Genetic Testing for Hereditary Cancer

INDEPENDENT CARE HEALTH PLAN

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Medicare Advantage Medical Coverage Policy

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Please refer to CMS website for the most current applicable CMS Online Manual System (IOMs)/National Coverage Determination (NCD)/ Local Coverage Determination (LCD)/Local Coverage Article (LCA)/ Transmittals.

Type	Title	ID Number	Jurisdiction Medicare	Applicable States/Territories

			Administrative Contractors (MACs)	
NCD	Next Generation Sequencing	90.2		
LCD	MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer MolDX: Molecular Diagnostic Tests (MDT) MolDX: Repeat Germline Testing	L39040 L36807 L38429	J5 - Wisconsin Physicians Service Insurance Corporation J8 - Wisconsin Physicians Service Insurance Corporation	IA, KS, MO, NE IN, MI
LCD	MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer MolDX: Molecular Diagnostic Tests (MDT) MolDX: Repeat Germline Testing	L39017 L36021 L38288	J15 - CGS Administrators, LLC (Part A/B MAC)	KY, OH
LCD	MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer MolDX: Molecular Diagnostic Tests (MDT) MolDX: Repeat Germline Testing	L38972 L35160 L38351	JE - Noridian Healthcare Solutions, LLC	CA, HI, NV, American Samoa, Guam, Northern Mariana Islands
LCD	MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer MolDX: Molecular Diagnostic Tests (MDT) MolDX: Repeat Germline Testing	L38974 L36256 L38353	JF - Noridian Healthcare Solutions, LLC	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY
LCD	Biomarkers for Oncology	L35396	JH - Novitas Solutions, Inc. (Part A/B MAC) JL - Novitas Solutions, Inc. (Part A/B MAC)	AR, CO, NM, OK, TX, LA, MS DE, D.C., MD, NJ, PA

LCD	MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer MolDX: Molecular Diagnostic Tests (MDT) MolDX: Repeat Germline Testing	L38966 L35025 L38274	JJ - Palmetto GBA (Part A/B MAC) JM - Palmetto GBA (Part A/B MAC)	AL, GA, TN NC, SC, VA, WV

Description

Genetic testing is a laboratory method that is performed to analyze an individual's deoxyribonucleic acid (DNA) to detect gene variants (mutations) associated with inherited conditions including hereditary cancer. Approximately 5 to 10 percent of all cancers are hereditary and genetic testing can help determine if a cancer is inherited. This type of testing may also be referred to as germline genetic testing. Testing is available for many cancers including, but not limited to, hereditary diffuse gastric cancer (HDGC), melanoma-pancreatic cancer syndrome, multiple endocrine neoplasia (MEN), paraganglioma (PGL)/pheochromocytoma (PCC), retinoblastoma and von Hippel Lindau syndrome.

Multigene (or expanded) panels analyze a broad set of genes simultaneously (as opposed to single gene testing that searches for variants in one specific gene) and have been proposed to evaluate the DNA of an individual with a personal and/or family history of more than one hereditary condition or syndrome or hereditary conditions/syndromes associated with more than one gene. Panels often include medically actionable genes but may also include those with unclear medical management. Targeted (or focused) multigene panels analyze a limited number of genes targeted to a specific condition.

Coverage Determination

iCare follows the CMS requirements that only allows coverage and payment for services that are reasonable and necessary for the diagnosis and treatment of illness or injury or to improve the functioning of a malformed body member except as specifically allowed by Medicare.

Genetic tests must demonstrate clinical utility, analytical and clinical validity and fulfill the CMS "reasonable and necessary" criteria. Analytic validity (test accurately identifies the gene variant), clinical validity (test identifies or predicts the clinically defined disorder) and clinical utility (test measurably improves clinical outcomes) of the genetic test is supported by generally accepted standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, specialty society recommendations, and views of physicians practicing in relevant clinical areas. The test must be ordered by a physician who is treating the beneficiary and the results will be used in the management of a beneficiary's specific medical problem.

