Local Coverage Article:
Billing and Coding: MolDX: Pharmacogenomics Testing (A58318)

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Contractor Information

CONTRACTOR NAME	CONTRACT TYPE	CONTRACT NUMBER	JURISDICTION	STATE(S)
Palmetto GBA	A and B MAC	10111 - MAC A	J - J	Alabama
Palmetto GBA	A and B MAC	10112 - MAC B	J - J	Alabama
Palmetto GBA	A and B MAC	10211 - MAC A	J - J	Georgia
Palmetto GBA	A and B MAC	10212 - MAC B	J - J	Georgia
Palmetto GBA	A and B MAC	10311 - MAC A	J - J	Tennessee
Palmetto GBA	A and B MAC	10312 - MAC B	J - J	Tennessee
Palmetto GBA	A and B and HHH MAC	11201 - MAC A	J - M	South Carolina
Palmetto GBA	A and B and HHH MAC	11202 - MAC B	J - M	South Carolina
Palmetto GBA	A and B and HHH MAC	11301 - MAC A	J - M	Virginia
Palmetto GBA	A and B and HHH MAC	11302 - MAC B	J - M	Virginia
Palmetto GBA	A and B and HHH MAC	11401 - MAC A	J - M	West Virginia
Palmetto GBA	A and B and HHH MAC	11402 - MAC B	J - M	West Virginia
Palmetto GBA	A and B and HHH MAC	11501 - MAC A	J - M	North Carolina
Palmetto GBA	A and B and HHH MAC	11502 - MAC B	J - M	North Carolina

Article Information

General Information

Article ID
A58318

Article Title
Billing and Coding: MolDX: Pharmacogenomics Testing

Article Type
Billing and Coding

AMA CPT / ADA CDT / AHA NUBC Copyright Statement
CPT codes, descriptions and other data only are

Original Effective Date
07/26/2020

Revision Effective Date
N/A

Revision Ending Date
N/A

Retirement Date
N/A

CMS National Coverage Policy

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

Article Guidance

Article Text:

The information in this article contains billing, coding or other guidelines that complement the Local Coverage Determination (LCD) for MolDX: Pharmacogenomics Testing L38294.

Relevant Articles:

Billing and Coding: MolDX: Testing of Multiple Genes A57503

Additional documentation requirements for coverage and billing:

Performing providers are required to acquire and retain records of the drugs under consideration for use or in use by the ordering physician that necessitate the use of ordered test.

MolDX may make available specific forms to assist with test Technical Assessments (TAs). Please follow the instructions on the MolDX website to assist with this process. If such forms are available that pertain to the test type in question, these forms are required for successful coverage determinations.

Billing instructions:

Only one test may be performed per date of service; the test should be the most likely to identify the necessary alleles/variants for the drug/drugs in question. This applies to both single gene tests and multigene panels. Multigene panels can be performed when (as defined in the policy):

1. More than one gene is reasonable and necessary for the safe use of the drug being considered or in use; or

2. More than one drug is in consideration or use that is associated with a gene-drug interaction

A multigene panel must include all relevant genes and variants for its intended use to be reasonable and necessary.

If, after the initial test is completed and additional testing is warranted and is reasonable and necessary as stated in the associated policy and as defined in the Repeat Germline Testing policy, an additional test may be subsequently performed. The medical necessity for the additional testing and the clinical decision making for the additional testing must be documented in the medical record. The CPT code set relevant to this policy is listed in the table below. If no CPT code is available for the gene being tested, the NOC code 81479 may be used. The identification of the proper recommended billing code is established as part of the test application process.

