Tier 2 Molecular Pathology Procedures

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➲ Terms and Conditions

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Policy Summary

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Overview

According to the American Medical Association (AMA) Current Procedural Terminology (CPT®) manual, molecular pathology procedures are medical laboratory procedures involving the analyses of nucleic acid to detect variants in genes that may be indicative of germline (e.g., constitutional disorders) or somatic (e.g., neoplasia) conditions, or to test for histocompatibility antigens (e.g., HLA). Code selection is typically based on the specific gene(s) that is being analyzed.

Codes that describe tests to assess for the presence of gene variants use common gene variant names. Typically, all of the listed variants would be tested. However, these lists are not exclusive. If other variants are also tested in the analysis, they would be included in the procedure and not reported separately. Full gene sequencing should not be reported using codes that assess for the presence of gene variants unless the CPT code specifically states full gene sequence in the code descriptor. In other words, you may only assign the CPT code that is described as “full gene sequence” if the test assay performed was a full gene sequence.

There are Tier 1 and Tier 2 molecular pathology procedure codes. Tier 1 codes generally describe testing for a specific gene or HLA locus. Tier 2 molecular pathology procedures represent procedures that are generally performed in lower volumes than Tier 1 molecular pathology procedures (e.g., the incidence of the disease being tested is rare). They are arranged by level of technical resources and interpretive work by the physician or other qualified healthcare professional.

Use the appropriate molecular pathology procedure level code that includes the specific analyte listed after the code descriptor. If the analyte/gene tested is not listed under one of the Tier 2 codes or is not represented by a Tier 1 code in CPT, use of the Not Otherwise Classified (NOC) CPT code is required.

Tier 1 and/or Tier 2 individual biomarker CPT codes should not be used for a single gene or any combination of genes when testing is performed as part of a Next-Generation Sequencing (NGS) or other multiplexing technology panel. Molecular pathology procedures have broad clinical and research applications. The following examples of applications may not be relevant to a Medicare member or may not meet a Medicare benefit category and/or reasonable and necessary threshold for coverage. Such examples include genetic testing and genetic counseling (when applicable) for:

- Disease risk;
- Carrier screening;

- Hereditary cancer syndromes;
- Gene expression profiling for certain cancers;
- Prenatal diagnostic testing;
- Diagnosis and monitoring non-cancer indications; and
- Several pharmacogenomic applications.

Guidelines

Tier 2 Molecular pathology procedures may be eligible for coverage when **all** of the following criteria are met:

- Alternative laboratory or clinical tests to definitively diagnose the disorder/identify the condition are unavailable or results are clearly equivocal; **and**
- Availability of a clinically valid test, based on published peer reviewed medical literature; **and**
- Testing assay(s) are Food and Drug Administration (FDA) approved/cleared or if LDT (lab developed test) or LDT protocol or FDA modified test(s) the laboratory documentation should support assay(s) analytical validity and clinical utility; **and**
- Results of the testing must directly impact treatment or management of the member; **and**
- For testing panels, including but not limited to, multiple genes or multiple conditions, and in cases where a tiered approach/method is clinically available, testing would be covered **only** for the number of genes or test that are reasonable and necessary to establish a diagnosis; **and**
- Individual has not previously received genetic testing for the disease/condition. (In general, diagnostic genetic testing for a disease should be performed once in a lifetime.)

A specific genetic test may only be performed once in a lifetime per member for inherited conditions; however, when medically reasonable and necessary, genetic testing may be done on acquired conditions such as malignancies (including separate malignancies developing at different times) as they are treated and are being followed, in order to assess response or other relevant clinical criteria. Likewise, there are situations where medical record and literature documentation are able to demonstrate that serial testing can be reasonably predicted to provide additional clinically useful information. When the record documents that this information, such as confirmed significant response to current therapy, is likely to assist in modifying treatment, serial testing can be considered reasonable and necessary and eligible for coverage.

Gene Identification

Covered

Specific diagnosis criteria for covered services can be found in the Applicable Codes section.

- **For CPT Code 81404**
  - CDKN2A (cyclin-dependent kinase inhibitor 2A)
  - FGFR2 is covered for patients who would otherwise be considered candidates for erdafitinib based on the FDA label
  - FGFR3 is reasonable and necessary for patients who would otherwise be considered candidates for erdafitinib based on the FDA label
  - MEN1 (multiple endocrine neoplasia 1) (e.g., multiple endocrine neoplasia type 1, Wermer syndrome), duplication/deletion
  - MEN2B
  - PRSS1 [protease, serine, 1 (trypsin 1)]
  - RET (ret-proto-oncogene) is considered medically necessary in patients with medullary CA of thyroid, multiple endocrine neoplasia, pheochromocytoma, and parathyroid tumors) to guide therapeutic decision making
  - VHL (von Hippel-Lindau tumor suppressor)
- **For CPT Code 81405**
  - MEN1 (multiple endocrine neoplasia 1) (e.g., multiple endocrine neoplasia type 1, Wermer syndrome), full gene sequence is considered medically necessary in patients with multiple endocrine neoplasia to guide therapeutic decision-making
  - MEN2A
  - RET (ret-proto-oncogene) is considered medically necessary in patients with medullary CA of thyroid, multiple endocrine neoplasia, pheochromocytoma, and parathyroid tumors) to guide therapeutic decision making
- **For CPT Code 81406**
  - ATP7B (ATPase, Cu++ transporting, beta polypeptide) is considered medically necessary in patients with symptoms of Wilson's disease to guide therapeutic decision making
  - RYR1 (Volatile anesthetics (class): desflurane, enflurane, halothane, isoflurane, methoxyflurane, sevoflurane, succinylcholine)

Non-Covered

The following individual Tier 2 genetic tests are unlikely to impact therapeutic decision-making, directly impact treatment, outcome and/or clinical management in the care of the member and will be denied as not medically necessary. (Please note that this list of non-covered genes is not exhaustive, and the fact that a specific gene is not mentioned does not mean it is covered. In addition, many genes have several names that are used. The most common names have been used in this policy.)