For jurisdictions with no Medicare guidance, iCare will utilize the MolDX program and Technical Assessments for molecular assays as the standard to evaluate clinical utility, analytical and clinical validity in conjunction with adhering to Medicare's reasonable and necessary requirement.

In interpreting or supplementing the criteria above and in order to determine medical necessity consistently, iCare may consider the criteria contained in the following:

General Criteria for Genetic Testing for Hereditary Cancer

Apply General Criteria for Genetic Testing for Hereditary Cancer when disease- or gene-specific criteria are not available on this medical coverage policy.

Genetic testing for hereditary cancer will be considered medically reasonable and necessary when the following requirements are met:

- Requirements of NCD 90.2 Section B2 have been met if test is next-generation sequencing (NGS); **AND**
- Test is FDA approved/cleared or Clinical Laboratory Evaluation Program (CLEP) approved; **AND**
- Analytic validity, clinical validity and clinical utility of the genetic test is supported by the MolDX program; **AND**
- Individual to be tested has a personal history of cancer;[14,15,16,17,18] **AND**
- Has a clinical indication for germline (inherited) testing for hereditary cancer;[14,15,16,17,18] **AND**
- Has a risk factor for germline cancer;[14,15,16,17,18] **AND**
- The test analyzes genes or genetic variants with definitive or well-established guidelines-based evidence (eg, National Comprehensive Cancer Network [NCCN]; category 1 or 2A recommendations) required for clinical decision making for its intended use that can be reasonably detected by the test;[14,15,16,17,18] **AND**
- A single gene or variant may be tested if it is the only gene or variant strongly or moderately associated with a cancer type[14,15,16,17,18]

***NCD 90.2** requires FDA approval for somatic testing only; germline (hereditary) tests that are not FDA approved/cleared may be reviewed using criteria from associated LCDs when the test is CLEP approved.

Criteria for Specific Hereditary Cancers

Hereditary Diffuse Gastric Cancer

***CDH1* full gene sequencing and deletion/duplication analysis** will be considered medically reasonable and necessary for hereditary diffuse gastric cancer when the following requirements are met:

- Genetic testing is limited to the *CHD1* gene;[14,15,16,17,18] **AND**
- Bilateral lobular breast cancer diagnosed before 70 years of age;[105] **OR**
- Diffuse gastric cancer (DGC) diagnosed prior to 50 years of age;[105] **OR**
- DGC and cleft lip/cleft palate;[105] **OR**
- DGC and is of Maori ethnicity;[105] **OR**
- DGC and lobular breast cancer, either cancer diagnosed prior to 70 years of age;[105] **OR**
- Individual to be tested meets the criteria above and has a first-, second- or third-degree relative with a pathogenic or likely pathogenic variant in the *CDH1* gene. Genetic testing should be limited to the known familial variant (KFV).[105]

Melanoma-Pancreatic Cancer Syndrome

***CDKN2A* full gene sequencing and deletion/duplication analysis** will be considered medically reasonable and necessary for melanoma-pancreatic cancer syndrome when the following requirements are met:

- Genetic testing is limited to the *CDKN2A* gene;[14,15,16,17,18] **AND**
- Individual to be tested has a personal history of invasive cutaneous melanoma and has a first-degree relative diagnosed with pancreatic cancer;[104] **OR**
- Individual to be tested has a personal history of invasive cutaneous melanoma and has a first-, second- or third-degree relative with a pathogenic or likely pathogenic variant in the *CDKN2A* gene. Genetic testing should be limited to the KFV.[104]

Multiple Endocrine Neoplasia Type 1

***MEN1* full gene sequencing and deletion/duplication analysis** will be considered medically reasonable and necessary for multiple endocrine neoplasia type 1 when the following requirements are met:

- Genetic testing is limited to the *MEN1* gene;[14,15,16,17,18] **AND**
- Individual to be tested has a personal history of either of the following:
  - 1 tumor type characteristic of MEN1 and has a first-, second- or third-degree relative diagnosed with at least 1 tumor type characteristic of MEN1;[108] **OR**
  - 2 tumor types characteristic of MEN1;[108] **OR**

