2.04.96	Genetic Testing for Statin-Induced Myopathy		
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Section:	2.0 Medicine	**Page:**	Page 1 of 11

Policy Statement

Genetic testing for the presence of variants in the *SLCO1B1* gene to identify patients at risk of statin-induced myopathy is considered **not medically necessary**.

Policy Guidelines

Genetics Nomenclature Update

The Human Genome Variation Society nomenclature is used to report information on variants found in DNA and serves as an international standard in DNA diagnostics. It is being implemented for genetic testing medical evidence review updates starting in 2017 (see Table PG1). The Society's nomenclature is recommended by the Human Variome Project, the Human Genome Organization, and by the Human Genome Variation Society itself.

The American College of Medical Genetics and Genomics and the Association for Molecular Pathology standards and guidelines for interpretation of sequence variants represent expert opinion from both organizations, in addition to the College of American Pathologists. These recommendations primarily apply to genetic tests used in clinical laboratories, including genotyping, single genes, panels, exomes, and genomes. Table PG2 shows the recommended standard terminology- "pathogenic," "likely pathogenic," "uncertain significance," "likely benign," and "benign"- to describe variants identified that cause Mendelian disorders.

Table PG1. Nomenclature to Report on Variants Found in DNA

Previous	Updated	Definition
Mutation	Disease-associated variant	Disease-associated change in the DNA sequence
	Variant	Change in the DNA sequence
	Familial variant	Disease-associated variant identified in a proband for use in subsequent targeted genetic testing in first-degree relatives

Table PG2. ACMG-AMP Standards and Guidelines for Variant Classification

Variant Classification	Definition
Pathogenic	Disease-causing change in the DNA sequence
Likely pathogenic	Likely disease-causing change in the DNA sequence
Variant of uncertain significance	Change in DNA sequence with uncertain effects on disease
Likely benign	Likely benign change in the DNA sequence
Benign	Benign change in the DNA sequence

ACMG: American College of Medical Genetics and Genomics; AMP: Association for Molecular Pathology.

Genetic Counseling

Experts recommend formal genetic counseling for patients who are at risk for inherited disorders and who wish to undergo genetic testing. Interpreting the results of genetic tests and understanding risk factors can be difficult for some patients; genetic counseling helps individuals understand the impact of genetic testing, including the possible effects the test results could have on the individual or their family members. It should be noted that genetic counseling may alter the utilization of genetic testing substantially and may reduce inappropriate testing; further, genetic counseling should be performed by an individual with experience and expertise in genetic medicine and genetic testing methods.

Coding

Effective January 1, 2018, the following CPT code is specific to testing for *SLCO1B1 (solute carrier organic anion transporter family, member 1B1)* (e.g., adverse drug reaction), V174A variant. *SLCO1B1* is no longer listed under code 81400:

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- **81328**: SLCO1B1 (solute carrier organic anion transporter family, member 1B1) (e.g., adverse drug reaction), gene analysis, common variant(s) (e.g., *5)

Description

HMG-CoA reductase inhibitors, or statins, which are widely used to treat hypercholesterolemia, can cause muscle-related adverse events. Serious myopathy (i.e., myositis, rhabdomyolysis) can also occur and may be associated with variants in the *SLCO1B1* gene. Commercially available tests for the presence of *SLCO1B1* variants are marketed for use in predicting the risk of myopathy for patients taking statins.

Related Policies

- N/A

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. The Boston Heart Statin Induced Myopathy (SLCO1B1) Genotype test and ARUP Laboratories Statin Sensitivity SLCO1B1 are available under the auspices of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the Food and Drug Administration has chosen not to require any regulatory review of this test.

Rationale

Background

Statins

HMG-CoA reductase inhibitors, or statin drugs, are the primary pharmacologic treatment for hypercholesterolemia worldwide. In the U. S., an estimated 38 million people took statins in 2008.[1,] The use of statins is associated with an approximately 30% reduction in cardiovascular events across a wide variety of populations.[2,]

Commercially Available *SLCO1B* Molecular Diagnostic Tests

Several commercial and academic labs offer genetic testing for statin-induced myopathy (*SLCO1B1*) variants, including Boston Heart Diagnostics and ARUP Laboratories. Other labs offer panel tests for drug metabolism that include the *SLCO1B1* gene; for example, ApolloGen.

