BlueCross BlueShield of Alabama

Name of Policy:

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

Policy #: 466
Category: Laboratory

Latest Review Date: May 2018
Policy Grade: C

Background/Definitions:

As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. *The technology must have final approval from the appropriate government regulatory bodies;*
2. *The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
3. *The technology must improve the net health outcome;*
4. *The technology must be as beneficial as any established alternatives;*
5. *The improvement must be attainable outside the investigational setting.*

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. *In accordance with generally accepted standards of medical practice; and*
2. *Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and*
3. *Not primarily for the convenience of the patient, physician or other health care provider; and*
4. *Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.*

Description of Procedure or Service:

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

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 the American Heart Association Scientific Sessions 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 biological role in atherosclerosis, lipid metabolism, coronary artery disease (CAD), or myocardial infarction (MI).

Analyses of prospective observational studies of cardiovascular health, and of the placebo arm of randomized controlled trials of statin interventions in at-risk populations have suggested a significant association between the arginine-to-tryptophan substitution at position 719 (Trp719Arg) single nucleotide polymorphism (rs20455) in *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 have 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.

Policy:

KIF6 Genotyping **does not meet** Blue Cross and Blue Shield of Alabama's criteria for coverage and is considered **investigational** for predicting cardiovascular risk and/or the effectiveness of statin therapy.

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the member's contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

The most recent literature review was performed through March 6, 2018.

Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.

KIF6 Genotyping

Clinical Context and Test Purpose

The purpose of testing for kinesin-like protein 6 (*KIF6)* gene variants in patients receiving statins therapy for coronary artery disease (CAD) is to inform a decision about whether an individual who has a variant is at a higher risk of a future cardiovascular event and therefore treatment with statin should be initiated or the existing dose of statin should be increased.

The questions addressed in this evidence review are: (1) Is there evidence that testing for variants in the *KIF6* gene variants has clinical validity?; and (2) Does patient management change in a way that would improve outcomes as a result of testing?

The following PICOTS were used to select literature to inform this review.

Patients

The population of interest includes patients who require or are being treated with statin treatment for primary or secondary prevention of cardiovascular disease.

Interventions

Genetic testing for variants in the *KIF6* gene to guide initiation or intensification of statin therapy.

Comparators

The comparator of interest is standard clinical care without genetic testing, in which decisions about medical therapy are based on standard lipid levels and risk factors for CAD (e.g., smoking, weight, diet, diabetes, family history of CAD). The intensity of therapies is based on a continued monitoring of response to treatment (e.g., achieving target LDL reduction).

Outcomes

The primary outcomes of interest for this review are CAD events and mortality over a ten year period. The potential harmful outcomes are those resulting from a false test result. False-positive test results can lead to initiation of unnecessary treatment and adverse effects from that treatment. False-negative test results could lead to under-treatment.

Timing
Decisions about choosing statin therapy are primarily driven by risks of CAD over a 10-year horizon.

Setting
Patients being treated with statins for primary prophylaxis for CAD are typically treated by general physicians or other primary care providers; those requiring statin therapy for secondary prevention may be treated by specialists or primary care providers. Consultations generally occur in outpatient care.

Technically Reliable
Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist. This evidence review focuses on the clinical validity and clinical utility.

Clinically Valid
A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Multiple studies have reported on the association between the *KIF6* Trp719Arg SNV and the risks of CAD and response to statin therapy, with varying results about the strength and direction of the association. These studies include early retrospective evaluations of prospective, observational studies (see Table 1, part 1); retrospective evaluations of the placebo arms of randomized controlled trials (RCTs) of statin therapy (see Table 1, part 2); large meta-analysis of 19 case-control studies (see Table 1, part 3); and finally retrospective evaluation of more recently conducted RCTs (see Table 1, part 4).

Patient populations in these studies include relatively unselected prevention cohorts and those with a higher risk of a CAD event. In prospective, observational studies and the placebo arms of RCTs, theTrp719Arg variant was positively associated with some CAD-related outcomes. In some RCTs, 719Arg variant carriers had larger decreases in coronary heart disease risk in association with statin treatment than non-carriers.

