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Origination Date	07/10/2024
Originated Department	Clinical Operations

Homocysteine Level Testing

Audience
Providers, Members, Brokers, MHC

Purpose

Medical policies provide general support for applying Mountain Health Co-Op member policy document coverage decisions and must reference the member-specific benefit plan document. The terms of the member-specific Policy document may differ from the standard benefit plan on which this medical policy is based. If there is a conflict between a member-specific policy document and the Mountain Health Co-Op medical policy, the member-specific policy document supersedes this medical policy. Any person(s) applying this medical policy must identify member eligibility, the member-specific policy document, and related policies or guidelines before applying this medical policy, including the existence of any state or federal guidance. Mountain Health Co-Op medical policies are designed for informational purposes only and are not an authorization, explanation of benefits, or contract. Receipt of benefits is subject to satisfaction of all terms and conditions of the member-specific policy document coverage. Mountain Health Co-Op reserves the sole discretionary right to modify all policies and guidelines at any time.

Definition

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 casecontrol studies have also suggested that elevated homocysteine is a risk factor for venous thromboembolism (VTE; pulmonary embolism, deep vein thrombosis).

Policy/Procedure

1. Commercial Plans/CHIP

Mountain Health Co-Op covers homocysteine testing in individuals suspected of having homocystinuria or in first-degree relatives of patients with homocystinuria.

Mountain Health Co-Op does NOT cover Homocysteine Level testing for cardiovascular disease as it is considered investigational.

Mountain Health Co-Op does NOT cover homocysteine plasma levels in the screening, evaluation, and management of patients with venous thromboembolism or risk of venous thromboembolism as it is considered INVESTIGATIONAL.

Mountain Health Co-Op does NOT cover Homocysteine Level testing for any other indication as it is considered investigational.

1. **Clinical Rationale**
   - **1.1** For individuals who are asymptomatic with the 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. The 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 pre-existing 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, with a subgroup analysis of patients from three 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 folic acid enriched grain 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.
   - **1.2** For individuals who are asymptomatic with the 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. The 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. Evidence from RCTs evaluating homocysteine-lowering interventions does not support the hypothesis that lowering homocysteine evels 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.

1.3 In its revised 2022 overview of homocysteine, UpToDate® concluded that patients with suspected homocystinuria should have their homocysteine levels tested along with first-degree relatives of patients diagnosed with homocystinuria. Furthermore, despite some limitations, clinical trials have generally found that reducing levels of homocysteine with B vitamin supplementation does not prevent cardiovascular disease or reduce the incidence of recurrent venous thromboembolism (VTE) or arterial thrombosis. Thus, they suggest not testing for or treating hyperhomocysteinemia, unless homocystinuria is suspected or confirmed.

Applicable Coding

CPT Codes

83090 Homocysteine

HCPCS Codes

No applicable codes

ICD-10 Codes

E72.11 Homocystinuria

Vendors

- **Personify**
- **HPS**

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Review/Revision/Approval History	
Date	Description
07/10/2024	**New Policy**
04/27/2026	**Reviewed and approved by Mountain Health CO-OP Policy Committee**

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