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Medicare Advantage Policy Manual **Policy ID:** M-GT20

Genetic and Molecular Diagnostics – Single Gene or Variant Testing

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IMPORTANT REMINDER

The Medicare Advantage Medical Policy manual is not intended to override the member Evidence of Coverage (EOC), which defines the insured's benefits, nor is it intended to dictate how providers are to practice medicine. Physicians and other health care providers are expected to exercise their medical judgment in providing the most appropriate care for the individual member.

The Medicare Advantage Medical Policies are designed to provide guidance regarding the decision-making process for the coverage or non-coverage of services or procedures in accordance with the member EOC and the Centers of Medicare and Medicaid Services (CMS) policies, when available. In the event of a conflict, applicable CMS policy or EOC language will take precedence over the Medicare Advantage Medical Policy. In the absence of CMS guidance for a requested service or procedure, the health plan may apply their Medical Policy Manual or MCG™ criteria, both of which are developed with an objective, evidence-based process using scientific evidence, current generally accepted standards of medical practice, and authoritative clinical practice guidelines.

Medicare and EOCs exclude from coverage, among other things, services or procedures considered to be investigational, cosmetic, or not medically necessary, and in some cases, providers may bill members for these non-covered services or procedures. Providers are encouraged to inform members in advance when they may be financially responsible for the cost of non-covered or excluded services.

DESCRIPTION

Genetic testing is a type of diagnostic laboratory testing performed to detect changes or variants in DNA, RNA, chromosomes, proteins, or certain metabolites. Human Genome Variation Society (HGVS) nomenclature[1] is used to describe variants found in DNA and serves as an international standard. According to this nomenclature, the term "variant" is used to describe a change in a DNA or protein sequence, replacing previously-used terms, such as "mutation." Pathogenic variants are variants associated with disease, while benign variants are not. The majority of genetic changes have unknown effects on human health, and these are referred to as variants of uncertain significance.

Genetic testing is done for several purposes, including but not limited to, diagnosing or predicting susceptibility for inherited conditions, screening for common disorders, or selecting appropriate treatments (also known as pharmacogenetic testing).

NOTE: See the "Policy Guidelines" below for important notes regarding Medicare and diagnostic laboratory and genetic testing services.

MEDICARE ADVANTAGE POLICY CRITERIA

I. See Table 1 to determine if a specific test is already addressed, with applicable Medicare references provided. While **not** all-inclusive, this table contains a list of tests with known Medicare coverage or non-coverage guidance. Some tests are never considered medically reasonable or necessary, while others may have criteria which must be met in order for the genetic test to be considered medically appropriate.

   a. Note the geographical location of the laboratory performing the test, and whether or not the given Medicare reference (LCD, LCA, MolDX guideline, etc.) applies to that geographical area. Table 3, found in the "*Policy Guidelines*" section below, provides a list of Medicare Administrative Contractors, or MACs, for each state. If the reference provided in Table 1 does not apply to the state where the laboratory testing will be performed, see Criterion II.
      i. If the Medicare reference is a Molecular Diagnostics (MolDX) Program guideline, see Table 2 (found in the "*Policy Guidelines*" section below) for a state listing to determine if the laboratory is located in a state that has adopted MolDX decisions.
   b. Codes included in Table 1 are provided as a courtesy only, and may not be the code(s) used, as individual laboratories may opt to use different coding when specific codes are not available.
      i. Note, do not limit searches to codes only because more than one criteria row may apply to the CPT or HCPCS code in question. Use Control+F to search the policy, and be sure to look for specific *genes, variants, and/or indication(s)* when applicable.

II. If the test in question is not part of Table 1, additional research and case-by-case review is necessary to determine the applicable Medicare guideline for genetic tests not addressed.

Table 1: Genetic Test, Performing Laboratory Location, and Medicare Coverage References

Back to Criteria

Important Note: This policy does **not** address panel testing, which is defined by MolDX as, "A predetermined set of medical tests composed of individual laboratory tests, related by medical condition, specimen type, frequency ordered, methodology or types of components to aid in the diagnosis/treatment of disease." MolDX adds, "the performance of multiple molecular biomarkers, regardless of whether the test requisition lists the tests as a panel or individually, and completed on a single sample to be a 'panel' of tests."[17] For coverage information regarding panel testing, see the Medicare Advantage medical policy for *Genetic and Molecular Diagnostics – Next Generation Sequencing and Genetic Panel Testing*, Genetic Testing, Policy No. M-64 (see Cross References)

Note: The tests listed in this table have known Medicare guidance available. Some tests are considered "not medically necessary," while others may have coverage criteria which must be met in order for the genetic test to be considered medically appropriate. Please review the "Medicare Rationale/Reference" source carefully. Note the geographical location of the laboratory performing the test, and whether or not the given Medicare reference applies to that geographical area. If it does not, see Criterion II.B.i in the "MEDICARE ADVANTAGE POLICY CRITERIA" section above.

TEST NAME & GENES *If known*	CODES *If known*	PERFORMING LABORATORY & LOCATION	MEDICARE RATIONALE / REFERENCE Back to Criteria
4q25-AF Risk Genotype	81479	Multiple	MolDX: 4q25-AF Risk Genotype Billing and Coding Guidelines (A55091) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: 4q25-AF Risk Genotype Billing and Coding Guidelines (A55090) *(Laboratories in CA and NV).*
9p21 Genotype Test	81479	Multiple	MolDX: 9p21 Genotype Test Billing and Coding Guideline (A55093) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: 9p21 Genotype Test Billing and Coding Guideline (A55092) *(Laboratories in CA and NV)*

Abbott RealTime IDH1, IDH2 (Abbott Molecular)	81120, 81121	Multiple	MolDX: Abbott RealTime IDH2 testing for Acute Myeloid Leukemia (AML) Billing and Coding Guidelines (A55712)*(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: Abbott RealTime IDH2 testing for Acute Myeloid Leukemia (AML) Billing and Coding Guidelines (A55711) *(Laboratories in CA and NV)* *NOTE: The above guidelines for the Abbott RealTime IDH2 test states: "This article reflects the FDA-approved indications on article creation date. MolDX will allow future FDA approved and amended indications for these tests." Therefore, as new FDA-approved medications and companion diagnostics (CDx) tests become available, more IDH2 tests may be allowed than what are indicated in the LCA. To view FDA-approved IDH1 and IDH2 tests and their corresponding medications, see the FDA web page for* List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools)*)*
ACVRL1 Gene Tests	81479	Multiple	MolDX: ENG and ACVRL1 Gene Tests Billing and Coding Guidelines (A55182) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: ENG and ACVRL1 Gene Tests Billing and Coding Guidelines (A55181) *(Laboratories in CA and NV)*
ALK Gene tests	81479	Multiple	*See the Noridian J-F web page for Approved Gene Testing, where ALK testing is listed as an approved test (Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY, CA, NV) (See the Noridian J-E web page for Approved Gene Testing for laboratories in CA and NV.)* *Some FDA-approved medications are connected to companion diagnostics (CDx) tests for ALK rearrangements. To view FDA-approved ALK tests and their corresponding medications, see the FDA web page for* List of Cleared or Approved Companion

			Diagnostic Devices (In Vitro and Imaging Tools). For other ALK testing not specifically listed as an FDA-approved CDx, clinical documentation must demonstrate how test results will be used in the management or diagnosis of an illness or condition)
Androgen Receptor (AR) Gene test	81173, 81174, 81204	Multiple	LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY) (Previously reported with 81401 [page 2] or 81405 [page 9]. Noncoverage of this test remains in place regardless of CPT code used until either MolDX or Noridian indicate coverage is available. Medical necessity is not determined by an assigned CPT code.)* LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV) (Previously reported with 81401 [page 2] or 81405 [page 9]. Noncoverage of this test remains in place regardless of CPT code used until either MolDX or Noridian indicate coverage is available. Medical necessity is not determined by an assigned CPT code.)* Biomarkers for Oncology (L35396)[17] (Published by Novitas) *(Until this contractor provides coverage guidance for this genetic test, language from this LCD which reads, "Biomarkers not addressed in this LCD or any other Novitas LCD will be considered not reasonable and necessary unless specifically covered by national policy" applies.)* Molecular Pathology Procedures (L35000) (Published by National Government Services) *(Laboratories in IL, MN, WI, CT, NY, ME, MA, NH, RI, VT) See the guideline specific to the gene or CPT code within the LCD. See also LCA A56199.*
Anti-dsDNA, High Salt/Avidity	0039U	UW Medicine	• The MolDX Program requires labs to submit a technology assessment (TA) to provide evidence of analytical and clinical validity (AV/CV), and clinical utility (CU). *(Noridian LCA A54554)* • The Noridian LCD L36256 states reimbursement is only allowed for “approved tests… for dates of service consistent with the effective date of the coverage determination” after MolDX review.

			• If a test does not have a coverage determination, then coverage is not allowed because evidence of clinical validity or utility has not been established via the TA review process. • This test is not considered medically reasonable and necessary under SSA §1862(a)(1)(A) until a MolDX review is complete and coverage is indicated by MolDX or Noridian.
APC Gene tests	See guideline for "Familial Adenomatous Polyposis (FAP) (includes Attenuated FAP [AFAP]) (APC gene testing) and MUTYH-Associated Polyposis (MAP) (formerly MYH-associated polyposis) (MUTYH gene testing)" testing below		
ApoE Genotype	81401	Multiple	MolDX: Biomarkers in Cardiovascular Risk Assessment (L36362) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY) (See also the LCA A55095)* MolDX: Biomarkers in Cardiovascular Risk Assessment (L36358)*(Laboratories in CA and NV) (See also the LCA A55094)*
Apolipoprotein E (apoE) Genotype Test	81401	Boston Heart Diagnostics, Massachusetts	National Government Services Inc. (NGS) LCD for Molecular Pathology Procedures (L35000) (Applies to the indicated performing laboratory) *See the guideline specific to the gene or CPT code within the LCD.*
Aspartoacyclase 2 Deficiency (ASPA) Testing	81200, 81479	Multiple	MolDX: Aspartoacyclase 2 Deficiency(ASPA) Testing Billing and Coding Guidelines (A55089) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: Aspartoacyclase 2 Deficiency(ASPA) Testing Billing and Coding Guidelines (A55088) *(Laboratories in CA and NV)*
ATM Gene Tests	81408 *(full gene sequencing)*, 0136U	Multiple	LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV)* **Note:** As an add-on code for *ATM* full gene sequencing testing, +RNAinsight™ for *ATM* by Ambry Genetics (0136U) is also non-covered if performed.