CPT codes

gene/test	**CPT**	**intended use for drug**
CFTR	81220	ivacaftor
CYP2B6	N/A	efavirez
CYP2C19	81225	Clopidogrel, voriconazole, SSRIs (class), tricyclic antidepressants (class)
CYP2C8	N/A	NSAIDs (class)

CYP2C9	81227	NSAIDs (class), phenytoin, warfarin,
HLA-B	81379, 81373	abacavir, allopurinol, oxcarbazepine, phenytoin
CYP4F2	N/A	Warfarin
VKORC1	81355	Warfarin
CYP2D6	81226, 0070U, 0071U, 0072U, 0073U, 0074U, 0075U, 0076U	atomoxetine, codeine, ondansetron, tropisetron, tamoxifen, SSRIs (class), tricyclic antidepressants (class)
CYP3A5	81231	Tacrolimus
DPYD	81232	Fluoropyrimidines (class)
G6PD	N/A	Rasburicase
HLA-A	81379, 81373	carbamazepine
IFNL3	81283	ribavirin, peginterferon-alpha-based regimens (class)
RYR1	81406	Volatile anethetics (class), succinylcholine
CACNA15	N/A	Volatile anethetics (class), succinylcholine
SCLO1B1	N/A	simvastatin
NUDT15	81306	Thiopurines (class)
TPMT	81335	Thiopurines (class)
UGT1A1	81350	Atazanavir
Panel	0030U	Warfarin

Table 1. Current CPIC guidelines as of July 15, 2020.

Gene	**CPT**	**Drug**	**Affected Subgroups+**

BCHE	N/A	Mivacurium	intermediate or poor metabolizers
BCHE	N/A	Succinylcholine	intermediate or poor metabolizers
CYP2B6	N/A	Efavirenz	poor metabolizers
CYP2C19	81225	Brivaracetam	intermediate or poor metabolizers
CYP2C19	81225	Citalopram	poor metabolizers
CYP2C19	81225	Clobazam	intermediate or poor metabolizers
CYP2C19	81225	Clopidogrel	intermediate or poor metabolizers
CYP2C19	81225	Flibanserin	poor metabolizers
CYP2C19	81225	Pantoprazole	poor metabolizers
CYP2C9	81227	Celecoxib	poor metabolizers
CYP2C9	81227	Dronabinol	intermediate or poor metabolizers
CYP2C9	81227	Erdafitinib	*3/*3 (poor metabolizers)
CYP2C9	81227	Flurbiprofen	poor metabolizers
CYP2C9	81227	Piroxicam	intermediate or poor metabolizers
CYP2C9	81227	Siponimod	intermediate or poor metabolizers
CYP2C9	81227	Warfarin	intermediate or poor metabolizers
CYP2D6	81226	Amphetamine	poor metabolizers
CYP2D6	81226	Aripiprazole	poor metabolizers

CYP2D6	81226	Aripiprazole Lauroxil	poor metabolizers
CYP2D6	81226	Atomoxetine	poor metabolizers
CYP2D6	81226	Brexpiprazole	poor metabolizers
CYP2D6	81226	Clozapine	poor metabolizers
CYP2D6	81226	Codeine	ultrarapid metabolizers
CYP2D6	81226	Deutetrabenazine	poor metabolizers
CYP2D6	81226	Eliglustat	ultrarapid, normal, intermediate, or poor metabolizers
CYP2D6	81226	Gefitinib	poor metabolizers
CYP2D6	81226	Iloperidone	poor metabolizers
CYP2D6	81226	Lofexidine	poor metabolizers
CYP2D6	81226	Meclizine	ultrarapid, intermediate, or poor metabolizers
CYP2D6	81226	Metoclopramide	poor metabolizers
CYP2D6	81226	Pimozide	poor metabolizers
CYP2D6	81226	Propafenone	poor metabolizers
CYP2D6	81226	Tetrabenazine	poor metabolizers
CYP2D6	81226	Thioridazine	poor metabolizers
CYP2D6	81226	Tramadol	Ultrarapid metabolizers3
CYP2D6	81226	Valbenazine	poor metabolizers
CYP2D6	81226	Venlafaxine	poor metabolizers
CYP2D6	81226	Vortioxetine	poor metabolizers

