Local Coverage Determination (LCD): Biomarkers Overview (L35062)

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Contractor Information

Contractor Name	Contract Type	Contract Number	Jurisdiction	State(s)
Novitas Solutions, Inc.	A and B MAC	04111 - MAC A	J - H	Colorado
Novitas Solutions, Inc.	A and B MAC	04112 - MAC B	J - H	Colorado
Novitas Solutions, Inc.	A and B MAC	04211 - MAC A	J - H	New Mexico
Novitas Solutions, Inc.	A and B MAC	04212 - MAC B	J - H	New Mexico
Novitas Solutions, Inc.	A and B MAC	04311 - MAC A	J - H	Oklahoma
Novitas Solutions, Inc.	A and B MAC	04312 - MAC B	J - H	Oklahoma
Novitas Solutions, Inc.	A and B MAC	04411 - MAC A	J - H	Texas
Novitas Solutions, Inc.	A and B MAC	04412 - MAC B	J - H	Texas
Novitas Solutions, Inc.	A and B MAC	04911 - MAC A	J - H	Colorado New Mexico Oklahoma Texas
Novitas Solutions, Inc.	A and B MAC	07101 - MAC A	J - H	Arkansas
Novitas Solutions, Inc.	A and B MAC	07102 - MAC B	J - H	Arkansas
Novitas Solutions, Inc.	A and B MAC	07201 - MAC A	J - H	Louisiana
Novitas Solutions, Inc.	A and B MAC	07202 - MAC B	J - H	Louisiana
Novitas Solutions, Inc.	A and B MAC	07301 - MAC A	J - H	Mississippi
Novitas Solutions, Inc.	A and B MAC	07302 - MAC B	J - H	Mississippi
Novitas Solutions, Inc.	A and B MAC	12101 - MAC A	J - L	Delaware
Novitas Solutions, Inc.	A and B MAC	12102 - MAC B	J - L	Delaware
Novitas Solutions, Inc.	A and B MAC	12201 - MAC A	J - L	District of Columbia
Novitas Solutions, Inc.	A and B MAC	12202 - MAC B	J - L	District of Columbia
Novitas Solutions, Inc.	A and B MAC	12301 - MAC A	J - L	Maryland
Novitas Solutions, Inc.	A and B MAC	12302 - MAC B	J - L	Maryland
Novitas Solutions, Inc.	A and B MAC	12401 - MAC A	J - L	New Jersey
Novitas Solutions, Inc.	A and B MAC	12402 - MAC B	J - L	New Jersey
Novitas Solutions, Inc.	A and B MAC	12501 - MAC A	J - L	Pennsylvania
Novitas Solutions, Inc.	A and B MAC	12502 - MAC B	J - L	Pennsylvania
Novitas Solutions, Inc.	A and B MAC	12901 - MAC A	J - L	District of Columbia Delaware Maryland New Jersey Pennsylvania

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LCD Information

Document Information

LCD ID
L35062

Original Effective Date
For services performed on or after 10/01/2015

Original ICD-9 LCD ID
L33640

Revision Effective Date
For services performed on or after 01/01/2018

LCD Title
Biomarkers Overview

Proposed LCD in Comment Period
N/A

Source Proposed LCD
N/A

Revision Ending Date
N/A

Retirement Date
N/A

Notice Period Start Date
10/13/2016

Notice Period End Date
11/30/2016

CMS National Coverage Policy
This LCD supplements but does not replace, modify or supersede existing Medicare applicable National Coverage Determinations (NCDs) or payment policy rules and regulations for biomarker overview services. Federal statute and subsequent Medicare regulations regarding provision and payment for medical services are lengthy. They are not repeated in this LCD. Neither Medicare payment policy rules nor this LCD replace, modify or supersede applicable state statutes regarding medical practice or other health practice professions acts, definitions and/or scopes of practice. All providers who report services for Medicare payment must fully understand and follow all existing laws, regulations and rules for Medicare payment for biomarker overview services and must properly submit only valid claims for them. Please review and understand them and apply the medical necessity provisions in the policy within the context of the manual rules. Relevant CMS manual instructions and policies regarding services may be found in the following Internet-Only Manuals (IOMs) published on the CMS Web site.

IOM Citations:

- CMS IOM, Publication 100-02, *Medicare Benefit Policy Manual*, Chapter 15, Section 80.1, 80.1.1, 80.1.2, 80.1.3, Laboratory services must meet applicable requirements of CLIA, and Section 280, Preventive and Screening Services.
- CMS IOM, Publication 100-08, *Medicare Program Integrity Manual*, Chapter 3
    - Section 3.4.1.3, Diagnosis Code Requirements.
    - Section 3.6.2.3, Limitation of Liability Determinations.

Social Security Act (Title XVIII) Standard References:

- Title XVIII of the Social Security Act, Section 1862(a)(1)(A) states that no Medicare payment shall be made for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury.
- Title XVIII of the Social Security Act, Section 1862(a)(7). This section excludes routine physical examinations.
- Title XVIII of the Social Security Act, Section 1833(e) states that no payment shall be made to any provider for any claim that lacks the necessary information to process the claim.
- Title XVIII of the Social Security Act, Section 1862(a)(1)(D) states that no Medicare payment may be made for any expenses incurred for items or services that are investigational or experimental.

Federal Register References:

- Title 42 Code of Federal Regulations (CFR) section 410.32(d)(3) indicates diagnostic tests are payable only when the physician who is treating the beneficiary for a specific medical problem and who uses the results in such treatment. Tests not ordered by the physician who is treating the beneficiary are not reasonable and necessary (see §411.15(k)(1) of this chapter).

Coverage Guidance
Coverage Indications, Limitations, and/or Medical Necessity

Notice: It is not appropriate to bill Medicare for services that are not covered (as described by this entire LCD) as if they are covered. When billing for non-covered services, use the appropriate modifier.

Compliance with the provisions in this policy may be monitored and addressed through post payment data analysis and subsequent medical review audits.

History/Background and/or General Information

The emergence of personalized laboratory medicine has been characterized by a multitude of testing options which may more precisely pinpoint management needs of individual patients. As a result, the growing compendium of biomarkers requires a more careful evaluation by both clinicians and laboratorians as to what testing configurations can more optimally realize the promises of personalized medicine. There are a plethora of burgeoning tools, including both gene-based (genomic) and protein-based (proteomic) assay formats, in tandem with more conventional (longstanding) flow cytometric, cytogenetic, etc. biomarkers. Classified somewhat differently, there are highly-diverse approaches ranging from single mutation biomarkers to multiple biomarker platforms, the latter of which often depend upon sophisticated biomathematical interpretative algorithms. This policy will provide guidance on the broad range of (recently coded) biomarkers, and how such a wide array of testing platforms can be best accommodated by this local Medicare Administrative Contractor.

Medicare coverage for screening of those individuals with a family history of certain disease is covered only for a limited number of services as listed in the Section 280 – Preventative and Screening Services of the IOM 100-02, *Medicare Benefit Policy Manual*, Chapter 15.