- Individual to be tested meets the criteria above and has a first-, second- or third-degree relative with a pathogenic or likely pathogenic variant in the *MEN1* gene. Genetic testing should be limited to the KFV.[108]

Multiple Endocrine Neoplasia Type 2

***RET* full gene sequencing and deletion/duplication analysis** will be considered medically reasonable and necessary for multiple endocrine neoplasia type 2 when the following requirements are met:

- Genetic testing is limited to the *RET* gene;[14,15,16,17,18] **AND**
- Individual to be tested has a personal history at least one of the following characteristics of MEN2;[108]
  - MTC
  - Parathyroid adenoma or hyperplasia
  - PCC; **OR**
- Individual to be tested diagnosed with MTC, parathyroid adenoma or hyperplasia or PCC and has a first-, second- or third-degree relative with a pathogenic or likely pathogenic variant in the *RET* gene. Genetic testing should be limited to the KFV.[108]

Multiple Endocrine Neoplasia Type 4

***CDKN1B* full gene sequencing and deletion/duplication analysis** will be considered medically reasonable and necessary for multiple endocrine neoplasia type 4 when the following requirements are met:

- Genetic testing is limited to the *CDKN1B* gene;[14,15,16,17,18] **AND**
- Personal history of one tumor type characteristic of MEN4;[100] **OR**
- Individual to be tested has a personal history of one tumor type characteristic of MEN4 and has a first-, second- or third-degree relative with a pathogenic or likely pathogenic variant in the *MEN4/MENX* gene. Genetic testing should be limited to the KFV.[100]

Paraganglioma and/or Pheochromocytoma

Paraganglioma and/or pheochromocytoma single gene or multigene panel testing (81437) and deletion/duplication analysis (81438) will be considered medically reasonable and necessary when the following requirements are met[108]:

- Personal history of PGL and/or PCC; **OR**
- Personal history of PGL and/or PCC and has a first-, second- or third-degree relative with a pathogenic or likely pathogenic variant in a gene associated with PGL or PCC. Genetic testing should be limited to the KFV.

Retinoblastoma

***RB1* full gene sequencing and deletion/duplication analysis** will be considered medically reasonable and necessary for retinoblastoma when the following requirements are met:

- Genetic testing is limited to the *RB1* gene;[14,15,16,17,18] **AND**
- Individual to be tested has been diagnosed with retinoblastoma by ophthalmoscopic examination and confirmed by imaging studies (eg, magnetic resonance imaging [MRI], ocular ultrasonography or optical coherence tomography [OCT]);[130] **OR**
- Individual to be tested has a personal history of retinoblastoma and has a first-, second- or third-degree relative with a pathogenic or likely pathogenic variant in the *RB1* gene. Genetic testing should be limited to the KFV.[130]

Von Hippel-Lindau Syndrome

***VHL* full gene sequencing and deletion/duplication analysis** will be considered medically reasonable and necessary for von Hippel-Lindau syndrome when the following requirements are met:

- Genetic testing is limited to the *VHL* gene;[14,15,16,17,18] **AND**
- Individual to be tested exhibits any of the following characteristics of VHL and a clinical diagnosis cannot be established[116]:
    - Clear cell RCC (ccRCC) diagnosed before 40 years of age
    - Endolymphatic sac tumor
    - Hemangioblastoma of the brain, retina or spine
    - Multiple (more than 1) bilateral ccRCC tumors diagnosed at any age
    - Multiple (more than 1) pancreatic cysts
    - Pancreatic neuroendocrine tumor
    - Pancreatic serous cystadenoma (more than 1)
    - Papillary cystadenoma of the epididymis or broad ligament
    - PCC
    - PGL of abdomen, neck or thorax
    - Retinal angioma; **OR**
- Individual to be tested has a personal history of von Hippel Lindau syndrome and has a first-, second- or third-degree relative with a pathogenic or likely pathogenic variant in the *VHL1* gene. Genetic testing should be limited to the KFV.[116]

The use of the criteria in this Medicare Advantage Medical Coverage Policy provides clinical benefits highly likely to outweigh any clinical harms. Services that do not meet the criteria above are not medically

necessary and thus do not provide a clinical benefit. Medically unnecessary services carry risks of adverse outcomes and may interfere with the pursuit of other treatments which have demonstrated efficacy.