- **For CPT Code 81404**
  - ACADS (acyl-CoA dehydrogenase)
  - AQP2 (aquaporin 2 [collecting duct])
  - ARX (aristaless related homeobox)
  - BTD (biotinidase)
  - CAV3 (caveolin 3) (e.g., CAV3-related distal myopathy, limb-girdle muscular dystrophy type 1C), full gene sequence
  - CLRN1 (clarin 1)
  - CYP1B1 (cytochrome P450, family 1, subfamily B, polypeptide 1)
  - EGR2 (early growth response 2) (e.g., Charcot-Marie-Tooth)
  - FKRP (Fukutin related protein)
  - FOXG1 (forkhead box G1)
  - FSHMD1A (facioscapulohumeral muscular dystrophy 1A) (e.g., facioscapulohumeral muscular dystrophy), evaluation to detect abnormal (e.g., deleted) alleles
  - FSHMD1A (facioscapulohumeral muscular dystrophy 1A) (e.g., facioscapulohumeral muscular dystrophy), characterization of haplotype(s) (i.e., chromosome 4A and 4B haplotypes)
  - HNF1B (HNF1 homeobox B)
  - HRAS (v-Ha-ras Harvey rat sarcoma viral oncogene homolog)
  - KCNJ10 (potassium inwardly rectifying channel, subfamily J, member 10)
  - SLC25A4 (solute carrier family 25 [mitochondrial carrier; adenine nucleotide translocation])
  - VWF (von Willebrand factor)
- **For CPT Code 81405**
  - ACADS (acyl-CoA dehydrogenase)
  - CASR (CAR, EIG8, extracellular calcium-sensing receptor, FHH, FIH, GPRC2A, HHC, HHC1, NSHPT, PCAR1)
  - CDKL5 (cyclin-dependent kinase-like 5)
  - CYP21A2 (cytochrome P450, family 21, subfamily A, polypeptide2)
  - HNF1B (HNF1 homeobox B)
  - MPZ (myelin protein zero)
  - NF2 (neurofibromin 2 [merlin])
  - TSC1 (tuberous sclerosis 1)
- **For CPT Code 81406**
  - ACADVL (acyl-CoA dehydrogenase, very long chain)
  - AIRE
  - CBS (cystathionine-beta-synthase)
  - CDKL5 (cyclin-dependent kinase-like 5)
  - DLAT (dihydrolipoamide S-acetyltransferase)
  - DLD (dihydrolipoamide dehydrogenase)
  - F8 (coagulation factor VIII)
  - GALT (galactose-1-phosphate uridylyltransferase)
  - HADHA [hydroxyacyl-CoA dehydrogenase/3-ketoacyl-CoA thiolase/enoyl-CoA hydratase (trifunctional protein) alpha subunit]
  - HEXA (hexosaminidase A, alpha polypeptide)
  - IVD
  - LMNA (lamin A/C)
  - NF2 [neurofibromin 2 (merlin)]
  - NSD1 (nuclear receptor binding SET domain protein 1)
  - PAH (phenylalanine hydroxylase)
  - PAX2 (paired box 2)
  - PDHA1 [pyruvate dehydrogenase (lipoamide) alpha1]
  - POLG (polymerase [DNA directed], gamma)
  - PRKAG2 (protein kinase, AMP-activated gamma 2 non-catalytic subunit)
  - PTPN11 (protein tyrosine phosphatase, non-receptor type 11)
  - RET (ret-proto-oncogene) (e.g., Hirschsprung disease), full gene sequence

- SLC9A6 [solute carrier family 9 (sodium/hydrogen exchanger) member 6]
- SOS1 (son of sevenless homolog 1)
- TAZ (tafazzin)
- TSC1 (tuberous sclerosis 1)
- TSC2 (tuberous sclerosis 2)
- UBE3A (ubiquitin protein ligase)

- **For CPT Code 81407, level 8 Molecular Pathology Procedures are noncovered**
- **For CPT Code 81408, level 9 Molecular Pathology Procedures are noncovered**

Based on the Centers for Medicare & Medicaid Services (CMS) Program Integrity Manual (100 - 08), this policy addresses the circumstances under which the item or service is reasonable and necessary under the Social Security Act, §1862(a)(1)(A). For laboratory services, a service can be reasonable and necessary if the service is safe and effective; not experimental or investigational (exception: routine costs of qualifying clinical trial services which meet the requirements of the Clinical Trials NCD and are considered reasonable and necessary); and appropriate, including the duration and frequency that is considered appropriate for the item or 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 need; and is at least as beneficial as an existing and available medically appropriate alternative.

Nationally Non-Covered Indications

Compliance with the provisions in this policy is subject to monitoring by post payment data analysis and subsequent medical review. Title XVIII of the Social Security Act, Section 1862(a)(1)(A) states " ...no Medicare payment shall be made for items or services which are not reasonable and necessary for the diagnosis and treatment of illness or injury..." Furthermore, it has been longstanding CMS policy that ***"tests that are performed in the absence of signs, symptoms, complaints, or personal history of disease or injury are not covered unless explicitly authorized by statute"***.

Screening services, such as pre - symptomatic genetic tests and services, used to detect an undiagnosed disease or disease predisposition are not a Medicare benefit and not covered. Similarly, Medicare may not reimburse the costs of tests/examinations that assess the risk of a condition unless the risk assessment clearly and directly effects the management of the patient.