ATP7B Gene Tests	81406, 81479	Multiple	MolDX: ATP7B Gene Tests Billing and Coding Guidelines (A55098) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: ATP7B Gene Tests Billing and Coding Guidelines A55097) *(Laboratories in CA and NV)*
Avise PG Assay	84999	Exagen Diagnostics	MolDX: Avise PG Assay Billing and Coding Guidelines (A54378) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: Avise PG Assay Billing and Coding Guidelines (A54376) *(Laboratories in CA and NV)*
BCKDHB Gene Test	81205, 81406	Multiple	MolDX: BCKDHB Gene Test Billing and Coding Guidelines (A55100) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: BCKDHB Gene Test Billing and Coding Guidelines (A55099) *(Laboratories in CA and NV)*
BCR-ABL	81206, 81207, 81208, 81479	Multiple	MolDX: Genetic Testing for BCR-ABL Negative Myeloproliferative Disease (L36186) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* • For coding assistance, see also the MolDX: BCR-ABL Coding and Billing Guidelines (A55600) MolDX: Genetic Testing for BCR-ABL Negative Myeloproliferative Disease (L36180) *(Laboratories in CA and NV)* • For coding assistance, see also the MolDX: BCR-ABL Coding and Billing Guidelines (A55595) **For both LCDs:** If a treating physician suspects a patient has myeloproliferative neoplasms (MPN) or myelodysplastic syndromes (MDS), it would be clinically appropriate to test BCR-ABL. No specific criteria are provided for this gene directly as this is considered “step one” in the LCDs, and would be considered “medically necessary” for these and related indications, as outlined

			in the LCDs. If performed with other genes (e.g., JAK2), this would be considered panel testing, and M-GT64 would apply. See Cross References. For BCR-ABL1 major and minor breakpoint fusion transcripts by the University of Iowa, reported with PLA code 0016U, apply the same BCR-ABL criteria used for 81206-81208 in the Wisconsin LCD for *MolDX: Genetic Testing for BCR-ABL Negative Myeloproliferative Disease* (L36815). For testing performed by BCR-ABL1 major and minor breakpoint fusion transcripts testing by Asuragen in Texas (also 0016U), see Novitas LCD L35396 (search by CPT code).
BCR-ABL Negative Myeloproliferative Disease Testing (JAK2 V617F, JAK2 exon 12 only, CALR, and MPL genes for myeloproliferative disease, or MPD) *(for single gene tests only)*	81206, 81207, 81208, 81219, 81270, 81402, 81403	Multiple	MolDX: Genetic Testing for BCR-ABL Negative Myeloproliferative Disease (L36186) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: Genetic Testing for BCR-ABL Negative Myeloproliferative Disease (L36180) *(Laboratories in CA and NV)* **For both LCDs:** If a treating physician suspects a patient has myeloproliferative neoplasms (MPN) or myelodysplastic syndromes (MDS), it would be clinically appropriate to test BCR-ABL. No specific criteria are provided for this gene directly as this is considered "step one" in the noted LCDs. Therefore, when used for the indications noted in these LCDs, BCR-ABL testing is considered medically necessary.
Bladder Tumor Marker *(with or without FISH technology)*	86294, 86316, 86386, 88120, 88121	Multiple	For ***general coverage and non-coverage criteria***: ✓ Bladder/Urothelial Tumor Markers (L36680) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* ✓ Bladder/Urothelial Tumor Markers (L36678) *(Laboratories in CA and NV)* For ***additional information for any testing requested with FISH***:

			✓ MolDX: Bladder Tumor Marker FISH Billing and Coding Guidelines (A55029) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* ✓ MolDX: Bladder Tumor Marker FISH Billing and Coding Guidelines (A55028) *(Laboratories in CA and NV)*
BLM Gene Analysis	81209	Multiple	MolDX: BLM Gene Analysis Billing and Billing Guidelines (A55114) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: BLM Gene Analysis Billing and Billing Guidelines (A55113) *(Laboratories in CA and NV)*
BRAF	81210	Multiple	MolDX: FDA-Approved BRAF Tests Billing and Coding Guidelines (A54420) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: FDA-Approved BRAF Tests Billing and Coding Guidelines (A54418) *(Laboratories in CA and NV)* *NOTE: The above guideline for* BRAF tests *states: "*This article reflects the FDA-approved indications on article creation date. MolDX will allow future FDA approved and amended indications for these tests.*" Therefore, as new FDA-approved medications and companion diagnostics (CDx) tests become available, more BRAF tests may be allowed than what are indicated in the LCA. To view FDA-approved BRAF tests and their corresponding medications, see the FDA web page for* List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools)*)*
BRCA1 and BRCA2 (hereditary breast cancer)	81162, 81163, 81164, 81165, 81166, 81167, 81212, 81215, 81216, 81217	Multiple	MolDX: BRCA1 and BRCA2 Genetic Testing (L36163) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: BRCA1 and BRCA2 Genetic Testing (*L36161*) *(Laboratories in CA and NV)*

			BRCA1 and BRCA2 Genetic Testing (L36499) *(Laboratories in FL)* MolDX: BRCA1 and BRCA2 Genetic Testing (L36082) *(Laboratories in NC, SC, VA, WV, AL, TN, or GA)*
CALR Genetic Testing	81219	Multiple	MolDX: Genetic Testing for BCR-ABL Negative Myeloproliferative Disease (L36186) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: Genetic Testing for BCR-ABL Negative Myeloproliferative Disease (L36180) *(Laboratories in CA and NV)*
CDH1 Genetic Testing	81406	Multiple	MolDX: CDH1 Genetic Testing Billing and Coding Guidelines (A55971) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: CDH1 Genetic Testing Billing and Coding Guidelines (A55970) *(Laboratories in CA and NV)* *For single gene testing, read the entire guideline as there may be exceptions to the MolDX non-coverage statement. For panel tests, see Cross References.*
CFTR Gene Analysis	81220, 81221, 81222, 81223, 81224	Multiple	MolDX: CFTR Gene Analysis Billing and Coding Guidelines (A55118) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: CFTR Gene Analysis Billing and Coding Guidelines (A55117) *(Laboratories in CA and NV)*
CHD7 Gene Analysis	81407, 81479	Multiple	MolDX: *CHD7* Gene Analysis Coding and Billing Guidelines (A55086) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)*

			MolDX: *CHD7* Gene Analysis Coding and Billing Guidelines (A55085) *(Laboratories in CA and NV)*
CHEK2 Gene Testing	81479	Multiple	LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV)*
Chimerism Testing	81265, 81266, 81267, 81268	Multiple	Short Tandem Repeat (STR) Markers and Chimerism (codes 81265-81268) Coding and Billing Guidelines (A54832) *(Published by Palmetto GBA, for laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY, CA, and NV)*)
Chromosome 1p-/19q-Deletion Analysis by Molecular Sequencing	81402	Multiple	Retired MolDX: Chromosome 1p/19q Deletion Analysis (L36542) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* Retired MolDX: Chromosome 1p/19q Deletion Analysis (L36557) *(Laboratories in CA and NV)* *(Both of the LCDs above state the scientific evidence for chromosome 1p-/19q-deletion analysis is still sound. The LCDs were retired due to operational issues for FISH codes related to this testing. Therefore, only use these retired LCDs to determine medically necessary indications for chromosome 1p-/19q-deletion analysis* **by molecular sequencing** *(81402). Do not use for chromosome 1p-/19q-deletion analysis by* **morphometric analysis** *[e.g. in situ hybridization [***FISH***] because appropriate use of these codes goes beyond the indications called out in these LCDs.)* Instructions: Highlight “L36542” or “L36557,” and press Control + C to copy. Click on either of the LCD links above (L36542 or L36557). Click “Search” in the list on the left-hand side, then enter (or paste) the LCD number into the “ID Search” field. The date of service can be left blank. Click the “Search Now” button.

cobas® 4800 BRAF V600 Test			See guideline for “BRAF” testing above
cobas EGFR Mutation Test			See guideline for “EGFR” testing below
cobas KRAS Test			See guideline for “KRAS” testing below
COL3A1 Gene Testing	81479	Multiple	LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV)*
Cytochrome p450 Genotyping	See individual genome below (i.e., CYP2B6, CYP2D6, etc)		
CYP1A1	81479	Multiple	LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV)*
CYP1A2	81479	Multiple	LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV)*
CYP1B1	81404, 81479	Multiple	LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV)*
CYP2B6	81479	Multiple	MolDX: CYP2B6 Test Billing and Coding Guidelines (A55178) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: CYP2B6 Test Billing and Coding Guidelines (A55177) *(Laboratories in CA and NV)*

CYP2C8	81479	Multiple	LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV)*
CYP2C9	81227, G9143	Multiple	MolDX: CYP2C19, CYP2D6, CYP2C9, and VKORC1 Genetic Testing (L36312) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: CYP2C19, CYP2D6, CYP2C9, and VKORC1 Genetic Testing (L36310) *(Laboratories in CA and NV)* CYP2C19, CYP2D6, CYP2C9, and VKORC1 Genetic Testing (L35698) *(Laboratories in FL)* *(See also "**Warfarin Response Testing"** guidelines below)*
CYP2C19	81225	Multiple	MolDX: CYP2C19, CYP2D6, CYP2C9, and VKORC1 Genetic Testing (L36312) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: CYP2C19, CYP2D6, CYP2C9, and VKORC1 Genetic Testing (L36310) *(Laboratories in CA and NV)* CYP2C19, CYP2D6, CYP2C9, and VKORC1 Genetic Testing (L35698) *(Laboratories in FL)* National Government Services Inc. (NGS) LCD for Molecular Pathology Procedures (L35000) *(Applies to laboratory testing performed by Boston Heart Diagnostics) See the guideline specific to the gene or CPT code within the LCD.*

	CYP2D6	81226, 0070U-0076U	Multiple	MolDX: CYP2C19, CYP2D6, CYP2C9, and VKORC1 Genetic Testing (L36312) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: CYP2C19, CYP2D6, CYP2C9, and VKORC1 Genetic Testing (L36310) *(Laboratories in CA and NV)* CYP2C19, CYP2D6, CYP2C9, and VKORC1 Genetic Testing (L35698) *(Laboratories in FL)* *Molecular Pathology Procedures (L35000) (Laboratories in MN [these include CYP2D6 testing by the Mayo Clinic, reported with0070U-0076U])*
	CYP3A4	81401, 81479	Multiple	LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV)*
	CYP3A5	81401, 81479	Multiple	LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV)*
	CYP4F2	81479	Multiple	LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV)*
	CYP7B1	81479	Multiple	LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)*

			LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV)*
	CYP11B1	81405	Multiple	LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV)*
	CYP17A1	81405	Multiple	LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV)*
	CYP21A2	81402, 81403, 81405	Multiple	LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV)*
Cytogenomic Constitutional Microarray Analysis		81228, 81229	Multiple	LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV)*
DPYD Gene Analysis				See Medicare Advantage medical policy for *Laboratory and Genetic Testing for Use of 5-Fluorouracil (5-FU) in Patients with Cancer*, Laboratory, Policy No. M-64 (see Cross References)
EGFR		81235	Multiple	MolDX: FDA-Approved EGFR Tests Billing and Coding Guidelines (A54424) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: FDA-Approved EGFR Tests Billing and Coding Guidelines (*A54422*) *(Laboratories in CA and NV)*

			NOTE: The above guideline for EGFR tests states: "This article reflects the FDA-approved indications on article creation date. MolDX will allow future FDA approved and amended indications for these tests." Therefore, as new FDA-approved medications and companion diagnostics (CDx) tests become available, more EGFR tests may be allowed than what are indicated in the LCA. To view FDA-approved EGFR tests and their corresponding medications, see the FDA web page for List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools)*)*
ENG Gene Tests	81403, 81405, 81406	Multiple	MolDX: ENG and ACVRL1 Gene Tests Billing and Coding Guidelines (A55182) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: ENG and ACVRL1 Gene Tests Billing and Coding Guidelines (A55181) *(Laboratories in CA and NV)*
ERBB2			*See row for HER2 below*
Familial Adenomatous Polyposis (FAP) (includes Attenuated FAP [AFAP]) (APC gene testing) and MUTYH-Associated Polyposis (MAP) (formerly MYH-associated polyposis) (MUTYH gene testing)	APC gene: 81201-81203 MUTYH gene: 81401, 81403, 81406, 81479	Multiple	***For APC Gene Testing (CPT codes 81201-81203) and MUTYH Full Gene Sequence Testing (CPT code 81406), Duplication/Deletion Testing (CPT code 81479), and Known Familial Variant Testing (CPT code 81403)****:* ✓ MolDX: APC and MUTYH Gene Testing (L36884) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* ✓ MolDX: APC and MUTYH Gene Testing (L36882) *(Laboratories in CA and NV)* ***For MUTYH Common Variant Testing (CPT code 81401)***: ✓ *See the Noridian J-F web page for Approved Gene Testing, where MUTYH testing is listed as an approved test (Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY) (See also the Noridian J-E web page for Approved Gene Testing for laboratories in CA and NV)*