Tests performed without relationship to treatment or diagnosis of a patient with no findings or history for a specific illness, symptom, complaint or injury unless set exclusion are so noted in Title 42 CFR, Section 411.15(a)(1).

Local Medicare coverage of such biomarkers must be predicated upon three fundamental principles:

First, there must be an underlying performance of acceptable, high-quality analytical validity for all such laboratory testing. As a result, the laboratory shall have available upon request:

- Analytical and clinical validation reports for Clinical Laboratory Improvement Amendments (CLIA), including the test description, intended use, and indications for testing.
- If applicable, all formal, written minutes and correspondences (including any Q & A and supporting documentation) with the New York State Department of Health (NYSDOH) or the US Food and Drug Administration.
- Most recent inspection results (including recommendations) or scheduled inspection(s) from CLIA, College of American Pathologists (CAP), or NYSDOH, as applicable.

Second, there must be an appreciation of evidence-in-transition where new biomarkers should be brought on-line in harmonization with their proven clinical validity/utility (CVU). Although analytical validity is an equally

important metric, it remains more outside of a payer's purview to conduct such detailed evaluations. Therefore, in the absence of a standard CVU referee process (e.g., although FDA labeling of biomarkers can be a helpful adjunct, it may not always be relevant), the key imperative is for medical necessity to be reflected by the clear articulation of a particular biomarker niche.

Third, there must be a recognized decision impact of such biomarkers by the clinical community. In other words, there must be acceptance/uptake of specific testing into patient management. It should be taken into account that to reach the medical necessity threshold, such acceptance should be based on the strongest evidence available, ideally from along the spectrum of high-quality masked, randomized controlled clinical trials, and much less preferably from lower levels of evidence, which are predicated upon expert opinion only without primary study data.

Per above, it is relevant to categorize biomarkers into functional clusters which, in turn, can enable longitudinal coverage guidance that is most relevant to the Medicare program mission:

The commercial availability does not ensure that a molecular diagnostic test is indicated for clinical application. Molecular diagnostic testing is a rapidly evolving science in which the significance of detecting specific mutations has yet to be clarified in many circumstances. Analytical and clinical validity as well as clinical utility are the responsibility of the provider, and all testing must meet standards of care.

Covered Indications

1.**GERMLINE (HEREDITARY) MUTATIONS**

Medicare considers genetic testing medically necessary to establish a molecular diagnosis of an inheritable disease when all of the following criteria are met:

- The beneficiary must display clinical features of an associated disease, but noting that coverage of molecular testing for carrier status or family studies is considered screening and is statutorily excluded from coverage; and
- The result of the test will directly impact the treatment being delivered to the beneficiary; and
- A definitive diagnosis remains uncertain after history, physical examination, pedigree analysis, genetic counseling, and completion of conventional diagnostic studies.

The following table delineates the coverage status for various germline mutations, based upon the above bulleted principles. No procedure-to-diagnosis based limitations will be implemented for the germline mutations contained in the table, with the expectation that such sound principles of genetic counseling* and testing have been implemented.

Germline Mutation	Coverage or Non-Coverage	CPT Code
DMD (dystrophin) (e.g., Duchenne/Becker muscular dystrophy) deletion analysis, and duplication analysis, if performed	Non-Covered	81161
Aortic dysfunction/dilation; genomic sequence panel	Non-Covered	81410
Aortic dysfunction/dilation; duplication/deletion analysis panel	Non-Covered	81411
Aspa gene	Non-Covered	81200
APC *adenomatous polyposis coli* full gene sequence	Covered	81201
APC known familial variants	Covered	81202
APC duplication/deletion	Covered	81203
Ashkenazi Jewish disorders	Non-Covered	81412
Bckdhb gene	Non-Covered	81205
Blm gene	Non-Covered	81209
Car ion chnnlpath inc 10 gns	Non-Covered	81413
Car ion chnnlpath inc 2 gns	Non-Covered	81414
Cftr gene com variants	Non-Covered	81220
Cftr gene known fam variants	Non-Covered	81221
Cftr gene dup/delet variants	Non-Covered	81222
Cftr gene full sequence	Non-Covered	81223

Germline Mutation	Coverage or Non-Coverage	CPT Code
Cftr gene intron poly t	Non-Covered	81224
Cytogen micrarray copy nmbr; for copy number or cgh microarray analysis	Non-Covered	81228
Cytogen micrarray copy nmbr; for copy number and SNP variants	Non-Covered	81229
Exome sequence analysis	Non-Covered (including for blood relatives)	81415
Exome sequence analysis; each comparator exome	Non-Covered (including for blood relatives)	81416
Exome re-evaluation	Non-Covered (including for blood relatives)	81417
Fancc gene	Covered	81242
Fetal chrmoml aneuploidy	Non-Covered	81420
Fmr1 gene detection	Non-Covered	81243
Fmr1 gene characterization	Non-Covered	81244
G6pc gene	Covered	81250
Gba gene	Covered	81251
GJB2 (gap junction protein, common variants)	Covered	81252
GJB2 known familial variants	Covered	81253
GJB6 gap junction protein gene analysis, common variants	Covered	81254
Genome sequence analysis	Non-Covered (including for blood relatives)	81425
Genome sequence analysis; each comparator genome	Non-Covered (including for blood relatives)	81426
Genome re-evaluation	Non-Covered (including for blood relatives)	81427
Hearing loss sequence analysis	Non-Covered	81430
Hearing dup/del analysis	Non-Covered	81431
Hereditary Retinal Panel	Non-Covered	81434
Hexa gene (Tay Sachs)	Covered	81255
Hfe gene	Covered	81256
Hba1/hba2 gene	Covered	81257
Hba1/hba2 gene fam vrnt	Covered	81258
Hba1/hba2 full gene sequence	Covered	81259
Hba1/hba2 gene dup/del vrnts	Covered	81269
Ikbkap gene	Non-Covered	81260
Hrdtry cardmypy gene panel	Non-Covered	81439
Mcoln1gene	Covered	81290
Mlh 1 gene; promoter methylation analysis	Covered	81288
Msh2 gene full seq	Covered	81295
Msh2 gene known variants	Covered	81296
Msh2 gene dup/delete variants	Covered	81297
Msh6 gene full seq	Covered	81298
Msh6 gene known variants	Covered	81299
Msh6 gene dup/delete variants	Covered	81300
Mitochondrial gene	Non-Covered	81440
Whole Mitochondrial genome; genomic sequence	Non-Covered	81460
Whole Mitochondrial genome; large deletion analysis	Non-Covered	81465
Mecp2 gene full seq (Rhetts)	Non-Covered	81302

Germline Mutation	Coverage or Non-Coverage	CPT Code
Mecp2 gene known variant (Rhetts)	Non-Covered	81303
Mecp2 gene dup/delete variants (Rhetts)	Non-Covered	81304
Mthfr gene	Non-Covered	81291
Noonan Spectrum Disorders	Non-Covered	81442
Pms2 gene full seq analysis	Covered	81317
Pms2 known familial variants	Covered	81318
Pms2 gene dup/delete variants	Covered	81319
PMP22 gene analysis, duplication/deletion	Covered	81324
PMP22 full sequence analysis	Covered	81325
PMP22 known familial variants	Covered	81326
Rbc dna hea 35 ag 11 bld grp	Covered	0001U
Smpd1 gene common variants	Non-Covered	81330
snrpn/ube3a gene	Non-Covered	81331
Serpina1 gene	Covered	81332
X-linked intellectual dblt; genomic sequence	Non-Covered	81470
X-linked intellectual dblt; duplication/deletion gene analysis	Non-Covered	81471

Note: The following two germline hereditary mutation tests will be considered medically necessary when performed for evaluation of venous thromboembolism. Please see ICD-10 Code group 3.

