# Genetic testing: hereditary cancer susceptibility

These services may or may not be covered by your HealthPartners plan. Please see your plan documents for your specific coverage information. If there is a difference between this general information and your plan documents, your plan documents will be used to determine your coverage.

## Administrative Process

**Prior authorization is sometimes required for BRCA1 and BRCA2 related tests.** Refer to the list in Related Content to find out whether prior authorization is required for a specific indication. Prior authorization requirements are based on both the procedure code (CPT) and primary diagnosis code (ICD-10-CM) associated with the genetic testing.

**Prior authorization is not required for BRCA1 and/or BRCA2 Targeted Variant Analysis-Ashkenazi Jewish Founder Variants**

**Prior authorization is not applicable for the following services as they are considered investigational/experimental:**

- ATM or CHEK2 Sequencing and/or Deletion/Duplication Analysis
- Targeted mRNA sequencing analysis for the interpretation of variants of unknown significance (0130U, 0133U, 0134U, 0136U, 0137U, 0138U, 0157U, 0158U, 0159U, 0160U, 0161U, 0162U)

**Prior authorization is required for the following services:**

- All other testing described in this policy below, and
- Testing that is associated with a procedure code listed in “Box A”, below.

Tests that require prior authorization will be reviewed for medical necessity of the testing as a whole. That is, a single coverage decision will apply to all of the tests, services, and/or procedure codes associated with the genetic test, whether they are requested/billed together or separately.

| **Box A: Genetic testing procedure codes that require prior authorization** |
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| Molecular pathology procedures, Tier 2 or unlisted (CPT 81400-81408, 81479) |
| Unlisted multianalyte assays (CPT 81599) |
| Any other listed or unlisted laboratory/pathology CPT code when it is used in association with a genetic test. |



## Policy Reference Table

*If available, codes are listed below for informational purposes only, and do not guarantee member coverage or provider reimbursement. The list may not be all-inclusive.*

| Coverage Criteria Sections | Example Tests (Labs) | Common CPT Codes | Common ICD10 Codes |
|---|---|---|---|
| Pan-Cancer Hereditary Cancer Susceptibility Panels | MyRisk (Myriad Genetics) | 81432, 81433 | C15-26, C50-58, Z17, Z80, Z85.0-Z85.9 |
| | Common Hereditary Cancers Panel (Invitae) | | |
| | CancerNext (Ambry Genetics) | | |
| | Tempus xG Hereditary Cancer Panel | | |
| | +RNAinsight with CancerNext (Ambry Genetics) | 0134U | |
| | GeneticsNow Comprehensive Germline Panel (GoPath Diagnostics) | 0474U | |
| Hereditary Breast Cancer Susceptibility Panels | VistaSeq Breast Cancer Panel (Labcorp)<br>Breast Cancer Panel (Invitae)<br>Breast Cancer STAT NGS Panel (Sequencing & | 81162, 81163, 81164, 81165, 81166, 81167, 81216, 81307, 81321, 81351, 81432, 81433 | C50, Z80.3, Z83, Z84, Z85, Z86 |

