Hereditary Polyposis Susceptibility Panels

A hereditary polyposis panel includes genes that are associated with inherited susceptibility to colon polyposis.

I. Genetic testing using a hereditary polyposis susceptibility panel is considered **medically necessary** when the member meets **BOTH** A and B:

   A. The member has a history of any of the following:

      1. 10 or more cumulative adenomas, **OR**
      2. Congenital hypertrophy of the retinal pigment epithelium (CHRPE), **OR**
      3. Desmoid tumor, **OR**
      4. Hepatoblastoma, **OR**
      5. Cribriform-morular variant of papillary thyroid cancer, **OR**
      6. A clinical diagnosis of serrated polyposis syndrome, with at least some adenomas, based on one of the following:

         a) 5 or more serrated polyps proximal to the rectum, all being 5mm or greater in size and at least 2 being 10mm or greater in size, **OR**

         b) More than 20 serrated polyps of any size distributed throughout the large bowel, with at least 5 or more being proximal to the rectum, **AND**

   B. The panel includes, at a minimum, sequencing of the following genes: *APC* and *MUTYH*.

II. Genetic testing using a hereditary polyposis susceptibility panel is considered **investigational** for all other indications.

III. mRNA sequencing analysis in genes associated with polyposis syndromes 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.

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RATIONALE AND REFERENCES

Hereditary Polyposis Susceptibility Panels

National Comprehensive Cancer Network (NCCN): Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, and Gastric (1.2025)

This guideline outlines scenarios in which individuals meet criteria for germline genetic testing for “all polyposis and [colorectal cancer] genes” (p.POLYP-1A). These include: personal history of 10-20 cumulative adenomas, congenital hypertrophy of retinal pigment epithelium (CHRPE), desmoid tumor, hepatoblastoma, cribriform-morular variant of papillary thyroid cancer, and clinically diagnosed serrated polyposis syndrome if adenomas are present (p. POLYP-1).

This guideline also notes that some individuals with a clinical diagnosis of serrated polyposis syndrome (defined as 5 or more serrated polyps proximal to the rectum all being 5mm or larger with 2 or more being 10 or more mm in size, or more than 20 serrated polyps of any size distributed throughout the colon, with 5 or more being proximal to the rectum) may carry pathogenic variants in *MUTYH* (biallelic) or *RNF43* (monoallelic)(p. SPS-1).

Some individuals will have variants of uncertain significance (VUS); post-test counseling should include considering referral to research studies for the purpose of learning the functional impact of VUSs such as variant reclassification programs through clinical labs or registries (p. EVAL-A, 8 of 9).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, and Gastric 1.2025
https://www.nccn.org/professionals/physician_gls/pdf/genetics_ceg.pdf

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