			(Clinical documentation must demonstrate how test results will be used in the management or diagnosis of an illness or condition).
FANCC Genetic Testing	81242	Multiple	MolDX: FANCC Genetic Testing Billing and Coding Guidelines (A55184) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: FANCC Genetic Testing Billing and Coding Guidelines (A55183) *(Laboratories in CA and NV)*
FLT3 Gene Testing	81245, 81246, 81479, 0023U, 0046U	Multiple (for single gene testing) *LeukoStrat® CDx FLT3 Mutation Assay and FLT3 ITD MRD by NGS, both by LabPMM LLC*	*See the Noridian J-F web page for Approved Gene Testing, where FLT3 testing is listed as an approved test (Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY) (See also the Noridian J-E web page for Approved Gene Testing for laboratories in CA and NV)* *NOTE: The above guidelines for other FDA-approved companion diagnostic (CDx) tests state MolDX approval may be allowed for the tests available and approved at that time, but that coverage may also be allowed for future FDA approved and amended indications for these tests. Therefore, as new FDA-approved medications and CDx tests become available, additional FLT3 testing may also be allowed. To view FDA-approved FLT3 tests and their corresponding medications, see the FDA web page for* List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools)*)*
FMR1 (Fragile X) Testing	81243, 81244	Multiple	MolDX: Fragile X Billing and Coding Guidelines Update (A55242) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: Fragile X Billing and Coding Guidelines Update (A55241) *(Laboratories in CA and NV)*
F2 gene testing			*See row for "Thrombophilia and/or Hypercoagulability Genetic Testing" below*

F5 gene testing			*See row for "Thrombophilia and/or Hypercoagulability Genetic Testing" below*
FSHD (FSHMD1A) Southern Blot Test	81404	Athena Diagnostics, Worcester, MA	Molecular Pathology Procedures (L35000) *(Applies to the indicated laboratory) Look for guidance specific to the FSHMD1A gene.*
FSHMD1A *(for laboratories in other states)*	81404	Multiple	LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV)*
GeneSight® MTHFR Test	81291	AssureRx Health, Inc., Mason, OH	The GeneSight® MTHFR test analyzes only the *MTHFR* gene. Therefore, see the LCA for MolDX: Genetic Testing for Hypercoagulability / Thrombophilia (Factor V Leiden, Factor II Prothrombin, and MTHFR) (L35984) *(Applies to the indicated laboratory) In the "Indications" section, look for guidance specific to the MTHFR gene.*
Glucosidase, Beta, Acid (GBA) Genetic Testing	81251	Multiple	MolDX: GBA Genetic Testing Billing and Coding Guidelines (A55244) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: GBA Genetic Testing Billing and Coding Guidelines (A55243) *(Laboratories in CA and NV)*
HAX1 Gene Sequencing	81479	Multiple	MolDX: HAX1 Gene Sequencing Billing and Coding Guidelines (A55252) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: HAX1 Gene Sequencing Billing and Coding Guidelines *(A55249) (Laboratories in CA and NV)*
HBA1/HBA2 Testing	81257, 81258, 81259, 81269	Multiple	LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)*

			LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV)* National Government Services Inc. (NGS) LCD for Molecular Pathology Procedures (L35000) *(Laboratories in IL, MN, WI, CT, NY, ME, MA, NH, RI, VT) See the guideline specific to the gene or CPT code within the LCD. See also LCA A56199.*
HBB Full Gene Sequencing	81401, 81403, 81404	Multiple	MolDX: HBB Gene Tests Billing and Coding Guidelines (A55254) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: HBB Gene Tests Billing and Coding Guidelines (A55253) *(Laboratories in CA and NV)*
Hemochromatosis (HFE Gene) Testing	81256	Multiple	*See the Noridian J-F web page for Approved Gene Testing, where HFE testing is listed as an approved test (Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY) (See also the Noridian J-E web page for Approved Gene Testing in CA and NV) (Search for HFE or 81256)* (Clinical documentation must demonstrate how test results will be used in the management or diagnosis of an illness or condition). National Government Services Inc. (NGS) LCD for Molecular Pathology Procedures (L35000) *(Laboratories in IL, MN, WI, CT, NY, ME, MA, NH, RI, VT) See the guideline specific to the gene or CPT code within the LCD. See also LCA A56199.*
HER2 Testing (includes DEPArray™ HER2)	81479, 0009U	Multiple	*See the Noridian J-F web page for Approved Gene Testing, where HER2 and ERBB2 testing are both listed as approved tests (Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY) (See also the Noridian J-E web page for Approved Gene Testing for CA and NV) (Search for HER2 or ERBB2 – apply coverage to both 81479 and 0009U)* (Clinical documentation must demonstrate how test results will be used in the management or diagnosis of an illness or condition).

HEXA Gene Analysis	81255, 81406	Multiple	MolDX: HEXA Gene Analysis Billing and Coding Guidelines (A55256) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: HEXA Gene Analysis Billing and Coding Guidelines (A55255) *(Laboratories in CA and NV)*
Human Leukocyte Antigen (HLA) Tests	Human Leukocyte Antigen (HLA) typing is commonly performed to assess compatibility of recipients and potential donors as a part of solid organ and hematopoietic stem cell/ bone marrow pretransplant testing. HLA testing is also performed to identify HLA alleles and allele groups (antigen equivalents) associated with specific diseases and individualized responses to drug therapy. See individual gene variant below (i.e., HLA-B*15:02, HLA-B*57:01, etc)		
Human Leukocyte Antigen (HLA) Typing	81370, 81371, 81372, 81373, 81374, 81375, 81376, 81377, 81378, 81379, 81380, 81381, 81382, 81383	Multiple	*See the Noridian J-F web page for Approved Gene Testing, where this testing is listed as an approved test (Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY) (See also the Noridian J-E web page for Approved Gene Testing for CA and NV) (Search for CPT code in question)* (Clinical documentation must demonstrate how test results will be used in the management or diagnosis of an illness or condition). Molecular Pathology Procedures for Human Leukocyte Antigen (HLA) Typing (L34518) *(Laboratories in FL)*
HLA-B*15:02	81381	Multiple	MolDX: HLA-B*15:02 Genetic Testing (L36149) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: HLA-B*15:02 Genetic Testing (L36145) *(Laboratories in CA and NV)*
HLA-B*5701 Testing	81381	Multiple	*See the Noridian J-F web page for Approved Gene Testing, where this testing is listed as an approved test (Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY) (See also the Noridian J-E web page for Approved Gene Testing for CA and NV) (Search for CPT code in question)* (Clinical documentation must demonstrate how

			test results will be used in the management or diagnosis of an illness or condition).
HLA-DQB1*06:02 Testing	81383	Multiple	For **narcolepsy**: ✓ MolDX: HLA-DQB1*06:02 Testing for Narcolepsy (L36544) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* ✓ MolDX: HLA-DQB1*06:02 Testing for Narcolepsy (L36551) *(Laboratories in CA and NV)* For **all other indications**: ✓ *See the Noridian J-F web page for Approved Gene Testing, where this testing is listed as an approved test (Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY) (See also the Noridian J-E web page for Approved Gene Testing for CA and NV) (Search for CPT code in question)* (Clinical documentation must demonstrate how test results will be used in the management or diagnosis of an illness or condition)
HTTLPR Gene Testing *(aka, HTT; 5HTT; OCD1; SERT; 5-HTT; SERT1; hSERT; 5-HTTLPR; or SLC6A4)*	81479	Multiple	MolDX: HTTLPR Gene Testing Coding and Billing Guidelines (A53480) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY, CA, NV) (Published by Palmetto GBA, for laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY, CA, and NV)*) See also the following: ✓ LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY) (Search by alternative names, such as SLC6A4)* ✓ LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV) (Search by alternative names, such as SLC6A4)*
HTT (Huntington Disease, or HD) Gene Testing	81271, 81274	Multiple	LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY) (Previously reported with 81401. Noncoverage of this test remains*

			in place regardless of CPT code used until either MolDX or Noridian indicate coverage is available. Medical necessity is not determined by an assigned CPT code.) LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV) (Previously reported with 81401 or 81405. Noncoverage of this test remains in place regardless of CPT code used until either MolDX or Noridian indicate coverage is available. Medical necessity is not determined by an assigned CPT code.)*
IDH1/IDH2 Gene Tests	81120, 81121	Multiple	*See the Noridian J-F web page for Approved Gene Testing, where IDH1 and IDH2 tests are listed as an approved test (Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY) (See also the Noridian J-E web page for Approved Gene Testing for CA and NV) (Search for CPT code and or gene in question. If a gene is listed as "approved" but with a more recent Tier 1 code, the coverage rationale still applies until a more specific coverage policy by MolDX or Noridian is available.)* (Clinical documentation must demonstrate how test results will be used in the management or diagnosis of an illness or condition). See also the guideline for "Abbott RealTime IDH2" testing above, if the request is specifically for this test.
IKBKAP Genetic Testing	81260	Multiple	MolDX: IKBKAP Genetic Testing Billing and Coding Guidelines (A55613) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: IKBKAP Genetic Testing Billing and Coding Guidelines (A55612) *(Laboratories in CA and NV)*
JAK2 Testing	81270, 81403, 0027U	Multiple	For **myeloproliferative disease**: ✓ See guideline for "BCR-ABL Negative Myeloproliferative Disease Testing"

			For JAK2 **single gene testing for all other indications**: ✓ *See the Noridian J-F web page for Approved Gene Testing, where JAK2 testing is listed as an approved test (Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY) (See also the Noridian J-E web page for Approved Gene Testing for CA and NV) (Search for JAK2)* (includes JAK2 Mutation by the University of Iowa, 0017U) (Clinical documentation must demonstrate how test results will be used in the management or diagnosis of an illness or condition) ✓ For JAK2 testing by the Mayo Clinic, see JAK2 testing criteria in LCD L35000 *(Laboratories in MN)*, or LCD L34519 *(Laboratories in FL)* **Note:** This gene is frequently tested as part of a genetic panel test. Therefore, view the health plan's medical policy for panel testing (see Cross References) to verify the correct Medicare coverage reference is used.
KIF6 Genotype	81479	Multiple	MolDX: KIF6 Genotype Billing and Coding Guidelines (A53576) *(Published by Palmetto GBA, for laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY, CA, NV)* See also the following: ✓ LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY) (Search by KIF6)* ✓ LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(For testing performed in California) (Search by KIF6)*
know error® DNA Specimen Provenance Assay	84999	Strand Diagnostics, Indianapolis, IN	*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..." The ***know error® system*** is a test performed

			to confirm a surgical biopsy sample belongs to the patient evaluated for treatment. Test results measure the quality of a process, rather than providing information to diagnose or treat a patient. Therefore, this test is not medically necessary based on Medicare guidelines. Wisconsin Physician Services (WPS) LCA for MolDX: know error® Billing and Coding Guidelines Update (A55172) (Published by WPS, for laboratories located in IN). *(See also the "Specimen Validity Testing" guideline below)*
KRAS Testing	81275	Multiple	MolDX: FDA-Approved KRAS Tests (A54500) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: FDA-Approved KRAS Tests (A54498) *(Laboratories in CA and NV)* *NOTE: The above guidelines for* KRAS tests *states: "This article reflects the FDA-approved indications on article creation date. MolDX will allow future FDA approved and amended indications for these tests." Therefore, as new FDA-approved medications and companion diagnostics (CDx) tests become available, more KRAS tests may be allowed than what are indicated in the LCA. To view FDA-approved KRAS tests and their corresponding medications, see the FDA web page for* List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools)*)*
L1CAM Gene Sequencing	81407	Multiple	MolDX: L1CAM Gene Sequencing Billing and Coding Guidelines (A55278) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: L1CAM Gene Sequencing Billing and Coding Guidelines (A55277) *(Laboratories in CA and NV)*