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Literature Review

The primary goal of pharmacogenomics testing and personalized medicine is to achieve better clinical outcomes in compared with the standard of care. Drug response varies greatly between individuals, and genetic factors are known to play a role. However, in most cases, the genetic variation only explains a modest portion of the variance in the individual response because clinical outcomes are also affected by a wide variety of factors including alternate pathways of metabolism and patient- and disease-related factors that may affect absorption, distribution, and elimination of the drug. Therefore, assessment of clinical utility cannot be made by a chain of evidence from clinical validity data alone. In such cases, evidence evaluation requires studies that directly demonstrate that the pharmacogenomic test alters clinical outcomes; it is not sufficient to demonstrate that the test predicts a disorder or a phenotype.

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function- including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, two domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Testing for *SLCO1B1* Variants To Guide Treatment

Clinical Context and Test Purpose

Statin-Induced Myopathy

Statins are associated with a known risk of muscle-related symptoms, which are the most common adverse events of statin drugs. Myopathy is a general term for muscle toxicity. Three categories of statin-induced myopathy were defined in 2002 by a joint committee of the American College of Cardiology, American Heart Association, and National Heart, Lung and Blood Institute,[3,]

- Statin-induced myalgia, defined as any muscle symptoms that occur without an elevation of serum creatinine kinase;
- Statin-induced myositis, defined as muscle symptoms with an elevation of serum creatinine kinase; and
- Statin-induced rhabdomyolysis, defined as markedly severe muscle symptoms with an elevation of creatinine kinase greater than ten times normal with an elevation in serum creatinine.

Statin-induced myalgia is the most common manifestation of myopathy; it is characterized by muscle pain, cramps, fatigue, and/or weakness.[4,] Myalgias without other clinical manifestations are not associated with clinically important adverse events and resolve when the statin is discontinued.

The incidence of myalgia varies widely. In clinical trials, it has been reported in 1.5% to 3.0% of patients; in most trials, the rate of myalgias in patients on statin therapy is not increased

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compared with placebo treatment.[5] In observational studies, higher rates of 10% to 15% have been reported.[2]

Myositis is much less common than myalgias, with an estimated rate of 5 per 100000 patient-years, and an estimated per-person incidence of 0.01%.[5] In virtually all cases, myositis resolves with discontinuation of the statin.

Rhabdomyolysis is the most severe clinical manifestation of statin-induced myopathy and can be life-threatening. The National Lipid Association estimated that rhabdomyolysis occurs at a rate of 1.6 per 100000 patient-years, and the U.S. Food and Drug Administration adverse events reporting system has estimated a rate of 0.7 per 100000 patient-years.[5] A systematic review by Law et al (2006) combined results from 20 clinical trials and estimated the rate of rhabdomyolysis to be 1.6 cases per 100000 patient-years.[6] Fatalities from statin-induced rhabdomyolysis can occur, but the mortality rate is not well-defined. The Food and Drug Administration has estimated that deaths from rhabdomyolysis occur at a rate of less than one death per million prescriptions.[3]

A number of clinical factors are associated with an increased risk of statin-induced myopathy. Statin dose is probably the strongest risk factor, with an estimated 6-fold increase for patients on high-dose[7] (age is also a strong risk factor). A study by Schech et al (2007) reported that patients older than 65 years of age required hospitalization for statin-induced myositis at a rate that was 4 times higher than for younger patients.[8] Some statins may be associated with a higher risk than others, and concomitant administration of certain drugs (e.g., gemfibrozil, amiodarone) has been associated with higher rates of statin myopathy in clinical trials.[7] Other factors that may be associated with myopathy include female sex and intense physical exercise.[7] The perceived risk of statin-induced myopathy may contribute to suboptimal statin use in patients with indications. It is estimated that less than 50% of patients in the U. S. who would benefit from statins are currently taking them, a substantial percentage of whom do not adhere to prescribed statin regimens.[1]

Genetic Factors Associated with Statin-Induced Myopathy

A variety of genetic factors are associated with statin myopathy. The cytochrome p450 system in the liver is the main pathway by which statins are metabolized. Numerous genetic variants in cytochrome p450 proteins affect the pharmacokinetics of statin metabolism and serum statin levels.[2] Other genetic variants affect statin metabolism, efficacy, and susceptibility to adverse events; these genetic variants involve variations in the apolipoproteins such as apo E, variations in the cholesterol ester transfer proteins, or variations in the coenzyme Q pathway.[1]