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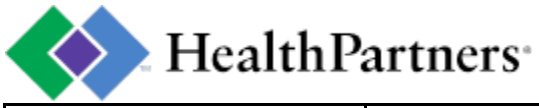
|---|---|---|---|
| | Deletion/Duplication) (Fulgent Genetics)<br>Breast Cancer - High Risk Panel (PreventionGenetics, part of Exact Sciences)<br>Breast Cancer High Risk Panel plus PALB2 (GeneDx) | | |
| | BRCAplus (Ambry Genetics) | 0129U | |
| Hereditary GI/Colon Cancer Susceptibility Panels | Colorectal Cancer (Invitae) | 81435, 81436 | C15-26, Z80, Z83, Z84, Z85, Z86 |
| | ColoNext (Ambry Genetics) | 0101U | |
| | +RNAinsight for ColoNext (Ambry Genetics) | 0130U, 0162U | |
| Hereditary Gastric Cancer Susceptibility Panels | Invitae Gastric Cancer Panel (Invitae) | 81201, 81203, 81292, 81294, 81295, 81297, 81298, 81300, 81317, 81319, 81403, 81404, 81405, 81406, 81408, 81479 | C16, Z80, Z85, Z86 |
| | Gastric Cancer Panel (PreventionGenetics, part of Exact Sciences) | | |
| Hereditary Pancreatic Cancer Susceptibility Panels | Pancreatic Cancer Panel (Invitae) | 81162, 81163, 81201, 81292, 81295, 81298, 81351, 81433, 81479 | C25, Z80, Z84, Z85, Z86 |
| | PancNext (Ambry Genetics) | | |
| Hereditary Polyposis Susceptibility Panels | Hereditary Polyposis Panel (PreventionGenetics, part of Exact Sciences) | 81201, 81203, 81406, 81479 | D12, K63.5, Z80, Z84, Z85, Z86 |
| | Adenomatous Polyposis Panel (Invitae) | | |
| Hereditary Prostate Cancer Susceptibility Panels | Hereditary Prostate Cancer Panel (Invitae) | 81162, 81292, 81295, 81351, 81479 | C61, Z80, Z84, Z85, Z86 |
| | ProstateNext (Ambry Genetics) | | |
| | +RNAinsight for ProstateNext (Ambry Genetics) | 0133U | |
| | ProstateNow Prostate Germline Panel (GoPath Diagnostics) | 0475U | |
| Hereditary Neuroendocrine Cancer Susceptibility Panels | Hereditary Paraganglioma-Pheochromocytoma Panel (Invitae) | 81437, 81438 | C74, C75, C7A, Z80, Z84, Z85, Z86 |
| | PGLNext (Ambry Genetics) | | |
| ***BRCA1* and *BRCA2* Gene Testing** | | | |
| *BRCA1/BRCA2* Targeted Variant or Known Familial Variant Analysis | BRCA1 or BRCA2 Targeted Variant-Single Test (GeneDx) | 81215, 81217 | C24.1, C50, C56, D05, Z17, Z80, Z83, Z84, Z85, Z86 |
| *BRCA1* and/or *BRCA2* Targeted Variant Analysis - Ashkenazi Jewish Founder Variants | BRCA1/2 Ashkenazi Jewish 3-Site Mutation Panel (Ambry Genetics) | 81212 | |
| | MultiSite 3 BRCAnalysis (Myriad Genetics) | | |
| *BRCA1/BRCA2* Sequencing and/or Deletion Duplication Analysis | Hereditary BRCA1/2 Panel (Invitae) | 81162, 81163, 81164, 81165, 81166, 81167, 81216 | |
| | BRCA1/2 Seq and Del/Dup (Ambry Genetics) | | |
| | +RNAinsight for BRCA1/2 (Ambry Genetics) | 0138U | |
| ***PALB2* Gene Testing** | | | |



