OVERVIEW
Homocysteine is an amino acid found in the blood; levels are inversely correlated with folate levels. Homocysteine has been evaluated as a potential marker of cardiovascular disease (CVD) in the general population and as a potential risk marker among people with CVD. The association between homocysteine-lowering interventions and risk of CVD has also been examined.

MEDICAL CRITERIA
Not applicable.

PRIOR AUTHORIZATION
Not applicable.

POLICY STATEMENT
BlueCHiP for Medicare
Measurement of plasma levels of homocysteine are not covered in the screening, evaluation and management of patients with the following indications due to the large amount of evidence that homocysteine-lowering interventions do not improve health outcomes:
- patients for cardiovascular disease
- patients with venous thromboembolism or risk of venous thromboembolism.

Commercial Products
Measurement of plasma levels of homocysteine is considered not medically necessary in the screening, evaluation and management of patients with the following indications due to the large amount of evidence that homocysteine-lowering interventions do not improve health outcomes:
- patients for cardiovascular disease
- patients with venous thromboembolism or risk of venous thromboembolism.

COVERAGE
Benefits may vary between groups and contracts. Please refer to the appropriate Evidence of Coverage, Subscriber Agreement for applicable not medically necessary benefits/coverage.

BACKGROUND
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 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-lowering 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.

CODING
Blue Chip for Medicare and Commercial Products
The following code is not covered or not medically necessary
83090 Assay of Homocystine

RELATED POLICIES
None

PUBLISHED
Provider Update, August 2018
Provider Update, December 2018
Provider Update, January 2017
Provider Update, August 2015

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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