- Factor II (F2 gene)
- Factor V (F5 gene)

* While not required for payment, NCCN Guidelines recommend referral to a cancer genetics professional with expertise and experience in cancer genetics prior to genetic testing and after genetic testing. Examples of cancer genetics professionals with expertise and experience in cancer genetics include: an American Board of Medical Genetics or American Board of Genetic Counseling certified or board eligible Clinical Geneticist, Medical Geneticist or Genetic Counselor not employed by a commercial genetic testing laboratory (excludes individuals employed by or contracted with a laboratory that is part of an Integrated Health System which routinely delivers health care services beyond just the laboratory test itself as these individuals are also considered independent); medical oncologist, obstetrician-gynecologist or other physician trained in medical cancer genetics, a genetic nurse credentialed as either a Genetic Clinical Nurse or an Advanced Practice Nurse in Genetics by either the Genetic Nursing Credentialing Commission (GNCC) or the American Nurses Credentialing Center (ANCC) who is not employed by a commercial genetic testing laboratory (excludes individuals employed by or contracted with a laboratory that is part of an Integrated Health System which routinely delivers health care services beyond just the laboratory test itself as these individuals are also considered independent).

2. **PHARMACOGENOMICS**

The cytochrome P450 (CYP450) gene superfamily is composed of many isoenzymes that are involved in the metabolism of many medications. Although this superfamily has more than 50 enzymes, six of them metabolize 90% of clinically used drugs. Each cytochrome P450 gene is named with CYP indicating it is part of the cytochrome P450 family. CYP2C19 metabolizes at least 10% of all commonly prescribed drugs, whereas CYP2D6 enzymes metabolize approximately 20-25%, and CYP2C9 metabolizes approximately 10%.

Human CYP genes are highly polymorphic. As a result, polymorphisms are classified into four groups based on the level of CYP enzyme activity and include poor (abolished activity), intermediate (reduced activity), extensive (normal activity) and ultra-rapid metabolizers (enhanced activity). Genetic variability or polymorphism in these enzymes may influence a patient’s response to commonly prescribed drug classes. The most pharmacologically and clinically relevant CYP polymorphisms are found in CYP2D6, CYP2C9, and CYP2C19. The genotypic rates vary by ethnicity.

A. **CYP2C19 Genotyping**

Background on CYP2C19 Testing

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.

The frequency of the various CYP2C19 metabolizer phenotypes has been estimated as follows:

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

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 Pharmaco-genetics 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 Helicobactor 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.

This policy limits CYP2C19 (CPT code 81225) genetic testing to patients with ACS undergoing PCI who are initiating or reinitiating Clopidogrel (Plavix) therapy.

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

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

B.**CYP2D6 Genotyping**

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.

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 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 galatamine, including information on treatment efficacy and tolerability.

- Donepezil (Aricept) is a drug used to treat 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 for CYP2D6

Genetic testing of the CYP2D6 gene is considered medically necessary to guide medical treatment 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

Indications considered not reasonable and necessary for CYP2D6

There is insufficient evidence to demonstrate that genetic testing for the CYP2D6 gene improves clinical outcomes for the following medications. Consequently, genetic testing for the CYP2D6 gene is considered investigational for the following:

- Antidepressants other than those listed above
- Antipsychotics
- Codeine
- Donepezil
- Galantamine
- Tamoxifen

3. **SOMATIC MUTATIONS, ONCOLOGY**:

- Please Refer to LCD L35396, Biomarkers for Oncology.

CYP2C9 Genotyping

- This policy does not address coverage with evidence development (CED) under section 1862(a)(1)(E). For CED coverage information related to CYP2C9 and VKORC1 for warfarin responsiveness please refer to the NCD for Pharmacogenomic Testing for Warfarin Response (90.1).

Biomarkers not addressed in this LCD or any other Novitas LCD will be considered not reasonable and necessary unless specifically covered by national policy. For frequency limitations please refer to the Utilization Guidelines section below.

Notice: This LCD imposes frequency limitations as well as diagnosis limitations that support diagnosis to procedure code automated denials. However, services performed for any given diagnosis must meet all of the indications and limitations stated in this policy, the general requirements for medical necessity as stated in CMS payment policy manuals, any and all existing CMS national coverage determinations, and all Medicare payment rules.

As published in CMS IOM 100-08, Chapter 13, Section 13.5.1, in order to be covered under Medicare, a service shall be reasonable and necessary. When appropriate, contractors shall describe the circumstances under which the proposed LCD for the service is considered reasonable and necessary under Section 1862 (a)(1)(A). Contractors shall consider a service to be reasonable and necessary if the contractor determines that the service is:

- Safe and effective.
- Not experimental or investigational (exception: routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 that meet the requirements of the Clinical Trials NCD are considered reasonable and necessary).
- Appropriate, including the duration and frequency that is considered appropriate for the service, in terms of whether it is:
    - Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member.
    - Furnished in a setting appropriate to the patient's medical needs and condition.
    - Ordered and furnished by qualified personnel.
    - One that meets, but does not exceed, the patient's medical needs.
    - At least as beneficial as an existing and available medically appropriate alternative.

The redetermination process may be utilized for consideration of services performed outside of the reasonable and necessary requirements in this LCD.

Summary of Evidence

N/A

Analysis of Evidence
(Rationale for Determination)

N/A

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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.

012x Hospital Inpatient (Medicare Part B only)
013x Hospital Outpatient
014x Hospital - Laboratory Services Provided to Non-patients
018x Hospital - Swing Beds
021x Skilled Nursing - Inpatient (Including Medicare Part A)
022x Skilled Nursing - Inpatient (Medicare Part B only)
023x Skilled Nursing - Outpatient
071x Clinic - Rural Health
072x Clinic - Hospital Based or Independent Renal Dialysis Center
073x Clinic - Freestanding
075x Clinic - Comprehensive Outpatient Rehabilitation Facility (CORF)
077x Clinic - Federally Qualified Health Center (FQHC)
083x Ambulatory Surgery Center
085x Critical Access Hospital

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.

Note: The contractor has identified the Bill Type and Revenue Codes applicable for use with the CPT/HCPCS codes included in this LCD. Providers are reminded that not all CPT/HCPCS codes listed can be billed with all Bill Type or Revenue Codes listed. CPT/HCPCS codes are required to be billed with specific Bill Type and Revenue Codes. Providers are encouraged to refer to the CMS IOM Pub. 100-04, *Medicare Claims Processing Manual*, for further guidance.