CYP2D6	81226	Carvedilol	poor metabolizers
CYP2D6	81226	Cevimeline	poor metabolizers
CYP2D6	81226	Codeine	poor metabolizers
CYP2D6	81226	Perphenazine	poor metabolizers
CYP2D6	81226	Tolterodine	poor metabolizers
CYP3A5	81231	Tacrolimus	intermediate or normal metabolizers
CYP4F2	N/A	Warfarin	V433M variant carriers
DPYD	81232	Capecitabine	intermediate or poor metabolizers
DPYD	81232	Fluorouracil	intermediate or poor metabolizer
HLA-A	81379, 81373	Carbamazepine	*31:01 allele positive
HLA-B	81379, 81373	Abacavir	*57:01 allele positive
HLA-B	81379, 81373	Carbamazepine	*15:02 allele positive
HLA-B	81379, 81373	Allopurinol	*58:01 allele positive
HLA-B	81379, 81373	Oxcarbazepine	*15:02 allele positive
HLA-B	81379, 81373	Pazopanib	*57:01 allele positive
HLA-DQA1	81379, 81373	Lapatinib	*02:01 allele positive
HLA-DRB1	81371	Lapatinib	*07:01 allele positive
NAT2	N/A	Amifampridine	poor metabolizers
NAT2	N/A	Amifampridine Phosphate	poor metabolizers

Nonspecific (NAT)	N/A	Isoniazid	poor metabolizers
Nonspecific (NAT)	N/A	Procainamide	poor metabolizers
Nonspecific (NAT)	N/A	Sulfamethoxazole and Trimethoprim	poor metabolizers
Nonspecific (NAT)	N/A	Sulfasalazine	poor metabolizers
SLCO1B1	N/A	Simvastatin	521 TC or 521 CC (intermediate or poor function transporters)
TPMT and/or NUDT15	81306, 81335	Azathioprine	intermediate or poor metabolizers
TPMT and/or NUDT15	81306, 81335	Mercaptopurine	intermediate or poor metabolizers
TPMT and/or NUDT15	81306, 81335	Thioguanine	intermediate or poor metabolizers
UGT1A1	81350	Belinostat	*28/*28 (poor metabolizers)
UGT1A1	81350	Irinotecan	*28/*28 (poor metabolizers)
UGT1A1	81350	Nilotinib	*28/*28 (poor metabolizers)
UGT1A1	81350	Pazopanib	*28/*28 (poor metabolizers)
VKORC1	81355	Warfarin	-1639G>A variant carriers

Table 2. Table of pharmacogenomic associations from the FDA for which the data support therapeutic recommendations or a potential impact on safety or response (from fda.gov/medical-devices/precision-medicine/table-phramacogenetic-associations) (last updated February 2020)

Covered multigene panels

Test name	**Company**	**Intended Use**
Genesight	Assurex health	Neuropsychiatric
NeuroIDgenetix	AltheaDx	Neuropsychiatric

Table 3. Multigene panel tests that have successfully completed a TA. These tests must fulfil all the criteria above and may be further limited to specific indications listed by ICD-10 codes, when applicable.

ICD-10 codes associated with intended uses

Intended Use	ICD-10	description
Neuropsychiatric	F32.1	Major depressive disorder, single episode, moderate
Neuropsychiatric	F32.2	Major depressive disorder, single episode, severe without psychotic features
Neuropsychiatric	F32.3	Major depressive disorder, single episode, severe with psychotic features
Neuropsychiatric	F32.4	Major depressive disorder, single episode, in partial remission
Neuropsychiatric	F32.9	Major depressive disorder, single episode, unspecified
Neuropsychiatric	F33.1	Major depressive disorder, recurrent, moderate
Neuropsychiatric	F33.2	Major depressive disorder, recurrent severe without psychotic features
Neuropsychiatric	F33.3	Major depressive disorder, recurrent, severe with psychotic symptoms
Neuropsychiatric	F33.40	Major depressive disorder, recurrent, in remission, unspecified
Neuropsychiatric	F33.41	Major depressive disorder, recurrent, in partial remission

Neuropsychiatric	F33.9	Major depressive disorder, recurrent, unspecified

Coding Information

CPT/HCPCS Codes

Group 1 Paragraph:

N/A

Group 1 Codes:

CODE	DESCRIPTION
81220	CFTR (CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR) (EG, CYSTIC FIBROSIS) GENE ANALYSIS; COMMON VARIANTS (EG, ACMG/ACOG GUIDELINES)
81225	CYP2C19 (CYTOCHROME P450, FAMILY 2, SUBFAMILY C, POLYPEPTIDE 19) (EG, DRUG METABOLISM), GENE ANALYSIS, COMMON VARIANTS (EG, *2, *3, *4, *8, *17)
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)
81227	CYP2C9 (CYTOCHROME P450, FAMILY 2, SUBFAMILY C, POLYPEPTIDE 9) (EG, DRUG METABOLISM), GENE ANALYSIS, COMMON VARIANTS (EG, *2, *3, *5, *6)
81231	CYP3A5 (CYTOCHROME P450 FAMILY 3 SUBFAMILY A MEMBER 5) (EG, DRUG METABOLISM), GENE ANALYSIS, COMMON VARIANTS (EG, *2, *3, *4, *5, *6, *7)
81232	DPYD (DIHYDROPYRIMIDINE DEHYDROGENASE) (EG, 5-FLUOROURACIL/5-FU AND CAPECITABINE DRUG METABOLISM), GENE ANALYSIS, COMMON VARIANT(S) (EG, *2A, *4, *5, *6)
81283	IFNL3 (INTERFERON, LAMBDA 3) (EG, DRUG RESPONSE), GENE ANALYSIS, RS12979860 VARIANT
81306	NUDT15 (NUDIX HYDROLASE 15) (EG, DRUG METABOLISM) GENE ANALYSIS, COMMON VARIANT(S) (EG, *2, *3, *4, *5, *6)
81335	TPMT (THIOPURINE S-METHYLTRANSFERASE) (EG, DRUG METABOLISM), GENE ANALYSIS, COMMON VARIANTS (EG, *2, *3)
81350	UGT1A1 (UDP GLUCURONOSYLTRANSFERASE 1 FAMILY, POLYPEPTIDE A1) (EG, DRUG METABOLISM, HEREDITARY UNCONJUGATED HYPERBILIRUBINEMIA [GILBERT SYNDROME]) GENE ANALYSIS, COMMON VARIANTS (EG, *28, *36, *37)