Many applications of the molecular pathology procedures are not covered services given lack of benefit category (preventive service) and/or failure to reach the reasonable and necessary threshold for coverage (based on quality of clinical evidence and strength of recommendation). Furthermore, payment of claims in the past (based on stacking codes) or in the future (based on the new code series) is not a statement of coverage since the service was not audited for compliance with program requirements and documentation supporting the reasonable and necessary testing for the member. Certain molecular pathology procedures may be subject to prepayment medical review (records requested) and paid claims must be supportable, if selected, for post payment audit. Molecular pathology tests for diseases or conditions that manifest severe signs or symptoms in newborns and in early childhood or that result in early death (e.g., Canavan disease) could be subject to automatic denials since these tests are not usually relevant to a member.

Documentation Guidelines

Providers are required to code to specificity; however, if an unlisted CPT code is used, the documentation must clearly identify the unique procedure performed. When multiple procedure codes are submitted on a claim (unique and/or unlisted) the documentation supporting each code should be easily identifiable. If on review UnitedHealthcare cannot link a billed code to the documentation, these services will be denied.

Because there are multiple biomarkers represented by each of the Tier 2 codes, when billing for these codes, it will be necessary to report the specific biomarker in the claim narrative/remarks. Report information in the narrative/remarks that provides ample information to uniquely identify the specific biomarker.

Providing the descriptive information for the Tier 2 molecular pathology code will assist in timely processing of claims. Failure to provide the information may result in delayed processing or claim denials.

Billing Claims with Multiple Biomarkers

There are typically submissions of claims where multiple biomarkers on the same date of service (DOS) can better support the further diagnosis, prognosis, or chemotherapy prediction of a neoplastic disease.

It would not be expected for providers to order multiple biomarkers on different DOS's, since the molecular evaluation of a particular neoplasm is typically comprehensive in nature.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

CPT Code	Description
81400	Molecular pathology procedure, Level 1 (short description)
81401	Molecular pathology procedure, Level 2 (short description)
81402	Molecular pathology procedure, Level 3 (short description)
81403	Molecular pathology procedure, Level 4 (short description)
81404	Molecular pathology procedure, Level 5 (short description)
81405	Molecular pathology procedure, Level 6 (short description)
81406	Molecular pathology procedure, Level 7 (short description)
81407	Molecular pathology procedure, Level 8 (short description)
81408	Molecular pathology procedure, Level 9 (short description)

Diagnosis Code	Description
CPT Code 81404 for FGFR2, FGFR3	
C67.0	Malignant neoplasm of trigone of bladder
C67.1	Malignant neoplasm of dome of bladder
C67.2	Malignant neoplasm of lateral wall of bladder
C67.3	Malignant neoplasm of anterior wall of bladder
C67.4	Malignant neoplasm of posterior wall of bladder
C67.5	Malignant neoplasm of bladder neck
C67.6	Malignant neoplasm of ureteric orifice
C67.7	Malignant neoplasm of urachus
C67.8	Malignant neoplasm of overlapping sites of bladder
CPT Code 81406 for RYR1	
T41.0X5A	Adverse effect of inhaled anesthetics, initial encounter
T41.0X5D	Adverse effect of inhaled anesthetics, subsequent encounter
T41.0X5S	Adverse effect of inhaled anesthetics, sequela
T41.0X6A	Underdosing of inhaled anesthetics, initial encounter
T41.0X6D	Underdosing of inhaled anesthetics, subsequent encounter
T41.0X6S	Underdosing of inhaled anesthetics, sequela
T41.1X5A	Adverse effect of intravenous anesthetics, initial encounter
T41.1X5D	Adverse effect of intravenous anesthetics, subsequent encounter
T41.1X5S	Adverse effect of intravenous anesthetics, sequela
T41.1X6A	Underdosing of intravenous anesthetics, initial encounter
T41.1X6D	Underdosing of intravenous anesthetics, subsequent encounter
T41.1X6S	Underdosing of intravenous anesthetics, sequela

Diagnosis Code	Description
CPT Codes 81404 and 81405 for RET – MEN Type 2	
C73	Malignant neoplasm of thyroid gland
C74.10	Malignant neoplasm of medulla of unspecified adrenal gland
C74.11	Malignant neoplasm of medulla of right adrenal gland
C74.12	Malignant neoplasm of medulla of left adrenal gland
C75.0	Malignant neoplasm of parathyroid gland
D35.1	Benign neoplasm of parathyroid gland
CPT Code 81406 for ATP7B	
E83.01	Wilson's disease

Non-Covered Diagnosis Code

Non-Covered Diagnosis Codes List

This list contains diagnosis codes that are **never covered when given as the primary reason for the test.** If a code from this section is given as the reason for the test and you know or have reason to believe the service may not be covered, call UnitedHealthcare to issue an Integrated Denial Notice (IDN) to the member and you. The IDN informs the member of their liability for the non-covered service or item and appeal rights. You must make sure the member has received the IDN prior to rendering or referring for non-covered services or items in order to collect payment.

