

Local Coverage Determination (LCD): MoIDX: CYP2C19, CYP2D6, CYP2C9, and VKORC1 Genetic Testing (L36312)

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Contractor Information

Contractor Name	Contract Type	Contract Number	Jurisdiction	State(s)
Noridian Healthcare Solutions, LLC	A and B MAC	02101 - MAC A	J - F	Alaska
Noridian Healthcare Solutions, LLC	A and B MAC	02102 - MAC B	J - F	Alaska
Noridian Healthcare Solutions, LLC	A and B MAC	02201 - MAC A	J - F	Idaho
Noridian Healthcare Solutions, LLC	A and B MAC	02202 - MAC B	J - F	Idaho
Noridian Healthcare Solutions, LLC	A and B MAC	02301 - MAC A	J - F	Oregon
Noridian Healthcare Solutions, LLC	A and B MAC	02302 - MAC B	J - F	Oregon
Noridian Healthcare Solutions, LLC	A and B MAC	02401 - MAC A	J - F	Washington
Noridian Healthcare Solutions, LLC	A and B MAC	02402 - MAC B	J - F	Washington
Noridian Healthcare Solutions, LLC	A and B MAC	03101 - MAC A	J - F	Arizona
Noridian Healthcare Solutions, LLC	A and B MAC	03102 - MAC B	J - F	Arizona
Noridian Healthcare Solutions, LLC	A and B MAC	03201 - MAC A	J - F	Montana
Noridian Healthcare Solutions, LLC	A and B MAC	03202 - MAC B	J - F	Montana
Noridian Healthcare Solutions, LLC	A and B MAC	03301 - MAC A	J - F	North Dakota
Noridian Healthcare Solutions, LLC	A and B MAC	03302 - MAC B	J - F	North Dakota
Noridian Healthcare Solutions, LLC	A and B MAC	03401 - MAC A	J - F	South Dakota
Noridian Healthcare Solutions, LLC	A and B MAC	03402 - MAC B	J - F	South Dakota
Noridian Healthcare Solutions, LLC	A and B MAC	03501 - MAC A	J - F	Utah
Noridian Healthcare Solutions, LLC	A and B MAC	03502 - MAC B	J - F	Utah
Noridian Healthcare Solutions, LLC	A and B MAC	03601 - MAC A	J - F	Wyoming
Noridian Healthcare Solutions, LLC	A and B MAC	03602 - MAC B	J - F	Wyoming
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LCD Information

Document Information

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LCD Title MoIDX: CYP2C19, CYP2D6, CYP2C9, and VKORC1 Genetic Testing	Revision Effective Date For services performed on or after 10/01/2018
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CMS National Coverage Policy

Title XVIII of the Social Security Act, §1862(a)(1)(A) allows coverage and payment for only those services that are considered to be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member

Title XVIII of the Social Security Act, §1833(e), prohibits Medicare payment for any claim which lack the necessary information to process the claim.

42 CFR 410.32(a) Diagnostic x-ray tests, diagnostic laboratory tests, and other diagnostic tests: Conditions 42CFR411.15(k)(1) Particular services excluded from coverage

CMS On-Line Manual, Publication 100-08, Medicare Program Integrity Manual, Chapter 3, §3.4.1.3, diagnosis code requirements

Coverage Guidance

Coverage Indications, Limitations, and/or Medical Necessity

This policy limits *CYP2C19* (CPT 81225) and *CYP2D6* (CPT 81226) genetic testing to defined indications. All other testing for *CYP2C19* and *CYP2D6* is non-covered until definitive clinical utility is established to justify coverage.

This policy non-covers *CYP2C9* (CPT 81227) and *VKORC1* (CPT 81355) genetic testing for all medications.

CYP2C19 Genotyping

Background on CYP2C19 Testing

The CYP450 gene superfamily is composed of many isoenzymes that are involved in the metabolism of about 75% of commonly prescribed drugs. *CYP2C19* metabolizes 15% of all currently used drugs, whereas *CYP2D6* enzymes metabolize approximately 20-25%, and *CYP2C9* metabolizes approximately 10%.

Genetic alterations or "polymorphisms" are common in these isoenzymes, with more than 30 polymorphisms identified in *CYP2C19*. These polymorphisms can lead to differences in individual drug response secondary to variation in metabolism.

