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Genetic and Molecular Diagnostics – Testing for Inherited Cancer Risk

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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, including care that may be both medically reasonable and necessary.

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 Centers of Medicare and Medicaid Services (CMS) policies and manuals, along with general CMS rules and regulations. 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 a specific CMS coverage determination for a requested service, item or procedure, the health plan may apply CMS regulations, as well as their Medical Policy Manual or other applicable utilization management vendor criteria developed with an objective, evidence-based process using scientific evidence, current generally accepted standards of medical practice, and authoritative clinical practice guidelines.

Some services or items may appear to be medically indicated for an individual but may be a direct exclusion of Medicare or the member's benefit plan. Medicare and member EOCs exclude from coverage, among other things, services or procedures considered to be investigational (experimental) or cosmetic, as well as services or items considered not medically reasonable and necessary under Title XVIII of the Social Security Act, §1862(a)(1)(A). 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. Members, their appointed representative, or a treating provider can request coverage of a service or item by submitting a pre-service organization determination prior to services being rendered.

DESCRIPTION

Genetic testing is testing performed to detect changes or variants in DNA, RNA, and/or chromosomes. 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.

Being born with variants in certain genes can increase an individual's risk for developing certain cancers. For example, pathogenic variants in the *BRCA1* and *BRCA2* genes are associated with the development of breast, ovarian, prostate, and other cancers. Additional genes are also linked to an increased risk of breast and ovarian cancer to a lesser degree. Other inherited cancer risk disorders include Lynch syndrome, in which mismatch repair gene variants cause an increased risk of colorectal cancer, and Li Fraumeni syndrome, in which germline (inherited) variants in the *TP53* gene increases the risk of a number of cancer types.

While genetic testing for inherited cancer syndromes in certain situations may improve health outcomes, there are also risks associated with genetic testing. Many inherited cancer risk panel tests include genes that have low or moderate penetrance and do not have any recommended changes for treatment or surveillance. Therefore, it is very important that any individual who is considering genetic testing understand all aspects of the test results. Candidates for genetic testing may wish to consult with a genetics professional who can explain in detail the benefits, risks, and limitations of a particular test.

Some genetic testing for inherited cancer syndromes may be eligible for Medicare coverage, while others are only eligible for coverage in select individuals or for certain conditions, and still others may not be eligible for coverage at all due to the nature of the Medicare program and the applicable requirements for reasonable and necessary services and diagnostic laboratory testing coverage.

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

MEDICARE ADVANTAGE POLICY CRITERIA

Note: The tables in this policy provide information regarding Medicare local carrier jurisdiction, specific genetic or molecular tests, as well as *types* or *categories* of tests.

I. See Table 2 to determine if a test is already addressed. This table contain a list of tests or types of tests with known Medicare coverage or non-coverage guidance. Some tests are never considered medically reasonable or necessary, while others have criteria which must be met for the test to be covered.

   a. Note, the genes and codes included in the tables are provided as a courtesy. Individual laboratories may choose to use different coding, and gene lists are subject to change.

   b. Some small panel tests may be reviewed by gene. If a panel test is not found in this Medicare Advantage Medical Policy, but **all** of the individual genes are addressed, the coverage decisions from the single gene policy for each individual gene may be applied **if** the applicable references are appropriate for the performing laboratory's service area.

II. If the test is not listed in Table 2, see Table 1 for a state listing to determine if the laboratory is located in a geographical area that has adopted MolDX guidelines.

a. For Medicare jurisdictions which **HAVE** adopted MolDX Program guidelines, additional research may be necessary for tests that are not included in Table 2.
b. For Medicare jurisdictions which have **NOT** adopted MolDX Program guidelines, additional research may need to be performed to determine the applicable Medicare guideline for tests performed in a geographical area that has not adopted MolDX guidelines, when not included within Table 2.

Table 1: 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			

Table 2: Testing for Inherited Cancer Risk in Patients with Cancer

Note: Medicare does not cover any genetic test for members due to family history alone. Medicare requires diagnostic tests – including genetic testing – to provide actionable data which will be used promptly by the treating physician for the management of an existing illness or condition. Testing due to family history alone is considered not medically necessary according to Title XVIII of the Social Security Act, Section 1862(a)(1)(A) where it 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 "Policy Guidelines" below). For all tests, please review the "Medicare Rationale/Reference" source carefully to determine whether criteria are met.