References

CMS National Coverage Determinations (NCDs)

Related NCDs: NCD 90.2 Next Generation Sequencing (NGS), NCD 190.3 Cytogenetic Studies, NCD 190.7 Human Tumor Stem Cell Drug Sensitivity Assays

CMS Local Coverage Determinations (LCDs) and Articles

LCD	Article	Contractor	Medicare Part A	Medicare Part B
ATP7B Gene Tests				
L36021 MolDX: Molecular Diagnostic Tests (MDT)	A54254 Billing and Coding: MolDX: ATP7B Gene Tests **Retired 04/23/2024**	CGS	KY, OH	KY, OH
N/A	A55097 Billing and Coding: MolDX: ATP7B Gene Tests **Retired 04/23/2024**	Noridian	AS, CA, GU, HI, MP, NV	AS, CA, GU, HI, MP, NV
N/A	A55098 Billing and Coding: MolDX: ATP7B Gene Tests **Retired 04/23/2024**	Noridian	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY
N/A	A53550 Billing and Coding: MolDX: ATP7B Gene Tests **Retired 04/23/2024**	Palmetto	AL, GA, NC, SC, TN, VA, WV	AL, GA, NC, SC, TN, VA, WV
L36807 MolDX: Molecular Diagnostic Tests (MDT)	A55143 Billing and Coding: MolDX: ATP7B Gene Tests **Retired 05/30/2024**	WPS*	IA, IN, KS, MI, MO, NE	IA, IN, KS, MI, MO, NE
BCKDHB Gene Test				
L36021 MolDX: Molecular Diagnostic Tests (MDT)	A54255 Billing and Coding: MolDX: BCKDHB Gene Test **Retired 05/08/2024**	CGS	KY, OH	KY, OH
N/A	A55099 Billing and Coding: MolDX: BCKDHB Gene Test **Retired 05/08/2024**	Noridian	AS, CA, GU, HI, MP, NV	AS, CA, GU, HI, MP, NV

LCD	Article	Contractor	Medicare Part A	Medicare Part B
BCKDHB Gene Test				
N/A	A55100 Billing and Coding: MolDX: BCKDHB Gene Test **Retired 05/08/2024**	Noridian	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY
L35025 MolDX: Molecular Diagnostic Tests (MDT)	A53600 Billing and Coding: MolDX: BCKDHB Gene Test **Retired 05/08/2024**	Palmetto	AL, GA, NC, SC, TN, VA, WV	AL, GA, NC, SC, TN, VA, WV
L36807 MolDX: Molecular Diagnostic Tests (MDT)	A55145 Billing and Coding: MolDX: BCKDHB Gene Test **Retired 05/30/2024**	WPS*	IA, IN, KS, MI, MO, NE	IA, IN, KS, MI, MO, NE
CDH1 Genetic Testing				
N/A	A54878 Billing and Coding: MolDX: CDH1 Genetic Testing **Retired 05/30/2024**	CGS	KY, OH	KY, OH
N/A	A55970 Billing and Coding: MolDX: CDH1 Genetic Testing **Retired 05/30/2024**	Noridian	AS, CA, GU, HI, MP, NV	AS, CA, GU, HI, MP, NV
N/A	A55971 Billing and Coding: MolDX: CDH1 Genetic Testing **Retired 05/30/2024**	Noridian	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY
N/A	A54835 Billing and Coding: MolDX: CDH1 Genetic Testing **Retired 05/30/2024**	Palmetto	AL, GA, NC, SC, TN, VA, WV	AL, GA, NC, SC, TN, VA, WV
L36807 MolDX: Molecular Diagnostic Tests (MDT)	A55622 Billing and Coding: MolDX: CDH1 Genetic Testing	WPS*	IA, IN, KS, MI, MO, NE	IA, IN, KS, MI, MO, NE
CHD7 Gene Analysis				
L36021 MolDX: Molecular Diagnostic Tests (MDT)	A54243 Billing and Coding: MolDX: CHD7 Gene Analysis Guidelines **Retired 04/25/2024**	CGS	KY, OH	KY, OH
N/A	A55085 Billing and Coding: MolDX: CHD7 Gene Analysis **Retired 04/25/2024**	Noridian	AS, CA, GU, HI, MP, NV	AS, CA, GU, HI, MP, NV
N/A	A55086 MolDX: CHD7 Gene Analysis Coding and Billing Guidelines **Retired 04/25/2024**	Noridian	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY
N/A	A53565 Billing and Coding: MolDX: CHD7 Gene Analysis **Retired 04/25/2024**	Palmetto	AL, GA, NC, SC, TN, VA, WV	AL, GA, NC, SC, TN, VA, WV
L36807 MolDX: Molecular Diagnostic Tests (MDT)	A55157 Billing and Coding: MolDX: CHD7 Gene Analysis **Retired 05/30/2024**	WPS*	IA, IN, KS, MI, MO, NE	IA, IN, KS, MI, MO, NE
ENG and ACVRL1 Gene Tests				
L36021 MolDX: Molecular Diagnostic Tests (MDT)	A54262 Billing and Coding: MolDX: ENG and ACVRL1 Gene Tests **Retired 04/18/2024**	CGS	KY, OH	KY, OH