CYP2C19 phenotypes include poor, intermediate, extensive and ultra-rapid metabolizers. The frequency of the various metabolizers phenotypes has been estimated as follows:

- 2-15% - poor metabolizers
- 18-45% - intermediate metabolizers
- 35-50% - extensive metabolizers
- 5-30% - ultra-rapid metabolizers

The genotypic rates vary by ethnicity. Approximately 2% of whites, 4% of blacks and 14% of Chinese are poor *CYP2C19* metabolizers.

Pharmacogenetic testing has been proposed to predict individual response to a variety of *CYP2C19*-metabolized drugs including clopidogrel, proton pump inhibitors, and tricyclic antidepressants, among others. In certain scenarios, an individual patient may benefit from genetic testing in determining dosage and likely response to specific medications.

Clopidogrel bisulfate (Plavix) is a widely prescribed medication to/for:

- Prevent blood clots in patients with acute coronary syndrome (ACS),
- Other cardiovascular (CV) disease-related events,
- Undergoing percutaneous coronary intervention

Clopidogrel response varies significantly due to genetic and acquired factors including obesity, smoking and non-compliance. Patients with poor response to clopidogrel may experience recurrent CV event or thrombotic events while taking clopidogrel. They are at greater risk for major adverse CV events such as heart attack, stroke and death. These individuals are typically poor to intermediate metabolizers of clopidogrel due to the presence of the associated *CYP2C19* polymorphisms. These individuals should be given an alternate treatment strategy (Plavix PI). As such, the clinical utility of *CYP2C19* genotyping has been supported with net benefits on improving health outcomes for individuals with ACS who are undergoing percutaneous coronary interventions (PCI). There is insufficient evidence of clinical utility of *CYP2C19* genotyping for individuals considering clopidogrel therapy for other indications, such as medical management of ACS without PCI, stroke, or peripheral artery disease.

With regards to *CYP2C19* testing for antidepressant treatment, recent evidence has suggested genetic testing prior to initiating certain tricyclic antidepressants, namely amitriptyline, due to the effects of the genotype on drug efficacy and safety. Use of this information to determine dosing has been proposed to improve clinical outcomes and reduce the failure rate of initial treatment. However, the Clinical Pharmacogenetics Implementation Consortium did not have enough evidence to make a strong recommendation for dose modification based on genotype, and a moderate recommendation was given based on data outside of randomized trials. Additionally, even with genotype information, a suggestion is given to start patients on low dose, gradually increasing to avoid adverse side effects. Consequently, genotyping is not needed with this approach.

Proton pump inhibitors are used to treat several gastric acid-related conditions including duodenal ulcer, gastric ulcer and gastroesophageal reflux disease. Proton pump inhibitors can also be used to treat *Helicobacter pylori*. Several proton pump inhibitors are metabolized by *CYP2C19*. However, there is insufficient data to warrant *CYP2C19* genotyping to determine health outcomes or adverse drug reactions in treatment with proton pump inhibitors.

With regards to Serotonin reuptake inhibitors, there is insufficient evidence to support *CYP2C19* genotyping to determine medical management for the treatment of obsessive compulsive disorder at this time.

Covered Indications

In summary, genetic testing of the *CYP2C19* gene is considered medically necessary for patients with ACS undergoing PCI who are initiating or reinitiating Clopidogrel (Plavix) therapy.

Non-covered Indications

Genetic testing for the *CYP2C19* gene is considered investigational at this time for the following medications including but not limited to:

- Amitriptyline
- Clopidogrel for indications other than above
- Proton pump inhibitors
- Selective serotonin reuptake inhibitors
- Warfarin

CYP2D6 Genotyping

Background on CYP2D6 Testing

Genetic alterations or “polymorphisms” are common in these isoenzymes, with more than 100 polymorphisms identified in *CYP2D6*. These polymorphisms can lead to differences in individual drug response secondary to variation in metabolism.

CYP2D6 phenotypes include poor, intermediate, extensive and ultra-rapid metabolizers. The frequency of the poor metabolizer phenotype varies by ethnicity with 7-10% in Caucasians, 1.9-7.3% in African- Americans, and ≤ 1% in most Asian populations studied. The extensive metabolizer phenotype, observed in 50% of Caucasians, is the most common in this population. Genetic variation, as well as drug-drug interactions, can influence the classification of *CYP2D6* metabolism into one of the above phenotypes. In addition, chronic dosing of a *CYP2D6* drug can inhibit its own metabolism over time as the concentration of the drug approaches a steady state.