TEST INFORMATION	MEDICARE RATIONALE / REFERENCE Back to Criteria
General Guidance for Hereditary (Germline) Cancer Tests *(CPT coding varies)* *(Initial testing only, see below for "repeat germline testing.")*	Hereditary cancers syndromes are caused by inherited (germline) variants that predispose an individual to cancer development. For hereditary cancer tests which **are** listed specifically by name within this policy (see below), use the reference(s) provided. For hereditary cancer tests **not** specifically listed by name within this policy: *Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY, CA, or NV:* • MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (L38974). *Companion article A58681 can be accessed directly from the LCD.* *Laboratories in CA or NV:* • MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (L38972) *Companion article A58679 can be accessed directly from the LCD.* According to the DEX™ Change Healthcare Registry website, the following tests are noted as **potentially covered** tests by MolDX for Medicare when above LCD criteria are met: • BRCAplus and BRCAplus-Expanded (81479, 0129U) (Ambry Genetics, CA) • BRCANext and BRCANext-Expanded (including +RNAinsight) (81479) (Ambry Genetics, CA) • CancerNext, CancerNext 37, and CancerNext-Expanded (including +RNAinsight) (81479, 0134U) (Ambry Genetics, CA) • ColoNext and ColoNext+RNAinsight (81479, 0101U) (Ambry Genetics, CA) • PancNext and PancNext+RNAinsight (81479) (Ambry Genetics, CA) • ProstateNext and ProstateNext+RNAinsight (81479) (Ambry Genetics, CA)
Repeat Germline Testing *(coding varies)*	*Laboratories in NC, SC, AL, GA, VA, or WV*: • MolDX: Repeat Germline Testing (L38274) *Companion article* A58017 *can be accessed directly from the LCD.*

	Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, or WY: • MolDX: Repeat Germline Testing (L38353) *Companion article A57332 can be accessed directly from the LCD.* *Laboratories in CA or NV*: • MolDX: Repeat Germline Testing (L38351) *Companion article A57331 can be accessed directly from the LCD.* *Laboratories in KY or OH*: • MolDX: Repeat Germline Testing (L38288) *Companion article A57141 can be accessed directly from the LCD.* *Laboratories in IA, KS, MO, NE, IN, or MI*: • MolDX: Repeat Germline Testing (L38429) *Companion article A57100 can be accessed directly from the LCD.*
ATM Gene Tests *(81408, 0136U)*	*Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY:* • MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (L38974) and associated article (A58681) *Laboratories in CA and NV:* • MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (L38972) and associated article (A56879) **Note**: All single-gene *ATM* tests that have completed a MolDX technology assessment (TA) are listed as "**not covered**." Therefore, all single-gene *ATM* tests are considered **not medically necessary**.
BRACAnalysis CDx *(BRCA1 and BRCA2) (81162)* Myriad Genetics (UT)	***Note: This guidance applies to tests ordered to diagnose a hereditary cancer syndrome*** *in an individual with cancer. For testing to select targeted treatment, see Policy Cross References.* • MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (L38974) *The companion article A58681 can be accessed directly from the LCD.* This test is listed in the DEX™ Change Healthcare Registry as "covered." Therefore, it may be considered medically necessary for patients who meet the LCD/article criteria.
BRCA1 and BRCA2 Genetic Testing Panels *(CPT coding varies)* Laboratories in AK, ID,	***Note: This guidance applies to tests ordered to diagnose a hereditary cancer syndrome*** *in an individual with cancer. For testing to select targeted treatment, see Policy Cross References.*

OR, WA, UT, AZ, MT, ND, SD, WY	*Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY:* • MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (L38974) *Companion article A58681 can be accessed directly from the LCD.* *Laboratories in CA or NV:* • MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (L38972) *Companion article A58679 can be accessed directly from the LCD.* *Laboratories in NC, SC, VA, WV, AL, TN, or GA:* • MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (L38966) *Companion article A58652 can be accessed directly from the LCD.* *Laboratories in FL:* • BRCA1 and BRCA2 Genetic Testing (L36499) *See all sections related to multi-gene panel testing within the LCD* See **General Guidance for Hereditary (Germline) Cancer Panel Tests** above.
CDH1 Gene Tests	*Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY:* • Billing and Coding: MolDX: CDH1 Genetic Testing (A55971) *Laboratories in CA and NV:* • Billing and Coding: MolDX: CDH1 Genetic Testing (A55970)
CHEK2 Gene Tests	*Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY:* • MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (L38974) and associated article (A58681) *Laboratories in CA and NV:* • MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (L38972) and associated article (A56879) **Note**: All single-gene *CHEK2* tests that have completed a TA for MolDX are listed as “not covered.” Therefore, all single-gene *CHEK2* tests are considered **not medically necessary**.