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| *PALB2* Targeted Variant Analysis | PALB2 Targeted Variant (GeneDx) | 81308 | C15-26, Z80, Z84, Z85, Z86 |
| *PALB2* Sequencing and/or Deletion/Duplication Analysis | PALB2 Sequencing PALB2 Deletion/Duplication (Quest) | 81307, 81479 | |
| | PALB2 with +RNA insight (Ambry Genetics) | 0137U | |
| ***ATM* and/or *CHEK2* Gene Testing** | | | |
| *ATM* or *CHEK2* Targeted Variant Analysis | ATM Targeted Variants - Single Test (GeneDx) | 81479 | C50, D05, Z80, Z84, Z85, Z86 |
| | CHEK2 Targeted Variants - Single Test (GeneDx) | | |
| *ATM* or *CHEK2* Sequencing and/or Deletion/Duplication Analysis | ATM Full Gene Sequencing and Deletion/Duplication (Invitae) | 81408, 81479 | |
| | Hereditary Breast Cancer via the CHEK2 Gene (PreventionGenetics, part of Exact Sciences) | 81479 | |
| | +RNAInsight for ATM (Ambry Genetics) | 0136U | |
| **Lynch Syndrome / Hereditary Nonpolyposis Colorectal Cancer (HNPCC)** | | | |
| MLH1, MSH2, MSH6, PMS2, or EPCAM Targeted Variant Analysis | MSH6 Targeted Variant PMS2 Targeted Variant EPCAM Targeted Variant (GeneDx) | 81299, 81318, 81479 | C15-22, C24-26, C53-57, Z80, Z84, Z85, Z86 |
| | Hereditary Nonpolyposis Colorectal Cancer (HNPCC): MLH1 (Known Mutation) (Labcorp) | 81293 | |
| | Hereditary Nonpolyposis Colorectal Cancer (HNPCC): MSH2 (Known Mutation) (Labcorp) | 81296 | |
| *MLH1, MSH2, MSH6 PMS2, EPCAM* Sequencing and/or Deletion/Duplication Analysis | HNPCC Concurrent (Ambry Genetics) | 81292, 81294, 81295, 81297, 81298, 81300, 81317, 81319, 81403 | |
| | Lynch Syndrome Panel (Invitae) | | |
| | CustomNext + RNA: MLH1, MSH2, MSH6, and/or PMS2 (Ambry Genetics) | 0158U, 0159U, 0160U, 0161U, 0162U | |
| ***BAP1*-Tumor Predisposition syndrome** | | | |
| *BAP1* Targeted Variant Analysis | BAP1: Site Specific Analysis (familial) (Univ of Pennsylvania School of Medicine-Genetic Diagnostic Laboratory) | 81403 | C22, C45, C64, C69, D22, D32, Z80, Z84, Z85, Z86 |
| *BAP1* Sequencing and/or Deletion/Duplication Analysis | BAP1 Full Gene Sequencing and Deletion/Duplication (Invitae) | 81479 | |
| **Birt-Hogg-Dube syndrome (BHDS)** | | | |
| *FLCN* Targeted Variant Analysis | FLCN Targeted Variant - Single Test (GeneDx) | 81479 | C65, D14.3, D23.9, Z84, Z85, Z86 |
| *FLCN* Sequencing and/or Deletion/Duplication Analysis | Birt-Hogg-Dube Syndrome Test (Invitae) | 81479 | |
| **Cowden Syndrome (CS)/PTEN Hamartoma Tumor Syndrome (PHTS)** | | | |
| *PTEN* Targeted Variant Analysis | PTEN Targeted Variant - Single Test (GeneDx) | 81322 | C15-21, C26, C50, C54, C55, C64, C73, D12, |

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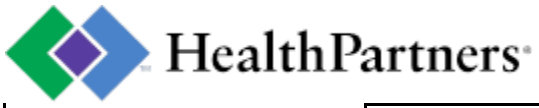
|---|---|---|---|
| *PTEN* Sequencing and/or Deletion/Duplication Analysis | PTEN Gene Sequencing and Del/Dup (GeneDx) | 81321, 81323 | D13, D17, D23, D24, F78, F84.0, Q75.3, Q87.89, Z80, Z84, Z85, Z86 |
| **Adenomatous Polyposis Conditions (Familial Adenomatous Polyposis Syndrome (FAP)/Attenuated FAP (AFAP) and *MUTYH*-Associated Polyposis Syndrome (MAP)** | | | |
| *APC* or *MUTYH* Targeted Variant Analysis | APC Targeted Variant - Single Test (GeneDx) | 81202 | C15-21, D12, Z80, Z84, Z85, Z86 |
| | MUTYH Targeted Variant - Single Test (GeneDx) | 81403, 81401 | |
| *APC* and/or *MUTYH* Sequencing and/or Deletion/Duplication Analysis | APC Seq and Del/Dup (Ambry Genetics) | 81201, 81203 | |
| | Familial Adenomatous Polyposis Test (Invitae) | | |
| | +RNAInsight for APC (Ambry Genetics | 0157U | |
| | MUTYH Full Gene Sequencing and Deletion/Duplication (Invitae) | 81406, 81479 | |
| **Familial Atypical Multiple Mole Melanoma Syndrome (FAMMM)** | | | |
| *CDKN2A* Targeted Variant Analysis | CDKN2A Targeted Variant - Single Test (GeneDx) | 81479 | C43, Z12.83, Z80, Z84, Z85, Z86 |
| *CDKN2A* Sequencing and/or Deletion/Duplication Analysis | CDKN2A Full Gene Sequencing and Deletion/Duplication (Invitae) | 81404, 81479 | |
| **Hereditary Diffuse Gastric Cancer (aka, Signet Ring Cell Gastric Cancer)** | | | |
| *CDH1* Targeted Variant Analysis | CDH1 Targeted Variant - Single Test (GeneDX) | 81479 | C16, C50, Q35, Q36, Z80, Z84, Z85, Z86 |
| *CDH1* Sequencing and/or Deletion/Duplication Analysis | CDH1 Full Gene Sequencing and Deletion/Duplication (Invitae) | 81406, 81479 | |
| **Juvenile Polyposis Syndrome (JPS)** | | | |
| *SMAD4* and/or *BMPR1A* Targeted Variant Analysis | Targeted Variant: SMAD4 (PreventionGenetics, part of Exact Sciences) | 81403 | C15-C26, D12, Z80, Z84, Z85, Z86 |
| | Targeted Variant: BMPR1A (PreventionGenetics, part of Exact Sciences) | 81403 | |
| *SMAD4* and/or *BMPR1A* Sequencing and/or Deletion/Duplication Analysis | Juvenile Polyposis Syndrome Panel (Invitae) | 81405, 81406, 81479 | |
| | BMPR1A, SMAD4 Gene Sequencing and Del/Dup (GeneDx) | | |
| **Hereditary Leiomyomatosis and Renal Cell Cancer (HLRCC)** | | | |
| *FH* Targeted Mutation Variant Analysis | FH Known Familial Mutation Analysis (University Hospitals) | 81403 | C44, C55, C64, D23, D25, Z84, Z85, Z86 |
| *FH* Sequencing and/or Deletion/Duplication Analysis | Hereditary Leiomyomatosis and Renal Cell Carcinoma (Ambry Genetics) | 81405, 81479 | |
| **Li-Fraumeni Syndrome (LFS)** | | | |
| *TP53* Targeted Variant Analysis | TP53 Targeted Variant - Single Test (GeneDx) | 81352 | C15-26, C30-41, C45, C47-49, C50, C71, C95.9, Z80, Z84, Z85, Z86 |
| *TP53* Sequencing and/or Deletion/Duplication Analysis | TP53 Full Gene Sequencing and Deletion/Duplication (Invitae) | 81351, 81479 | |