LPA-Aspirin Genotype	81479	Multiple	MolDX: LPA-Aspirin Genotype Coding and Billing Guidelines (A53467) *(Published by Palmetto GBA, for laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY, CA, and NV)*)
LPA-Intron 25 Genotype	81479	Multiple	MolDX: LPA-Intron 25 Genotype Coding and Billing Guidelines (A53468) *(Published by Palmetto GBA, for laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY, CA, NV)*)
Lyme ImmunoBlots IgM and IgG tests	0041U, 0042U	IgeneX	• The MolDX Program requires labs to submit a technology assessment (TA) to provide evidence of analytical and clinical validity (AV/CV), and clinical utility (CU). *(Noridian LCA A54552)* • The Noridian LCD L35160 states reimbursement is only allowed for "approved tests… for dates of service consistent with the effective date of the coverage determination" after MolDX review. • If a test does not have a coverage determination, then coverage is not allowed because evidence of clinical validity or utility has not been established via the TA review process. • This test is not considered medically reasonable and necessary under SSA §1862(a)(1)(A) until a MolDX review is complete and coverage is indicated by MolDX or Noridian.
Lynch Syndrome (MLH1, MSH2, MSH6, PMS2 and EPCAM single gene tests only)	81210, 81288, 81292, 81293, 81294, 81295, 81296, 81297, 81298, 81299, 81300, 81301, 81317, 81318, 81319, 81403, 81479	Multiple	MolDX: Genetic Testing for Lynch Syndrome (L36374) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY) (Note the following statement: "For coverage, the treating physician/pathologist is expected to follow the stepped approach outlined for LS screening and targeted MMR testing in this policy.")* MolDX: Genetic Testing for Lynch Syndrome (L36370) *(Laboratories in CA and NV) (Note the following statement: "For coverage, the treating physician/pathologist is expected to follow the stepped approach outlined for LS screening and targeted MMR testing in this policy.")* Genetic Testing for Lynch Syndrome *(*L34912*) (Laboratories in FL)*

MCOLN1 Genetic Testing	81290	Multiple	MolDX: MCOLN1 Genetic Testing Billing and Coding Guidelines (A55284) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: MCOLN1 Genetic Testing Billing and Coding Guidelines (A55283) *(Laboratories in CA and NV)*
MECP2 Genetic Testing	81302, 81303, 81304, 81479	Multiple	MolDX: MECP2 Genetic Testing Billing and Coding Guidelines (A55286) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)*
MGMT Gene Promoter	81287	Multiple	MolDX: MGMT Promoter Methylation Analysis (L36192) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: MGMT Promoter Methylation Analysis *(*L36188*)* *(Laboratories in CA and NV)*
miR-31now™	0069U	GoPath Laboratories	National Government Services Inc. (NGS) LCD for Molecular Pathology Procedures (L35000) *(Applies to the indicated laboratory)* (NGS is the Medicare contractor assigned jurisdiction over this laboratories service area. While the LCD does not specifically call out this test by name or by code, coverage may be available for this test if the clinical documentation demonstrates how test results will be used in the management or diagnosis of an illness or condition. According to the LCD L35000, under "Indications," diagnostic genetic testing should only be performed once per lifetime. Therefore, if the member has received genetic testing for colorectal cancer in the past, there must be documentation of why there is a need for repeat testing [pre- or post-therapy testing to determine member response to therapy, etc.]).
MMACHC Testing	81404	Multiple	MolDX: MMACHC Test Coding and Billing Guidelines (A55289) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)*

			MolDX: MMACHC Genetic Testing Billing and Coding Guidelines (A55288) *(Laboratories in CA and NV)*
MPL (Myeloproliferative Leukemia Virus Oncogene) Gene Tests	81402, 81479	Multiple	For full gene sequence testing (CPT 81479): ✓ LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* ✓ LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV)* For ***myeloproliferative disease***: ✓ See guideline for "BCR-ABL Negative Myeloproliferative Disease Testing"
MRDx BCR-ABL Test	0040U	MolecularMD	MolDX: Genetic Testing for BCR-ABL Negative Myeloproliferative Disease (L36180) *(Applies to the indicated laboratory)* **Note:** As with other BCR-ABL single gene tests, the Palmetto LCA A53531 includes PLA code 0040U as another code for reporting a specific BCR-ABL test. With respect to coverage criteria, if a treating physician suspects a patient has myeloproliferative neoplasms (MPN) or myelodysplastic syndromes (MDS), it would be clinically appropriate to test BCR-ABL. No specific criteria are provided for this gene directly as this is considered "step one" in the noted LCDs. The MRDx® BCR-ABL test was FDA approved as "a companion diagnostic for Chronic Myeloid Leukemia (CML) patients in the chronic phase (CP) being treated with Tasigna® who may be candidates for treatment discontinuation and monitoring of treatment-free remission (TFR)." Therefore, when used for this FDA-approved purpose, this test would be considered medically necessary. *NOTE: MolDX guidelines for other FDA-approved companion diagnostic (CDx) tests state MolDX approval may be allowed for the tests available and approved at that time, but that coverage may also be allowed for future FDA approved and amended indications for these tests. Therefore, as new FDA-approved medications and CDx tests become available, additional testing may also be allowed.*

			To view the FDA-approved MRDx BCR-ABL test and its corresponding medications, see the FDA web page for List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools)*)*
MUTYH Gene Tests			See guideline for "Familial Adenomatous Polyposis (FAP) (includes Attenuated FAP [AFAP]) (APC gene testing) and MUTYH-Associated Polyposis (MAP) (formerly MYH-associated polyposis) (MUTYH gene testing)" testing above
myPAP™ DNA test	84999	Multiple	MolDX: myPap™ Billing and Coding Guidelines (A55293) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: myPap™ Billing and Coding Guidelines (A55292) *(Laboratories in CA and NV)*
NPM1 Gene Testing	81310, 0049U	Multiple (for single gene testing) *NPM1 MRD by NGS by LabPMM LLC*	*See the Noridian J-F web page for Approved Gene Testing, where NPM1 testing in listed as an approved test (Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY) (See also the Noridian J-E web page for Approved Gene Testing for CA and NV.) (Search for NPM1)* (Clinical documentation must demonstrate how test results will be used in the management or diagnosis of an illness or condition). *NOTE: MolDX guidelines for other FDA-approved companion diagnostic (CDx) tests state MolDX approval may be allowed for the tests available and approved at that time, but that coverage may also be allowed for future FDA approved and amended indications for these tests. Therefore, as new FDA-approved medications and CDx tests become available, additional NPM1 testing may also be allowed. To view FDA-approved NPM1 tests and their corresponding medications, see the FDA web page for* List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools)*)*
NRAS Gene Testing	81311, 81479	Multiple	MolDX: NRAS Genetic Testing (L36339) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)*

			MolDX: NRAS Genetic Testing (L36335) *(Laboratories in CA and NV)*
NSD1 Gene Tests	81403, 81405, 81406	Multiple	MolDX: NSD1 Gene Tests Billing and Coding Guidelines (A55615) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: NSD1 Gene Tests Billing and Coding Guidelines (A55609) *(Laboratories in CA and NV)*
PALB2 Gene Testing	81406 *(full gene sequencing)*, 0137U	Multiple	LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV)* **Note:** As an add-on code for *PALB2* full gene sequencing testing, +RNAinsight™ for *PALB2* by Ambry Genetics (0137U) is also non-covered if performed.
PathFinderTG®	81479	RedPath Integrated Pathology, Pittsburgh, PA	Loss-of-Heterozygosity Based Topographic Genotyping with PathfinderTG® (L34864)[18] (Published by Novitas, and applies to the indicated laboratory)
PAX6 Gene Sequencing	81479	Multiple	MolDX: PAX6 Gene Sequencing Billing and Coding Guidelines (A55632) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: PAX6 Gene Sequencing Billing and Coding Guidelines (A55625) *(Laboratories in CA and NV)*
PIK3CA	81404	Multiple	MolDX: PIK3CA Gene Tests Billing and Coding Guidelines (A55602) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: PIK3CA Gene Tests Billing and Coding Guidelines (A55597) *(Laboratories in CA and NV)*
PolypDX™	0002U	Multiple	Biomarkers for Oncology (L35396)[17] (Published by Novitas, and applies to all labs) *(Search for 0002U)*

PTCH1 Gene Testing	81479	Multiple	MolDX: PTCH1 Gene Testing Billing and Coding Guidelines (A55618) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: PTCH1 Gene Testing Billing and Coding Guidelines (A55608 *for laboratories located in California)*
RBC Phenotyping, molecular	81403, 0001U	Multiple	MolDX: Molecular RBC Phenotyping (L36171) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* *(See also the Noridian LCD* L36167 *(Laboratories in CA and NV)*
Real-time quaking-induced conversion for prion detection (RT-QuIC)	0035U	*National Prion Disease Pathology Surveillance Center*	• The MolDX Program requires labs to submit a technology assessment (TA) to provide evidence of analytical and clinical validity (AV/CV), and clinical utility (CU). *(Noridian LCA A54552)* • The Noridian LCD L35160 states reimbursement is only allowed for "approved tests… for dates of service consistent with the effective date of the coverage determination" after MolDX review. • If a test does not have a coverage determination, then coverage is not allowed because evidence of clinical validity or utility has not been established via the TA review process. • This test is not considered medically reasonable and necessary under SSA §1862(a)(1)(A) until a MolDX review is complete and coverage is indicated by MolDX or Noridian.
RPS19 Gene Tests	81403, 81405	Multiple	MolDX: RPS19 Gene Tests Billing and Coding Guidelines (A55614) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: RPS19 Gene Tests Billing and Coding Guidelines (A55610) *(Laboratories in CA and NV)*
Screening DNA (Deoxyribonucleic acid) stool tests • ***ColoSure™*** • ***PreGen-Plus™***	81479	Multiple, including OncoMethylome for ColoSure™ and LabCorp for PreGen-Plus™	NCD for Colorectal Cancer Screening Tests (210.3) *For Cologuard™ (Exact Sciences Laboratories), see Cross References for other genetic testing policies*

SEPT9 Gene Test	81327	Multiple	MolDX: SEPT9 Gene Test Billing and Coding Guidelines (A55628) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: SEPT9 Gene Test Billing and Coding Guidelines (A55623) *(Laboratories in CA and NV)*
Short Tandem Repeat (STR) Markers	81265, 81266, 81267, 81268	Multiple	Short Tandem Repeat (STR) Markers and Chimerism (codes 81265-81268) Coding and Billing Guidelines (A54832) *(Published by Palmetto GBA, for laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY, CA, NV)*)
SLCO1B1 Genotype	81400	Multiple	MolDX: SLCO1B1 Genotype Billing and Coding Guidelines (A55630) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: SLCO1B1 Genotype Billing and Coding Guidelines (A55626) *(Laboratories in CA and NV)*
SMPD1 Genetic Testing	81330, 81403	Multiple	MolDX: SMPD1 Genetic Testing Billing and Coding Guidelines (A55631) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: SMPD1 Genetic Testing Billing and Coding Guidelines (A55627) *(Laboratories in CA and NV)*
Specimen Validity Testing Example: ToxLok	81479, 84999, 0079U	Multiple, including InSource Diagnostics and Agena Bioscience, Inc. for ToxLox	Controlled Substance Monitoring and Drugs of Abuse Testing (L36668) *(Laboratories in CA, such as ToxLok, 0079U) (In the "Non-Covered Services" section, see the guidance specific to specimen validity testing)* **For specimen validity testing in general**: *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..." *(See also Medicare Benefit Policy Manual, Chapter 16 - General Exclusions From Coverage, §20 - Services*

			Not Reasonable and Necessary). Specimen validity tests (i.e., tests performed to confirm a surgical biopsy sample belongs to the patient evaluated for treatment, or tests that measure the quality of a process) are not medically necessary based on Medicare guidelines because they do not provide information to diagnose or treat a patient or condition. *(Applies to all laboratories, regardless of location)*
STAT3 Gene Testing	81405	Multiple	MolDX: STAT3 Gene Testing Billing and Coding Guidelines (A55481) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: STAT3 Gene Testing Billing and Coding Guidelines (A55480) *(Laboratories in CA and NV)*
SULT4A1 Genetic Testing	81479	Multiple	MolDX: SULT4A1 Genetic Testing Billing and Coding Guidelines (A55601) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: SULT4A1 Genetic Testing Billing and Coding Guidelines (A55596) *(Laboratories in CA and NV)*
TERC Gene Tests	81479	Multiple	MolDX: TERC Gene Tests Billing and Coding Guidelines (A55616) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: TERC Gene Tests Billing and Coding Guidelines (A55611) *(Laboratories in CA and NV)*
therascreen® EGFR RGQ PCR Kit			See guideline for "EGFR" testing above
therascreen® KRAS PCR Kit			See guideline for "KRAS" testing above
Thrombophilia and/or Hypercoagulability Genetic Testing (F5, F2, F9, and/or MTHFR genes)	81238, 81240, 81241, 81291, 81403, 81405	Multiple	For **hypercoagulability / thrombophilia testing, *except for F9 testing***: ✓ MolDX: Genetic Testing for Hypercoagulability / Thrombophilia (Factor V Leiden, Factor II Prothrombin, and