Pharmacogenetic testing has been proposed to predict individual response to a variety of *CYP2D6*-metabolized drugs including tamoxifen, antidepressants, opioid analgesics, and tetrabenazine for chorea, among others. In certain scenarios, an individual patient may benefit from this genetic testing in determining dosage and likely response to specific medications.

Tamoxifen

Available evidence fails to support direct evidence of clinical utility for testing of *CYP2D6* in treatment with tamoxifen. Tamoxifen metabolism and the causes for resistance are complex rather than the result of a single polymorphism.

Antidepressants

In regards to *CYP2D6* testing for antidepressant treatment, there was insufficient evidence in the past to support testing to determine treatment. More recently, evidence has supported the use of genetic testing prior to initiating certain tricyclic antidepressants due to the effects of genotype on drug efficacy and safety. Use of this information to determine dosing can improve clinical outcomes and reduce the failure rate of initial treatment. However, there is insufficient evidence for *CYP2D6* genotyping for individuals considering antipsychotic medications or other antidepressants with *CYP2D6* as a metabolizing enzyme.

Codeine

In addition, the role of *CYP2D6* genotyping has been evaluated for use in opioid analgesic drug therapy, specifically codeine analgesia. The efficacy and toxicity, including severe or life-threatening toxicity after normal doses of codeine has been linked to an individual's *CYP2D6* genotype. However, genotyping would indicate avoidance of codeine due to risk of adverse events in only 1-2% of the populations, and there is considerable variation in the degree of severity of adverse events, with most not classified as serious. Furthermore, codeine is widely used without genotyping. At this time, there is insufficient evidence to support clinical utility of genotyping for management of codeine therapy.

Tetrabenazine

The dosing of tetrabenazine is based, in part, on *CYP2D6* genotyping. However, a recent study suggests that the necessity to genotype may need to be reconsidered. The Xenazine® manufacturer package insert indicates that poor metabolizers of *CYP2D6* should not exceed a maximum dose of 50 mg/day.

Drugs for Alzheimer's Disease

Galantamine is an antidementia drug used in the treatment of Alzheimer's disease. Studies have been performed that reveal the *CYP2D6* genotype significantly influences galantamine concentrations in blood. Still other studies have revealed that urinary assays for *CYP2D6* phenotype are technically feasible. At this time, the association between phenotype and drug responsiveness remains unknown. It has been suggested that confirmation studies in larger populations are necessary to establish evidence regarding individuals most likely to benefit from galantamine, including information on treatment efficacy and tolerability.

Donepezil (Aricept) is a drug used to treat an Alzheimer's disease. Some studies have reported an influence of the *CYP2D6* on the response to treatment with this drug. Other studies suggest that therapy based on *CYP2D6* genotype is unlikely to be beneficial for treating Alzheimer's disease patients in routine clinical practice. Additional studies are needed to determine the efficacy and utility of *CYP2D6* genotyping in those patients who are treated with donepezil.

Covered Indications

In summary, genetic testing of the *CYP2D6* gene is considered medically necessary to guide medical treatment and/or dosing for individuals for whom initial therapy is planned with:

- Amitriptyline or nortriptyline for treatment of depressive disorders
- Tetrabenazine doses greater than 50 mg/day, or re-initiation of therapy with doses greater than 50 mg/day

Non-covered Indications

There is insufficient evidence to demonstrate that genetic testing for the *CYP2D6* gene improves clinical outcomes. Consequently, genetic testing for the *CYP2D6* gene is considered investigational including but not limited to the following medications:

- Antidepressants other than those listed above
- Antipsychotics

- Codeine
- Donepezil
- Galantamine
- Tamoxifen

CYP2C9 Genotyping

Background on CYP2C9 Testing

CYP2C9 metabolizes approximately 10-15% of all currently used drugs. Genetic alternations or “polymorphisms” are common in these isoenzymes, with 57 polymorphisms identified in *CYP2C9*, which can lead to differences in individual drug response secondary to variation in metabolism.

Pharmacogenetic testing has been proposed to predict individual response to a variety of *CYP2C9*-metabolized drugs including celecoxib, fluorbipofen, fluvoxamine and warfarin, among others. In certain scenarios, an individual patient may benefit from this genetic testing in determining dosage and likely response to specific medications. However, there is insufficient evidence to support *CYP2C9* genotyping to determine medical management and alter outcomes at this time.