However, a large meta-analysis of 19 case-control studies found no association between the Trp719Arg SNV and nonfatal CAD. A major limitation of this meta-analysis was the exclusion of fatal coronary disease events and inability to examine whether the effect on risk was modified by statin therapy. In addition to the findings of the meta-analysis, none of several, large genome-wide association studies for CAD or myocardial infarction reported any SNVs at the *KIF6* locus as significant. Retrospective analyses of data from major RCTs published from 2011 to 2012 was consistent with the meta-analytic results and statins were equally effective at reducing cardiovascular event rates among carriers and non-carriers of the *KIF6* variant.

In a retrospective analysis of two prospective trials, Arsenault et al (2012) investigated whether *KIF6* variant carriers obtain more benefit from high-dose statin therapy. The benefit was similar

across all groups, except for those with homozygous variants, in whom there was a statistically significant benefit with a higher statin dose. However, the genotype by treatment interaction was not significant.

The conflicting results on the *KIF6* variant, CHD, and treatment outcomes might have been explained in a meta-analysis by Ference et al (2011). Reviewers selected 37 case-control studies, prospective cohort studies, or randomized trial treatment allocation arms (each considered as a separate cohort), which together enrolled 144,931 participants and reported 27,465 CHD events. The *KIF6* genotype, particularly the Trp719Arg SNV carrier status, was not associated with increased risk of CHD event. However, for each millimole per liter increase in low-density lipoprotein cholesterol (LDL-C), *KIF6* variant carriers experienced a 15% greater increase in the relative risk of CHD compared with non-carriers (ratio of relative risk, 1.15; 95% confidence interval [CI], 1.06 to 1.25, p=0.001). Similarly, the decrease in risk for each mmol/L decrease in LDL was 13% higher for variant carriers. Also included in the meta-analysis were 8 randomized trials of statin therapy involving 50,060 participants and 7307 CHD events. *KIF6* variant carriers derived a greater clinical benefit for each millimole per liter reduction in LDL-C during treatment with a statin than did non-carriers (ratio of relative risk, 0.87; 95% CI, 0.77 to 0.99; p=0.038). Thus, the results suggest that the *KIF6* Trp719Arg variant increases vulnerability to LDL-C. This result might explain why *KIF6* variant carriers appear to derive greater clinical benefit from a statin even though the variant itself does not appear to affect the ability of the statin to lower LDL-C, nor does it appear to be independently associated with the risk of CHD on average. However, "the association between the *KIF6* variant and the risk of CHD will vary according to the average LDL cholesterol level of the population(s) under study." This association may explain some of the conflicting reports of *KIF6* genotype association with CHD.

Table 1: Results of Individual Studies Investigating Differential Effects of *KIF6* Genotype on CV Outcomes and a Meta-Analysis of the Association Between *KIF6* Genotype and CAD Outcomes

Study	**Patients Evaluated**	***KIF6* Association Evaluated**	**Results: Observational Study or Placebo Arm, *KIF6*V carriers vs. non-carriers (95% CI)**	**Results: Statin Arm vs. Placebo Arm (unless otherwise stated) (95% CI)**
Part 1 *KIF6* variant association with CAD outcomes in retrospective evaluations of prospective, observational studies				
Morrison et al 2007 Retrospective evaluation of ARIC study	U.S. individuals aged 45–64 years	MI, CHD death, or coronary revascularization	HR: 1.09 (95% CI,1.00-1.19)	N/A
Shiffman et al 2008 Retrospective evaluation of CHS	Adults aged 65 years and older	Incident MI	HR: 1.29 (90% CI, 1.1-1.52)* (95% CI, 1.06-1.6)**	N/A
Shiffman et al 2008 Retrospective evaluation of WHS	Healthy Caucasian American women	Incident CHD event (MI, coronary revascularization, or CV-related death) or incident ischemic stroke	CHD HR: 1.24 (95% CI, 1.04-1.46) MI HR: 1.34 (95% CI, 1.02-1.75) Stroke HR: not sig.	N/A
Part 2 *KIF6* variant association with CAD outcomes in retrospective evaluations of randomized, controlled trials of statin therapy				
Iakoubova et al 2008 Retrospective	Caucasian MI survivors with total	Recurrent fatal or non-fatal MI	HR: 1.50 (95% CI, 1.05-2.15)	Among *KIF6V* carriers:

evaluation of CARE study	cholesterol <240 mg/dL			HR: 0.63 (0.46–0.87) Among non-carriers: HR: 0.80 (0.52–1.24)
Shiffman et al 2010 Retrospective evaluation of CARE study	MI survivors (all ethnicities) with total cholesterol <240 mg/dL	Recurrent fatal or non-fatal MI		Adjusted for self-reported ethnicity, Among *KIF6*V carriers: HR: 0.63 (0.49-0.83) Among non-carriers: HR: 1.01 (0.69-1.45)
Iakoubova et al 2008 Nested case-control study from WOSCOPS trial	Men with hyper-cholesterolemia but no history of MI	Nonfatal MI, revascularization procedures, or death from CHD	OR: 1.55 (95% CI, 1.14-2.09)	Among *KIF6*V carriers: HR: 0.50 (0.38–0.68) Among non-carriers: HR: 0.91 (0.64–1.28)
Iakoubova et al 2008 Retrospective evaluation of PROVE IT-TIMI	Patients hospitalized for MI or high-risk unstable angina	Composite endpoint: all-cause mortality, MI, unstable angina, or stroke	(no placebo arm)	Intensive vs. moderate statin therapy arms among: *KIF6*V carriers HR: 0.59 (0.45-0.77), Non-*KIF6*V carriers HR: 0.94 (0.70-1.27)
Iakoubova et al 2010 Retrospective evaluation of PROSPER study	Older patients with preexisting vascular disease	Composite endpoint: death from CHD, nonfatal MI, or fatal/ nonfatal stroke	HR: 1.28 (95% CI, 0.98-1.69)	Among *KIF6*V carriers: HR: 0.66 (0.52-0.86) Among non-carriers: HR: 0.94 (0.69-1.28)
	Older patients at increased risk for vascular disease			No benefit
Part 3 Meta-analysis of *KIF6* variant association with CAD outcomes				
Assimes et al 2010 Meta-analysis of 19 case-control studies	(Various) 17,000 cases, 39,369 controls	CAD cases with and without a diagnosis of non-fatal MI	OR: 0.98 (95% CI, 0.95-1.02)	N/A
Part 4 Recent publications: *KIF6* variant association with CAD outcomes in retrospective evaluations of RCTs of statin therapy				
Ridker et al 2011 Retrospective evaluation of prospective JUPITER study Rosuvastatin vs. placebo	Men and women free of diabetes or prior cardiovascular disease	Composite: CV death, nonfatal MI, nonfatal stroke, hospitalization for unstable angina, or arterial revascularization,	HR=0.91 (95% CI, 0.66-1.26)	Among *KIF6*V carriers: HR:0.61 (0.43-0.87) Among non-carriers: HR:0.59 (0.39-0.88) P-interact=0.90

Hopewell et al 2011 Retrospective evaluation of prospective Heart Protection Study Simvastatin vs. placebo	Individuals at high risk for or a previous diagnosis of CV disease	Composite: CHD death, nonfatal MI, strokes, coronary or noncoronary revascularizations	No significant effect on risk of major CV events, regardless of modeling approach (p= 0.54 to 0.76)	Among *KIF6*V carriers: 23% (16% - 29%) Among non-carriers: 24% (17% - 31%) P-interact=0.4 to 0.7
Hoffmann et al 2011 Retrospective evaluation of 4D prospective study Atorvastatin vs. placebo	Patients with T2DM and <2 year prior hemodialysis treatment	Composite: death from cardiac causes, MI, or stroke	HR=0.83 (95% CI, 0.66–1.05)	Among statin-treated, *KIF6V* carriers vs non-carriers: HR=0.96 (0.76–1.23)
Arsenault et al 2012 Retrospective evaluation of prospective TNT (80 vs. 10 mg/day atorvastatin) and IDEAL (80 mg/day atorvastatin vs. 20-40 mg/day simvastatin) studies	TNT: patients with stable CHD and LDL-C levels<130 mg/dL	Composite: coronary death, nonfatal MI, resuscitation after cardiac arrest and fatal or nonfatal stroke	N/A	Among *KIF6V* carriers: 0.85 (0.66-1.11) Among homozygote carriers: 0.44 (0.23-0.84) Among non-carriers: 0.81 (0.59-1.11) P-interact=0.81
	IDEAL: patients with a history of MI			Among *KIF6V* carriers: 0.91 (0.58-1.43) Among homozygote carriers: 0.88 (0.62-1.07) Among non-carriers: 0.85 (0.67-1.10), P-interact=0.91
Akao et al. 2012 Retrospective study of participants in PROSPER (PROspective Study of Pravastatin in the Elderly at Risk) trial, randomized to pravastatin 40 mg/day or placebo	Individuals with a history of, or risk factors for, vascular disease	MI or stroke	Homozygote HR=0.47, p=0.03 For women on pravastatin only; not significant after correction for multiple comparisons	N/A