COLARIS® AP*, *COLARIS AP® PLUS *(with or without Colorectal and Polyposis Panel)* and ***COLARIS® PLUS + myRisk Update*** Myriad Genetics (UT)	• MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (L38974). *Companion article A58681 can be accessed directly from the LCD.* According to the DEX™ Change Healthcare Registry website, these tests are listed as "not covered" by MolDX. Therefore, these tests are considered **not medically necessary**.
Colon Cancer and Lynch Syndrome Genetic Tests *(coding varies)*	*Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY:* • MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (L38974). *Companion article A58681 can be accessed directly from the LCD.* *Laboratories in CA and NV:* • MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (L38972). *Companion article A58679 can be accessed directly from the LCD.* *Laboratories in FL:* • Genetic Testing for Lynch Syndrome (L34912) *Companion article A57450 can be accessed directly from the LCD.* According to this LCD, a stepped testing approach is required, which includes MSI/IHC testing as the first step, or a multigene panel *inclusive* of MSI testing. If a lab is unable to perform the stepped testing approach outlined in the LCD, multiple germ-line gene testing will be covered by Medicare only for the findings noted under the "**MMR Germline Gene Mutation Testing Exception**" subheading. See **General Guidance for Hereditary (Germline) Cancer Panel Tests** above.
Familial Adenomatous Polyposis (FAP) and MUTYH-Associated Polyposis (MAP) Tests *(APC and/or MUTYH) (81479)*	*Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY, CA, or NV:* • MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (L38974) *Companion article A58681 can be accessed directly from the LCD.* *Laboratories in CA and NV* • MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (L38972). *Companion article A58679 can be accessed directly from the LCD.* See **General Guidance for Hereditary (Germline) Cancer Panel Tests** above.

Myriad myRisk™ Hereditary Cancer Test *(48 genes)* Myriad Genetics (UT)	***Note:*** *There are two versions of the myRisk™ test. Check the test version and use the appropriate guidance (see row below).* • MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (L38974) *Companion article A58681 can be accessed directly from the LCD.* The myRisk™ Hereditary Cancer test is listed in the DEX™ Change Healthcare Registry as "**covered**." Therefore, it may be considered medically necessary when LCD criteria are met.
Myriad myRisk™ Hereditary Cancer Update Test *(33 genes)* Myriad Genetics (UT)	***Note:*** *There are two versions of the myRisk™ test. Check the test version and use the appropriate guidance (see row above).* • MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (L38974) (The companion article A58681 can be accessed directly from the LCD). See **General Guidance for Hereditary (Germline) Cancer Panel Tests** above. The myRisk™ Hereditary Cancer Update test is listed in the DEX™ Change Healthcare Registry as "not covered." Therefore, it is considered **not medically reasonable or necessary**.
PALB2 Gene Tests *(81307, 81308, 0137U)*	*Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY:* • MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (L38974) and associated article (A58681) *Laboratories in CA and NV:* • MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (L38972) and associated article (A56879) **Note**: All single-gene *PALB2* tests that have completed a TA for MolDX are listed as "not covered." Therefore, all single-gene *PALB2* tests are considered **not medically necessary**, including the add-on test +RNAinsight™ for *PALB2* by Ambry Genetics (0137U).
RenalNext *(including +RNAinsight) (81479)* Ambry Genetics (CA)	• MolDX: Molecular Diagnostic Tests (MDT) (L35160). According to the DEX™ Registry, this test is listed as "covered".
TP53 Gene Tests	*Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY:* • Billing and Coding: MolDX: TP53 Gene Test (A55487) *Laboratories in CA and NV:* • Billing and Coding: MolDX: TP53 Gene Test (A55484)