Variations in the *SLCO1B1* gene also affect statin metabolism and are among the most well studied genetic variants. These variants are the genetic markers for which there are commercially available tests. This gene codes for a transporter protein that is part of the solute carrier organic ion transporter system, which mediates the influx and metabolism of statins in the liver.[2] Single-nucleotide variants in this gene are associated with variations in the risk of statin-induced myopathy. The T/T allele is the wild-type and associated with the lowest risk of myopathy. The C/C allele is associated with the highest risk of myopathy, and the T/C allele with intermediate risk. The T allele has a prevalence of approximately 87%, and the C allele has a prevalence of approximately 13%.[4]

Other genes have been studied, including *ABCB1*, which encodes ATP-binding cassette (ABC) transporters subfamily B member 1 (ABCB1/P-glycoprotein 1), *ABCG2*, which encodes ABC transporters subfamily G member 2 (ABCG2/breast cancer resistance protein), and the coenzyme Q2 (COQ2) homolog gene. Other studies have evaluated the association between variants in the *GATM* gene and statin-induced myopathy (the *GATM* gene encodes a glycine amidinotransferase that is the rate-limited enzyme in creatine biosynthesis). However, it should be noted that the association between variants has not been consistently replicated.[9]

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Genetic Testing

The purpose of genetic testing for *SLCO1B1* variants in patients who are taking statin drugs is to inform a decision whether patients identified as at risk for statin-associated myopathy should continue taking specific statin drugs. Genome-wide association studies have found that *SLCO1B1* variants are associated with statin-induced myopathy. The Study of the Effectiveness of Additional Reductions in Cholesterol and Homcysteine (Collaboration Group (2008) published a genome-wide association study based on data from an RCT of 12064 patients assigned to simvastatin 20 mg or 80 mg.[4,] Of the patients in the 80-mg statin group, 0.8% had elevated serum creatinine kinase levels more than 10 times normal, and an additional 0.8% had creatinine kinase levels that were more than 3 times normal. The *SLCO1B1* locus was the single-nucleotide variant that had a strong association with myopathy. The cumulative risk of developing myopathy after 6 years of treatment with simvastatin 80 mg was 0.6% for patients with the T/T allele, 3% for patients with the T/C allele, and 18% for patients with the C/C allele.

The Study of the Effectiveness of Additional Reductions in Cholesterol and Homcysteine investigators replicated the association of the *SLCO1B1* genetic variant with myopathy in 16664 patients from the Heart Protection Study. In this trial, all patients were treated with simvastatin 40 mg; 0.1% were identified with creatinine kinase levels greater than 10 times normal. *SLCO1B1* variants were strongly associated with myopathy in this replication study.

Some evidence has suggested that the association between myopathy and *SLCO1B1* genotype is most pronounced for simvastatin. The Statin Response Examined by Genetic Haplotype Markers study was a randomized trial that examined statin response and safety by the dose of statin, statin type, and presence of genetic markers.[10,] A total of 509 patients were randomized to various doses of atorvastatin, pravastatin, or simvastatin and followed for adverse events, including myopathy. The presence of at least 1 variant on the *SLCO1B1* gene was associated with an increased rate of adverse events with the risk of adverse events being 19% with no variant alleles, 27% with 1 variant allele, and 50% with 2 variant alleles (p=0.01 for trend). The association between *SLCO1B1* gene status and adverse event rates did not appear to be present for patients who received pravastatin.

In a subanalysis of a prospective population-based cohort study of chronic diseases in the elderly population, de Keyser et al (2014) evaluated whether *SLCO1B1* variants modify the risk of adverse drug reactions during statin therapy among 2080 patients who received simvastatin or atorvastatin and had *SLCO1B1* genotype available.[11,] The study's primary outcome was a reduction in statin dose or a switch to another statin-lowering drug as an indicator of an adverse drug reaction. Among simvastatin users, the T>C variant was significantly associated with the primary outcome. Patients with the CC genotype had a hazard ratio for dose decrease or switch of 1.74 (95% confidence interval [CI], 1.05 to 2.88). A similar association was not seen among atorvastatin users.