Individuals with low enzyme activity for *CYP2C9* substrates are at risk of adverse drug reactions. However, pharmacogenetic testing for individuals being treated with drugs, such as warfarin, may experience little or no benefit from testing. This is, in part, because the *CYP2C9* genotype accounts for only part of the variability in drug sensitivity.

Warfarin

While there is extensive literature regarding warfarin and the *CYP2C9* genotype, the clinical utility of such testing remains unproven at this time. In fact, pharmacogenetic testing for warfarin treatment has been recommended against by the American College of Medical Genetics and the American College of Chest Physicians. These guidelines suggest that genetic testing for warfarin metabolism is not medically necessary, and evidence of clinical utility remains to be proven. Obstacles for determining clinical utility have been reviewed with suggestions for researchers in this area.

Celecoxib

In addition, limited information is available regarding celecoxib metabolism in individuals with *CYP2C9* polymorphisms. More trials are needed to determine clinical utility and appropriateness of pharmacogenetic testing in this population.

Covered Indications

Effective August 3, 2009, the Centers for Medicare & Medicaid Services (CMS) believes that the available evidence supports that coverage with evidence development (CED) under §1862(a)(1)(E) of the Social Security Act (the Act) is appropriate for pharmacogenomic testing of *CYP2C9* or *VKORC1* alleles to predict warfarin responsiveness by any method, and is therefore covered only when provided to Medicare beneficiaries who are candidates for anticoagulation therapy with warfarin who:

- Have not been previously tested for *CYP2C9* or *VKORC1* alleles; and

- Have received fewer than five days of warfarin in the anticoagulation regimen for which the testing is ordered; and
- Are enrolled in a prospective, randomized, controlled clinical study when that study meets the standards as set forth in National Coverage Determination 90.1.

Non-covered Indications

All other coverage for genetic testing for the *CYP2C9* gene is considered investigational at this time. There is currently no proven clinical utility related to any medication, including but not limited to:

- Celecoxib
- Fluoribiprofen
- Flovoxamine

VKORC1 Genotyping

Background on *VKORC1* Testing

The vitamin K epoxide reductase complex subunit 1, encoded by the gene *VKORC1*, is critical in the vitamin K pathway for coagulation. Warfarin therapy targets *VKORC1* to reduce clotting risk.

Variation in response to warfarin therapy has been linked to genetic variations. Retrospective study of European-American patients undergoing long term warfarin therapy identified 5 major haplotypes that were most predictive of approximately 25% of variance in warfarin dose. These are classified into A: low dose haplotype and B: high dose haplotype. This was validated in two European-American populations. Average maintenance dose for A/A haplotypes was approximately 2.7 mg per day; 4.9 mg per day for A/B, and 6.2 mg per day for B/B ($p < 0.001$).

Review by the American College of Medical Genetics (2008) confirmed the analytic validity of testing *VKORC1* and confirmed that there is sufficient evidence to support association with final therapeutic dose of warfarin. However, safe warfarin dosing requires careful monitoring and there is insufficient evidence is available to support routine *VKORC1* genotyping for determination of final dosing. Further study in prospective clinical trials are needed to determine clinical utility.

Clinical Pharmacogenetics Implementation Consortium guidelines recommend that pharmacogenetic algorithms be used to determine ideal dosing, and recommend including *VKORC1* genotyping when available. However the evidence from randomized prospective trials is limited, and impact on clinical outcomes is not yet known, limiting the ability to recommend that genotyping be performed for initial warfarin prescribing.

Prospective study of 30 healthy subjects assessed for warfarin dosing with daily INR measurements determined that *VKORC1* ($p=0.02$) variant carriers require lower cumulative doses of warfarin to achieve $INR \geq 2.0$. Participants who carried variants in both *CYP2C9* and *VKORC1* required fewer days to achieve $INR \geq 2.0$ that wild type subjects ($p=0.01$) resulting in an estimated genetic contribution to dose variability of 62%.

Meta-analysis of *CYP2C9* and *VKORC1* genotypes influence the risk of hemorrhagic complications in warfarin treated patients and increase the risk for over-coagulation and hemorrhagic complications with *CYP2C9**3 carriers. No significant association was noted between *VKORC1* genotypes and hemorrhagic complications.