VistaSeq® Panels *(coding varies),* LabCorp (any state)	• MolDx: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (L38974). *Companion article A58681 can be accessed directly from the LCD. See* ***General Guidance for Hereditary (Germline) Cancer Panel Tests*** *above.* According to the DEX™ Change Healthcare Registry website, the following VistaSeq® tests are listed as "covered" by MolDX for Medicare and therefore may be considered medically necessary for patients who meet the LCD/article criteria.: • *Brain/CNS/PNS Cancer Profile* • *Breast and GYN Cancer Profile* • *Breast Cancer Profile* • *Colorectal Cancer Profile* • *Comprehensive Cancer Panel* • *Endocrine Cancer Profile* • *Hereditary Cancer Panel (with BRCA)* • *High/Moderate Risk Breast Cancer Profile* • *High Risk Colorectal Cancer Profile* • *Lynch Syndrome Panel* • *Pancreatic Cancerl* • *Prostate Panel* • *Renal Cell Cancer Profile* The following tests are listed as "not covered" test by the DEX™ Change Healthcare Registry website. Therefore, they are considered **not medically necessary**. • *APC Comprehensive* • *GYN Cancer Profile* • *Hereditary Cancer Panel Without BRCA*

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,[1,2]
- Not be excluded from coverage by statute, regulation, National Coverage Determination, (NCD), or Local Coverage Determination (LCD)[2]
- 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 signs and/or symptoms;[3,4] This also means services determined to be not medically necessary for any reason (including lack of safety and efficacy because it is an investigational service) are non-covered.[5]
- Be ordered by a physician who is treating the beneficiary;[6,7]
- Provide data that would be directly used in the management of a beneficiary's specific medical problem.[6,7]

In order for the referring physician to effectively manage their patient's specific medical problem using genetic or molecular diagnostic testing, the genetic tests performed must be used to assist in the management/treatment of the beneficiary. Therefore, it is important for referring physicians to be familiar with all specific genetic tests they order to ensure all test result components are clinically actionable.

In addition to the above Medicare requirements, when making coverage decision policies, under Chapter 13 of the Medicare Program Integrity Manual, Medicare allows contractors to consider a service "reasonable and necessary" when the service is appropriate for the member's condition. This includes appropriateness in duration, frequency, and that the service is furnished in accordance with accepted standards of medical practice for the condition, furnished in a setting appropriate to the medical needs and condition, ordered and furnished by qualified personnel, that the service meets, but does not exceed, the medical need; and is at least as beneficial as an existing and available medically appropriate alternative.[8]

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)

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 the test.[13-15]

The MolDX program will affect diagnostic services reported with the following CPT/HCPCS codes: (13)

Code Category/Description	2018 MolDx Code Range
Tier 1	81161-81383
Tier 2	81400-81408
Genomic Sequencing Procedures	81410-81471
Molecular Multianalyte Assays (MAAA)	81490-81595
MAAA Admin. Codes	MAAA codes for molecular tests only
Immunology	86152-86153
PLA	PLA codes for molecular tests only
Cytology	88120-88121
The following NOC codes are in scope for molecular tests only	81479, 81599, 84999, 85999, 86849, 87999

For testing performed by a laboratory outside of the Medicare Advantage Organization's (MAO) 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."[16]

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."[17]

REQUIRED DOCUMENTATION

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 or panel;
    a. The DEX Z-code as assigned by DEX™ Diagnostics Exchange and/or a copy of the decision letter by the MolDX Program would also be beneficial in making timely and efficient coverage determinations;
2. Name of the performing laboratory;

3. The exact gene(s) and/or mutations 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.); and,
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

1. Genetic and Molecular Diagnostics – Next Generation Sequencing, Genetic Panels, and Biomarker Testing, Genetic Testing, Policy No. M-GT64
2. Genetic and Molecular Diagnostics – Testing for Cancer Diagnosis, Prognosis, and Treatment Selection, Policy No. M-GT83
3. COVID-19 Testing, Laboratory, Policy No. M-LAB74