Danik et al (2013) evaluated the role of *SLCO1B1* variants as effect modifiers for clinical myalgia in the Prevention: an Intervention Trial Evaluating Rosuvastatin trial, which randomized subjects to rosuvastatin (20 mg/d) or placebo.[12,] Among the 4404 subjects allocated to rosuvastatin, there was no significant association between *SLCO1B1* gene status and either muscle symptoms or a diagnosis of rhabdomyolysis, myopathy, or myositis.

Based on the evidence for a link between *SLCO1B1* variants and simvastatin-associated myopathy, testing for *SLCO1B1* variants could potentially result in changes in medications that would reduce the risk of adverse drug reactions.

The question addressed in this evidence review is: Does testing for *SLCO1B1* variants improve the net health outcome in patients treated with statins?

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

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Patients
The relevant population of interest are individuals who are on statin therapy.

Interventions
The intervention of interest is testing for *SLCO1B1* variants. Asymptomatic patients are typically placed on statin therapy by primary care physicians. Symptomatic patients are referred to cardiologists.

Comparators
The following practice is currently being used to manage statin therapy: standard of care treatment without *SLCO1B1*testing.Asymptomatic patients are typically placed on statin therapy by primary care physicians. Symptomatic patients are referred to cardiologists.

Outcomes
The general outcomes of interest are statin-associated myopathy events while on therapy and long-term cardiovascular events such as myocardial infarction and hospitalizations.

The onset of statin-associated myopathy typically occurs weeks to months after initiating statin therapy but can occur at any time.

Systematic Review
In their meta-analysis, Xiang et al (2018) assessed the association between SLCO1B1 T521C and 521T alleles and the risk of statin-induced myopathy.[13] Fourteen cohort and case-control studies were included, with a total of 3265 myopathy patients and 7743 controls. Findings of several studies suggested that 521TT carries a statistically less significant risk of statin-induced myopathy compared to the other alleles studied (i.e., 521CC, 521TC, 521CC + TC). In addition, 521C was also associated with a greater risk of statin-induced myopathy than 521T. These studies all had significant heterogeneity. The authors also evaluated the association of SLCO1B1 T521C and the risk of myopathy when taking different types of statins. They found a statistically significant risk for 521CC + TC individuals on simvastatin (odds ratio, 2.35; 95% CI, 1.08 to 5.12; $P = .032$) or rosuvastatin (odds ratio, 1.69; 95% CI, 1.07 to 2.67; $P=.024$) compared with 521TT. The 521C allele was also associated with a greater risk of myopathy from taking cerivastatin (odds ratio, 1.95; 95% CI, 1.47 to 2.57; $P < .001$). The heterogeneity among studies of statin types for SLCO1B1 T521C and myopathy risk was not statistically significant. Publication bias could not be ruled out in several studies.

Randomized Controlled Trials
Vassy et al (2018) conducted a systematic review of *SLCO1B1* testing of patient and clinical outcomes.[14] They identified 5 pilot studies and an RCT by Voora (2017) that studied how *SLCO1B1* test results influence patient outcomes (see Table 1).[15] Voora (2017) recruited patients who had discontinued statin therapy due to suspected side effects (73% reported myalgia, 25% of patients were *SLCO1B1*5* carriers). Patients were randomized to immediate or delayed results of *SLCO1B1* testing, stratified based on *SLCO1B1*5* genotype (carriers vs noncarriers) and clinic site. The primary outcome was adherence as assessed by the Morisky Medication Adherence Scale. Secondary outcomes included low-density lipoprotein cholesterol (LDL-C), Brief Pain Inventory, and 12-Item Short-Form Health Survey. Voora (2017) reported a significant difference between groups in LDL-C at three months, but not in other outcome measures (see Table 2). Limitations in trial design might have affected adherence to medications and self-reporting on questionnaires (see Tables 3 and 4).

Table 1. Summary of Key RCT Characteristics

Study	Countries	Dates	Sites	Participants	Interventions	
					Active	Comparator
Voora (2017)[15]	U.S.	2013-2016	3	159 nonusers of statin therapy due to suspected side effects	Immediate results of *SLCO1B1* variant testing	Delayed (8 mo) results of *SLCO1B1* variant testing

RCT: randomized controlled trial.

