myRisk Hereditary Cancer Testing

Introduction

myRisk™ Hereditary Cancer testing is addressed by this guideline.

Procedures addressed

The inclusion of any procedure code in this table does not imply that the code is under management or requires prior authorization. Refer to the specific Health Plan's procedure code list for management requirements.

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<thead>
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<th>Procedure addressed by this guideline</th>
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What are hereditary cancer syndromes

Definition

When a mutation in a single gene causes a significantly increased risk for certain cancers, it is called a hereditary cancer syndrome. Hereditary cancer syndromes are usually characterized by a pattern of specific cancer types occurring together in the same family, younger cancer diagnosis ages than usual, and/or other co-existing non-cancer conditions.

• Most cancer is sporadic and believed to be caused by a mix of behavioral/lifestyle, environmental, and inherited risk factors. However, about 5-10% of cancers are believed to have a major inherited component.¹

• There are more than 50 hereditary cancer syndromes.¹ Some of the most common are listed below with associated cancers:²

  o Hereditary breast and ovarian cancer syndrome (HBOC): breast, ovarian/fallopian tube/primary peritoneal cancer, pancreatic, prostate cancers
  o Lynch syndrome: colorectal, endometrial, small bowel, stomach, ovarian, pancreatic, ureteral and renal pelvis, biliary tract, brain, sebaceous adenoma, and keratoacanthoma tumors
  o Familial adenomatous polyposis: colorectal and other gastrointestinal cancers, gastrointestinal tract polyps (adenomas, fundic gland), osteomas, desmoids, thyroid cancer and hepatoblastoma
- MUTYH-associated polyposis: colorectal and other gastrointestinal cancers, adenomas, hyperplastic polyps
- Cowden syndrome: benign and malignant tumors of the breast, endometrium, and thyroid; cancer and polyps (hamartomas) in the colon and rectum
- Li Fraumeni syndrome: soft tissue sarcoma, osteosarcoma, leukemia, melanoma, and cancer of the breast, pancreas, colon, adrenal cortex, stomach, esophagus and brain
- Peutz-Jeghers syndrome: polyps (hamartomas) in the stomach, small intestine and colon, and pancreas, lung, breast, uterine and ovarian cancer

- Many hereditary cancer syndromes can include the same types of cancer and therefore have overlapping clinical findings (e.g., breast cancer is a feature of HBOC caused by BRCA mutations, Li Fraumeni syndrome, Cowden syndrome, and others). Sometimes, the pattern of cancers in the family or pathognomonic features makes the underlying syndrome clear. However, in many cases it can be difficult to reliably diagnose hereditary cancer syndromes based on clinical and family history alone.

**Test information**

- Until recently, most sequencing tests used the Sanger sequencing methodology that was originally developed in the 1970s. Sanger sequencing is labor intensive and did not lend itself to high-throughput applications.
- Next generation sequencing (NGS), which is also sometimes called massively parallel sequencing, was developed in 2005 to allow larger scale and more efficient gene sequencing. NGS relies on sequencing many copies of small pieces of DNA simultaneously and using bioinformatics to assemble the sequence.
- The efficiency of NGS has led to an increasing number of large, multi-gene testing panels. NGS panels that test several genes at once are particularly well-suited to conditions caused by more than one gene or where there is considerable clinical overlap between conditions making it difficult to reliably narrow down likely causes. As a result, several laboratories have begun to combine genes involved in causing various hereditary cancer syndromes, which often have both of those characteristics.
- myRisk Hereditary Cancer testing, performed by Myriad, is a hereditary cancer syndrome multi-gene panel that utilizes NGS technology. This test simultaneously analyzes 29 genes that have been identified to increase an individual’s risk of cancer.
Guidelines and evidence

- The National Comprehensive Cancer Network (NCCN) makes the following general recommendations for using multi-gene panels in evaluating risk for breast and ovarian and colorectal cancers and now includes this option in some management algorithms:\textsuperscript{4,5}
  
  o "Multi-gene testing is a new and rapidly growing field, but there is currently a lack of evidence regarding proper procedure and risk management strategies that should follow testing, especially when mutations are found for moderate-penetrance genes and when a VUS is found. For this reason, the NCCN panel recommends that multi-gene testing be offered in the context of professional genetic expertise, with pre- and post-test counseling being offered."
  