MTHFR) (L36159) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)*

- ✓ MolDX: Genetic Testing for Hypercoagulability / Thrombophilia (Factor V Leiden, Factor II Prothrombin, and MTHFR) (L36155) *(Laboratories in CA and NV)*
- ✓ *See the statement that reads, "Genetic testing for these genes for all risk factors, signs, symptoms, diseases, or conditions, including cardiovascular risk assessment, are non-covered except for pregnant patients."*

For **cardiovascular risk assessment*, except for F9 testing***:

- ✓ MolDX: Biomarkers in Cardiovascular Risk Assessment (L36362) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)*
- ✓ MolDX: Biomarkers in Cardiovascular Risk Assessment (L36358) for *(Laboratories in CA and NV)*
  - o *See the "Gene Mutations (any methodology) and Genomic Profiling" section of each LCD for MTHFR, F2, and F5 genes*
- ✓ National Government Services Inc. (NGS) LCD for Molecular Pathology Procedures (L35000) *(Laboratories in IL, MN, WI, CT, NY, ME, MA, NH, RI, VT) See the guideline specific to the gene or CPT code within the LCD.*

For **F9 (coagulation factor IX) testing**:

- ✓ LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)*
- ✓ LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV)*

			✓ National Government Services Inc. (NGS) LCD for Molecular Pathology Procedures (L35000) *(Laboratories in IL, MN, WI, CT, NY, ME, MA, NH, RI, VT*
ThxID™ BRAF V600/K			See guideline for "BRAF" testing above
Tick-Borne Relapsing Fever Borrelia (TBRF) ImmunoBlots IgM and IgG tests	0043U, 0044U	*IgeneX*	• The MolDX Program requires labs to submit a technology assessment (TA) to provide evidence of analytical and clinical validity (AV/CV), and clinical utility (CU). *(Noridian LCA A54552)* • The Noridian LCD L35160 states reimbursement is only allowed for "approved tests… for dates of service consistent with the effective date of the coverage determination" after MolDX review. • If a test does not have a coverage determination, then coverage is not allowed because evidence of clinical validity or utility has not been established via the TA review process. • This test is not considered medically reasonable and necessary under SSA §1862(a)(1)(A) until a MolDX review is complete and coverage is indicated by MolDX or Noridian.
TP53 Gene Test	81404, 81405	Multiple	MolDX: TP53 Gene Test Billing and Coding Guidelines (A55487) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: TP53 Gene Test Billing and Coding Guidelines (A55484) *(Laboratories in CA and NV)*
TPMT Gene Testing	81335, 81401	Multiple	*See the Noridian J-F web page for Approved Gene Testing, where TPMT testing in listed as an approved test (Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY) (See also the Noridian J-E web page for Approved Gene Testing for CA and NV.) (Search for TPMT, and* apply guideline to either 81401 or 81335) (Clinical documentation must demonstrate how test results will be used in the management or diagnosis of an illness or condition)
Transthyretin (TTR) Amyloidosis Gene Testing	81403, 81404	Multiple	LCD attachment for L36256, Excluded Test List – as of 08/01/2016 *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* LCD attachment for L35160, Excluded Test List – as of 08/01/2016 *(Laboratories in CA and NV)*

Twins Zygosity PLA	0060U	Natera, Inc.	*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..." *(See also Medicare Benefit Policy Manual, Chapter 16 - General Exclusions From Coverage, §20 - Services Not Reasonable and Necessary).* A test to determine twin zygosity (identical vs. fraternal twin) does not treat or diagnose an illness. Therefore, this test is not medically reasonable or necessary under Medicare.*(See also similar non-coverage language for twin zygosity testing in the MolDX LCA A54832 for short tandem repeat (STR) and chimerism testing above.)*
TYMS Gene Analysis			See Medicare Advantage medical policy for *Laboratory and Genetic Testing for Use of 5-Fluorouracil (5-FU) in Patients with Cancer*, Laboratory, Policy No. M-64 (see Cross References)
UGT1A1 Gene Analysis	81350	Multiple	MolDX: UGT1A1 Gene Analysis Billing and Coding Guidelines (A55483) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: UGT1A1 Gene Analysis Billing and Coding Guidelines (A55482) *(Laboratories in CA and NV)*
UroVysion Bladder Kit			See guideline for "Bladder Tumor Marker FISH" above
VEGFR2 Tests	81479	Multiple	MolDX: VEGFR2 Tests Billing and Coding Guidelines (A55469) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: VEGFR2 Tests Billing and Coding Guidelines (A55468) *(Laboratories in CA and NV)*
VKORC1	81355, G9143	Multiple	MolDX: CYP2C19, CYP2D6, CYP2C9, and VKORC1 Genetic Testing (L36312) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY)* MolDX: CYP2C19, CYP2D6, CYP2C9, and VKORC1 Genetic Testing (L36310) *(Laboratories in CA and NV)*

			CYP2C19, CYP2D6, CYP2C9, and VKORC1 Genetic Testing (L35698) *(Laboratories in FL)* *(See also "**Warfarin Response Testing"** guidelines below)*
Vysis ALK Break Apart Fish Probe Kit (Abbot)			See guideline for "ALK Gene Tests" above
Ventana ALK (D5F3) CDx Assay (Ventana Medical Systems)			See guideline for "ALK Gene Tests" above
Warfarin Response Testing • ***CYP2C9*** • ***VKORC1***	81227, 81355, G9143	Multiple	Pharmacogenomic Testing for Warfarin Response (90.1) *(All laboratories)* *(See also separate rows for CYP2C9 and VKORC1 testing, where LCD L36312 or L36310 are applied.) (laboratories in CA and NV)*
Xpresys Lung® and Xpresys Lung 2® (XL2, or BDX-XL2)	81599, 0080U	Integrated Diagnostics, Inc. (aka Indi®) (Seattle, WA)	MolDX: Xpresys Lung (L37062) *(Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY) (Note, coverage outlined in this LCD is limited to only XL2. The clinical utility for the earlier version of Xpresys Lung® is not noted as demonstrated in the same way XL2 has been demonstrated. Therefore, Xpresys Lung® is not considered medically necessary. Only XL2 is eligible for coverage.)*
YouScript Plavix *The YouScript Plavix test analyzes only the CYP2C19 gene*	81225	Genelex, Seattle, WA	MolDX: CYP2C19, CYP2D6, CYP2C9, and VKORC1 Genetic Testing (L36312) *(Applies to the indicated laboratory)*
**Scroll to the "All Versions" section at the bottom of the LCD or LCA to access prior versions.			

POLICY GUIDELINES

Important Notes Regarding Diagnostic Laboratory and Genetic Testing Services

Medicare and Medical Necessity

According to Medicare guidelines, Medicare coverage is contingent upon the services meeting certain requirements to determine medical necessity. In order to be considered a covered service, Medicare requires that the service in question:

- Fall within a defined Medicare benefit category,[2,3]
- Not be excluded from coverage by statute, regulation, National Coverage Determination, (NCD), or Local Coverage Determination (LCD)[3]
- Be considered medically necessary, as required per the Social Security Act, §1862(a)(1)(A). This means the service must be considered reasonable and necessary in the diagnosis or treatment of an illness or injury, or to rule out or confirm a suspected diagnosis because the patient has a sign and/or symptoms.[4,5] This also means services that are determined to be **not** medically necessary for any reason (including lack of safety and efficacy because it is an investigational service) are non-covered.[6]
- Be ordered by a physician who is treating the beneficiary;[7,8]
- Provide data that would be directly used in the management of a beneficiary's specific medical problem.[7,8]

"In order to be paid under this benefit category, a diagnostic test must be ordered by a physician who is treating the beneficiary and the results used in the management of a beneficiary's specific medical problem. Although many molecular diagnostic tests may provide valid and useful information, they do not meet this definition."[12]

Services excluded from coverage

Tests performed in the absence of signs, symptoms, complaints, personal history of disease, or injury are not covered, except when there is a statutory provision that explicitly covers a specific screening test. Tests that confirm a diagnosis or known information, and tests to determine risk for developing a disease or condition are also excluded test services.[9-12]

In addition, specimen validity testing to ensure a specimen has not been compromised or tests performed to measure the quality of a process are also non-covered by Medicare because they do not provide information to diagnose or treat a patient and therefore, are "not reasonable and necessary for the diagnosis and treatment of illness or injury."

Molecular Diagnostic Services Program (MolDX)

The Medicare Molecular Diagnostic Services Program (MolDX) was developed in 2011 to identify and establish coverage and reimbursement for molecular diagnostic tests, and is maintained by Palmetto GBA. Palmetto evaluates genetic tests to determine analytical and clinical validity and clinical utility, as well as confirming that each test meets Medicare criteria (described below). Palmetto MolDX guidelines provide assessments and indicate coverage or non-coverage of each test.[13,14]

Some Medicare contractors have adopted the MolDX program guidelines for their services areas. The MolDX program covers the following Medicare Jurisdictions[13]:

- JE A/B MAC, which covers California, Nevada, Hawaii and the US Pacific Territories of Guam, American Samoa and the Northern Marianas, administered by Noridian Healthcare Solutions
- JF A/B MAC, which covers Oregon, Washington, Idaho, Utah, Montana, Wyoming, Nevada, Arizona, North Dakota, South Dakota, Alaska, and the Aleutian Islands, administered by Noridian Healthcare Solutions
- JM A/B MAC, which covers North Carolina, South Carolina, Virginia, and West Virginia, administered by Palmetto GBA
- J5 A/B MAC, which covers Iowa, Kansas, Missouri, and Nebraska, administered by WPS Government Health Administrators
- J8 A/B MAC, which covers Michigan and Indiana, administered by WPS Government Health Administrators
- J15 A/B MAC, which covers Ohio and Kentucky, administered by CGS Administrators, LLC
- JJ A/B MAC, which covers Alabama, Georgia, and Tennessee, administered by Palmetto GBA

Table 2: MolDX Program and Medicare Jurisdictions Back to Criteria

Medicare jurisdictions which have adopted the MolDX Program are indicated below (MolDX site). If the performing laboratory is not located in one of the marked states, MolDX guidelines should not apply. Other Medicare guidance may be available.

STATE	MolDX?	STATE	MolDX?	STATE	MolDX?
Alabama	X	Alaska	X	Arizona	X
Arkansas		California	X	Colorado	
Connecticut		Delaware		Florida	
Georgia	X	Hawaii	X	Idaho	X
Illinois		Indiana	X	Iowa	X
Kansas	X	Kentucky	X	Louisiana	
Maine		Maryland		Massachusetts	
Michigan	X	Minnesota		Mississippi	

Missouri	X	Montana	X	Nebraska	X
Nevada	X	New Hampshire		New Jersey	
New Mexico		New York		North Carolina	X
North Dakota	X	Ohio	X	Oklahoma	
Oregon	X	Pennsylvania		Rhode Island	
South Carolina	X	South Dakota	X	Tennessee	X
Texas		Utah	X	Vermont	
Virginia	X	Washington	X	West Virginia	X
Wisconsin		Wyoming			

For testing performed by a laboratory outside of the MAO's service area

"A MAC outside of the plan's service area sometimes has exclusive jurisdiction over a Medicare covered item or service. In some instances, one Medicare A/B MAC processes all of the claims for a particular Medicare-covered item or service for all Medicare beneficiaries around the country. This generally occurs when there is only one supplier of a particular item, medical device or diagnostic test (for example; certain pathology and lab tests furnished by independent laboratories). In this situation, MA plans must follow the coverage requirements or LCD of the MAC that enrolled the supplier and processes all of the Medicare claims for that item, test or service."(15)

In addition, "Jurisdiction of claims for laboratory services furnished by an independent laboratory normally lies with the carrier serving the area in which the laboratory test is performed. However, there are some situations where a regional or national lab chain jurisdiction is with a single carrier."(16)

Table 3: States and Medicare Contractor (MAC) Jurisdictions	Back to Criteria
If the genetic test is performed in this state….	**The MAC for the service area is…**
Alaska, Arizona, Idaho, Montana, North Dakota, Oregon, South Dakota, Washington, Utah, Wyoming	Noridian Healthcare Solutions, LLC (J-F)
California, Hawaii, Nevada, American Samoa, Guam, Northern Mariana Islands	Noridian Healthcare Solutions, LLC (J-E)
Alabama, Georgia, North Carolina, South Carolina, Tennessee, Virginia, West Virginia	Palmetto GBA *(this is also the MolDX Program Contractor)*
Iowa, Indiana, Kansas, Michigan, Missouri, Nebraska	Wisconsin Physicians Service Insurance Corporation (WPS)

If the genetic test is performed in this state….	The MAC for the service area is…
Kentucky, Ohio	CGS Administrators, LLC
Connecticut, Illinois, Maine, Massachusetts, Minnesota, New Hampshire, New York, Rhode Island, Vermont, Wisconsin	National Government Services, Inc.
Arkansas, Colorado, Washington DC, Texas, Delaware, Louisiana, Maryland, Mississippi, New Jersey, New Mexico, Oklahoma, Pennsylvania	Novitas Solutions, Inc.
Florida, Puerto Rico, Virgin Islands	First Coast Service Options, Inc.