LCD	Article	Contractor	Medicare Part A	Medicare Part B
ENG and ACVRL1 Gene Tests				
N/A	A55181 Billing and Coding: MolDX: ENG and ACVRL1 Gene Tests **Retired 04/18/2024**	Noridian	AS, CA, GU, HI, MP, NV	AS, CA, GU, HI, MP, NV
N/A	A55182 Billing and Coding: MolDX: ENG and ACVRL1 Gene Tests **Retired 04/18/2024**	Noridian	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY
N/A	A53536 Billing and Coding: MolDX: ENG and ACVRL1 Gene Tests **Retired 04/18/2024**	Palmetto	AL, GA, NC, SC, TN, VA, WV	AL, GA, NC, SC, TN, VA, WV
L36807 MolDX: Molecular Diagnostic Tests (MDT)	A55159 Billing and Coding: MolDX: ENG and ACVRL1 Gene Tests **Retired 05/30/2024**	WPS*	IA, IN, KS, MI, MO, NE	IA, IN, KS, MI, MO, NE
FGFR2 and FGFR3 Gene Tests				
L38586 MolDX: Prognostic and Predictive Molecular Classifiers for Bladder Cancer	A58065 Billing and Coding: MolDX: Prognostic and Predictive Molecular Classifiers for Bladder Cancer	CGS	KY, OH	KY, OH
L38647 MolDX: Prognostic and Predictive Molecular Classifiers for Bladder Cancer	A58181 Billing and Coding: MolDX: Prognostic and Predictive Molecular Classifiers for Bladder Cancer	Noridian	AS, CA, GU, HI, MP, NV	AS, CA, GU, HI, MP, NV
L38649 MolDX: Prognostic and Predictive Molecular Classifiers for Bladder Cancer	A58187 Billing and Coding: MolDX: Prognostic and Predictive Molecular Classifiers for Bladder Cancer	Noridian	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY
L38576 MolDX: Prognostic and Predictive Molecular Classifiers for Bladder Cancer	A58028 Billing and Coding: MolDX: Prognostic and Predictive Molecular Classifiers for Bladder Cancer	Palmetto	AL, GA, NC, SC, TN, VA, WV	AL, GA, NC, SC, TN, VA, WV
L38684 Prognostic and Predictive Molecular Classifiers for Bladder Cancer	A58211 Billing and Coding: MolDX: Prognostic and Predictive Molecular Classifiers for Bladder Cancer	WPS*	IA, IN, KS, MI, MO, NE	IA, IN, KS, MI, MO, NE
Genetic Testing for Cardiovascular Disease				
L39084 Genetic Testing for Cardiovascular Disease	A58797 Billing and Coding: Genetic Testing for Cardiovascular Disease	First Coast	FL, PR, VI	FL, PR, VI
L39082 Genetic Testing for Cardiovascular Disease	A58795 Billing and Coding: Genetic Testing for Cardiovascular Disease	Novitas	AR, CO, DC, DE, LA, MD, MS, NJ, NM, OK, PA, TX	AR, CO, DC, DE, LA, MD, MS, NJ, NM, OK, PA, TX
HEXA Gene Analysis				
L36021 MolDX: Molecular Diagnostic Tests (MDT)	A54268 Billing and Coding: MolDX: HEXA Gene Analysis **Retired 05/08/2024**	CGS	KY, OH	KY, OH

LCD	Article	Contractor	Medicare Part A	Medicare Part B
HEXA Gene Analysis				
N/A	A55255 Billing and Coding: MolDX: HEXA Gene Analysis **Retired 05/08/2024**	Noridian	AS, CA, GU, HI, MP, NV	AS, CA, GU, HI, MP, NV
N/A	A55256 Billing and Coding: MolDX: HEXA Gene Analysis **Retired 05/08/2024**	Noridian	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY
L35025 MolDX: Molecular Diagnostic Tests (MDT)	A53598 Billing and Coding: MolDX: HEXA Gene Analysis **Retired 05/08/2024**	Palmetto	AL, GA, NC, SC, TN, VA, WV	AL, GA, NC, SC, TN, VA, WV
L36807 MolDX: Molecular Diagnostic Tests (MDT)	A55168 Billing and Coding: MolDX: HEXA Gene Analysis **Retired 05/30/2024**	WPS*	IA, IN, KS, MI, MO, NE	IA, IN, KS, MI, MO, NE
L1CAM Gene Sequencing				
L36021 MolDX: Molecular Diagnostic Tests (MDT)	A54274 Billing and Coding: MolDX: L1CAM Gene Sequencing Guidelines	CGS	KY, OH	KY, OH
N/A	A55277 Billing and Coding: MolDX: L1CAM Gene Sequencing **Retired 05/24/2024**	Noridian	AS, CA, GU, HI, MP, NV	AS, CA, GU, HI, MP, NV
N/A	A55278 Billing and Coding: MolDX: L1CAM Gene Sequencing **Retired 05/24/2024**	Noridian	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY
L35025 MolDX: Molecular Diagnostic Tests (MDT)	A53659 Billing and Coding: MolDX: L1CAM Gene Sequencing **Retired 05/24/2024**	Palmetto	AL, GA, NC, SC, TN, VA, WV	AL, GA, NC, SC, TN, VA, WV
L36807 MolDX: Molecular Diagnostic Tests (MDT)	A55192 Billing and Coding: MolDX: L1CAM Gene Sequencing **Retired 06/27/2024**	WPS*	IA, IN, KS, MI, MO, NE	IA, IN, KS, MI, MO, NE
MMACHC Test				
L36021 MolDX: Molecular Diagnostic Tests (MDT)	A54209 Billing and Coding: MolDX: MMACHC Test **Retired 05/30/2024**	CGS	KY, OH	KY, OH
N/A	A55288 Billing and Coding: MolDX: MMACHC Test **Retired 05/30/2024**	Noridian	AS, CA, GU, HI, MP, NV	AS, CA, GU, HI, MP, NV
N/A	A55289 Billing and Coding: MolDX: MMACHC Test **Retired 05/30/2024**	Noridian	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY
L35025 MolDX: Molecular Diagnostic Tests (MDT)	A54035 Billing and Coding: MolDX: MMACHC Test **Retired 05/30/2024**	Palmetto	AL, GA, NC, SC, TN, VA, WV	AL, GA, NC, SC, TN, VA, WV
L36807 MolDX: Molecular Diagnostic Tests (MDT)	A55191 Billing and Coding: MolDX: MMACHC Test **Retired 06/27/2024**	WPS*	IA, IN, KS, MI, MO, NE	IA, IN, KS, MI, MO, NE