0300 Laboratory - General Classification
0301 Laboratory - Chemistry
0302 Laboratory - Immunology
0303 Laboratory - Renal Patient (Home)
0304 Laboratory - Non-Routine Dialysis
0305 Laboratory - Hematology
0306 Laboratory - Bacteriology & Microbiology
0307 Laboratory - Urology
0309 Laboratory - Other Laboratory
0310 Laboratory Pathology - General Classification
0311 Laboratory Pathology - Cytology
0312 Laboratory Pathology - Histology
0314 Laboratory Pathology - Biopsy
0319 Laboratory Pathology - Other Laboratory Pathology

CPT/HCPCS Codes
Group 1 Paragraph:

Note: Providers are reminded to refer to the long descriptors of the CPT codes in their CPT book.

Please note: At this time, only the CPT codes listed in ICD-10 code group paragraphs 1 through 5 are subject to diagnosis-to-procedure code limitations. Please refer to the list of CPT/HCPCS codes at the beginning of each ICD -10 code group paragraph for appropriate diagnosis-to-procedure code limitations.

Group 1 Codes:
81201 Apc gene full sequence
81202 Apc gene known fam variants
81203 Apc gene dup/delet variants
81225 Cyp2c19 gene com variants
81226 Cyp2d6 gene com variants
81240 F2 gene
81241 F5 gene
81242 Fancc gene
81250 G6pc gene
81251 Gba gene
81252 Gjb2 gene full sequence
81253 Gjb2 gene known fam variants
81254 Gjb6 gene com variants
81255 Hexa gene
81256 Hfe gene
81257 Hba1/hba2 gene
81258 Hba1/hba2 gene fam vrnt
81259 Hba1/hba2 full gene sequence
81265 Str markers specimen anal
81266 Str markers spec anal addl
81267 Chimerism anal no cell selec
81268 Chimerism anal w/cell select
81269 Hba1/hba2 gene dup/del vrnts
81288 Mlh1 gene
81290 Mcoln1 gene
81295 Msh2 gene full seq
81296 Msh2 gene known variants
81297 Msh2 gene dup/delete variant
81298 Msh6 gene full seq
81299 Msh6 gene known variants
81300 Msh6 gene dup/delete variant
81317 Pms2 gene full seq analysis
81318 Pms2 known familial variants

81319 Pms2 gene dup/delet variants
81324 Pmp22 gene dup/delet
81325 Pmp22 gene full sequence
81326 Pmp22 gene known fam variant
81332 Serpina1 gene
81370 Hla i & ii typing lr
81371 Hla i & ii type verify lr
81372 Hla i typing complete lr
81373 Hla i typing 1 locus lr
81374 Hla i typing 1 antigen lr
81375 Hla ii typing ag equiv lr
81376 Hla ii typing 1 locus lr
81377 Hla ii type 1 ag equiv lr
81378 Hla i & ii typing hr
81379 Hla i typing complete hr
81380 Hla i typing 1 locus hr
81381 Hla i typing 1 allele hr
81382 Hla ii typing 1 loc hr
81383 Hla ii typing 1 allele hr
81490 Autoimmune rheumatoid arthr
81595 Cardiology hrt trnspl mrna
0001U Rbc dna hea 35 ag 11 bld grp

Group 2 Paragraph:

Coverage for these codes is addressed in the NCD for Pharmacogenomic Testing for Warfarin Response (90.1). Please refer to the NCD for details.

Group 2 Codes:
81227 Cyp2c9 gene com variants
81355 Vkorc1 gene

Group 3 Paragraph:

The following CPT codes are non-covered.

Group 3 Codes:
81161 Dmd dup/delet analysis
81200 Aspa gene
81205 Bckdhb gene
81209 Blm gene
81220 Cftr gene com variants
81221 Cftr gene known fam variants
81222 Cftr gene dup/delet variants
81223 Cftr gene full sequence
81224 Cftr gene intron poly t
81228 Cytogen micrarray copy nmbr
81229 Cytogen m array copy no&snp
81243 Fmr1 gene detection
81244 Fmr1 gene characterization
81260 Ikbkap gene
81291 Mthfr gene
81302 Mecp2 gene full seq
81303 Mecp2 gene known variant
81304 Mecp2 gene dup/delet variant
81330 Smpd1 gene common variants

81331 Snrpn/ube3a gene
81410 Aortic dysfunction/dilation
81411 Aortic dysfunction/dilation
81412 Ashkenazi jewish assoc dis
81413 Car ion chnnlpath inc 10 gns
81414 Car ion chnnlpath inc 2 gns
81415 Exome sequence analysis
81416 Exome sequence analysis
81417 Exome re-evaluation
81420 Fetal chrmoml aneuploidy
81425 Genome sequence analysis
81426 Genome sequence analysis
81427 Genome re-evaluation
81430 Hearing loss sequence analys
81431 Hearing loss dup/del analys
81434 Hereditary retinal disorders
81439 Hrdtry cardmypy gene panel
81440 Mitochondrial gene
81442 Noonan spectrum disorders
81460 Whole mitochondrial genome
81465 Whole mitochondrial genome
81470 X-linked intellectual dblt
81471 X-linked intellectual dblt

ICD-10 Codes that Support Medical Necessity
Group 1 Paragraph:
It is the provider's responsibility to select codes carried out to the highest level of specificity and selected from the ICD-10-CM code book appropriate to the year in which the service is rendered for the claim(s) submitted.

Medicare is establishing the following limited coverage for **CPT code 81225-CYP2C19.**

Group 1 Codes:

ICD-10 Codes	Description
I25.10	Atherosclerotic heart disease of native coronary artery without angina pectoris
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
I25.5	Ischemic cardiomyopathy
I25.6	Silent myocardial ischemia
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
I25.760	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
I25.790	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
I25.810	Atherosclerosis of coronary artery bypass graft(s) without angina pectoris
I25.812	Atherosclerosis of bypass graft of coronary artery of transplanted heart without angina pectoris
I25.83	Coronary atherosclerosis due to lipid rich plaque
I25.84	Coronary atherosclerosis due to calcified coronary lesion