REFERENCES

1. Medicare Coverage Determination Process
2. Medicare Managed Care Manual, Ch. 4 - Benefits and Beneficiary Protections, §10.2 - Basic Rule
3. Title XVIII of the Social Security Act, §1862(a)(1)(A)
4. Medicare Benefit Policy Manual, Chapter 16 - General Exclusions From Coverage, §20 - Services Not Reasonable and Necessary
5. Medicare Claims Processing Manual, Chapter 23 - Fee Schedule Administration and Coding Requirements, §30 - Services Paid Under the Medicare Physician's Fee Schedule, Subsection A
6. 42 CFR §410.32(a)
7. Medicare Benefit Policy Manual, Ch. 15 – Covered Medical and Other Health Services, §80.1 - Clinical Laboratory Services
8. Medicare Program Integrity Manual, Chapter 13 – Local Coverage Determinations, §13.5.4 - Reasonable and Necessary Provision in an LCD
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 Program

13. Noridian Healthcare Solutions - Palmetto GBA MolDX Program for Jurisdiction F
14. Molecular Diagnostics Program (MolDX®) Manual
15. Palmetto GBA Molecular Diagnostic Tests and Medicare web page
16. Medicare Managed Care Manual, Ch. 4 - Benefits and Beneficiary Protections, §90.4.1 - MACS with Exclusive Jurisdiction over a Medicare Item or Service
17. Medicare Claims Processing Manual, Chapter 16 - Laboratory Services, §50.5 - Jurisdiction of Laboratory Claims
18. Novitas Article Biomarkers for Oncology (A52986) *(This reference can be found on the Medicare Coverage Database website)*

CODING

NOTE: The recently added 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.[18] 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.

For laboratories in the health plan's service area, instructions regarding the reporting of next generation sequencing (NGS), targeted tumor panels, or comprehensive genomic profile (CGP) testing, see the Noridian article *MolDX: Defining Panel Services in MolDX* (A59687) for coding expectations.

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	0101U	Hereditary colon cancer disorders (eg, Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis); genomic sequence analysis panel utilizing a combination of NGS, Sanger, MLPA and array CGH, with MRNA analytics to resolve variants of unknown significance when indicated [15 genes (sequencing and deletion/duplication), EPCAM and GREM1 (deletion/duplication only)]
	0102U	Hereditary breast cancer-related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence analysis panel utilizing a combination of NGS, Sanger, MLPA and array CGH, with MRNA analytics to resolve variants of unknown significance when indicated [17 genes (sequencing and deletion/duplication)]
	0103U	Hereditary ovarian cancer (eg, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence analysis panel utilizing a combination of NGS, Sanger, MLPA and array CGH, with MRNA analytics to resolve variants of unknown significance when indicated [24 genes (sequencing and deletion/duplication); EPCAM (deletion/duplication only)]
	0129U	Hereditary breast cancer–related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer), genomic sequence analysis and deletion/duplication analysis panel (ATM, BRCA1, BRCA2, CDH1, CHEK2, PALB2, PTEN, and TP53)
	0130U	Hereditary colon cancer disorders (eg, Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis), targeted mRNA sequence analysis panel (APC, CDH1, CHEK2, MLH1, MSH2, MSH6,

	MUTYH, PMS2, PTEN, and TP53) (List separately in addition to code for primary procedure) (Use 0130U in conjunction with 81435, 0101U)
0131U	Hereditary breast cancer–related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer), targeted mRNA sequence analysis panel (13 genes) (List separately in addition to code for primary procedure) (Use 0131U in conjunction with 81162, 81432, 0102U)
0132U	Hereditary ovarian cancer–related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer), targeted mRNA sequence analysis panel (17 genes) (List separately in addition to code for primary procedure) (Use 0132U in conjunction with 81162, 81432, 0103U)
0133U	Hereditary prostate cancer–related disorders, targeted mRNA sequence analysis panel (11 genes) (List separately in addition to code for primary procedure) (Use 0133U in conjunction with 81162)
0134U	Hereditary pan cancer (eg, hereditary breast and ovarian cancer, hereditary endometrial cancer, hereditary colorectal cancer), targeted mRNA sequence analysis panel (18 genes) (List separately in addition to code for primary procedure) (Use 0134U in conjunction with 81162, 81432, 81435)
0135U	Hereditary gynecological cancer (eg, hereditary breast and ovarian cancer, hereditary endometrial cancer, hereditary colorectal cancer), targeted mRNA sequence analysis panel (12 genes) (List separately in addition to code for primary procedure) (Use 0135U in conjunction with 81162)
0136U	ATM (ataxia telangiectasia mutated) (eg, ataxia telangiectasia) mRNA sequence analysis (List separately in addition to code for primary procedure)
0137U	PALB2 (partner and localizer of BRCA2) (eg, breast and pancreatic cancer) mRNA sequence analysis (List separately in addition to code for primary procedure)
0138U	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) mRNA sequence analysis (List separately in addition to code for primary procedure)
0157U	APC (APC regulator of WNT signaling pathway) (eg, familial adenomatosis polyposis [FAP]) mRNA sequence analysis (List separately in addition to code for primary procedure)
0158U	MLH1 (mutL homolog 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
0159U	MSH2 (mutS homolog 2) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
0160U	MSH6 (mutS homolog 6) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
0161U	PMS2 (PMS1 homolog 2, mismatch repair system component) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
0162U	Hereditary colon cancer (Lynch syndrome), targeted mRNA sequence analysis panel (MLH1, MSH2, MSH6, PMS2) (List separately in addition to code for primary procedure)