LCD	Article	Contractor	Medicare Part A	Medicare Part B
NSD1 Gene Tests				
L36021 MolDX: Molecular Diagnostic Tests (MDT)	A54291 Billing and Coding: MolDX: NSD1 Gene Tests **Retired 04/30/2024**	CGS	KY, OH	KY, OH
N/A	A55609 Billing and Coding: MolDX: NSD1 Gene Tests **Retired 04/30/2024**	Noridian	AS, CA, GU, HI, MP, NV	AS, CA, GU, HI, MP, NV
N/A	A55615 Billing and Coding: MolDX: NSD1 Gene Tests **Retired 04/30/2024**	Noridian	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY
L35025 MolDX: Molecular Diagnostic Tests (MDT)	A53585 Billing and Coding: MolDX: NSD1 Gene Tests **Retired 04/30/2024**	Palmetto	AL, GA, NC, SC, TN, VA, WV	AL, GA, NC, SC, TN, VA, WV
L36807 MolDX: Molecular Diagnostic Tests (MDT)	A55198 Billing and Coding: MolDX: NSD1 Gene Tests **Retired 05/30/2024**	WPS*	IA, IN, KS, MI, MO, NE	IA, IN, KS, MI, MO, NE
Pharmacogenomics Testing				
L38394 MolDX: Pharmacogenomics Testing	A58324 Billing and Coding: MolDX: Pharmacogenomics Testing	CGS	KY, OH	KY, OH
L38335 MolDX: Pharmacogenomics Testing	A57384 Billing and Coding: MolDX: Pharmacogenomics Testing	Noridian	AS, CA, GU, HI, MP, NV	AS, CA, GU, HI, MP, NV
L38337 MolDX: Pharmacogenomics Testing	A57385 Billing and Coding: MolDX: Pharmacogenomics Testing	Noridian	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY
L38294 MolDX: Pharmacogenomics Testing	A58318 Billing and Coding: MolDX: Pharmacogenomics Testing	Palmetto	AL, GA, NC, SC, TN, VA, WV	AL, GA, NC, SC, TN, VA, WV
L38435 MolDX: Pharmacogenomics Testing	A58395 Billing and Coding: MolDX: Pharmacogenomics Testing	WPS*	IA, IN, KS, MI, MO, NE	IA, IN, KS, MI, MO, NE
L39073 Pharmacogenomics Testing	A58812 Billing and Coding: Pharmacogenomics Testing	First Coast	FL, PR, VI	FL, PR, VI
L39063 Pharmacogenomics Testing	A58801 Billing and Coding: Pharmacogenomics Testing	Novitas	AR, CO, DC, DE, LA, MD, MS, NJ, NM, OK, PA, TX	AR, CO, DC, DE, LA, MD, MS, NJ, NM, OK, PA, TX
RPS19 Gene Tests				
L36021 MolDX: Molecular Diagnostic Tests (MDT)	A54299 Billing and Coding: MolDX: RPS19 Gene Tests **Retired 04/30/2024**	CGS	KY, OH	KY, OH
N/A	A55610 Billing and Coding: MolDX: RPS19 Gene Tests **Retired 04/30/2024**	Noridian	AS, CA, GU, HI, MP, NV	AS, CA, GU, HI, MP, NV
N/A	A55614 Billing and Coding: MolDX: RPS19 Gene Tests **Retired 04/30/2024**	Noridian	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY
L35025 MolDX: Molecular Diagnostic Tests (MDT)	A53587 Billing and Coding: MolDX: RPS19 Gene Tests **Retired 04/30/2024**	Palmetto	AL, GA, NC, SC, TN, VA, WV	AL, GA, NC, SC, TN, VA, WV

LCD	Article	Contractor	Medicare Part A	Medicare Part B
RPS19 Gene Tests				
N/A	A55205 Billing and Coding: MolDX: RPS19 Gene Tests **Retired 05/30/2024**	WPS*	IA, IN, KS, MI, MO, NE	IA, IN, KS, MI, MO, NE
STAT3 Gene Testing				
L36021 MolDX: Molecular Diagnostic Tests (MDT)	A54284 Billing and Coding: MolDX: STAT3 Gene Testing **Retired 04/24/2024**	CGS	KY, OH	KY, OH
N/A	A55480 Billing and Coding: MolDX: STAT3 Gene Testing **Retired 04/24/2024**	Noridian	AS, CA, GU, HI, MP, NV	AS, CA, GU, HI, MP, NV
N/A	A55481 Billing and Coding: MolDX: STAT3 Gene Testing **Retired 04/24/2024**	Noridian	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY
N/A	A53562 Billing and Coding: MolDX: STAT3 Gene Testing **Retired 04/24/2024**	Palmetto	AL, GA, NC, SC, TN, VA, WV	AL, GA, NC, SC, TN, VA, WV
L36807 MolDX: Molecular Diagnostic Tests (MDT)	A55209 Billing and Coding: MolDX: STAT3 Gene Testing **Retired 05/30/2024**	WPS*	IA, IN, KS, MI, MO, NE	IA, IN, KS, MI, MO, NE
General Molecular Diagnostic Tests				
L34519 Molecular Pathology Procedures	A57451 Billing and Coding: Molecular Pathology Procedures	First Coast	FL, PR, VI	FL, PR, VI
	A58918 Billing and Coding: Molecular Pathology and Genetic Testing			
L35062 Biomarkers Overview	A58917 Billing and Coding: Molecular Pathology and Genetic Testing	Novitas	AR, CO, DC, DE, LA, MD, MS, NJ, NM, OK, PA, TX	AR, CO, DC, DE, LA, MD, MS, NJ, NM, OK, PA, TX
L35000 Molecular Pathology Procedures	A56199 Billing and Coding: Molecular Pathology Procedures	NGS	CT, IL, MA, ME, MN, NH, NY, RI, VT, WI	CT, IL, MA, ME, MN, NH, NY, RI, VT, WI
L36021 MolDX: Molecular Diagnostic Tests (MDT)	A56973 Billing and Coding: MolDX: Molecular Diagnostic Tests (MDT)	CGS	KY, OH	KY, OH
	A54901 Billing and Coding: MolDX: Targeted and Comprehensive Genomic Profile Next Generation Sequencing Testing in Cancer			
L35025 MolDX: Molecular Diagnostic Tests (MDT)	A56853 Billing and Coding: MolDX: Molecular Diagnostic Tests (MDT)	Palmetto	AL, GA, NC, SC, TN, VA, WV	AL, GA, NC, SC, TN, VA, WV
L35160 MolDX: Molecular Diagnostic Tests (MDT)	A57526 Billing and Coding: MolDX: Molecular Diagnostic Tests (MDT)	Noridian	AS, CA, GU, HI, MP, NV	AS, CA, GU, HI, MP, NV
L36256 MolDX: Molecular Diagnostic Tests (MDT)	A57527 Billing and Coding: MolDX: Molecular Diagnostic Tests (MDT)	Noridian	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY

LCD	Article	Contractor	Medicare Part A	Medicare Part B
General Molecular Diagnostic Tests				
L36807 MolDX: Molecular Diagnostic Tests (MDT)	A57772 Billing and Coding: MolDX: Molecular Diagnostic Tests (MDT)	WPS*	IA, IN, KS, MI, MO, NE	IA, IN, KS, MI, MO, NE
*__Note__: Wisconsin Physicians Service Insurance Corporation: Contract Number 05901 applies only to WPS Legacy Mutual of Omaha MAC A Providers.				

CMS Benefit Policy Manual

Chapter 15; §§ 80.1 - 80.1.3, 80.6 Clinical Laboratory Services

CMS Claims Processing Manual

Chapter 12; § 60 Payment for Pathology Services
Chapter 16, § 10.2 General Explanation of Payment; § 20 Calculation of Payment Rates - Clinical Laboratory Test Fee Schedules; § 40 Billing for Clinical Laboratory Tests

Others

CMS IOM 100-08, Medicare Program Integrity Manual, Chapter 13, Section13.5.4 Reasonable and Necessary Provisions in LCDs
Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for the Use of Potent Volatile Anesthetic Agents and Succinylcholine in the Context of RYR1 or CACNA1S Genotypes
CMS Clinical Laboratory Fee Schedule, CMS Website
Pharmacogenomic Biomarkers in Drug Labeling, FDA website
Palmetto GBA MolDx Website
Palmetto GBA MolDx Manual, Palmetto GBA MolDx Website

Guideline History/Revision Information

Revisions to this summary document do not in any way modify the requirement that services be provided and documented in accordance with the Medicare guidelines in effect on the date of service in question.

Date	Summary of Changes

11/01/2024	**Related Policies**
	• Removed reference link to the:
	  ○ Medicare Advantage Policy Guideline titled:
	  ▪ *Biomarkers in Cardiovascular Risk Assessment*
	  ▪ *Blood Product Molecular Antigen Typing* (retired Nov. 1, 2024)
	  ▪ *Genetic Testing for Cardiovascular Disease* (retired Nov. 1, 2024)
	  ○ Medicare Advantage Coverage Summary titled *Molecular Pathology/Molecular Diagnostics/Genetic Testing*

08/01/2024	**Policy Summary**
	Gene Identification
	Covered
	• Revised list of covered indications:
	For CPT Code 81400
	  ○ Removed:
	  ▪ ACE
	  ▪ F13B
	  ▪ F5
	  ▪ F7
	  ▪ FGB
	For CPT Code 81401
	  ○ Removed:
	  ▪ CBFB-MYH11
	  ▪ E2A/PBX1

Date	Summary of Changes
	▪ EML4-ALK ▪ ETV6-RUNX1 ▪ EWSR1/ERG ▪ EWSR1/FLI1 ▪ EWSR1/WT1 ▪ F11 coagulation factor XI ▪ FGFR3 ▪ FIP1L1-PDGFR ▪ FOXO1/PAX3 ▪ FOXO1/PAX7 ▪ MT-RNR1 ▪ MUTYH [mutY homolog (E. coli)] ▪ NPM/ALK ▪ PAX8/PPARG ▪ RUNX1/RUNX1T1 *For CPT Code 81403* ○ Removed: ▪ EpCAM ▪ F8 (coagulation factor VIII) ▪ FGFR3 ▪ VHL (von Hippel-Lindau tumor suppressor) Non-Covered • Revised list of non-covered indications: *For CPT Code 81400* ○ Removed: ▪ ABCC8 ▪ ACADM ▪ AGTR1 ▪ CCR5 ▪ CLRN1 ▪ DYT1 (TOR1A) ▪ IL28B ▪ IVD ▪ TOR1A *For CPT Code 81401* ○ Removed: ▪ ABCC8 ▪ ADRB2 ▪ APOE ▪ CFH/ARMS2 ▪ DEK/NUP214 ▪ GALT (galactose-1-phosphate uridylyltransferase) ▪ H19 ▪ KCNQ10T1 (KCNQ1 overlapping transcript 1) ▪ MEG3/DLK1 ▪ MLL/AFF ▪ MT-ATP6 ▪ MT-ND4 ▪ MT-ND6 ▪ MT-ND5 [mitochondrially encoded tRNA leucine 1 (UUA/G), mitochondrially encoded NADH dehydrogenase 5] ▪ MT-TK (mitochondrially encoded tRNA lysine) ▪ MT-TL1 ▪ MT-TS1 ▪ PRSS1 [protease, serine, 1 (trypsin 1)] *For CPT Code 81402* ○ Removed:

