

Corporate Medical Policy

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

File Name: kif6_genotyping_for_predicting_cardiovascular_risk
Origination: 2/2011
Last CAP Review: 4/2012
Next CAP Review: 4/2013
Last Review: 5/2012

Description of Procedure or Service

Genetic testing to determine the KIF6 Trp719Arg variant status of patients is being evaluated as a prognostic test to predict risk of future cardiovascular events and/or as a pharmacogenetic test to predict response to statin therapy, particularly in high-risk patients.

Background:

Analysis of prospective observational studies of cardiovascular health, and of the placebo arm of randomized controlled trials of statin intervention in at-risk populations have suggested a significant association between the Trp719Arg single nucleotide polymorphism (SNP; rs20455) in kinesin-like protein 6 (KIF6) and the development of clinical coronary artery disease (CAD). Approximately 60 percent 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 risk, or at decreased risk of CAD or recurrent myocardial infarction (MI), depending on the intensity of the statin therapy. These results supported the development of a KIF6 Trp719Arg genotyping test for use as a predictor of CAD risk and of the likely effectiveness of statin therapy.

Celera Corporation now a wholly owned subsidiary of Quest Diagnostics, Inc., holds a U.S. patent relating to methods of determining heart attack risk by detecting the KIF6 gene variant and reduction of such increased risk by statin therapy. Celera's Berkeley HeartLab subsidiary has been offering KIF6 genotyping (KIF6-StatinCheck™ Genotype Test) since July 2008. San Francisco General Hospital's Clinical Chemistry Laboratory (University of California, San Francisco), is the only non-Celera lab to obtain a license to develop a KIF6 LTD; a small number of clinical labs/health care groups have negotiated with Celera to offer the test by sending it to BHL (e.g., Aurora Health Care of Milwaukee, WI).

Regulatory Status:

The KIF6 genotyping test is not a manufactured test kit and has not been reviewed by the Food and Drug Administration. Rather, it is a laboratory-developed test (LTD), offered by clinical laboratories licensed under CLIA for high-complexity testing. The company submitted a Premarket Approval application to the U.S. Food and Drug Administration (FDA) in January, 2011, for their KIF6 Genotyping Assay performed on Abbott's m2000™ instrument system. However, on April 7, the FDA sent a letter to Celera indicating that its application is not approvable "without major amendment." The data and publications submitted were deemed "insufficient to demonstrate the safety and effectiveness of the device for its proposed intended use." The agency indicated that additional data on clinical utility may be required, which could include conducting a randomized controlled clinical trial.

*****Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

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Policy

KIF6 Genotyping is considered investigational for all applications. BCBSNC does not provide coverage for investigational services or procedures.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When KIF6 Genotyping is covered

Not applicable

When KIF6 Genotyping is not covered

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

Policy Guidelines

The data supporting the association of the KIF6 Trp719Arg SNP with CAD outcomes are contradictory. The most recent evidence from large populations at different levels of vascular risk do not support a significant association with future CAD outcomes. Moreover, the biologic function of the KIF6 protein is currently unknown. Thus, the clinical validity for the KIF6 genotyping test has not been shown. The most recent results of treatment trials indicate that the efficacy of statin treatment appears to be similar in carriers and non-carriers of the mutation. It has not been determined whether the results of the test can be used to improve patient management decisions and improve outcomes.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: There is currently no specific CPT code for this testing. A combination of the molecular diagnostic CPT codes 83890-83912 would most likely be used.

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

BCBSA Medical Policy Reference Manual [Electronic Version], 2.04.67, 1/13/11

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Medical Director review 2/2011

Specialty Matched Consultant Advisory Panel review 4/2011

Senior Medical Director – 5/2011

Allingham-Hawkins D, Lea A, Levine S. KIF6 p.Trp719Arg testing to assess risk of coronary artery disease and/or statin response. PLoS Curr 2010; 2:RRN1191. Retrieved on March 21, 2012 from <http://knol.google.com/k/diane-allingham-hawkins/kif6-p-trp719arg-testing-to-assess-risk/1i0b298tuv2uk/3#>

Ridker PM, MacFadyen JG, Glynn RJ et al. Kinesin-like protein 6 (KIF6) polymorphism and the efficacy of rosuvastatin in primary prevention. Circ Cardiovasc Genet 2011; 4(3):312-7. Retrieved on March 21, 2012 from <http://circgenetics.ahajournals.org/content/4/3/312.full.pdf+html>

Arsenault BJ, Boekholdt SM, Hovingh GK et al. The 719Arg Variant of KIF6 and Cardiovascular Outcomes in Statin-Treated, Stable Coronary Patients of the TNT and IDEAL Prospective Studies. Circ Cardiovasc Genet 2011. Retrieved on March 21, 2012 from <http://circgenetics.ahajournals.org/content/5/1/51.full.pdf+html>

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.67, 2/9/12

Specialty Matched Consultant Advisory Panel review 4/2012

Policy Implementation/Update Information

- 5/10/11 New Evidenced Based Guideline implemented. KIF6 Genotyping is not recommended for predicting cardiovascular risk and/or the effectiveness of statin therapy. Medical Director review 2/2011. Specialty Matched Consultant Advisory Panel review 4/2011. (mco)
- 5/24/11 Evidence Based Guideline converted to Corporate Medical Policy. “KIF6 Genotyping is considered investigational for predicting cardiovascular risk and/or the effectiveness of statin therapy.” Reviewed with Senior Medical Director 5/13/2011. Notification given 5/24/11. Policy effective 8/30/11. (mco)
- 5/15/12 Specialty Matched Consultant Advisory panel review 4/2012. References updated. Policy Guidelines updated. Description section updated. (mco)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.