STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

Testing for Hereditary Cancer Susceptibility Syndromes Using Multi-Gene Panels

LAB-012

Iowa Medicaid Program:	Prior Authorization	**Effective Date:**	6/1/2023
Revision Number:	2	**Last Rev Date:**	1/19/2024
Reviewed By:	Medicaid Medical Director	**Next Rev Date:**	1/17/2025
Approved By:	Medicaid Clinical Advisory Committee	**Approved Date:**	1/20/2023

Descriptive Narrative

An estimated 5-10 percent of cancers have a heritable component, and a growing number of hereditary cancer syndromes have been recognized. Identifying pathogenic variants in genes associated with hereditary cancer syndromes can uncover genomic mechanisms that have predictive, diagnostic, and prognostic utility for patients and are used to improve their medical or surgical management. Traditionally, testing of genes associated with hereditary cancers was performed based on specific gene-disease relationships and personal or family history, often in a single-gene reflex fashion. However, the growing number of genes known to be associated with hereditary cancer syndromes and the overlap between clinical presentations has challenged this paradigm.

A common example is the overlap in cancer risk between carriers of genes typically associated with hereditary breast and ovarian cancer (HBOC) and genes associated with Lynch syndrome. Multi-syndrome panel testing for hereditary cancer syndromes may be appropriate when concern exists that gene variants may be missed by more narrowly focused testing due to genetic and phenotypic heterogeneity identified in the assessment. BRCA1 and BRCA2 have historically been the most frequently tested genes in HBOC. It is now estimated that more than half of the individuals with hereditary breast cancer carry pathogenic variants in genes other than BRCA1/2.

Genetic testing for hereditary cancer may be pursued in different ways:

- A more traditional approach involves conducting focused testing for pathogenic variants in the most likely gene or limited set of genes for patients who meet high-risk clinical criteria for a suspected single hereditary cancer syndrome.
- Focused multigene panels use next-generation sequencing (NGS) to identify variants and evaluate their pathogenicity in a small number of selected genes strongly associated with a suspected hereditary cancer syndrome.

- NGS multi-syndrome panels search for pathogenic variants in larger numbers of specified genes relevant to more than one hereditary cancer syndrome. Many panels include genes with both strong and moderate associations with disease.

The National Comprehensive Cancer Network (NCCN) guidelines have also expanded to incorporate testing of multiple genes into medical management recommendations.

As a result of the complexity of overlapping hereditary cancer syndromes and the number of potential genes or panels available for use, it becomes crucial that a qualified health professional, such as a certified genetic counselor, be involved in the process. The role of this health professional would include elements of the following:

- A personal medical and surgical history of the patient,
- A three-generation pedigree,
- Identification of elements in the personal and family history that would be suggestive of a hereditary cancer syndrome,
- Selection of an appropriate panel of tests that would confirm or exclude the syndrome(s) in question,
- Exclusion of gene tests that are currently not associated with cancer or variants of unknown significance,
- Pre- and post-test counseling regarding the outcomes of testing and how it can influence the medical or surgical management of that individual.

Criteria

Testing for hereditary cancer susceptibility syndromes using multi-gene panels is medically necessary when **ALL** the following are met:

1. Member is 18 years of age or older; **AND**
2. Results of testing will impact medical or surgical management; **AND**
3. The ordering health professional is from **ONE** of the following specialties:
   a. Certified genetic counselor; OR
   b. Oncologist; OR
   c. Breast surgeon; OR
   d. Gynecologic oncologist; **AND**
4. The member meets criteria for testing for **ONE** of the following:
   a. Hereditary breast and ovarian cancer syndrome (please refer to specific policy); **OR**
   b. Lynch syndrome (please refer to specific policy); **AND**
5. All genes in the panel have peer-reviewed, clinical validity data which have been shown to be associated with the cancer(s) in the personal and/or family history for the individual being tested (for example NCCN Guidelines category 1 or 2A; **AND**
6. The panel does not contain genes without a known association with cancer or variants of unknown significance (VUS); **AND**
7. The qualified health professional **is not** employed by the laboratory performing the testing.