Date	Summary of Changes
	▪ CYP21A2 ▪ Chromosome 18q- ▪ MEFV (Mediterranean fever) (e.g., familial Mediterranean fever) ▪ TRD ▪ Uniparental disomy (UPD) *For CPT Code 81403* ○ Removed: ▪ ANG (angiogenin, ribonuclease, RNase A family, 5) ▪ GJB1 (gap junction protein, beta 1) (e.g., Charcot-Marie-Tooth X-linked), full gene sequence ▪ HRAS (v-Ha-ras Harvey rat sarcoma viral oncogene homolog Costello syndrome) ▪ MT-RNR1 (mitochondrially encoded 12S RNA) ▪ MT-TS1 (mitochondrially encoded tRNA serine 1) *For CPT Code 81404* ○ Removed: ▪ MMACHC [methylmalonic aciduria (cobalamin deficiency) cblC type, with homocystinuria] *For CPT Code 81405* ○ Removed: ▪ ENG ▪ NSD1 ▪ RPS19 ▪ STAT3 *For CPT Code 81406* ○ Removed: ▪ BCKDHB (branched-chain keto acid dehydrogenase E1, beta polypeptide) ▪ CDH1, full gene sequence ▪ ENG **Documentation Guidelines** • Revised language to indicate: ○ Providers are required to code to specificity; however, if an unlisted CPT code is used, the documentation must clearly identify the unique procedure performed ○ When multiple procedure codes are submitted on a claim (unique and/or unlisted), the documentation supporting each code should be easily identifiable ○ If on review UnitedHealthcare cannot link a billed code to the documentation, these services will be denied ○ Because there are multiple biomarkers represented by each of the Tier 2 codes, when billing for these codes, it will be necessary to report the specific biomarker in the claim narrative/remarks; report information in the narrative/remarks that provides ample information to uniquely identify the specific biomarker ○ Providing the descriptive information for the Tier 2 molecular pathology code will assist in timely processing of claims ○ Failure to provide the information may result in delayed processing or claim denials **Applicable Codes** ***Diagnosis Codes*** For CPT Code 81406 for MUTYH • Removed list of applicable codes: C18.0, C18.1, C18.2, C18.3, C18.4, C18.5, C18.6, C18.7, C18.8, C19, C20, D12.0, D12.1, D12.2, D12.3, D12.4, D12.5, D12.7, D12.8, Z85.038, and Z86.010 **References** ***CMS Local Coverage Determinations (LCDs) and Articles*** • Updated list of applicable reference links to reflect the most current information • Added notation to indicate the Wisconsin Physicians Service Insurance Company (WPS) Contract Number 05901 applies only to WPS Legacy Mutual of Omaha MAC A Providers ***UnitedHealthcare Commercial Policies*** • Removed list of applicable reference links

Date	Summary of Changes
	Administrative • Archived previous policy version MPG381.17

Purpose

The Medicare Advantage Policy Guideline documents are generally used to support UnitedHealthcare Medicare Advantage claims processing activities and facilitate providers' submission of accurate claims for the specified services. The document can be used as a guide to help determine applicable:

- Medicare coding or billing requirements, and/or
- Medical necessity coverage guidelines; including documentation requirements.

UnitedHealthcare follows Medicare guidelines such as NCDs, LCDs, LCAs, and other Medicare manuals for the purposes of determining coverage. It is expected providers retain or have access to appropriate documentation when requested to support coverage. Please utilize the links in the References section above to view the Medicare source materials used to develop this resource document. This document is not a replacement for the Medicare source materials that outline Medicare coverage requirements. Where there is a conflict between this document and Medicare source materials, the Medicare source materials will apply.

Terms and Conditions

The Medicare Advantage Policy Guidelines are applicable to UnitedHealthcare Medicare Advantage Plans offered by UnitedHealthcare and its affiliates.

These Policy Guidelines are provided for informational purposes, and do not constitute medical advice. Treating physicians and healthcare providers are solely responsible for determining what care to provide to their patients. Members should always consult their physician before making any decisions about medical care.

Benefit coverage for health services is determined by the member specific benefit plan document* and applicable laws that may require coverage for a specific service. The member specific benefit plan document identifies which services are covered, which are excluded, and which are subject to limitations. In the event of a conflict, the member specific benefit plan document supersedes the Medicare Advantage Policy Guidelines.

Medicare Advantage Policy Guidelines are developed as needed, are regularly reviewed and updated, and are subject to change. They represent a portion of the resources used to support UnitedHealthcare coverage decision making. UnitedHealthcare may modify these Policy Guidelines at any time by publishing a new version of the policy on this website. Medicare source materials used to develop these guidelines include, but are not limited to, CMS National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Medicare Benefit Policy Manual, Medicare Claims Processing Manual, Medicare Program Integrity Manual, Medicare Managed Care Manual, etc. The information presented in the Medicare Advantage Policy Guidelines is believed to be accurate and current as of the date of publication and is provided on an "AS IS" basis. Where there is a conflict between this document and Medicare source materials, the Medicare source materials will apply.

You are responsible for submission of accurate claims. Medicare Advantage Policy Guidelines are intended to ensure that coverage decisions are made accurately based on the code or codes that correctly describe the health care services provided. UnitedHealthcare Medicare Advantage Policy Guidelines use Current Procedural Terminology (CPT®), Centers for Medicare and Medicaid Services (CMS), or other coding guidelines. References to CPT® or other sources are for definitional purposes only and do not imply any right to reimbursement or guarantee claims payment.

Medicare Advantage Policy Guidelines are the property of UnitedHealthcare. Unauthorized copying, use, and distribution of this information are strictly prohibited.

*For more information on a specific member's benefit coverage, please call the customer service number on the back of the member ID card or refer to the Administrative Guide.