ICD-10 Codes	Description
I25.89	Other forms of chronic ischemic heart disease
I25.9	Chronic ischemic heart disease, unspecified
I63.013	Cerebral infarction due to thrombosis of bilateral vertebral arteries
I63.033	Cerebral infarction due to thrombosis of bilateral carotid arteries
I63.113	Cerebral infarction due to embolism of bilateral vertebral arteries
I63.133	Cerebral infarction due to embolism of bilateral carotid arteries
I63.213	Cerebral infarction due to unspecified occlusion or stenosis of bilateral vertebral arteries
I63.233	Cerebral infarction due to unspecified occlusion or stenosis of bilateral carotid arteries
I63.313	Cerebral infarction due to thrombosis of bilateral middle cerebral arteries
I63.323	Cerebral infarction due to thrombosis of bilateral anterior cerebral arteries
I63.333	Cerebral infarction to thrombosis of bilateral posterior cerebral arteries
I63.343	Cerebral infarction to thrombosis of bilateral cerebellar arteries
I63.413	Cerebral infarction due to embolism of bilateral middle cerebral arteries
I63.423	Cerebral infarction due to embolism of bilateral anterior cerebral arteries
I63.433	Cerebral infarction due to embolism of bilateral posterior cerebral arteries
I63.443	Cerebral infarction due to embolism of bilateral cerebellar arteries
I63.511	Cerebral infarction due to unspecified occlusion or stenosis of right middle cerebral artery
I63.512	Cerebral infarction due to unspecified occlusion or stenosis of left middle cerebral artery
I63.513	Cerebral infarction due to unspecified occlusion or stenosis of bilateral middle cerebral arteries
I63.519	Cerebral infarction due to unspecified occlusion or stenosis of unspecified middle cerebral artery
I63.523	Cerebral infarction due to unspecified occlusion or stenosis of bilateral anterior cerebral arteries
I63.533	Cerebral infarction due to unspecified occlusion or stenosis of bilateral posterior cerebral arteries
I63.543	Cerebral infarction due to unspecified occlusion or stenosis of bilateral cerebellar arteries
I63.59	Cerebral infarction due to unspecified occlusion or stenosis of other cerebral artery
I66.01	Occlusion and stenosis of right middle cerebral artery
I66.02	Occlusion and stenosis of left middle cerebral artery
I66.03	Occlusion and stenosis of bilateral middle cerebral arteries
I66.8	Occlusion and stenosis of other cerebral arteries
Z79.02	Long term (current) use of antithrombotics/antiplatelets

Group 2 Paragraph:

Medicare is establishing the following coverage for **CPT code 81226- CYP2D6.**

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
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
F32.89	Other specified depressive episodes
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

ICD-10 Codes	Description
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
G10	Huntington's disease

Group 3 Paragraph:

Medicare is establishing the following limited coverage for **CPT codes 81240 and 81241:**

Group 3 Codes:

ICD-10 Codes	Description
I82.91	Chronic embolism and thrombosis of unspecified vein

Group 4 Paragraph:

Medicare is establishing the following limited coverage for **CPT code 81490**:

Group 4 Codes:

ICD-10 Codes	Description
M05.011	Felty's syndrome, right shoulder
M05.012	Felty's syndrome, left shoulder
M05.021	Felty's syndrome, right elbow
M05.022	Felty's syndrome, left elbow
M05.031	Felty's syndrome, right wrist
M05.032	Felty's syndrome, left wrist
M05.041	Felty's syndrome, right hand
M05.042	Felty's syndrome, left hand
M05.051	Felty's syndrome, right hip
M05.052	Felty's syndrome, left hip
M05.061	Felty's syndrome, right knee
M05.062	Felty's syndrome, left knee
M05.071	Felty's syndrome, right ankle and foot
M05.072	Felty's syndrome, left ankle and foot
M05.09	Felty's syndrome, multiple sites
M05.111	Rheumatoid lung disease with rheumatoid arthritis of right shoulder
M05.112	Rheumatoid lung disease with rheumatoid arthritis of left shoulder
M05.121	Rheumatoid lung disease with rheumatoid arthritis of right elbow
M05.122	Rheumatoid lung disease with rheumatoid arthritis of left elbow
M05.131	Rheumatoid lung disease with rheumatoid arthritis of right wrist
M05.132	Rheumatoid lung disease with rheumatoid arthritis of left wrist
M05.141	Rheumatoid lung disease with rheumatoid arthritis of right hand
M05.142	Rheumatoid lung disease with rheumatoid arthritis of left hand
M05.151	Rheumatoid lung disease with rheumatoid arthritis of right hip
M05.152	Rheumatoid lung disease with rheumatoid arthritis of left hip
M05.161	Rheumatoid lung disease with rheumatoid arthritis of right knee
M05.162	Rheumatoid lung disease with rheumatoid arthritis of left knee
M05.171	Rheumatoid lung disease with rheumatoid arthritis of right ankle and foot
M05.172	Rheumatoid lung disease with rheumatoid arthritis of left ankle and foot
M05.19	Rheumatoid lung disease with rheumatoid arthritis of multiple sites
M05.211	Rheumatoid vasculitis with rheumatoid arthritis of right shoulder

ICD-10 Codes	Description
M05.212	Rheumatoid vasculitis with rheumatoid arthritis of left shoulder
M05.221	Rheumatoid vasculitis with rheumatoid arthritis of right elbow
M05.222	Rheumatoid vasculitis with rheumatoid arthritis of left elbow
M05.231	Rheumatoid vasculitis with rheumatoid arthritis of right wrist
M05.232	Rheumatoid vasculitis with rheumatoid arthritis of left wrist
M05.241	Rheumatoid vasculitis with rheumatoid arthritis of right hand
M05.242	Rheumatoid vasculitis with rheumatoid arthritis of left hand
M05.251	Rheumatoid vasculitis with rheumatoid arthritis of right hip
M05.252	Rheumatoid vasculitis with rheumatoid arthritis of left hip
M05.261	Rheumatoid vasculitis with rheumatoid arthritis of right knee
M05.262	Rheumatoid vasculitis with rheumatoid arthritis of left knee
M05.271	Rheumatoid vasculitis with rheumatoid arthritis of right ankle and foot
M05.272	Rheumatoid vasculitis with rheumatoid arthritis of left ankle and foot
M05.29	Rheumatoid vasculitis with rheumatoid arthritis of multiple sites
M05.311	Rheumatoid heart disease with rheumatoid arthritis of right shoulder
M05.312	Rheumatoid heart disease with rheumatoid arthritis of left shoulder
M05.321	Rheumatoid heart disease with rheumatoid arthritis of right elbow
M05.322	Rheumatoid heart disease with rheumatoid arthritis of left elbow
M05.331	Rheumatoid heart disease with rheumatoid arthritis of right wrist
M05.332	Rheumatoid heart disease with rheumatoid arthritis of left wrist
M05.341	Rheumatoid heart disease with rheumatoid arthritis of right hand
M05.342	Rheumatoid heart disease with rheumatoid arthritis of left hand
M05.351	Rheumatoid heart disease with rheumatoid arthritis of right hip
M05.352	Rheumatoid heart disease with rheumatoid arthritis of left hip
M05.361	Rheumatoid heart disease with rheumatoid arthritis of right knee
M05.362	Rheumatoid heart disease with rheumatoid arthritis of left knee
M05.371	Rheumatoid heart disease with rheumatoid arthritis of right ankle and foot
M05.372	Rheumatoid heart disease with rheumatoid arthritis of left ankle and foot
M05.39	Rheumatoid heart disease with rheumatoid arthritis of multiple sites
M05.411	Rheumatoid myopathy with rheumatoid arthritis of right shoulder
M05.412	Rheumatoid myopathy with rheumatoid arthritis of left shoulder
M05.421	Rheumatoid myopathy with rheumatoid arthritis of right elbow
M05.422	Rheumatoid myopathy with rheumatoid arthritis of left elbow
M05.431	Rheumatoid myopathy with rheumatoid arthritis of right wrist
M05.432	Rheumatoid myopathy with rheumatoid arthritis of left wrist
M05.441	Rheumatoid myopathy with rheumatoid arthritis of right hand
M05.442	Rheumatoid myopathy with rheumatoid arthritis of left hand
M05.451	Rheumatoid myopathy with rheumatoid arthritis of right hip
M05.452	Rheumatoid myopathy with rheumatoid arthritis of left hip
M05.461	Rheumatoid myopathy with rheumatoid arthritis of right knee
M05.462	Rheumatoid myopathy with rheumatoid arthritis of left knee
M05.471	Rheumatoid myopathy with rheumatoid arthritis of right ankle and foot
M05.472	Rheumatoid myopathy with rheumatoid arthritis of left ankle and foot
M05.49	Rheumatoid myopathy with rheumatoid arthritis of multiple sites
M05.511	Rheumatoid polyneuropathy with rheumatoid arthritis of right shoulder
M05.512	Rheumatoid polyneuropathy with rheumatoid arthritis of left shoulder
M05.521	Rheumatoid polyneuropathy with rheumatoid arthritis of right elbow
M05.522	Rheumatoid polyneuropathy with rheumatoid arthritis of left elbow
M05.531	Rheumatoid polyneuropathy with rheumatoid arthritis of right wrist
M05.532	Rheumatoid polyneuropathy with rheumatoid arthritis of left wrist
M05.541	Rheumatoid polyneuropathy with rheumatoid arthritis of right hand
M05.542	Rheumatoid polyneuropathy with rheumatoid arthritis of left hand
M05.551	Rheumatoid polyneuropathy with rheumatoid arthritis of right hip
M05.552	Rheumatoid polyneuropathy with rheumatoid arthritis of left hip
M05.561	Rheumatoid polyneuropathy with rheumatoid arthritis of right knee
M05.562	Rheumatoid polyneuropathy with rheumatoid arthritis of left knee
M05.571	Rheumatoid polyneuropathy with rheumatoid arthritis of right ankle and foot
M05.572	Rheumatoid polyneuropathy with rheumatoid arthritis of left ankle and foot

