Medical Policy
KIF6 Genotyping for Predicting Cardiovascular Risk and/or Effectiveness of Statin Therapy

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Policy Number: 129
BCBSA Reference Number: 2.04.67
NCD/LCD: NA

Related Policies
None

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

KIF6 genotyping is considered INVESTIGATIONAL for predicting cardiovascular risk and/or the effectiveness of statin therapy.

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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<td>Commercial PPO and Indemnity</td>
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<td>Medicare HMO BlueSM</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.

CPT Codes
There is no specific CPT code for this service.

Description
Kinesin-like protein 6 (KIF6) belongs to the kinesin superfamily of proteins involved in intracellular transport. The exact function of the KIF6 gene product is as yet undetermined. It has been reported that the gene is not expressed in the vasculature, the primary site of atherosclerosis, but is expressed in low levels in the brain, connective tissue, colon, eye, pharynx, skin, and testes. In contrast, a study presented at a 2010 American Heart Association scientific session reported on data derived from tissue immunohistochemistry, locating KIF6 protein in macrophages surrounding neovessels and in foam cells in human atherosclerotic lesions. Nevertheless, there is no strong evidence that KIF6 protein plays a direct biologic role in atherosclerosis, lipid metabolism, coronary artery disease (CAD), or myocardial infarction.

Analyses of prospective observational studies of cardiovascular health and the placebo arm of randomized controlled trials (RCTs) of statin interventions in at-risk populations have suggested a significant association between the arginine-to-tryptophan substitution at position 719 (Trp719Arg) singlenucleotide polymorphism (rs20455) in KIF6 and the development of clinical CAD. Approximately 60% of the population carries the putative KIF6 high-risk 719Arg allele. Moreover, carriers of the 719Arg allele in the treatment arms of the statin trials appeared to be at no increased or decreased risk of CAD or recurrent MI, depending on the intensity of the statin therapy. These results have supported the development of a KIF6 Trp719Arg genotyping test for use as a predictor of CAD risk and the likely effectiveness of statin therapy.

Summary
Genetic testing to determine kinesin-like protein 6 (KIF6) Trp719Arg variant status is being evaluated as a prognostic test to predict the risk of future cardiovascular events and as a pharmacogenetic test to predict response to statin therapy, particularly in high-risk patients.

For individuals who are asymptomatic with risk of cardiovascular disease and undergoing treatment with statin therapy who receive testing for KIF6 Trp719Arg variant status, the evidence includes secondary analyses of randomized controlled trials (RCTs), case-control studies, and 1 quasi-experimental singlearm study. Relevant outcomes are overall survival, test accuracy and validity, change in disease status, morbid events, and medication use. Data supporting the association between KIF6 variant status and coronary artery disease (CAD) outcomes are contradictory. The most recent evidence from large populations with different vascular disease risk levels has not supported a significant association between CAD risk and the presence of the variant. Further, studies of the association between response to statin therapy and KIF6 variant status are also mixed. However, a large meta-analysis has shown that carriers of the KIF6 variant derive greater clinical benefit from low-density lipoprotein cholesterol reduction (a 13% reduction in the risk of CAD outcomes) compared with noncarriers. However, no prospective RCTs have evaluated the impact of testing for KIF6 variants on changes in clinical management (eg, intensifying the statin treatment in carriers, use of alternate approaches for lipid management in noncarriers) or outcomes. One nonrandomized study has suggested that subjects who received KIF6 genotype results had greater adherence to statin therapy, but, overall, it is uncertain whether testing for KIF6 variants will alter the clinical management decisions. The clinical utility of KIF6 testing has not been established. The evidence is insufficient to determine the effects of the technology on health outcomes.

Policy History

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<th>Date</th>
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<tr>
<td>7/2017</td>
<td>New references added from BCBSA National medical policy.</td>
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<tr>
<td>3/2015</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:
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

References
15. Wellcome Trust Case Control Consortium. Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls. Nature. Jun 7 2007;447(7145):661-678. PMID 17554300