REQUIRED DOCUMENTATION

The information below **must** be submitted for review to determine whether policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome:

The following information is required in order to determine medical necessity and potential Medicare coverage for a genetic or molecular diagnostic test. *[See Title XVIII of the Social Security Act, §1833(e), which states no payment may be made unless information necessary to determine payment has been submitted)]*

1. The specific name of the genetic or molecular diagnostic test;
2. Name of the performing laboratory;
3. The exact gene(s) and/or variants being tested:
4. Applicable CPT and/or HCPCS code(s)
5. Brief explanation of how the results of genetic testing are necessary to guide treatment decisions relevant to the member's personal medical history. Tests performed for the following purposes are a few examples:
   - Diagnose an illness when signs/symptoms are displayed; or,
   - Rule out a diagnosis when signs/symptoms are displayed; or
   - Guide treatment planning for a previously diagnosed illness (i.e., whether to perform surgery, determine chemotherapy treatment, choose between medication options, etc.).
6. Medical records relevant to the testing being performed. This includes:
   - History and physical examinations by the referring physician,
   - Conventional testing and outcomes, and
   - Conservative treatment provided, if applicable.

CROSS REFERENCES

Genetic and Molecular Diagnostics – Next Generation Sequencing and Genetic Panel Testing, Genetic Testing, Policy No. M-64

Chemoresistance and Chemosensitivity Assays (CSRAs), Laboratory, Policy No. M-06

Laboratory and Genetic Testing for Use of 5-Fluorouracil (5-FU) in Patients with Cancer, Laboratory, Policy No. M-64

REFERENCES

1. den Dunnen, JT, Dalgleish, R, Maglott, DR, et al. HGVS Recommendations for the Description of Sequence Variants: 2016 Update. Human mutation. 2016 Jun;37(6):564-9. PMID: 26931183
2. Medicare Coverage Determination Process
3. Medicare Managed Care Manual, Ch. 4 - Benefits and Beneficiary Protections, §10.2 - Basic Rule
4. Title XVIII of the Social Security Act, §1862(a)(1)(A)
5. Medicare Benefit Policy Manual, Chapter 16 - General Exclusions From Coverage, §20 - Services Not Reasonable and Necessary
6. Medicare Claims Processing Manual, Chapter 23 - Fee Schedule Administration and Coding Requirements, §30 - Services Paid Under the Medicare Physician's Fee Schedule, Subsection A
7. 42 CFR §410.32(a)
8. Medicare Benefit Policy Manual, Ch. 15 – Covered Medical and Other Health Services, §80.1 - Clinical Laboratory Services
9. Federal Register / Vol. 66, No. 226 / Friday, November 23, 2001
10. Medicare Claims Processing Manual, Chapter 16 – Laboratory Services, §120.1, Negotiated Rulemaking Implementation*(See section regarding "Clarification of the Use of the Term 'Screening' or 'Screen'")*
11. Medicare National Coverage Determinations (NCD) Coding Policy Manual and Change Report January 2013
12. Palmetto GBA MolDX: Excluded Tests (M00105, V2)
13. Palmetto GBA MolDX: Molecular Diagnostic Services Program (M00103, V5)
14. Noridian Healthcare Solutions Jurisdiction F (J-F) and MolDX
15. Medicare Managed Care Manual, Ch. 4 - Benefits and Beneficiary Protections, §90.4.1 - MACS with Exclusive Jurisdiction over a Medicare Item or Service
16. Medicare Claims Processing Manual, Chapter 1 - General Billing Requirements, §10.1.5.4 - Independent Laboratories
17. Palmetto GBA MolDX: Molecular Test Panel Edit Alert (M00101)
18. Novitas LCA for Biomarkers for Oncology (A52986)
19. Retired Noridian LCA for Molecular Genetic testing (A52932) (Scroll to the "Public Version(s)" section at the bottom of the LCD for links to prior versions if necessary.)

CODING

NOTE: The newly added (2013) CPT® codes for molecular genetic testing are often non-specific as evidenced by the CPT range 81400-81408. Many of the tests listed for these codes are not covered by Medicare. In order to properly adjudicate claims for molecular genetic testing, the actual test name being performed must be included in the narrative section of the claim.[19]

In addition, HCPCS S-codes are not payable by Medicare, and therefore, are not payable for the health plan's Medicare Advantage members.

Codes	Number	Description
CPT	81105	Human platelet antigen 1 genotyping (HPA-1), ITGB3 (integrin, beta 3 [platelet glycoprotein iiia], antigen CD61 [GPIIIA]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-1A/B (L33P)
	81106	Human platelet antigen 2 genotyping (HPA-2), GP1BA (glycoprotein ib [platelet], alpha polypeptide [GPIBA]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-2A/B (T145M)
	81107	Human platelet antigen 3 genotyping (HPA-3), ITGA2B (integrin, alpha 2b [platelet glycoprotein IIB of IIB/IIIA complex], antigen CD41 [GPIIB]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-3A/B (I843S)
	81108	Human platelet antigen 4 genotyping (HPA-4), ITGB3 (integrin, beta 3 [platelet glycoprotein IIIA], antigen CD61 [GPIIIA]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-4A/B (R143Q)
	81109	Human platelet antigen 5 genotyping (HPA-5), ITGA2 (integrin, alpha 2 [CD49B, alpha 2 subunit of VLA-2 receptor] [GPIA]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant (eg, HPA-5A/B (K505E))
	81110	Human platelet antigen 6 genotyping (HPA-6W), ITGB3 (integrin, beta 3 [platelet glycoprotein IIIA, antigen CD61] [GPIIIA]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-6A/B (R489Q)
	81111	Human platelet antigen 9 genotyping (HPA-9W), ITGA2B (integrin, alpha 2b [platelet glycoprotein IIB of IIB/IIIA complex, antigen CD41] [GPIIB]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-9A/B (V837M)
	81112	Human platelet antigen 15 genotyping (HPA-15), CD109 (CD109 molecule) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-15A/B (S682Y)
	81120	*IDH1 (isocitrate dehydrogenase 1 [NADP+], soluble) (eg, glioma)*, common variants (eg, R132H, R132C)
	81121	*IDH2 (isocitrate dehydrogenase 2 [NADP+], mitochondrial)* (eg, glioma), common variants (eg, R140W, R172M)
	81161	*DMD (dystrophin)* (e.g., Duchenne/Becker muscular dystrophy) deletion analysis and duplication analysis, if performed

81162	*BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated)* (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis (ie, detection of large gene rearrangements)
81163	*BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated)* (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81164	; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81165	*BRCA1 (BRCA1, DNA repair associated)* (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81166	; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81167	*BRCA2 (BRCA2, DNA repair associated)* (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81170	*ABL1 (ABL proto-oncogene 1, non-receptor tyrosine kinase)* (eg, acquired imatinib tyrosine kinase inhibitor resistance), gene analysis, variants in the kinase domain
81171	*AFF2 (AF4/FMR2 family, member 2 [FMR2])* (eg, fragile X mental retardation 2 [FRAXE]) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
81172	; characterization of alleles (eg, expanded size and methylation status)
81173	*AR (androgen receptor)* (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; full gene sequence
81174	; known familial variant
81175	*ASXL1 (additional sex combs like 1, transcriptional regulator)* (eg, myelodysplastic syndrome, myeloproliferative neoplasms, chronic myelomonocytic leukemia), gene analysis; full gene sequence
81176	; targeted sequence analysis (eg, exon 12)
81177	*ATN1 (atrophin 1)* (eg, dentatorubral-pallidoluysian atrophy) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81178	*ATXN1 (ataxin 1)* (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81179	*ATXN2 (ataxin 2)* (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81180	*ATXN3 (ataxin 3)* (eg, spinocerebellar ataxia, Machado-Joseph disease) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81181	*ATXN7 (ataxin 7)* (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81182	*ATXN8OS (ATXN8 opposite strand [non-protein coding])* (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81183	*ATXN10 (ataxin 10) (eg, spinocerebellar ataxia)* gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81184	*CACNA1A (calcium voltage-gated channel subunit alpha1 A)* (eg, spinocerebellar ataxia) gene analysis; evaluation to detect abnormal (eg, expanded) alleles

81185	*CACNA1A (calcium voltage-gated channel subunit alpha1 A)* (eg, spinocerebellar ataxia) gene analysis; full gene sequence
81186	*CACNA1A (calcium voltage-gated channel subunit alpha1 A)* (eg, spinocerebellar ataxia) gene analysis; known familial variant
81187	*CNBP (CCHC-type zinc finger nucleic acid binding protein)* (eg, myotonic dystrophy type 2) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81188	*CSTB (cystatin B) (eg, Unverricht-Lundborg disease)* gene analysis; evaluation to detect abnormal (eg, expanded) alleles
81189	*CSTB (cystatin B) (eg, Unverricht-Lundborg disease)* gene analysis; full gene sequence
81190	*CSTB (cystatin B) (eg, Unverricht-Lundborg disease)* gene analysis; known familial variant(s)
81200	*ASPA (aspartoacylase)* (eg, Canavan disease) gene analysis, common variants (eg, E285A, Y231X)
81201	*APC (adenomatous polyposis coli)* (eg, familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; full gene sequence
81202	; known familial variants
81203	; duplication/deletion variants
81204	*AR (androgen receptor)* (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; characterization of alleles (eg, expanded size or methylation status)
81205	*BCKDHB (branched-chain keto acid dehydrogenase E1, beta polypeptide)* (eg, maple syrup urine disease) gene analysis, common variants (eg, R183P, G278S, E422X)
81206	*BCR/ABL1 (t(9;22))* (eg, chronic myelogenous leukemia) translocation analysis; major breakpoint, qualitative or quantitative
81207	; minor breakpoint, qualitative or quantitative
81208	; other breakpoint, qualitative or quantitative
81209	*BLM (Bloom syndrome, RecQ helicase-like)* (eg, Bloom syndrome) gene analysis, 2281del6ins7 variant
81210	*BRAF (B-Raf proto-oncogene, serine/threonine kinase)* (eg, colon cancer, melanoma), gene analysis, V600E variant(s)
~~81211~~	~~*BRCA1, BRCA2 (breast cancer 1 and 2)* (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and common duplication/deletion variants in BRCA1 (ie, exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-20 del 26kb, exon 22 del 510bp, exon 8-9 del 7.1kb)~~ *(Code deleted 01/01/2019)*
81212	*BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; 185delAG, 5385insC, 6174delT variants*
~~81213~~	~~; uncommon duplication/deletion variants~~ *(Code deleted 01/01/2019)*
~~81214~~	~~*BRCA1 (breast cancer 1)* (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and common duplication/deletion variants (ie, exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-20 del 26kb, exon 22 del 510bp, exon 8-9 del 7.1kb)~~ *(Code deleted 01/01/2019)*