ICD-10 Codes	Description
M05.59	Rheumatoid polyneuropathy with rheumatoid arthritis of multiple sites
M05.611	Rheumatoid arthritis of right shoulder with involvement of other organs and systems
M05.612	Rheumatoid arthritis of left shoulder with involvement of other organs and systems
M05.621	Rheumatoid arthritis of right elbow with involvement of other organs and systems
M05.622	Rheumatoid arthritis of left elbow with involvement of other organs and systems
M05.631	Rheumatoid arthritis of right wrist with involvement of other organs and systems
M05.632	Rheumatoid arthritis of left wrist with involvement of other organs and systems
M05.641	Rheumatoid arthritis of right hand with involvement of other organs and systems
M05.642	Rheumatoid arthritis of left hand with involvement of other organs and systems
M05.651	Rheumatoid arthritis of right hip with involvement of other organs and systems
M05.652	Rheumatoid arthritis of left hip with involvement of other organs and systems
M05.661	Rheumatoid arthritis of right knee with involvement of other organs and systems
M05.662	Rheumatoid arthritis of left knee with involvement of other organs and systems
M05.671	Rheumatoid arthritis of right ankle and foot with involvement of other organs and systems
M05.672	Rheumatoid arthritis of left ankle and foot with involvement of other organs and systems
M05.69	Rheumatoid arthritis of multiple sites with involvement of other organs and systems
M05.711	Rheumatoid arthritis with rheumatoid factor of right shoulder without organ or systems involvement
M05.712	Rheumatoid arthritis with rheumatoid factor of left shoulder without organ or systems involvement
M05.721	Rheumatoid arthritis with rheumatoid factor of right elbow without organ or systems involvement
M05.722	Rheumatoid arthritis with rheumatoid factor of left elbow without organ or systems involvement
M05.731	Rheumatoid arthritis with rheumatoid factor of right wrist without organ or systems involvement
M05.732	Rheumatoid arthritis with rheumatoid factor of left wrist without organ or systems involvement
M05.741	Rheumatoid arthritis with rheumatoid factor of right hand without organ or systems involvement
M05.742	Rheumatoid arthritis with rheumatoid factor of left hand without organ or systems involvement
M05.751	Rheumatoid arthritis with rheumatoid factor of right hip without organ or systems involvement
M05.752	Rheumatoid arthritis with rheumatoid factor of left hip without organ or systems involvement
M05.761	Rheumatoid arthritis with rheumatoid factor of right knee without organ or systems involvement
M05.762	Rheumatoid arthritis with rheumatoid factor of left knee without organ or systems involvement
M05.771	Rheumatoid arthritis with rheumatoid factor of right ankle and foot without organ or systems involvement
M05.772	Rheumatoid arthritis with rheumatoid factor of left ankle and foot without organ or systems involvement
M05.79	Rheumatoid arthritis with rheumatoid factor of multiple sites without organ or systems involvement
M05.811	Other rheumatoid arthritis with rheumatoid factor of right shoulder
M05.812	Other rheumatoid arthritis with rheumatoid factor of left shoulder
M05.821	Other rheumatoid arthritis with rheumatoid factor of right elbow
M05.822	Other rheumatoid arthritis with rheumatoid factor of left elbow
M05.831	Other rheumatoid arthritis with rheumatoid factor of right wrist
M05.832	Other rheumatoid arthritis with rheumatoid factor of left wrist
M05.841	Other rheumatoid arthritis with rheumatoid factor of right hand
M05.842	Other rheumatoid arthritis with rheumatoid factor of left hand
M05.851	Other rheumatoid arthritis with rheumatoid factor of right hip
M05.852	Other rheumatoid arthritis with rheumatoid factor of left hip
M05.861	Other rheumatoid arthritis with rheumatoid factor of right knee
M05.862	Other rheumatoid arthritis with rheumatoid factor of left knee
M05.871	Other rheumatoid arthritis with rheumatoid factor of right ankle and foot
M05.872	Other rheumatoid arthritis with rheumatoid factor of left ankle and foot
M05.89	Other rheumatoid arthritis with rheumatoid factor of multiple sites
M06.011	Rheumatoid arthritis without rheumatoid factor, right shoulder
M06.012	Rheumatoid arthritis without rheumatoid factor, left shoulder
M06.021	Rheumatoid arthritis without rheumatoid factor, right elbow
M06.022	Rheumatoid arthritis without rheumatoid factor, left elbow
M06.031	Rheumatoid arthritis without rheumatoid factor, right wrist
M06.032	Rheumatoid arthritis without rheumatoid factor, left wrist
M06.041	Rheumatoid arthritis without rheumatoid factor, right hand
M06.042	Rheumatoid arthritis without rheumatoid factor, left hand