Randomized controlled study assessing 109 adult patients and the influence of *VKORC1* genotyping data on

clinical outcomes of initial warfarin dosing was performed. Primary endpoints included time in therapeutic range over 90 days and number of anticoagulation visits. Hospitalizations, emergency visits, time to reach therapeutic dose, INR >4, hemorrhagic events, thrombotic events and mortality were secondary endpoints. No difference in the primary endpoints was noted between patients who received initial dosing by clinical and genotype information as compared to those whose initial dosing was determined by clinical information alone. No statistical difference was noted between either group in secondary events, however fewer of these events were noted among patients whose dosing included genotypic data.

Covered Indications

Effective August 3, 2009, the Centers for Medicare & Medicaid Services (CMS) believes that the available evidence supports that coverage with evidence development (CED) under §1862(a)(1)(E) of the Social Security Act (the Act) is appropriate for pharmacogenomic testing of *CYP2C9* or *VKORC1* alleles to predict warfarin responsiveness by any method, and is therefore covered only when provided to Medicare beneficiaries who are candidates for anticoagulation therapy with warfarin who:

- Have not been previously tested for *CYP2C9* or *VKORC1* alleles; and
- Have received fewer than five days of warfarin in the anticoagulation regimen for which the testing is ordered; and
- Are enrolled in a prospective, randomized, controlled clinical study when that study meets the standards as set forth in National Coverage Determination 90.1.

Non-covered Indications

Genetic testing for the *VKORC1* gene is considered investigational at this time for all other medications.

Summary of Evidence

NA

Analysis of Evidence (Rationale for Determination)

NA

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Coding Information

Bill Type Codes:

Contractors may specify Bill Types to help providers identify those Bill Types typically used to report this service. Absence of a Bill Type does not guarantee that the policy does not apply to that Bill Type. Complete absence of all Bill Types indicates that coverage is not influenced by Bill Type and the policy should be assumed to apply equally to all claims.

N/A

Revenue Codes:

Contractors may specify Revenue Codes to help providers identify those Revenue Codes typically used to report this service. In most instances Revenue Codes are purely advisory. Unless specified in the policy, services reported under other Revenue Codes are equally subject to this coverage determination. Complete absence of all Revenue Codes indicates that coverage is not influenced by Revenue Code and the policy should be assumed to apply equally to all Revenue Codes.

N/A

CPT/HCPCS Codes

Group 1 Paragraph: N/A

Group 1 Codes:

81225 CYP2C19 (CYTOCHROME P450, FAMILY 2, SUBFAMILY C, POLYPEPTIDE 19) (EG, DRUG METABOLISM), GENE ANALYSIS, COMMON VARIANTS (EG, *2, *3, *4, *8, *17)

81479 UNLISTED MOLECULAR PATHOLOGY PROCEDURE

Group 2 Paragraph: N/A

Group 2 Codes:

81226 CYP2D6 (CYTOCHROME P450, FAMILY 2, SUBFAMILY D, POLYPEPTIDE 6) (EG, DRUG METABOLISM), GENE ANALYSIS, COMMON VARIANTS (EG, *2, *3, *4, *5, *6, *9, *10, *17, *19, *29, *35, *41, *1XN, *2XN, *4XN)

81479 UNLISTED MOLECULAR PATHOLOGY PROCEDURE

Group 3 Paragraph: N/A

Group 3 Codes:

81227 CYP2C9 (CYTOCHROME P450, FAMILY 2, SUBFAMILY C, POLYPEPTIDE 9) (EG, DRUG METABOLISM), GENE ANALYSIS, COMMON VARIANTS (EG, *2, *3, *5, *6)

81355 VKORC1 (VITAMIN K EPOXIDE REDUCTASE COMPLEX, SUBUNIT 1) (EG, WARFARIN METABOLISM), GENE ANALYSIS, COMMON VARIANT(S) (EG, -1639G>A, C.173+1000C>T)

ICD-10 Codes that Support Medical Necessity

Group 1 Paragraph: N/A

Group 1 Codes:

ICD-10 Codes	Description
I20.0	Unstable angina
I20.1	Angina pectoris with documented spasm
I20.8	Other forms of angina pectoris
I20.9	Angina pectoris, unspecified
I21.09	ST elevation (STEMI) myocardial infarction involving other coronary artery of anterior wall
I21.11	ST elevation (STEMI) myocardial infarction involving right coronary artery
I21.19	ST elevation (STEMI) myocardial infarction involving other coronary artery of inferior wall
I21.29	ST elevation (STEMI) myocardial infarction involving other sites
I21.3	ST elevation (STEMI) myocardial infarction of unspecified site
I21.4	Non-ST elevation (NSTEMI) myocardial infarction
I21.9	Acute myocardial infarction, unspecified
I21.A1	Myocardial infarction type 2
I21.A9	Other myocardial infarction type
I24.0	Acute coronary thrombosis not resulting in myocardial infarction
I24.1	Dressler's syndrome
I24.8	Other forms of acute ischemic heart disease
I24.9	Acute ischemic heart disease, unspecified
I25.110	Atherosclerotic heart disease of native coronary artery with unstable angina pectoris
I25.111	Atherosclerotic heart disease of native coronary artery with angina pectoris with documented spasm
I25.118	Atherosclerotic heart disease of native coronary artery with other forms of angina pectoris

ICD-10 Codes	Description
I25.119	Atherosclerotic heart disease of native coronary artery with unspecified angina pectoris
I25.700	Atherosclerosis of coronary artery bypass graft(s), unspecified, with unstable angina pectoris
I25.701	Atherosclerosis of coronary artery bypass graft(s), unspecified, with angina pectoris with documented spasm
I25.708	Atherosclerosis of coronary artery bypass graft(s), unspecified, with other forms of angina pectoris
I25.709	Atherosclerosis of coronary artery bypass graft(s), unspecified, with unspecified angina pectoris
I25.710	Atherosclerosis of autologous vein coronary artery bypass graft(s) with unstable angina pectoris
I25.711	Atherosclerosis of autologous vein coronary artery bypass graft(s) with angina pectoris with documented spasm
I25.718	Atherosclerosis of autologous vein coronary artery bypass graft(s) with other forms of angina pectoris
I25.719	Atherosclerosis of autologous vein coronary artery bypass graft(s) with unspecified angina pectoris
I25.720	Atherosclerosis of autologous artery coronary artery bypass graft(s) with unstable angina pectoris
I25.721	Atherosclerosis of autologous artery coronary artery bypass graft(s) with angina pectoris with documented spasm
I25.728	Atherosclerosis of autologous artery coronary artery bypass graft(s) with other forms of angina pectoris
I25.729	Atherosclerosis of autologous artery coronary artery bypass graft(s) with unspecified angina pectoris
I25.730	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with unstable angina pectoris
I25.731	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with angina pectoris with documented spasm
I25.738	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with other forms of angina pectoris
I25.739	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with unspecified angina pectoris
I25.750	Atherosclerosis of native coronary artery of transplanted heart with unstable angina
I25.751	Atherosclerosis of native coronary artery of transplanted heart with angina pectoris with documented spasm
I25.758	Atherosclerosis of native coronary artery of transplanted heart with other forms of angina pectoris
I25.759	Atherosclerosis of native coronary artery of transplanted heart with unspecified angina pectoris
I25.760	Atherosclerosis of bypass graft of coronary artery of transplanted heart with unstable angina
I25.761	Atherosclerosis of bypass graft of coronary artery of transplanted heart with angina pectoris with documented spasm
I25.768	Atherosclerosis of bypass graft of coronary artery of transplanted heart with other forms of angina pectoris
I25.769	Atherosclerosis of bypass graft of coronary artery of transplanted heart with unspecified angina pectoris
I25.790	Atherosclerosis of other coronary artery bypass graft(s) with unstable angina pectoris
I25.791	Atherosclerosis of other coronary artery bypass graft(s) with angina pectoris with documented spasm
I25.798	Atherosclerosis of other coronary artery bypass graft(s) with other forms of angina pectoris
I25.799	Atherosclerosis of other coronary artery bypass graft(s) with unspecified angina pectoris

Group 2 Paragraph: N/A

Group 2 Codes:

ICD-10 Codes	Description
F31.30	Bipolar disorder, current episode depressed, mild or moderate severity, unspecified
F31.31	Bipolar disorder, current episode depressed, mild
F31.32	Bipolar disorder, current episode depressed, moderate
F31.4	Bipolar disorder, current episode depressed, severe, without psychotic features
F31.5	Bipolar disorder, current episode depressed, severe, with psychotic features
F31.60	Bipolar disorder, current episode mixed, unspecified
F31.61	Bipolar disorder, current episode mixed, mild
F31.62	Bipolar disorder, current episode mixed, moderate
F31.63	Bipolar disorder, current episode mixed, severe, without psychotic features
F31.64	Bipolar disorder, current episode mixed, severe, with psychotic features