CODE	DESCRIPTION
81355	VKORC1 (VITAMIN K EPOXIDE REDUCTASE COMPLEX, SUBUNIT 1) (EG, WARFARIN METABOLISM), GENE ANALYSIS, COMMON VARIANT(S) (EG, -1639G>A, C.173+1000C>T)
81371	HLA CLASS I AND II TYPING, LOW RESOLUTION (EG, ANTIGEN EQUIVALENTS); HLA-A, -B, AND -DRB1 (EG, VERIFICATION TYPING)
81373	HLA CLASS I TYPING, LOW RESOLUTION (EG, ANTIGEN EQUIVALENTS); ONE LOCUS (EG, HLA-A, -B, OR -C), EACH
81379	HLA CLASS I TYPING, HIGH RESOLUTION (IE, ALLELES OR ALLELE GROUPS); COMPLETE (IE, HLA-A, -B, AND -C)
81406	MOLECULAR PATHOLOGY PROCEDURE, LEVEL 7 (EG, ANALYSIS OF 11-25 EXONS BY DNA SEQUENCE ANALYSIS, MUTATION SCANNING OR DUPLICATION/DELETION VARIANTS OF 26-50 EXONS, CYTOGENOMIC ARRAY ANALYSIS FOR NEOPLASIA)
0030U	DRUG METABOLISM (WARFARIN DRUG RESPONSE), TARGETED SEQUENCE ANALYSIS (IE, CYP2C9, CYP4F2, VKORC1, RS12777823)
0070U	CYP2D6 (CYTOCHROME P450, FAMILY 2, SUBFAMILY D, POLYPEPTIDE 6) (EG, DRUG METABOLISM) GENE ANALYSIS, COMMON AND SELECT RARE VARIANTS (IE, *2, *3, *4, *4N, *5, *6, *7, *8, *9, *10, *11, *12, *13, *14A, *14B, *15, *17, *29, *35, *36, *41, *57, *61, *63, *68, *83, *XN)
0071U	CYP2D6 (CYTOCHROME P450, FAMILY 2, SUBFAMILY D, POLYPEPTIDE 6) (EG, DRUG METABOLISM) GENE ANALYSIS, FULL GENE SEQUENCE (LIST SEPARATELY IN ADDITION TO CODE FOR PRIMARY PROCEDURE)
0072U	CYP2D6 (CYTOCHROME P450, FAMILY 2, SUBFAMILY D, POLYPEPTIDE 6) (EG, DRUG METABOLISM) GENE ANALYSIS, TARGETED SEQUENCE ANALYSIS (IE, CYP2D6-2D7 HYBRID GENE) (LIST SEPARATELY IN ADDITION TO CODE FOR PRIMARY PROCEDURE)
0073U	CYP2D6 (CYTOCHROME P450, FAMILY 2, SUBFAMILY D, POLYPEPTIDE 6) (EG, DRUG METABOLISM) GENE ANALYSIS, TARGETED SEQUENCE ANALYSIS (IE, CYP2D7-2D6 HYBRID GENE) (LIST SEPARATELY IN ADDITION TO CODE FOR PRIMARY PROCEDURE)
0074U	CYP2D6 (CYTOCHROME P450, FAMILY 2, SUBFAMILY D, POLYPEPTIDE 6) (EG, DRUG METABOLISM) GENE ANALYSIS, TARGETED SEQUENCE ANALYSIS (IE, NON-DUPLICATED GENE WHEN DUPLICATION/MULTIPLICATION IS TRANS) (LIST SEPARATELY IN ADDITION TO CODE FOR PRIMARY PROCEDURE)
0075U	CYP2D6 (CYTOCHROME P450, FAMILY 2, SUBFAMILY D, POLYPEPTIDE 6) (EG, DRUG METABOLISM) GENE ANALYSIS, TARGETED SEQUENCE ANALYSIS (IE, 5' GENE DUPLICATION/MULTIPLICATION) (LIST SEPARATELY IN ADDITION TO CODE FOR PRIMARY PROCEDURE)
0076U	CYP2D6 (CYTOCHROME P450, FAMILY 2, SUBFAMILY D, POLYPEPTIDE 6) (EG, DRUG METABOLISM) GENE ANALYSIS, TARGETED SEQUENCE ANALYSIS (IE, 3' GENE DUPLICATION/ MULTIPLICATION) (LIST SEPARATELY IN ADDITION TO CODE FOR

CODE	DESCRIPTION
	PRIMARY PROCEDURE)

CPT/HCPCS Modifiers

Group 1 Paragraph:

N/A

Group 1 Codes:

N/A

ICD-10 Codes that Support Medical Necessity

Group 1 Paragraph:

N/A

Group 1 Codes:

ICD-10 CODE	DESCRIPTION
F32.1	Major depressive disorder, single episode, moderate
F32.2	Major depressive disorder, single episode, severe without psychotic features
F32.3	Major depressive disorder, single episode, severe with psychotic features
F32.4	Major depressive disorder, single episode, in partial remission
F32.9	Major depressive disorder, single episode, unspecified
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
F33.9	Major depressive disorder, recurrent, unspecified

ICD-10 Codes that DO NOT Support Medical Necessity

N/A

Additional ICD-10 Information

N/A

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

Other Coding Information

N/A

Revision History Information

N/A

Associated Documents

Related Local Coverage Document(s)

LCD(s)
L38294 - MolDX: Pharmacogenomics Testing

Related National Coverage Document(s)

N/A

Statutory Requirements URL(s)

N/A

Rules and Regulations URL(s)

N/A

CMS Manual Explanations URL(s)

N/A

Other URL(s)

N/A

Public Version(s)

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Keywords

N/A