ICD-10 Codes	Description
M06.051	Rheumatoid arthritis without rheumatoid factor, right hip
M06.052	Rheumatoid arthritis without rheumatoid factor, left hip
M06.061	Rheumatoid arthritis without rheumatoid factor, right knee
M06.062	Rheumatoid arthritis without rheumatoid factor, left knee
M06.071	Rheumatoid arthritis without rheumatoid factor, right ankle and foot
M06.072	Rheumatoid arthritis without rheumatoid factor, left ankle and foot
M06.08	Rheumatoid arthritis without rheumatoid factor, vertebrae
M06.09	Rheumatoid arthritis without rheumatoid factor, multiple sites
M06.1	Adult-onset Still's disease
M06.211	Rheumatoid bursitis, right shoulder
M06.212	Rheumatoid bursitis, left shoulder
M06.221	Rheumatoid bursitis, right elbow
M06.222	Rheumatoid bursitis, left elbow
M06.231	Rheumatoid bursitis, right wrist
M06.232	Rheumatoid bursitis, left wrist
M06.241	Rheumatoid bursitis, right hand
M06.242	Rheumatoid bursitis, left hand
M06.251	Rheumatoid bursitis, right hip
M06.252	Rheumatoid bursitis, left hip
M06.261	Rheumatoid bursitis, right knee
M06.262	Rheumatoid bursitis, left knee
M06.271	Rheumatoid bursitis, right ankle and foot
M06.272	Rheumatoid bursitis, left ankle and foot
M06.28	Rheumatoid bursitis, vertebrae
M06.29	Rheumatoid bursitis, multiple sites
M06.311	Rheumatoid nodule, right shoulder
M06.312	Rheumatoid nodule, left shoulder
M06.321	Rheumatoid nodule, right elbow
M06.322	Rheumatoid nodule, left elbow
M06.331	Rheumatoid nodule, right wrist
M06.332	Rheumatoid nodule, left wrist
M06.341	Rheumatoid nodule, right hand
M06.342	Rheumatoid nodule, left hand
M06.351	Rheumatoid nodule, right hip
M06.352	Rheumatoid nodule, left hip
M06.361	Rheumatoid nodule, right knee
M06.362	Rheumatoid nodule, left knee
M06.371	Rheumatoid nodule, right ankle and foot
M06.372	Rheumatoid nodule, left ankle and foot
M06.38	Rheumatoid nodule, vertebrae
M06.39	Rheumatoid nodule, multiple sites
M06.811	Other specified rheumatoid arthritis, right shoulder
M06.812	Other specified rheumatoid arthritis, left shoulder
M06.821	Other specified rheumatoid arthritis, right elbow
M06.822	Other specified rheumatoid arthritis, left elbow
M06.831	Other specified rheumatoid arthritis, right wrist
M06.832	Other specified rheumatoid arthritis, left wrist
M06.841	Other specified rheumatoid arthritis, right hand
M06.842	Other specified rheumatoid arthritis, left hand
M06.851	Other specified rheumatoid arthritis, right hip
M06.852	Other specified rheumatoid arthritis, left hip
M06.861	Other specified rheumatoid arthritis, right knee
M06.862	Other specified rheumatoid arthritis, left knee
M06.871	Other specified rheumatoid arthritis, right ankle and foot
M06.872	Other specified rheumatoid arthritis, left ankle and foot
M06.88	Other specified rheumatoid arthritis, vertebrae
M06.89	Other specified rheumatoid arthritis, multiple sites

Group 5 Paragraph:

Medicare is establishing the following coverage for CPT code 81595- CARDIOLOGY ALLOMAP:

Group 5 Codes:

ICD-10 Codes	Description
Z48.21	Encounter for aftercare following heart transplant
Z94.1	Heart transplant status

ICD-10 Codes that DO NOT Support Medical Necessity
Group 1 Paragraph:

All those not listed under the "ICD-10 Codes that Support Medical Necessity" section of this policy

Group 1 Codes:

ICD-10 Codes	Description
XX000	Not Applicable

ICD-10 Additional Information Back to Top

General Information

Associated Information

Documentation Requirements

1. All documentation must be maintained in the patient's medical record and made available to the contractor upon request.
2. Every page of the record must be legible and include appropriate patient identification information (e.g., complete name, dates of service(s)). The documentation must include the legible signature of the physician or non-physician practitioner responsible for and providing the care to the patient.
3. The submitted medical record must support the use of the selected ICD-10-CM code(s). The submitted CPT/HCPCS code must describe the service performed.
4. The medical record documentation must support the medical necessity of the services as directed in this policy.

Utilization Guidelines

In accordance with CMS Ruling 95-1 (V), utilization of these services should be consistent with locally acceptable standards of practice, whereby more than once per lifetime testing is not deemed medically necessary, except under special clinical scenarios which will be handled through the redetermination process. The medical record must support the medical necessity of the increased frequency.

CPT code 81490, Autoimmune (rheumatoid arthritis), is limited to two services per rolling year per beneficiary.

Sources of Information
Contractor is not responsible for the continued viability of websites listed.

Aetna Clinical Policy Bulletin: Genetic Testing (Number: 0140)

Altar CA, Hornberger J, Shewade A, et al. Clinical validity of cytochrome P450 metabolism and serotonin gene variants in psychiatric pharmacotherapy. *Int Rev Psychiatry*, 2013; 25(5): 509-533.

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human subjects. *Neuropsychopharmacology*, 2007; 32(5): 1011-1020.

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de Leon J, Susce MT, Pan R, et al. The CYP2D6 poor metabolizer phenotype may be associated with risperidone adverse drug reactions and discontinuation. *J Clin Psychiatry*, 2005; 66(1): 15-27.

El-Mallakh RS, Roberts RJ, El-Mallakh PL, et al. Pharmacogenomics in Psychiatric Practice. *Clin Lab Med*. 2016; 36:507-523. Doi: 10.1016/j.cll.2016.05.001

Erk S, Meyer-Lindenberg A, Linden DE, et al. Replication of brain function effects of a genome-wide supported psychiatric risk variant in the CACNA1C gene and new multi-locus effects. *Neuroimage*, 2014; 94: 147-154.

Ferreira MA, O'Donovan MC, Meng YA, et al. Collaborative genome-wide association analysis supports a role for ANK3 and CACNA1C in bipolar disorder. *Nat Genet*, 2008; 40(9): 1056-1058.

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http://www.ncbi.nlm.nih.gov/books/NBK1440/

http://ghr.nlm.nih.gov/gene/HFE

http://ghr.nlm.nih.gov/gene/HBA1

http://www.ncbi.nlm.nih.gov/books/NBK1435/

http://ghr.nlm.nih.gov/gene/HBA2

http://ghr.nlm.nih.gov/condition/familial-dysautonomia

http://www.ncbi.nlm.nih.gov/books/NBK1180/

http://ghr.nlm.nih.gov/gene/KCNH2

http://www.ncbi.nlm.nih.gov/books/NBK1129/ + Input from Palmetto GBA.

http://ghr.nlm.nih.gov/condition/mucolipidosis-type-iv

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http://ghr.nlm.nih.gov/gene/MTHFR

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There were extensive in-person consultations with both CAC representatives and nationally-recognized experts in order to assist with the above medical necessity language and procedure-to-diagnosis code pairings.