Examples of multi-gene panels may include (but are not limited to) the following:

Multi-Gene Panel	Lab
MyRisk	Myriad
VistaSeq	LabCorp
Comprehensive Common Cancer Panel	GeneDx
Common Hereditary Cancer Panel	Invitae
Riscover - Comprehensive	Progenity
Breast & Gyn Cancer Panel	Invitae
Riskguard	Exact Sciences

Coding

The following list of codes is provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS/CPT code is inappropriate.

HCPCS	Description
81432	Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence analysis panel, must include sequencing of at least 10 genes, always including BRCA1, BRCA2, CDH1, MLH1, MSH2, MSH6, PALB2, PTEN, STK11, and TP53.
81433	Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); duplication/deletion analysis panel, must include analyses for BRCA1, BRCA2, MLH1, MSH2, and STK11.
81435	Hereditary colon cancer disorders (e.g., Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis); genomic sequence analysis panel, must include sequencing of at least 10 genes, including APC, BMPR1A, CDH1, MLH1, MSH2, MSH6, MUTYH, PTEN, SMAD4, and STK11.
81436	Hereditary colon cancer disorders (e.g., Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis); duplication/deletion analysis panel, must include analysis of at least 5 genes, including MLH1, MSH2, EPCAM, SMAD4, and STK11.

Compliance

1. Should conflict exist between this policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual and as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in

the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

EncoderPro.

Exact Sciences website: Riskguard | Exact Sciences.

Hulick P. Next-generation DNA sequencing (NGS): principles and clinical applications. UpToDate. Topic last updated: August 10, 2022.

Robsone ME, Bradbury AR, Arun B, et al. American Society of Clinical Oncology Policy statement update: genetic and genomic testing for cancer susceptibility. J Clin Oncol. 2015;33:3660-3667.

Multi-syndrome Panel Testing to aid in Management of Patients Suspected of having a hereditary Cancer Syndrome. Precision Medicine Insights. Hayes Review. Nov 18, 2020.

BRCA-Related Cancer: Risk Assessment, Genetic Counseling, and Genetic Testing. United States Preventive Services Task Force: Final Recommendation Statement. August 20, 2019. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/brca-related-cancer-risk-assessment-genetic-counseling-and-genetic-testing.

Family Cancer Syndromes. Genetics and Cancer. American Cancer Society. Last revised September 14, 2022. https://www.cancer.org/healthy/cancer-causes/genetics/family-cancer-syndromes.html.

MolDX: Next-Generation Sequencing Lab-Developed Tests for Inherited Cancer Syndromes. DL38972. CMS Local Coverage Determination. Posted 7/22/2021. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?LCDId=38971&ContrId=364.

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Price KS, Svenson A, King E, Ready K, Lazarin GA. Inherited cancer in the age of next-generation sequencing. Biol Res Nurs. 2018;20(2):192-204.

Genetic/Familial High-Risk Assessment: Colorectal. NCCN Clinical Practice Guidelines in Oncology. Version1.2-22 – June 8, 2022. Multigene Panel Testing for Lynch Syndrome and Other Cancer Risk Genes. Pp. 11-13.

Genetic/Familial High-Risk Assessment: Breast, Ovarian and Pancreatic. NCCN Clinical Practice Guidelines in Oncology. Version 1.2023 – September 7, 2022. Choice of Multi-Gene Testing. Pp. 12-13.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version

Signature

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Signature

Change Date	Changed By	Description of Change	Version
1/19/2024	CAC	Annual review.	2

Signature
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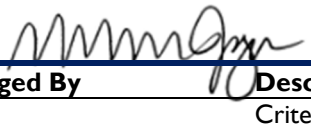

Change Date	Changed By	Description of Change	Version
1/20/2023	CAC	Criteria implementation.	1

Signature
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