81215	*BRCA1 (BRCA1, DNA repair associated)* (eg, hereditary breast and ovarian cancer) gene analysis; known familial variant
81216	*BRCA2 (BRCA2, DNA repair associated)* (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81217	; known familial variant
81218	*CEBPA (CCAAT/enhancer binding protein [C/EBP], alpha)* (eg, acute myeloid leukemia), gene analysis, full gene sequence
81219	*CALR (calreticulin)* (eg, myeloproliferative disorders), gene analysis, common variants in exon 9
81220	*CFTR (cystic fibrosis transmembrane conductance regulator)* (eg, cystic fibrosis) gene analysis; common variants (eg, ACMG/ACOG guidelines)
81221	; known familial variants
81222	; duplication/deletion variants
81223	; full gene sequence
81224	; intron 8 poly-T analysis (eg, male infertility)
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)
81228	Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number variants (eg, bacterial artificial chromosome [BAC] or oligo-based comparative genomic hybridization [CGH] microarray analysis)
81229	; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants for chromosomal abnormalities
81230	*CYP3A4 (cytochrome P450 family 3 subfamily A member 4)* (eg, drug metabolism), gene analysis, common variant(s) (eg, *2, *22)
81231	*CYP3A5 (cytochrome P450 family 3 subfamily A member 5)* (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *5, *6, *7)
81233	*BTK (Bruton's tyrosine kinase)* (eg, chronic lymphocytic leukemia) gene analysis, common variants (eg, C481S, C481R, C481F)
81234	*DMPK (DM1 protein kinase)* (eg, myotonic dystrophy type 1) gene analysis; evaluation to detect abnormal (expanded) alleles
81235	*EGFR (epidermal growth factor receptor)* (eg, non-small cell lung cancer) gene analysis, common variants (eg, exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q)
81236	*EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit)* (eg, myelodysplastic syndrome, myeloproliferative neoplasms) gene analysis, full gene sequence
81237	*EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit)* (eg, diffuse large B-cell lymphoma) gene analysis, common variant(s) (eg, codon 646)
81238	*F9 (coagulation factor IX)* (eg, hemophilia B), full gene sequence

81239	*DMPK (DM1 protein kinase)* (eg, myotonic dystrophy type 1) gene analysis; characterization of alleles (eg, expanded size)
81240	*F2 (prothrombin, coagulation factor II)* (eg, hereditary hypercoagulability) gene analysis, 20210G>A variant
81241	*F5 (coagulation factor V)* (eg, hereditary hypercoagulability) gene analysis, Leiden variant
81242	*FANCC (Fanconi anemia, complementation group C)* (eg, Fanconi anemia, type C) gene analysis, common variant (eg, IVS4+4A>T)
81243	*FMR1 (fragile X mental retardation 1)* (eg, fragile X mental retardation) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
81244	; characterization of alleles (eg, expanded size and promoter methylation status)
81245	*FLT3 (fms-related tyrosine kinase 3)* (eg, acute myeloid leukemia), gene analysis; internal tandem duplication (ITD) variants (ie, exons 14, 15)
81246	; tyrosine kinase domain (TKD) variants (eg, D835, I836)
81247	*G6PD (glucose-6-phosphate dehydrogenase)* (eg, hemolytic anemia, jaundice), gene analysis; common variant(s) (eg, a, a-)
81248	; known familial variant(s)
81249	; full gene sequence
81250	*G6PC (glucose-6-phosphatase, catalytic subunit)* (eg, Glycogen storage disease, type 1a, von Gierke disease) gene analysis, common variants (eg, R83C, Q347X)
81251	*GBA (glucosidase, beta, acid)* (eg, Gaucher disease) gene analysis, common variants (eg, N370S, 84GG, L444P, IVS2+1G>A)
81252	*GJB2 (gap junction protein, beta 2, 26kDa, connexin 26)* (eg, nonsyndromic hearing loss) gene analysis; full gene sequence
81253	; known familial variants
81254	*GJB6 (gap junction protein, beta 6, 30kDa, connexin 30)* (eg, nonsyndromic hearing loss) gene analysis, common variants (eg, 309kb [del(GJB6-D13S1830)] and 232kb [del(GJB6-D13S1854)])
81255	*HEXA (hexosaminidase A [alpha polypeptide])* (eg, Tay-Sachs disease) gene analysis, common variants (eg, 1278insTATC, 1421+1G>C, G269S)
81256	*HFE (hemochromatosis)* (eg, hereditary hemochromatosis) gene analysis, common variants (eg, C282Y, H63D)
81257	*HBA1/HBA2 (alpha globin 1 and alpha globin 2)* (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis, for common deletions or variant (eg, Southeast Asian, Thai, Filipino, Mediterranean, alpha3.7, alpha4.2, alpha20.5, and Constant Spring)
81258	*HBA1/HBA2 (alpha globin 1 and alpha globin 2)* (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; known familial variant
81259	; full gene sequence
81260	*IKBKAP (inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein)* (eg, familial dysautonomia) gene analysis, common variants (eg, 2507+6T>C, R696P)

81261	*IGH@ (Immunoglobulin heavy chain locus)* (eg, leukemias and lymphomas, B-cell), gene rearrangement analysis to detect abnormal clonal population(s); amplified methodology (eg, polymerase chain reaction)
81262	; direct probe methodology (eg, Southern blot)
81263	*IGH@ (Immunoglobulin heavy chain locus)* (eg, leukemia and lymphoma, B-cell), variable region somatic mutation analysis
81264	*IGK@ (Immunoglobulin kappa light chain locus)* (eg, leukemia and lymphoma, B-cell), gene rearrangement analysis, evaluation to detect abnormal clonal population(s)
81265	Comparative analysis using Short Tandem Repeat (STR) markers; patient and comparative specimen (eg, pre-transplant recipient and donor germline testing, post-transplant non-hematopoietic recipient germline [eg, buccal swab or other germline tissue sample] and donor testing, twin zygosity testing, or maternal cell contamination of fetal cells)
81266	; each additional specimen (eg, additional cord blood donor, additional fetal samples from different cultures, or additional zygosity in multiple birth pregnancies) (List separately in addition to code for primary procedure)
81267	Chimerism (engraftment) analysis, post transplantation specimen (eg, hematopoietic stem cell), includes comparison to previously performed baseline analyses; without cell selection
81268	; with cell selection (eg, CD3, CD33), each cell type
81269	*HBA1/HBA2 (alpha globin 1 and alpha globin 2)* (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; duplication/deletion variants
81270	*JAK2 (Janus kinase 2)* (eg, myeloproliferative disorder) gene analysis, p.Val617Phe (V617F) variant
81271	*HTT (huntingtin) (eg, Huntington disease)* gene analysis; evaluation to detect abnormal (eg, expanded) alleles
81272	*KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog)* (eg, gastrointestinal stromal tumor [GIST], acute myeloid leukemia, melanoma), gene analysis, targeted sequence analysis (eg, exons 8, 11, 13, 17, 18)
81273	*KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog)* (eg, mastocytosis), gene analysis, D816 variant(s)
81274	*HTT (huntingtin) (eg, Huntington disease)* gene analysis; characterization of alleles (eg, expanded size)
81275	*KRAS (Kirsten rat sarcoma viral oncogene homolog)* (eg, carcinoma) gene analysis; variants in exon 2 (eg, codons 12 and 13)
81276	; additional variant(s) (eg, codon 61, codon 146)
81283	*IFNL3 (interferon, lambda 3)* (eg, drug response), gene analysis, rs12979860 variant
81284	*FXN (frataxin) (eg, Friedreich ataxia)* gene analysis; evaluation to detect abnormal (expanded) alleles
81285	*FXN (frataxin) (eg, Friedreich ataxia)* gene analysis; evaluation to detect abnormal (expanded) alleles
81286	*FXN (frataxin) (eg, Friedreich ataxia)* gene analysis; full gene sequence
81287	*MGMT (O-6-methylguanine-DNA methyltransferase)* (eg, glioblastoma multiforme), promoter methylation analysis

81288	*MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2)* (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; promoter methylation analysis
81289	*FXN (frataxin) (eg, Friedreich ataxia)* gene analysis; known familial variant(s)
81290	*MCOLN1 (mucolipin 1)* (eg, Mucolipidosis, type IV) gene analysis, common variants (eg, IVS3-2A>G, del6.4kb)
81291	*MTHFR (5,10-methylenetetrahydrofolate reductase)* (eg, hereditary hypercoagulability) gene analysis, common variants (eg, 677T, 1298C)
81292	*MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2)* (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81293	; known familial variants
81294	; duplication/deletion variants
81295	*MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1)* (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81296	; known familial variants
81297	; duplication/deletion variants
81298	*MSH6 (mutS homolog 6 [E. coli])* (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81299	; known familial variants
81300	; duplication/deletion variants
81301	Microsatellite instability analysis (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) of markers for mismatch repair deficiency (eg, BAT25, BAT26), includes comparison of neoplastic and normal tissue, if performed
81302	*MECP2 (methyl CpG binding protein 2)* (eg, Rett syndrome) gene analysis; full sequence analysis
81303	; known familial variant
81304	; duplication/deletion variants
81305	*MYD88 (myeloid differentiation primary response 88)* (eg, Waldenstrom's macroglobulinemia, lymphoplasmacytic leukemia) gene analysis, p.Leu265Pro (L265P) variant
81306	*NUDT15 (nudix hydrolase 15)* (eg, drug metabolism) gene analysis, common variant(s) (eg, *2, *3, *4, *5, *6)
81310	*NPM1 (nucleophosmin)* (eg, acute myeloid leukemia) gene analysis, exon 12 variants
81311	*NRAS (neuroblastoma RAS viral [v-ras] oncogene homolog)* (eg, colorectal carcinoma), gene analysis, variants in exon 2 (eg, codons 12 and 13) and exon 3 (eg, codon 61)
81312	*PABPN1 (poly[A] binding protein nuclear 1)* (eg, oculopharyngeal muscular dystrophy) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81313	*PCA3/KLK3 (prostate cancer antigen 3 [non-protein coding]/kallikrein-related peptidase 3 [prostate specific antigen])* ratio (eg, prostate cancer)

	81314	*PDGFRA (platelet-derived growth factor receptor, alpha polypeptide)* (eg, gastrointestinal stromal tumor [GIST]), gene analysis, targeted sequence analysis (eg, exons 12, 18)
	81315	*PML/RARalpha, (t(15;17))*, *(promyelocytic leukemia/retinoic acid receptor alpha)* (eg, promyelocytic leukemia) translocation analysis; common breakpoints (eg, intron 3 and intron 6), qualitative or quantitative
	81316	; single breakpoint (eg, intron 3, intron 6 or exon 6), qualitative or quantitative
	81317	*PMS2 (postmeiotic segregation increased 2 [S. cerevisiae])* (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
	81318	; known familial variants
	81319	; duplication/deletion variants
	81320	*PLCG2 (phospholipase C gamma 2)* (eg, chronic lymphocytic leukemia) gene analysis, common variants (eg, R665W, S707F, L845F)
	81321	*PTEN (phosphatase and tensin homolog)* (eg, Cowden syndrome, *PTEN* hamartoma tumor syndrome) gene analysis; full sequence analysis
	81322	; known familial variant
	81323	; duplication/deletion variant
	81324	*PMP22 (peripheral myelin protein 22)* (eg, Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; duplication/deletion analysis
	81325	; full sequence analysis
	81326	; known familial variant
	81327	*SEPT9 (Septin9) (eg, colorectal cancer)* promoter methylation analysis
	81328	*SLCO1B1 (solute carrier organic anion transporter family, member 1B1)* (eg, adverse drug reaction), gene analysis, common variant(s) (eg, *5)
	81329	*SMN1 (survival of motor neuron 1, telomeric)* (eg, spinal muscular atrophy) gene analysis; dosage/deletion analysis (eg, carrier testing), includes SMN2 (survival of motor neuron 2, centromeric) analysis, if performed
	81330	*SMPD1(sphingomyelin phosphodiesterase 1, acid lysosomal)* (eg, Niemann-Pick disease, Type A) gene analysis, common variants (eg, R496L, L302P, fsP330)
	81331	*SNRPN/UBE3A (small nuclear ribonucleoprotein polypeptide N and ubiquitin protein ligase E3A)* (eg, Prader-Willi syndrome and/or Angelman syndrome), methylation analysis
	81332	*SERPINA1 (serpin peptidase inhibitor, clade A, alpha-1 antiproteinase, antitrypsin, member 1)* (eg, alpha-1-antitrypsin deficiency), gene analysis, common variants (eg, *S and *Z)
	81333	*TGFBI (transforming growth factor beta-induced)* (eg, corneal dystrophy) gene analysis, common variants (eg, R124H, R124C, R124L, R555W, R555Q)
	81334	*RUNX1 (runt related transcription factor 1)* (eg, acute myeloid leukemia, familial platelet disorder with associated myeloid malignancy), gene analysis, targeted sequence analysis (eg, exons 3-8)
	81335	*TPMT (thiopurine S-methyltransferase)* (eg, drug metabolism), gene analysis, common variants (eg, *2, *3)

