Policy Group - Cardiology. No changes to policy statements.
4/2009	Reviewed - Medical Policy Group – Cardiology. No changes to policy statements.
4/2008	Reviewed - Medical Policy Group -Cardiology. No changes to policy statements.
3/2008	New Policy effective 3/2008 describing ongoing non-coverage.

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](#)

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