Abbreviations: CAD, coronary artery disease; CHD, coronary heart disease; CV, cardiovascular; MI, myocardial infarction; T2DM, type 2 diabetes mellitus; OR, odds ratio; HR, hazard ratio; CI, confidence interval; N/A, not applicable; MI, myocardial infarction; ARIC, Atherosclerosis Risk in Communities cohort; CHS, Cardiovascular Health Study; CARE, Cholesterol and Recurrent Events trial; WOSCOPS, West of Scotland Coronary Prevention Study; PROVE IT-TIMI 22, Pravastatin or Atorvastatin Evaluation and Infection Therapy: Thrombolysis in Myocardial Infarction 22 trial; WHS, Women's Health Study; PROSPER, PROspective Study of Pravastatin in the Elderly at Risk; JUPITER, Justification for Use of Statins in Primary Prevention, An Intervention Trial Evaluating Rosuvastatin; TNT, Treating to New Targets; IDEAL, Incremental Decrease in End Points Through Aggressive Lipid-Lowering.
*Published. **Calculated from published data.

Section Summary: Clinically Valid

There is uncertainty about the clinical validity of genetic testing for *KIF6* Trp719Arg SNV due to conflicting results on the association between *KIF6* variant carrier status and the risks of CAD and to conflicting results of the association between *KIF6* variant carrier status and response to statin therapy.

Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

The potential clinical utility of genetic testing for *KIF6* includes confirmation of the diagnosis and evaluating whether there is a modifiable treatment option that would lower the risk of CAD for that individual.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from randomized controlled trials.

Charland et al, 2014 reported the results of a prospective, nonrandomized, open-label, single-center trial designed to compare statin adherence at six months in those who learned about their *KIF6* carrier status versus those who do not. Patients older than 18 years of age who were new to statin therapy (with no pharmacy electronic claims for statins in prior six months before the index date) were enrolled and *KIF6* genotyping was performed. *KIF6*-carrier status results were mailed to all individuals including information on association between *KIF6* carriers and higher coronary heart disease risk reduction with statins. Patients not contacted for study participation were matched 1:1 with the final *KIF6*-tested group based on age, sex, index statin prescription fill channel (mail or retail pharmacy), and a number of unique chronic medications within 180 days of the statin index date to serve as controls. A secondary control cohort was created from patients who were contacted about the study and made aware that their statin adherence might be routinely monitored, but who declined study participation with *KIF6* testing. The primary study outcomes were statin prescription adherence and persistence, assessed using prescription claims records. Adherence was calculated as the proportion of days covered; subjects were adherent if they had 80% or more of days covered. The proportion of patients categorized as adherent to statin therapy was 18.4% higher for the *KIF6*-tested group (63.4%; 95% CI, 59.6% to 67.1%) than for the matched controls (45.0%; 95% CI, 41.1% to 48.8%; $p<0.001$), and 12.7% higher than for the secondary control group (50.7%; 95% CI, 47.7% to 52.6%; $p<0.001$). While this study reported an association between receipt of *KIF6*-genotype testing results and higher statin adherence, the nonrandomized study design and the baseline group differences limit the validity of the results. Potential for bias in the self-selection of healthier patients for *KIF6* genotyping and the inability to isolate the incremental effects of receiving the *KIF6* genotype results over other aspects of study participation limit the conclusions that can be drawn about the effect of *KIF6* genotyping on adherence.

Chain of Evidence
Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

The conflicting evidence on clinical validity does not permit conclusions on clinical utility.

Section Summary: Clinical Utility
The clinical utility of genetic testing for the *KIF6* variant has not been established. It is unclear whether genetic testing for *KIF6* variant alters the clinical management decisions. One nonrandomized study suggested that subjects who received *KIF6* genotype results exhibited greater adherence to statin therapy, but the nonrandomized trial design and the baseline group differences limit the validity of the results. The potential for selection bias of healthier patients who volunteered for *KIF6* genotyping and the inability to isolate the incremental effects of receiving the *KIF6* genotype results over other aspects of trial participation restrict the conclusions that can be drawn about the effect of *KIF6* genotyping on adherence. More importantly, no study has demonstrated whether *KIF6* testing leads to changes in clinical management which leads to reduction in the risk of CAD.