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| | Li-Fraumeni Syndrome, TP53 Sequencing and Deletion/Duplication (Quest Diagnostics) | | |
| **Multiple Endocrine Neoplasia - Type 1 (MEN1)** | | | |
| *MEN1* Targeted Variant Analysis | MEN1 Targeted Variant - Single Test (GeneDx) | 81479 | C25, C75.0, D35.2, E31.2, Z80, Z84, Z85, Z86 |
| *MEN1* Sequencing and/or Deletion/Duplication Analysis | MEN1 Gene Sequencing and Del/Dup (GeneDx) | 81404, 81405 | |
| | Multiple Endocrine Neoplasia Type 1 Test (Invitae) | | |
| **Multiple Endocrine Neoplasia Type 2 (MEN2)** | | | |
| *RET* Targeted Variant Analysis | RET Targeted Variant - Single Test (GeneDx) | 81404 | C73-75, C7A, D3A, Z80, Z84, Z85, Z86 |
| *RET* Sequencing and/or Deletion/Duplication Analysis | RET Full Gene Sequencing and Deletion/Duplication (Invitae) | 81406, 81479, S3840 | |
| **Nevoid Basal Cell Carcinoma Syndrome (NBCC) (aka Gorlin syndrome)** | | | |
| *PTCH1* and/or *SUFU* Targeted Variant Analysis | Targeted Variant: PTCH1 or SUFU (GeneDx) | 81479 | C44, C71.6, G93, M27.4, Z84, Z85, Z86 |
| *PTCH1* and *SUFU* Sequencing and/or Deletion/Duplication Analysis | Basal Cell Nevus Syndrome Panel (Invitae) | 81479 | |
| **Hereditary Paraganglioma/Pheochromocytoma Syndrome (PGL/PCC)** | | | |
| *MAX, SDHA, SDHAF2, SDHB, SDHC, SDHD,* or *TMEM127* Targeted Variant Analysis | SDHB, SDHD, SDHC, MAX, SDHAF2, or TMEM127 Targeted Variant - Single Test (GeneDx) Targeted Variants: MAX, SDHAF2, TMEM127 (PreventionGenetics, part of Exact Sciences) | 81479 | C7A, C74.1, D35.00, D44.7, Z84, Z85, Z86 |
| *MAX, SDHA, SDHAF2, SDHB, SDHC, SDHD,* and/or *TMEM127* Sequencing and/or Deletion/Duplication Analysis | SHDB Full Gene Sequencing and Deletion/Duplication (Invitae) | 81405, 81479 | |
| | SDHA Full Gene Sequencing and Deletion/Duplication (Invitae) | 81406, 81479 | |
| | SDHC Full Gene Sequencing and Deletion/Duplication (Invitae) | 81404, 81405 | |
| | SDHD Full Gene Sequencing and Deletion/Duplication (Invitae) | 81404, 81479 | |
| | MAX Full Gene Sequencing and Deletion/Duplication (Invitae) | 81479 | |
| | SDHAF2 Full Gene Sequencing and Deletion/Duplication (Invitae) | | |
| | TMEM127 Full Gene Sequencing and Deletion/Duplication (Invitae) | | |
| **Peutz-Jeghers Syndrome (PJS)** | | | |
| *STK11* Targeted Variant Analysis | STK11 Targeted Variant - Single Test (GeneDx) | 81479 | C50, Q85.8, Z80, Z84, Z85, Z86 |
| *STK11* Sequencing and/or Deletion/Duplication Analysis | STK11 Gene Sequencing & Del/Dup (GeneDx) | 81404, 81405 | |
| **Retinoblastoma** | | | |
| *RB1* Targeted Variant Analysis | Retinoblastoma: Site Specific Analysis (Familial) (Univ of | 81403 | C69, C75.3, Z80, Z84, Z85, Z86 |