Coverage Limitations

US Government Publishing Office. Electronic code of federal regulations: part 411 – 42 CFR § 411.15 - Particular services excluded from coverage

The following tests may not be considered a benefit (statutory exclusion):

- Tests considered screening in the absence of clinical signs and symptoms of disease that are not specifically identified by the law;[112] **OR**
- Tests that confirm a diagnosis or known information;[112] **OR**
- Tests to determine risk for developing a disease or condition;[112] **OR**
- Tests performed to measure the quality of a process;[112] **OR**
- Tests without diagnosis specific indications;[112] **OR**
- Tests identified as investigational by available literature and/or the literature supplied by the developer and are not a part of a clinical trial[112]

These treatments and services fall within the Medicare program's statutory exclusion that prohibits payment for items and services that have not been demonstrated to be reasonable and necessary for the diagnosis and treatment of illness or injury (§1862(a)(1) of the Act). Other services/items fall within the Medicare program's statutory exclusion at 1862(a)(12), which prohibits payment.

The following items will not be considered medically reasonable and necessary:

- Any laboratory test that investigates the same germline genetic content, for the same genetic information, that has already been tested in the same individual[14,15,16,17,18, 24, 25, 26, 27, 28]
- Deletion/duplication analysis is obtained as part of the sequencing procedure but submitted as an independent analysis
- Genetic tests that have not demonstrated clinical utility, analytical and clinical validity via the MolDX Program
- Multigene panel if only a single gene on the panel is considered reasonable and necessary

- Panels with genes that are not relevant to the individual's personal and family history[14,15,16,17,18]
- Repeat germline testing (testing is limited to once-in-a-lifetime)[24, 25, 26, 27, 28,30]

A review of the current medical literature shows that the evidence is insufficient to determine that these services are standard medical treatments. There remains an absence of randomized, blinded clinical studies examining benefit and long-term clinical outcomes establishing the value of these services in clinical management.

Coding Information

Any codes listed on this policy are for informational purposes only. Do not rely on the accuracy and inclusion of specific codes. Inclusion of a code does not guarantee coverage and/or reimbursement for a service or procedure.

CPT® Code(s)	Description	Comments
81437	Hereditary neuroendocrine tumor disorders (eg, medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma); genomic sequence analysis panel, must include sequencing of at least 6 genes, including MAX, SDHB, SDHC, SDHD, TMEM127, and VHL	
81438	Hereditary neuroendocrine tumor disorders (eg, medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma); duplication/deletion analysis panel, must include analyses for SDHB, SDHC, SDHD, and VHL	
81479	Unlisted molecular pathology procedure	
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
No code(s) identified		

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Appendix

Appendix A
Family Relationships

Degree of Relationship	Relative of the Individual to be Tested
First-degree	Child, full-sibling, parent
Second-degree	Aunt, uncle, grandchild, grandparent, nephew, niece, half-sibling
Third-degree	First cousin, great aunt, great-uncle, great-grandchild, great-grandparent, half-aunt, half-uncle

Appendix B
Tumor Types Characteristic of MEN1[108]

Adrenal adenoma
Bronchial carcinoid
Gastric carcinoid
Pancreatic or duodenal neuroendocrine tumor (gastrinoma, glucagonoma, insulinoma, VIPoma/ somatostatinoma)
Parathyroid adenoma or hyperplasia
Pituitary adenoma
Primary hyperparathyroidism
Thymic carcinoid

Appendix C
Tumor Types Characteristic of MEN4[100]

Pancreatic or duodenal neuroendocrine tumor (gastrinoma, glucagonoma, insulinoma, VIPoma/ somatostatinoma) Papillary thyroid cancer
Parathyroid adenoma or hyperplasia
Pituitary adenoma

Change Summary

- 01/01/2024 New Policy.