Other Contractor Policies

First Coast Service Options (FCSO) LCD, L35366, CYP2C19, CYP2D6, CYP2C9, and VKORC1 Genetic Testing

Palmetto GBA

Contractor Medical Directors

Bibliography

N/A

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Revision History Information

Revision History Date	Revision History Number	Revision History Explanation	Reason(s) for Change
01/01/2018	R15	LCD revised and published on 01/25/2018 effective for dates of service on and after 01/01/2018 to reflect the annual CPT/HCPCS code updates. The following CPT code(s) have been added to the Group 1 codes with no diagnosis limitations applied and have also been added to the Germline Mutation Table as covered: 81258, 81259, and 81269. For the following CPT code(s) either the short description and/or the long description has been changed. Depending on which description is used in this LCD, there may not be any change in how the codes display in the document: 81257 (Group 1 CPT code) and 81439 (Group 3 CPT code). 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; therefore, not all the fields included on the LCD are applicable as noted in this policy.	• Revisions Due To CPT/HCPCS Code Changes
12/14/2017	R14	LCD revised and published on 12/14/2017 to add the statement from L35396-Biomarkers for Oncology in order to provide clarification regarding biomarkers considered reasonable and necessary.	• Other (Clarification)

Revision History Date	Revision History Number	Revision History Explanation	Reason(s) for Change
10/01/2017	R13	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; therefore, not all the fields included on the LCD are applicable as noted in this policy. LCD revised and published on 10/05/2017 effective for dates of service on and after 10/01/2017 to reflect the ICD-10 Annual Code Updates. The following ICD-10 code(s) have undergone a descriptor change - Group 1 Codes: I63.323, I63.333, I63.513, I63.523, I63.533. Effective for dates of service on and after 08/09/2017 the following ICD-10 code has been added to Group 5 codes: Z94.1. Group 1 Paragraph statement has been revised to clarify that only CPT codes listed in ICD-10 code groups 1 through 5 are subject to diagnosis-to-procedure code limitations at this time.	• Revisions Due To ICD-10-CM Code Changes • Other (Inquiry and Clarification)
02/01/2017	R12	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; therefore, not all the fields included on the LCD are applicable as noted in this policy. LCD revised and published on 05/11/2017 effective for dates of service on and after 02/01/2017 to add CPT/HCPCS code 0001U to Group 1 CPT codes and to the Germline Table as covered; there are no diagnosis code limitations applied at this time.	• Revisions Due To CPT/HCPCS Code Changes
01/01/2017	R11	LCD revised and published on 03/16/2017 to add sources submitted for a reconsideration request to add a six-gene panel for Major Depressive Disorder. No change has been made to the content of the policy.	• Reconsideration Request
01/01/2017	R10	LCD revised and published on 01/12/2017 effective for dates of service on and after 01/01/2017 to reflect the annual CPT/HCPCS code updates. The following CPT/HCPCS codes 81280, 81281, and 81282 have been deleted and therefore removed from group 3 of the LCD. The following CPT/HCPCS codes 81413, 81414, and 81439 have been added to group 3 of the LCD. The Germline Mutation Table has been modified to reflect the changes.	• Revisions Due To CPT/HCPCS Code Changes
12/01/2016	R9	LCD posted for notice on 10/13/2016 with a notice end date of 11/30/2016. LCD becomes effective for dates of service on and after 12/01/2016. 05/19/2016 DL35062 Draft LCD Posted for Comment.	• Automated Edits to Enforce Reasonable & Necessary Requirements
10/01/2016	R8	LCD revised and published on 09/29/2016 effective for dates of service on and after 10/01/2016 to reflect the ICD-10 Annual Code Updates. The following ICD-10 code(s) have been added to Group 1: I63.013, I63.033, I63.113, I63.133, I63.213, I63.233, I63.313, I63.323, I63.333, I63.343, I63.413, I63.423, I63.433, I63.443, I63.513, I63.523, I63.533, and I63.543. The following ICD-10 code has been added to Group 2: F32.89. The dual diagnosis requirement in Group 1 for CPT code 81225 has been removed effective for dates of service on and after 10/01/2015.	• Other (Inquiry) • Revisions Due To ICD-10-CM Code Changes
01/01/2016	R7	LCD revised and published on 01/28/2016 effective for dates of service on and after 01/01/2016 to reflect the annual CPT/HCPCS code updates. The following CPT/HCPCS code has been added to the Germline Mutation table as covered and to Group 1 Codes: *81162*. For the following CPT/HCPCS code either the short description and/or the long description was changed. Depending on which description is used in this LCD, there may not be any change in how the code displays in the document: *81355*. The following CPT/HCPCS code has been deleted: *81412*.	• Revisions Due To CPT/HCPCS Code Changes
10/01/2015	R6		

Revision History Date	Revision History Number	Revision History Explanation	Reason(s) for Change
		LCD revised and published 09/11/2015 to add many sources submitted with reconsideration request to add Genecept Assay. No changes made to the content of LCD.	• Reconsideration Request
10/01/2015	R5	LCD revised and published on 06/25/2015.	• New/Updated Technology • Revisions Due To CPT/HCPCS Code Changes
10/01/2015	R4	LCD revised and published on 08/14/2014 to clarify that effective 07/01/2014 an indefinite suspension of requests for new local coverage appropriateness protocols was implemented.	• Provider Education/Guidance
10/01/2015	R3	LCD revised and published on 07/24/2014, effective for dates of service on or after 10/01/2014 to remove the age restrictions from the following biomarkers: Mlh 1 gene full seq, Mlh 1 gene known variants, Mlh 1 gene dup/delete variant, Microsatellite instability, PTEN gene analysis, full sequence, PTEN gene known familial variants, PTEN gene duplication/deletion.	• Provider Education/Guidance
10/01/2015	R2	LCD revised and published on 06/26/2014 to delete a reference to the Coverage with Evidence (CED) process, which is not exactly the same as the local coverage appropriateness protocol approach described in this LCD effective for dates of service on or after 10/01/2014.	• Other (Clarification)
10/01/2015	R1	LCD revised to delete selected age-based limits in an effort to be more compliant/consistent with December 2013 United States Preventive Services Task Force (USPSTF) recommendations on BRCA1 and BRCA2 gene mutation testing in response to a reconsideration request. (LCD updated 05/15/2014)	• Reconsideration Request

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Associated Documents

Attachments N/A

Related Local Coverage Documents LCD(s) L35396 - Biomarkers for Oncology L36715 - BRCA1 and BRCA2 Genetic Testing

Related National Coverage Documents NCD(s) 90.1 - Pharmacogenomic Testing for Warfarin Response

Public Version(s) Updated on 01/19/2018 with effective dates 01/01/2018 - N/A Updated on 12/08/2017 with effective dates 12/14/2017 - 12/31/2017 Updated on 09/29/2017 with effective dates 10/01/2017 - 12/13/2017 Updated on 05/05/2017 with effective dates 02/01/2017 - 09/30/2017 Updated on 03/10/2017 with effective dates 01/01/2017 - 01/31/2017 Updated on 01/06/2017 with effective dates 01/01/2017 - N/A Some older versions have been archived. Please visit the MCD Archive Site to retrieve them. Back to Top

Keywords

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