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|---|---|---|---|
| | Pennsylvania School of Medicine-Genetic Diagnostic Laboratory) | | |
| *RB1* Sequencing and/or Deletion/Duplication Analysis | RB1 Full Gene Sequencing and Deletion/Duplication (Invitae) | 81479, S3841 | |
| **Von Hippel-Lindau Syndrome (VHL)** | | | |
| *VHL* Targeted Variant Analysis | VHL Known Mutation (Children's Hospital of Philadelphia - Division of Genomic Diagnostics) | 81403 | C64, C7A, D3A, D35.00, K86.2, N28, N50.3, Q85.8, Z80, Z84, Z85, Z86 |
| *VHL* Sequencing and/or Deletion/Duplication Analysis | VHL Full Gene Sequencing and Deletion/Duplication (Invitae) | 81403, 81404, S3842 | |
| | VHL Gene Sequencing and Del/Dup (GeneDx) | | |



## Coverage

### 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.).

1. Genetic testing using a pan-cancer hereditary cancer susceptibility panel is considered **medically necessary** when:
   - A. The member is 18 years or older, **and**
   - B. The member meets at least one of the following:
     - i. The member meets clinical criteria for *BRCA1* and *BRCA2* sequencing and/or deletion/duplication analysis, **or**
     - ii. The member meets clinical criteria for Lynch syndrome/HNPCC *MLH1*, *MSH2*, *MSH6*, *PMS2*, or *EPCAM* sequencing and/or deletion/duplication analysis, **and**
   - C. The panel includes, at a minimum, sequencing of the following genes: *BRCA1*, *BRCA2*, *EPCAM*, *MLH1*, *MSH2*, *MSH6*, *PMS2***.**
2. Genetic testing using a pan-cancer hereditary cancer susceptibility panel is considered **investigational** for all other indications.
3. Hereditary cancer susceptibility panel targeted mRNA sequencing analysis for the interpretation of variants of unknown significance, when billed in addition, 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.

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### Hereditary Breast Cancer Susceptibility Panels

A hereditary breast cancer susceptibility panel includes genes that are associated with inherited susceptibility to breast cancer.

1. Genetic testing using a hereditary breast cancer susceptibility panel is considered **medically necessary** when:
   - A. The member meets *BRCA1* and *BRCA2* Sequencing and/or Deletion/Duplication analysis, **and**
   - B. The panel includes, at a minimum, sequencing of the following genes: *BRCA1* and *BRCA2*.
2. Genetic testing using a STAT hereditary breast cancer panel is considered **medically necessary** when:
   - A. The member meets any of the above criteria, **and**
   - B. The member requires a rapid turn-around-time for decision making related to surgical interventions and treatment.
3. Genetic testing using a hereditary breast cancer susceptibility panel is considered **investigational** for all other indications.

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### Hereditary GI/Colon Cancer Susceptibility Panels

A hereditary colorectal cancer susceptibility panel includes genes that are associated with inherited susceptibility to colorectal cancer.