0235U	PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome), full gene analysis, including small sequence changes in exonic and intronic regions, deletions, duplications, mobile element insertions, and variants in non-uniquely mappable regions
0238U	Oncology (Lynch syndrome), genomic DNA sequence analysis of MLH1, MSH2, MSH6, PMS2, and EPCAM, including small sequence changes in exonic and intronic regions, deletions, duplications, mobile element insertions, and variants in non-uniquely mappable regions
0474U	Hereditary pan-cancer (eg, hereditary sarcomas, hereditary endocrine tumors, hereditary neuroendocrine tumors, hereditary cutaneous melanoma), genomic sequence analysis panel of 88 genes with 20 duplications/deletions using next generation sequencing (NGS), Sanger sequencing, blood or saliva, reported as positive or negative for germline variants, each gene
0475U	Hereditary prostate cancer related disorders, genomic sequence analysis panel using next-generation sequencing (NGS), Sanger sequencing, multiplex ligation-dependent probe amplification (MLPA), and array comparative genomic hybridization (CGH), evaluation of 23 genes and duplications/deletions when indicated, pathologic mutations reported with a genetic risk score for prostate cancer
81162	BRCA1 (BRCA1, DMA 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	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; 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	BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; 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)
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
81212	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; 185delAG, 5385insC, 6174delT variants
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
81288	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; promoter methylation analysis
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
81307	PALB2 (partner and localizer of BRCA2) (eg, breast and pancreatic cancer) gene analysis; full gene sequence
81308	;known familial variant
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
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
81351	TP53 (tumor protein 53) (eg, Li-Fraumeni syndrome) gene analysis; full gene sequence
81352	;targeted sequence analysis (eg, 4 oncology)
81353	;known familial variant
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

81432	Hereditary breast cancer-related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer, hereditary pancreatic cancer, hereditary prostate cancer), genomic sequence analysis panel, 5 or more genes, interrogation for sequence variants and copy number variants; genomic sequence analysis panel, must include sequencing of at least 10 genes, including BRCA1, BRCA2, CDH1, MLH1, MSH2, MSH6, PALB2, PTEN, STK11, and TP53
~~81433~~	~~;duplication/deletion analysis panel, must include analyses for BRCA1, BRCA2, MLH1, MSH2, and STK11~~ (Deleted 01/01/2025)
81435	Hereditary colon cancer-related disorders (eg, Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis), genomic sequence analysis panel, 5 or more genes, interrogation for sequence variants and copy number variants; genomic sequence analysis panel, must include analysis of at least 10 genes, including APC, BMPR1A, CDH1, MLH1, MSH2, MSH6, MUTYH, PTEN, SMAD4, and STK11
~~81436~~	~~;duplication/deletion of gene analysis panel, must include analysis of at least 5 genes, including MLH1, MSH2, EPCAM, SMAD4, and STK11~~ (Deleted 01/01/2025)
81437	Hereditary neuroendocrine tumor-related disorders (eg, medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma), genomic sequence analysis panel, 5 or more genes, interrogation for sequence variants and copy number variants; genomic sequence analysis panel, must include sequencing of at least 6 genes, including MAX, SDHB, SDHC, SDHD, TMEM127, and VHL
~~81438~~	~~;duplication/deletion analysis panel, must include analyses for SDHB, SDHC, SDHD, and VHL~~ (Deleted 01/01/2025)
81479	Unlisted molecular pathology procedure
81599	Unlisted multianalyte assay with algorithmic analysis
84999	Unlisted chemistry procedure

***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.*