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Table 2. Summary of Key RCT Results

Study	Morisky Medication Adherence Scale (SD)	LDL-C (mg/dL) at 3 Months (SD)	LDL-C (mg/dL) at 8 Months (SD)	Brief Pain Inventory Score	SF-12 Score
Voora (2017)[15,]					
N	119	148	119	119	119
Immediate	6.8 (1.7)	132 (42)	129 (38)	NR	NR
Delayed	7.1 (1.3)	144 (43)	141 (44)	NR	NR
p	0.75	0.04	0.07	*NS*	*NS*

LDL-C: low-density lipoprotein cholesterol; NR: not reported; *NS*: not significant; RCT: randomized controlled trial; SF-12: 12-Item Short-Form Health Survey; SD: standard deviation.

The purpose of the limitations tables (see Tables 3 and 4) is to display notable limitations identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of the evidence supporting the position statement. The limitations stated in these tables are specific to the current review and do not reflect a comprehensive assessment.

Table 3. Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Voora (2017)[15,]			2. Participation in the study might have increased medication adherence		1, 2. 8 mo might be insufficient to evaluate medication adherence

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 4. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Voora (2017)[15,]		1, 2. Patients were not blinded, which might have affected adherence and questionnaire responses				

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4.Comparative treatment effects not calculated.

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Several institutions have implemented electronic medical record-based clinical decision support systems to guide statin dosing and follow-up for patients started on a statin using a patients' *SLCO1B1* status.[7,16,] It should be noted that all studies seeking to demonstrate that such support systems are associated with improved clinical outcomes have been found to be lacking.

Summary of Evidence
For individuals who are taking statin drugs who receive genetic testing for *SLCO1B1* variants, the evidence includes a systematic review and an RCT. The relevant outcomes are symptoms, quality of life, morbid events, and treatment-related morbidity. Direct evidence for clinical utility in this setting would come from studies demonstrating that using the *SLCO1B1* genotype to inform statin therapy (statin dose or choice of a specific drug) has positive outcomes in terms of lower rates of myopathy with adequate lipid control and tolerability of alternative treatments. The systematic review findings suggested that certain alleles carry less risk of statin-induced myopathy compared with others. One RCT was identified that evaluated adherence to medication and lipid control in patients whose physicians were informed of the *SLCO1B1* haplotype at the beginning or at the end of the study. No significant benefits were identified in adherence to medications or in pain with knowledge of the *SLCO1B1* haplotype status. There was a decrease in LDL-C at three months but not at eight months in the active intervention group. Interpretation of this trial is limited due to the lack of blinding of participants and short-term outcomes, which might have affected adherence to medications and patient responses on questionnaires. The evidence is insufficient to determine the effects of the technology on health outcomes.

Supplemental Information
Practice Guidelines and Position Statements
The Clinical Pharmacogenetics and Pharmacogenomics Implementation Consortium (2012) issued guidelines for *SLCO1B* genotypes and simvastatin-induced myopathy, which were updated in 2014.[17,] These guidelines on patient management for various *SLCO1B* genotypes recommended prescribing a lower dose or considering an alternative statin and considering routine creatinine kinase surveillance in patients with *SLCO1B* genotypes consistent with intermediate or low statin metabolism.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
Some currently ongoing and unpublished trials that might influence this review are listed in Table 5.

Table 5. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT02871934	Clinical Safety and Efficacy of Pharmacogenetics in Veteran Care	408	Dec 2020

NCT: national clinical trial.

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Documentation for Clinical Review

- No records required

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms

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of the Policy. Inclusion or exclusion of codes does not constitute or imply member coverage or provider reimbursement.

NMN
The following services may be considered not medically necessary.

Type	Code	Description
CPT®	81328	SLCO1B1 (solute carrier organic anion transporter family, member 1B1) (e.g., adverse drug reaction), gene analysis, common variant(s) (e.g., *5)
HCPCS	None	

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
02/01/2017	BCBSA Medical Policy adoption
01/01/2018	Policy revision without position change Coding Update
01/01/2019	Policy revision without position change
02/01/2020	Annual review. No change to policy statement. Literature review updated.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) 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 the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

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Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

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