ICD-10 Codes

Description

F31.75	Bipolar disorder, in partial remission, most recent episode depressed
F31.76	Bipolar disorder, in full remission, most recent episode depressed
F31.77	Bipolar disorder, in partial remission, most recent episode mixed
F31.78	Bipolar disorder, in full remission, most recent episode mixed
F31.9	Bipolar disorder, unspecified
F32.9	Major depressive disorder, single episode, unspecified
F33.0	Major depressive disorder, recurrent, mild
F33.1	Major depressive disorder, recurrent, moderate
F33.2	Major depressive disorder, recurrent severe without psychotic features
F33.3	Major depressive disorder, recurrent, severe with psychotic symptoms
F33.40	Major depressive disorder, recurrent, in remission, unspecified
F33.41	Major depressive disorder, recurrent, in partial remission
F33.42	Major depressive disorder, recurrent, in full remission
F33.9	Major depressive disorder, recurrent, unspecified
F53.0	Postpartum depression
G10	Huntington's disease

ICD-10 Codes that DO NOT Support Medical Necessity N/A

ICD-10 Additional Information [Back to Top](#)

General Information

Associated Information

N/A

Sources of Information

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NA

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Revision History Information

Revision History Date	Revision History Number	Revision History Explanation	Reason(s) for Change
10/01/2018	R4	<p>09/19/2018: At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.</p> <p>LCD is revised to add ICD-10 F53.0 to Group 2 diagnoses due to 2019 ICD-10 code updates.</p>	<ul style="list-style-type: none"> • Creation of Uniform LCDs With Other MAC Jurisdiction • Revisions Due To ICD-10-CM Code Changes
10/01/2017	R3	<p>02/06/2018: At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.</p> <p>LCD is revised to remove <i>Title XVIII of the Social Security Act, §1862(a)(1)(D) items and services related to research and experimentation</i> from the CMS National Coverage Policy section.</p>	<ul style="list-style-type: none"> • Creation of Uniform LCDs With Other MAC Jurisdiction
10/01/2017	R2	<p>09/08/2017: At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.</p> <p>Added the following codes under ICD-10 Codes that Support Medical Necessity , Group 1:I25.111, I25.118, I25.119, I25.701, I25.708, I25.709, I25.711, I25.718, I25.719, I25.721, I25.728, I25.729, I25.731, I25.738, I25.739, I25.751, I25.758, I25.759, I25.761, I25.768, I25.769, I25.791, I25.798 and I25.799 effective 6/1/2017.</p> <p>Added ICD-10 codes I21.9, I21.A1, I21.A9 due to the 2017 Annual ICD-10 Code Update.</p>	<ul style="list-style-type: none"> • Creation of Uniform LCDs With Other MAC Jurisdiction • Revisions Due To ICD-10-CM Code Changes
07/08/2016	R1	<p>Effective 07/08/2016, CPT code 81479 is added to groups 1 & 2 under the "CPT/HCPCS Codes " section, per the MoIDX contractor. The Part A LCD (L36311) is retired and Part A contract numbers are added to the Part B LCD so that they will have the same LCD number in the Medicare Coverage Database.</p>	<ul style="list-style-type: none"> • Creation of Uniform LCDs With Other MAC Jurisdiction

**Revision
History
Date**

**Revision
History
Number**

Revision History Explanation

**Reason(s) for
Change**

- Revisions Due To CPT/HCPCS Code Changes

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Associated Documents

Attachments N/A

Related Local Coverage Documents Article(s) [A54237](#) - (MCD Archive Site) [A54749](#) - (MCD Archive Site)

Related National Coverage Documents N/A

Public Version(s) Updated on 09/26/2018 with effective dates 10/01/2018 - N/A [Updated on 02/06/2018 with effective dates 10/01/2017 - 09/30/2018](#) [Updated on 09/09/2017 with effective dates 10/01/2017 - N/A](#) Some older versions have been archived. Please visit the [MCD Archive Site](#) to retrieve them. [Back to Top](#)

Keywords

- genetic
- MoDx
- genotyping
- pharmacogenetic
- CYP2C19
- CYP2D6
- CYP2C9
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