1. Genetic testing using a hereditary colorectal cancer susceptibility panel is considered **medically necessary** when:
   - A. The member meets at least one of the following:

i. The member has a personal history of, or at least one blood relative with, any of the following:
a) At least 10 adenomatous polyps, **or**
b) At least 2 hamartomatous polyps, **or**
c) At least 5 serrated polyps/lesions proximal to the rectum, **or**
ii. The member meets clinical criteria for Lynch syndrome/HNPCC *MLH1*, *MSH2*, *MSH6*, *PMS2*, or *EPCAM* Sequencing and/or Deletion/Duplication Analysis, **and**

B. The panel includes, at a minimum, sequencing of the following genes: *APC, BMPR1A, EPCAM*, *MLH1, MSH2, MSH6, MUTYH, PMS2*, *PTEN, SMAD4, STK11*, and *TP53***.**

2. Genetic testing using a hereditary colorectal cancer susceptibility panel is considered **investigational** for all other indications.

3. Hereditary colorectal cancer susceptibility panel targeted mRNA sequencing analysis for the interpretation of variants of unknown significance, when billed in addition, 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.

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## Hereditary Gastric Cancer Susceptibility Panels

A hereditary gastric cancer panel includes genes that are associated with inherited susceptibility to gastric (stomach) cancer.

1. Genetic testing using a hereditary gastric susceptibility panel is considered **medically necessary** when:
A. The member is 18 years or older, **and**
B. The member meets sequencing and/or deletion/duplication clinical criteria for at least one of the following:
i. Lynch syndrome/hereditary non-polyposis colorectal cancer, **or**
ii. Hereditary diffuse gastric cancer, **or**
iii. Juvenile Polyposis Syndrome, **or**
iv. Peutz-Jeghers Syndrome, **or**
v. Adenomatous Polyposis Syndromes, **and**
C. The panel includes, at a minimum, sequencing of the following genes: *APC, BMPR1A*, *CDH1, EPCAM, MLH1, MSH2, MSH6, PMS2*, *SMAD4, STK11*.
2. Genetic testing using a hereditary gastric cancer susceptibility panel is considered **investigational** for all other indications.

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## Hereditary Pancreatic Cancer Susceptibility Panels

A hereditary pancreatic cancer susceptibility panel includes genes that are associated with inherited susceptibility to pancreatic cancer.

1. Genetic testing using a hereditary pancreatic cancer susceptibility panel is considered **medically necessary** when:
A. The member is 18 years or older, **and**
B. The member meets criteria for *BRCA1* and *BRCA2* sequencing and/or deletion/duplication analysis, **and**
C. The panel includes, at a minimum, sequencing of the following genes: *ATM*, *BRCA1, BRCA2, CDKN2A, EPCAM, MLH1, MSH2, MSH6, PALB2, STK11*, *TP53*.
2. Genetic testing using a hereditary pancreatic cancer susceptibility panel is considered **investigational** for all other indications.

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## Hereditary Polyposis Susceptibility Panels

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

1. Genetic testing using a hereditary polyposis panel is considered **medically necessary** when:
A. The member meets criteria for sequencing and/or deletion/duplication analysis for Familial Adenomatous Polyposis (FAP)/Attenuated FAP (AFAP) and *MUTYH*-Associated Polyposis Syndrome (MAP), **and**
B. The panel includes, at a minimum, sequencing of the following genes: *APC* and *MUTYH*.
2. Genetic testing using a hereditary polyposis panel is considered **investigational** for all other indications.

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## Hereditary Prostate Cancer Susceptibility Panels

A hereditary prostate cancer susceptibility panel is one that includes genes that are associated with inherited susceptibility to prostate cancer.

1. Genetic testing using a hereditary prostate cancer susceptibility panel is considered **medically necessary** when:
   - A. The member is 18 years or older, **and**
   - B. The member has a personal history of any of the following:
     - i. Metastatic prostate cancer, **or**
     - ii. High- or very-high risk localized prostate cancer, **or**
     - iii. Intermediate risk prostate cancer with intraductal/cribriform histology, **or**
   - C. The member has a personal history of prostate cancer and any of the following:
     - i. One or more close relatives with any of the following:
       - a) Breast cancer at or under age 50, **or**
       - b) Triple-negative breast cancer at any age, **or**
       - c) Male (sex assigned at birth) breast cancer at any age, **or**
       - d) Ovarian cancer at any age, **or**
       - e) Exocrine pancreatic cancer at any age, **or**
       - f) Metastatic, very-high-risk, or high-risk prostate cancer at any age, **or**
     - ii. Three or more close relatives with prostate cancer (any grade) and/or breast cancer on the same side of the family including the member with prostate cancer, **or**
     - iii. Ashkenazi Jewish ancestry, **or**
   - D. The member has a first-degree blood relative meeting any of the criteria above, **or**
   - E. The member's probability of having a *BRCA1* or *BRCA2* pathogenic variant is greater than 2.5% based on prior probability models (examples: Tyrer-Cuzick, BRCApro, CanRisk), **and**
   - F. The panel includes, at a minimum, sequencing of the following genes: *BRCA1*, *BRCA2*.
2. Genetic testing using a hereditary prostate cancer susceptibility panel is considered **investigational** for all other indications.
3. Hereditary prostate cancer susceptibility panel targeted mRNA sequencing analysis for the interpretation of variants of unknown significance, when billed in addition, 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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## Hereditary Neuroendocrine Cancer Susceptibility Panels