  o “Testing of unaffected family members when no affected member is available should be considered. Significant limitations of interpreting test results should be discussed.”
  
  o “When more than one gene can explain an inherited cancer syndrome, then multi-gene testing may be more efficient and/or cost effective.”
  
  o “As commercially available tests differ in the specific genes analyzed (as well as classification of variants and many other factors), choosing the specific laboratory and test panel is important.”
  
  o “Multi-gene testing can include ‘intermediate’ penetrant (moderate-risk) genes. For many of these genes, there is limited data on the degree of cancer risk and there are no clear guidelines on risk management for carriers of mutations. Not all genes included on available multi-gene tests are necessarily clinically actionable.” If a moderate risk gene mutation is identified, “gene carriers should be encouraged to participate in clinical trials or genetic registries.”
  
  o “Mutations in many breast cancer susceptibility genes involved in DNA repair may be associated with rare autosomal recessive conditions.” Therefore, multi-gene testing may unexpectedly reveal that an individual and their family are at an increased risk for these conditions.
  
  o “There is an increased likelihood of finding variants of unknown significance when testing for mutations in multiple genes.”

- The American College of Medical Genetics and Genomics published a policy statement that offers general guidance on the clinical application of large-scale sequencing focusing primarily on whole exome and whole genome testing. However, some of the recommendations regarding counseling around unexpected results and variants of unknown significance and minimum requirements for reporting apply to many applications of NGS sequencing applications.\textsuperscript{6}
Criteria

This guideline applies ONLY to myRisk Hereditary Cancer testing performed by Myriad Genetics. For all other Hereditary Cancer Syndrome Multigene panels, please refer to the guideline titled, *Hereditary Cancer Syndrome Multigene Panels*.

**myRisk Hereditary Cancer testing will be reimbursed when the following criteria are met:**

- Pre and post-test genetic counseling by an appropriate provider (as deemed by the Health Plan policy), AND
- No known cancer-causing mutation in the family, AND
- No previous hereditary cancer syndrome multigene panel testing, AND
- No previous hereditary cancer syndrome testing for any gene on the myRisk panel, AND
- Member meets criteria for at least one of the following options based on current eviCore guidelines:
  - BRCA Analysis,** OR
  - Lynch Syndrome Genetic Testing,*** OR
  - Two other separate hereditary cancer syndromes, not BRCA1/2 or Lynch syndrome, that are included on the panel, AND
- Rendering laboratory is a qualified provider of service per the Health Plan policy.

** Please refer to the *BRCA Analysis* guideline for criteria

*** Please refer to the *Lynch Syndrome Genetic Testing* guideline for criteria

**myRisk Hereditary Cancer Testing Update will be reimbursed when the following criteria are met:**

- Pre and post-test genetic counseling by an appropriate provider (as deemed by the Health Plan policy), AND
- No known cancer-causing mutation in the family, AND
- No previous cancer-causing mutation in the family, AND
- Testing for one condition, for which the member meets eviCore criteria, was performed and billed separately. A multi-gene panel is now being considered as a reflex and will be billed at a rate comparable to single syndrome pricing, AND
- Member meets medical necessity criteria for at least one additional condition included in the panel that was not already tested (e.g., hereditary breast and ovarian cancer was already performed, but Lynch syndrome criteria are also met). Please refer to test-specific guidelines for details.
  - Although not a complete list, the following are considered separate conditions:
- Hereditary breast cancer - this includes both BRCA1/2 and PALB2. (Note that if BRCA1/2 testing was already performed and PALB2 criteria are now met, PALB2 testing alone would be reimbursable and not myRisk Update).
  - Lynch syndrome
  - Li-Fraumeni
  - Familial adenomatous polyposis
  - Cowden syndrome, AND

- Rendering laboratory is a qualified provider of service per the Health Plan policy.

References

   Available at: http://www.cancer.gov/about-cancer/causes-prevention/genetics/genetic-testing-fact-sheet