Summary of Evidence
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 one quasi-experimental single-arm 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 presence of the variant. Further, studies of the association between response to statin therapy and *KIF6* variant status are 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 randomized clinical trials (RCTs) have evaluated the impact of testing for *KIF6* variants on changes in clinical management (e.g., intensifying the statin treatment in carriers, use of alternate approaches for lipid management in non-carriers) or outcomes. One nonrandomized study suggested that subjects who received *KIF6* genotype results had greater adherence to statin therapy, but overall it is uncertain if testing for *KIF6* variants alters 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.

Practice Guidelines and Position Statements
No reference to *KIF6* genotyping was found in the 2010 joint American College of Cardiology Foundation/American Heart Association Practice Guidelines on the Assessment of Cardiovascular Risk in Asymptomatic Adults.

In 2013, ACC/AHA issued joint guidelines on the assessment of cardiovascular risk that does not address *KIF6* genotyping.

U.S. Preventive Services Task Force Recommendations
No U.S. Preventive Services Task Force (USPSTF) recommendations for *KIF6* genotyping in CHD risk or use of KIF6 genotyping to guide the selection or use of statin therapy have been identified.

Key Words:
Cardiovascular genotyping, Genetic testing, cardiovascular risk, Statin pharmacogenetics, *KIF6* genotyping, Pharmacogenetic testing, statins, Celera

Approved by Governing Bodies:
Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests (LDTs) must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments (CLIA). Laboratories that offer LDTs must be licensed by CLIA for high-complexity testing. To date, the U.S. Food and Drug Administration (FDA) has chosen not to require any regulatory review of this test.

In January 2011, Celera Corp. submitted a premarket approval application to FDA for its *KIF6* Genotyping Assay performed using Abbott's m2000™ instrument system. On April 7, FDA informed Celera that its application was 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." FDA indicated that additional data on clinical utility might be required, which could include conducting a randomized controlled trial. An online search in 2017 found no update.

Now a wholly owned subsidiary of Quest Diagnostics, Celera Corp, holds a U.S. patent on methods of determining coronary heart disease (CHD) risk through detection of the *KIF6* gene variant and reduction of such increased risk by atorvastatin and pravastatin therapy, and offers the "Cardio IQ™ *KIF6* Genotype."

Benefit Application:
Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.
ITS: Home Policy provisions apply
FEP: Special benefit consideration may apply. Refer to member's benefit plan. FEP does not consider investigational if FDA approved and will be reviewed for medical necessity.

Current Coding:
CPT codes:

81479	Unlisted molecular pathology procedure **(effective 01/01/13)**

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Policy History:

Medical Policy Group, February 2011 **(3)**
Medical Policy Administration Committee, February 2011
Available for comment February 24th through April 11, 2011
Medical Policy Group, February 2012 **(2)**: 2012 Update – Key Points & References
Medical Policy Group, January 2013 **(1)**: Update to Coding with addition of code 81479 and deletion of code range 83890-83914
Medical Policy Panel, February 2013
Medical Policy Group, February 2013 **(1):** Update to Key Points and References; no change to policy statement
Medical Policy Panel, February 2014
Medical Policy Group, February 2014 **(1):** Update to Descriptions, Key Points and References; no change to policy statement
Medical Policy Panel, February 2015
Medical Policy Group, February 2015 **(3):** 2015 Update to Key Points and References; no change to policy statement
Medical Policy Panel, February 2016
Medical Policy Group, February 2016 **(3)**: 2016 Updates to Key Points; no change in policy statement
Medical Policy Panel, May 2017
Medical Policy Group, June 2017 **(3):** 2017 Updates to Description, Key Points & Approved by Governing Bodies; No References added and no change in policy statement.
Medical Policy Panel, July 2017
Medical Policy Group, August 2017 **(3):** Updates to Key Points; removed Previous Coding section for codes deleted 1/1/13; No References added and no change in policy statement.
Medical Policy Panel, May 2018
Medical Policy Group, May 2018 **(4):** Updates to Key Points. No change in policy statement.