A hereditary neuroendocrine cancer susceptibility panel is one that includes genes that are associated with inherited susceptibility to a neuroendocrine cancer.

1. Genetic testing using a hereditary neuroendocrine cancer susceptibility panel is considered **medically necessary** when:
   - A. The member has a diagnosis of at least one of the following:
     - i. Adrenocortical carcinoma, **or**
     - ii. Paraganglioma/pheochromocytoma, **or**
     - iii. Parathyroid adenoma or primary hyperparathyroidism before age 30, **or**
     - iv. Multiple parathyroid adenomas, **or**
     - v. Multigland hyperplasia without obvious secondary cause, **or**
     - vi. Recurrent primary hyperparathyroidism, **or**
     - vii. Gastrinoma, **or**
     - viii. Duodenal or pancreatic neuroendocrine tumor, **or**
     - ix. A first-degree relative meeting any of the above criteria, but is not available for testing, **or**
   - B. The member meets criteria for *MEN1* sequencing and/or deletion/duplication analysis, **or**
   - C. The member meets criteria for *RET* sequencing and/or deletion/duplication analysis.
2. Genetic testing using a hereditary neuroendocrine cancer susceptibility panel is considered **investigational** for all other indications.

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

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## BRCA1 and BRCA2 Gene Testing

### BRCA1 or BRCA2 Targeted Variant or Known Familial Variant Analysis

1. *BRCA1* or *BRCA2* targeted variant or known familial variant analysis for hereditary cancer susceptibility is considered **medically necessary** when:
   - A. The member is 18 years or older, **and**
   - B. One of the following:
     - i. The member has a family history of a known *BRCA1* or *BRCA2* pathogenic or likely pathogenic variant, **or**
     - ii. A pathogenic or likely pathogenic variant in *BRCA1* or *BRCA2* was identified by tumor profiling in the member and germline analysis has not yet been performed.

2. *BRCA1* or *BRCA2* targeted variant analysis for hereditary cancer susceptibility is considered **investigational** for all other indications.

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**BRCA1 and/or BRCA2 Targeted Variant Analysis - Ashkenazi Jewish Founder Variants**

1. *BRCA1* and *BRCA2* targeted variant analysis for the 185delAG, 5385insC, 6174delT variants is considered **medically necessary** when:
   - A. The member is 18 years or older, **and**
   - B. The member is of Ashkenazi Jewish ancestry (at least one grandparent of Ashkenazi Jewish ancestry)

2. *BRCA1* and *BRCA2* targeted variant analysis for the 185delAG, 5385insC, 6174delT variants is considered **investigational** for all other indications.

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**BRCA1 and BRCA2 Sequencing and/or Deletion/Duplication Analysis**

