

Pan-Cancer Hereditary Cancer Susceptibility Panels

A pan-cancer hereditary cancer susceptibility panel includes genes that are associated with inherited susceptibility to several different types of cancer (e.g., breast cancer, colon cancer, stomach cancer, etc.).

- I. Genetic testing using a pan-cancer hereditary cancer susceptibility panel is considered **medically necessary** when the member meets **BOTH** A and B:
 - A. The member has one of the following:
 1. A personal history, or a close relative with a personal history, of one of the following cancers ≤ 50 years of age:
 - a) Breast cancer, **OR**
 - b) Colorectal cancer, **OR**
 - c) Endometrial cancer, **OR**
 2. The member has a personal history of one of the following:
 - a) Pancreatic cancer at any age, **OR**
 - b) Metastatic prostate cancer at any age, **OR**
 3. Ovarian, peritoneal, or fallopian tube cancer at any age, **OR**
 4. The member's personal or family history is suspicious for more than one hereditary cancer syndrome, **AND**
 - B. The panel includes, at a minimum, sequencing of the following genes: *BRCA1*, *BRCA2*, *EPCAM*, *MLH1*, *MSH2*, *MSH6*, *PMS2*.
- II. Genetic testing using a pan-cancer hereditary cancer susceptibility panel is considered **investigational** for all other indications.
- III. Hereditary cancer susceptibility panel targeted mRNA sequencing analysis for the interpretation of variants of unknown significance is considered **investigational** because it is typically either considered an existing component

of the genetic testing process for quality assurance or follow up testing without proven utility.

NOTE: If a multigene cancer panel is performed, the appropriate panel code should be used.

¹ Targeted testing rather than sequencing has a role in some hereditary cancer syndromes. For example, a single variant in the *HOXB13* gene has been linked to prostate cancer risk.

DEFINITIONS

1. **Close relatives** include first, second, and third degree blood relatives:
 - a. **First-degree relatives** are parents, siblings, and children
 - b. **Second-degree relatives** are grandparents, aunts, uncles, nieces, nephews, grandchildren, and half siblings
 - c. **Third-degree relatives** are great grandparents, great aunts, great uncles, great grandchildren, and first cousins

REFERENCES

1. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Genetic/Familial High-Risk Assessment: Genetic/Familial High-Risk Assessment: Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate. Version 2.2025.
https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf.

2. NCCN Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, and Gastric guidelines (1.2025).
https://www.nccn.org/professionals/physician_gls/pdf/genetics_colon.pdf.
3. “Use of Multi-Gene Panel Testing.” Position Statement from National Society of Genetic Counselors.
<https://www.nsgc.org/Policy-Research-and-Publications/Position-Statements/Position-Statements/Post/use-of-multi-gene-panel-tests>. Adopted, 2017, Reaffirmed 2020 and 2023.
4. “Selection of Germline Genetic Testing Panels in Patients With Cancer: ASCO Guideline”. Practice Guideline from The American Society of Clinical Oncology.
<https://ascopubs.org/doi/pdfdirect/10.1200/JCO.24.00662>. Published May 17, 2024.