81336	*SMN1 (survival of motor neuron 1, telomeric)* (eg, spinal muscular atrophy) gene analysis; full gene sequence
81337	*SMN1 (survival of motor neuron 1, telomeric)* (eg, spinal muscular atrophy) gene analysis; known familial sequence variant(s)
81340	*TRB@ (T cell antigen receptor, beta)* (eg, leukemia and lymphoma), gene rearrangement analysis to detect abnormal clonal population(s); using amplification methodology (eg, polymerase chain reaction)
81341	; using direct probe methodology (eg, Southern blot)
81342	*TRG@ (T cell antigen receptor, gamma)* (eg, leukemia and lymphoma), gene rearrangement analysis, evaluation to detect abnormal clonal population(s)
81343	*PPP2R2B (protein phosphatase 2 regulatory subunit Bbeta)* (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81344	*TBP (TATA box binding protein) (eg, spinocerebellar ataxia)* gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81345	*TERT (telomerase reverse transcriptase)* (eg, thyroid carcinoma, glioblastoma multiforme) gene analysis, targeted sequence analysis (eg, promoter region)
81350	*UGT1A1 (UDP glucuronosyltransferase 1 family, polypeptide A1)* (eg, irinotecan metabolism), gene analysis, common variants (eg, *28, *36, *37)
81355	*VKORC1 (vitamin K epoxide reductase complex, subunit 1)* (eg, warfarin metabolism), gene analysis, common variant(s) (eg, -1639G>A, c. 173+1000C>T)
81361	*HBB (hemoglobin, subunit beta)* (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); common variant(s) (eg, HBS, HBC, HBE)
81362	; known familial variant(s)
81363	; duplication/deletion variant(s)
81364	; full gene sequence
81370	*HLA Class I and II typing, low resolution* (eg, antigen equivalents); *HLA-A, -B, -C, -DRB1/3/4/5, and -DQB1*
81371	; *HLA-A, -B, and -DRB1* (eg, verification typing)
81372	*HLA Class I typing, low resolution* (eg, antigen equivalents); complete (ie, *HLA-A, -B, and -C*)
81373	; one locus (eg, HLA-A, -B, or -C), each
81374	; one antigen equivalent (eg, B*27), each
81375	*HLA Class II typing, low resolution* (eg, antigen equivalents); *HLA-DRB1/3/4/5 and -DQB1*
81376	; one locus (eg, HLA-DRB1, -DRB3/4/5, -DQB1, -DQA1, -DPB1, or -DPA1), each
81377	; one antigen equivalent, each
81378	*HLA Class I and II typing, high resolution* (ie, alleles or allele groups), *HLA-A, -B, -C, and -DRB1*
81379	*HLA Class I typing, high resolution* (ie, alleles or allele groups); complete (ie, HLA-A, -B, and -C)
81380	; one locus (eg, HLA-A, -B, or -C), each
81381	; one allele or allele group (eg, B*57:01P), each

	81382	*HLA Class II typing, high resolution* (ie, alleles or allele groups); one locus (eg, HLA-DRB1, -DRB3/4/5, -DQB1, -DQA1, -DPB1, or -DPA1), each
	81383	; one allele or allele group (eg, HLA-DQB1*06:02P), each
	81400	Molecular pathology procedure, Level 1
	81401	Molecular pathology procedure, Level 2
	81402	Molecular pathology procedure, Level 3
	81403	Molecular pathology procedure, Level 4
	81404	Molecular pathology procedure, Level 5
	81405	Molecular pathology procedure, Level 6
	81406	Molecular pathology procedure, Level 7
	81407	Molecular pathology procedure, Level 8
	81408	Molecular pathology procedure, Level 9
	81479	Unlisted molecular pathology procedure
	81504	Oncology (tissue of origin), microarray gene expression profiling of > 2000 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as tissue similarity scores
	81507	Fetal aneuploidy (trisomy 21, 18, and 13) DNA sequence analysis of selected regions using maternal plasma, algorithm reported as a risk score for each trisomy
	81519	Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 21 genes, utilizing formalin-fixed paraffin embedded tissue, algorithm reported as recurrence score
	81538	Oncology (lung), mass spectrometric 8-protein signature, including amyloid A, utilizing serum, prognostic and predictive algorithm reported as good versus poor overall survival
	81599	Unlisted multianalyte assay with algorithmic analysis
	84999	Unlisted chemistry procedure
	88299	Unlisted cytogenetic study
	0004M	Scoliosis, DNA analysis of 53 single nucleotide polymorphisms (SNPs), using saliva, prognostic algorithm reported as a risk score
	0002U	Oncology (colorectal), quantitative assessment of three urine metabolites (ascorbic acid, succinic acid and carnitine) by liquid chromatography with tandem mass spectrometry (LC-MS/MS) using multiple reaction monitoring acquisition, algorithm reported as likelihood of adenomatous polyps *(used for PolypDX™)*
	0009U	Oncology (breast cancer), ERBB2 (HER2) copy number by FISH, tumor cells from formalin fixed paraffin embedded tissue isolated using image-based dielectrophoresis (DEP) sorting, reported as ERBB2 gene amplified or non-amplified
	0016U	Oncology (hematolymphoid neoplasia), RNA, BCR/ABL1 major and minor breakpoint fusion transcripts, quantitative PCR amplification, blood or bone marrow, report of fusion not detected or detected with quantitation
	0017U	Oncology (hematolymphoid neoplasia), JAK2 mutation, DNA, PCR amplification of exons 12-14 and sequence analysis, blood or bone marrow, report of JAK2 mutation not detected or detected
	~~0020U~~	~~Drug test(s), presumptive, with definitive confirmation of positive results, any number of drug classes, urine, with specimen verification including DNA~~

	~~authentication in comparison to buccal DNA, per date of service~~ *(Code deleted 10/01/2018)*
0023U	Oncology (acute myelogenous leukemia), DNA, genotyping of internal tandem duplication, p.D835, p.I836, using mononuclear cells, reported as detection or non-detection of FLT3 mutation and indication for or against the use of midostaurin
0027U	*JAK2 (Janus kinase 2)* (eg, myeloproliferative disorder) gene analysis, targeted sequence analysis exons 12-15
~~0028U~~	~~*CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6)* (eg, drug metabolism) gene analysis, copy number variants, common variants with reflex to targeted sequence analysis~~ *(Code deleted 10/01/2018)*
0031U	*CYP1A2 (cytochrome P450 family 1, subfamily A, member 2)* (eg, drug metabolism) gene analysis, common variants (ie, *1F, *1K, *6, *7)
0032U	*COMT (catechol-O-methyltransferase)* (drug metabolism) gene analysis, c.472G>A (rs4680) variant
0035U	Neurological disorder (eg prion disease), protein, pathogenic prion protein, real-time quaking-induced conversion, CSF, diagnostic, report result as positive or negative
0039U	Autoimmunity (Systemic Lupus Erythematosus, SLE), detection of high avidity antidsDNA antibodies, ELISA assay, serum, reported as quantitative number for therapeutic decision making
0040U	Oncology (hematolymphoid neoplasia), mRNA, BCR-ABL1, major breakpoint fusion transcript, quantitative RT-PCR amplification, blood, report of molecular response (MR) and BCR-ABL ratio %IS
0041U	Borrelia burgdorferi, antibody detection of 5 recombinant protein groups, by immunoblot, IgM
0042U	Borrelia burgdorferi, antibody detection of 5 recombinant protein groups, by immunoblot, IgG
0043U	Tick-borne relapsing fever Borrelia group, antibody detection to 4 recombinant protein groups, by immunoblot, IgM
0044U	Tick-borne relapsing fever Borrelia group, antibody detection to 4 recombinant protein groups, by immunoblot, IgG
0046U	*FLT3 (fms-related tyrosine kinase 3)* (eg, acute myeloid leukemia) internal tandem duplication (ITD) variants, quantitative
0049U	*NPM1 (nucleophosmin)* (eg, acute myeloid leukemia) gene analysis, quantitative
0060U	Twin zygosity, genomic targeted sequence analysis of chromosome 2, using circulating cell-free fetal DNA in maternal blood
0069U	Oncology (colorectal), microRNA, RT-PCR expression profiling of miR-31-3p, formalin-fixed paraffin-embedded tissue, algorithm reported as an expression score
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 primary procedure)
	0079U	Comparative DNA analysis using multiple selected single-nucleotide polymorphisms (SNPs), urine and buccal DNA, for specimen identity verification
	0136U	ATM (ataxia telangiectasia mutated) (eg, ataxia telangiectasia) mRNA sequence analysis (List separately in addition to code for primary procedure) (Use 0136U in conjunction with 81408)
	0137U	PALB2 (partner and localizer of BRCA2) (eg, breast and pancreatic cancer) mRNA sequence analysis (List separately in addition to code for primary procedure) (Use 0137U in conjunction with 81406)
HCPCS	G0452	Molecular pathology procedure; physician interpretation and report
	G9143	Warfarin responsiveness testing by genetic technique using any method, any number of specimen(s)
	S3800	Genetic testing for amyotrophic lateral sclerosis (ALS) *(Not valid for Medicare purposes)*
	S3840	DNA analysis for germline mutations of the RET proto-oncogene for susceptibility to multiple endocrine neoplasia type 2 *(Not valid for Medicare purposes)*
	S3841	Genetic testing for retinoblastoma *(Not valid for Medicare purposes)*
	S3842	Genetic testing for Von Hippel-Lindau disease *(Not valid for Medicare purposes)*
	S3844	DNA analysis of the connexin 26 gene (GJB2) for susceptibility to congenital, profound deafness *(Not valid for Medicare purposes)*
	S3845	Genetic testing for alpha thalassemia *(Not valid for Medicare purposes)*
	S3846	Genetic testing for hemoglobin E beta-thalassemia *(Not valid for Medicare purposes)*

	S3849	Genetic testing for Niemann-Pick disease *(Not valid for Medicare purposes)*
	S3850	Genetic testing for sickle cell anemia *(Not valid for Medicare purposes)*
	S3852	DNA analysis for APOE epsilon 4 allele for susceptibility to Alzheimer's disease *(Not valid for Medicare purposes)*
	S3853	Genetic testing for muscular dystrophy *(Not valid for Medicare purposes)*
	S3855	Genetic testing for detection of mutations in the presenilin-1 gene *(Not valid for Medicare purposes)*
	S3861	Genetic testing, sodium channel, voltage-gated, type V, alpha subunit (SCN5A) and variants for suspected Brugada syndrome *(Not valid for Medicare purposes)*
	S3865	Comprehensive gene sequence analysis for hypertrophic cardiomyopathy *(Not valid for Medicare purposes)*
	S3866	Genetic analysis for a specific gene mutation for hypertrophic cardiomyopathy (HCM) in an individual with a known HCM mutation in the family *(Not valid for Medicare purposes)*
	S3870	Comparative genomic hybridization (CGH) microarray testing for developmental delay, autism spectrum disorder and/or intellectual disability *(Not valid for Medicare purposes)*

***IMPORTANT NOTE:** Medicare Advantage medical policies use the most current Medicare references available at the time the policy was developed. Links to Medicare references will take viewers to external websites outside of the health plan's web control as these sites are not maintained by the health plan.*