1. *BRCA1* and *BRCA2* sequencing and/or deletion/duplication analysis for hereditary breast and/or ovarian cancer susceptibility is considered **medically necessary** when:
   - A. The member is 18 years or older, **and**
   - B. The member has a personal history of any of the following:
     - i. Male (sex assigned at birth) breast cancer, **or**
     - ii. Triple-negative breast cancer, **or**
     - iii. Breast cancer diagnosed at age 65 or younger, **or**
     - iv. Epithelial ovarian cancer (including fallopian tube cancer or peritoneal cancer), **or**
     - v. Exocrine pancreatic or ampullary cancer, **or**
     - vi. Metastatic prostate cancer, **or**
     - vii. High- or very-high-risk group prostate cancer, **or**
     - viii. Multiple primary breast cancers (diagnosed synchronously or metachronously), **or**
   - C. The member has a personal history of breast cancer **and** any of the following:
     - i. Ashkenazi Jewish ancestry, **or**
     - ii. One or more close relatives with any of the following:
       - a) Female (sex assigned at birth) breast cancer diagnosed at age 50 years or younger, **or**
       - b) Male (sex assigned at birth) breast cancer, **or**
       - c) Ovarian cancer, **or**
       - d) Pancreatic cancer, **or**
       - e) Prostate cancer that is either metastatic, intermediate-risk with intraductal/cribriform histology, or high- or very-high-risk group, **or**
     - iii. Three or more total diagnoses of breast cancer and/or prostate cancer (any grade) on the same side of the family including the member with breast cancer, **or**
   - D. The member has a first- or second-degree relative meeting any of the above criteria, **or**
   - E. The member has metastatic breast cancer and is being considered for systemic treatment using PARP inhibitors, **or**
   - F. The member has high-risk, HER2-negative breast cancer and is being considered for adjuvant treatment with olaparib, **or**
   - G. The member's probability of having a BRCA1 or BRCA2 pathogenic variant is greater than 2.5% based on prior probability models (examples: Tyrer-Curzick, BRCApro, CanRisk).

2. *BRCA1* and *BRCA2* sequencing and/or deletion/duplication analysis for hereditary breast and/or ovarian cancer susceptibility is considered **investigational** for all other indications.

3. *BRCA1* and *BRCA2* mRNA sequencing analysis for the interpretation of variants of unknown significance, when billed in addition, 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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## PALB2 Gene Testing

**PALB2 Targeted Variant Analysis**

1. *PALB2* targeted variant analysis for hereditary breast and/or ovarian cancer susceptibility is considered **medically necessary** when:
   - A. The member is 18 years or older, **and**
   - B. One of the following:
     - i. The member has a family history of a known pathogenic or likely pathogenic variant in *PALB2*, **or**
     - ii. A pathogenic or likely pathogenic variant in *PALB2* was identified by tumor profiling in the member, and germline analysis has not yet been performed.

2. *PALB2* targeted variant analysis for hereditary breast and/or ovarian cancer susceptibility is considered **investigational** for all other indications.

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**PALB2 Sequencing and/or Deletion/Duplication Analysis**

1. *PALB2* sequencing and/or deletion/duplication analysis for hereditary breast and/or ovarian cancer susceptibility is considered **medically necessary** when:
   - A. The member is 18 years or older, **and**
   - B. One of the following:
     - i. The member has a personal history of any of the following:
       - a) Male (sex assigned at birth) breast cancer, **or**
       - b) Triple-negative breast cancer, **or**
       - c) Breast cancer diagnosed at age 50 or younger, **or**
       - d) Epithelial ovarian cancer (including fallopian tube cancer or peritoneal cancer), **or**
       - e) Exocrine pancreatic or ampullary cancer, **or**
       - f) Multiple primary breast cancers **(**diagnosed synchronously or metachronously), **or**
       - g) Metastatic prostate cancer, **or**
     - ii. The member has a personal history of breast cancer **and** any of the following:
       - a) Ashkenazi Jewish ancestry, **or**
       - b) One or more close relatives with any of the following:
         - (a) Female (sex assigned at birth) breast cancer diagnosed at age 50 years or younger, **or**
         - (b) Male (sex assigned at birth) breast cancer, **or**
         - (c) Ovarian cancer, **or**
         - (d) Exocrine pancreatic cancer, **or**
       - c) Three or more total diagnoses of breast cancer in the member and/or close blood relatives, **or**
     - iii. The member has a first- or second-degree relative meeting any of the above criteria, **or**
     - iv. The member has metastatic breast cancer and is being considered for systemic treatment decisions using PARP inhibitors, **or**
     - v. The member has high-risk, HER2-negative breast cancer and is being considered for adjuvant treatment with olaparib, **or**
     - vi. The member's probability of having a BRCA1 or BRCA2 pathogenic variant is greater than 2.5% based on prior probability models (examples: Tyrer-Curzick, BRCApro, CanRisk).
2. *PALB2* sequencing and/or deletion/duplication analysis for hereditary breast and/or ovarian cancer susceptibility is considered **investigational** for all other indications.
3. *PALB2* mRNA sequencing analysis for the interpretation of variants of unknown significance, when billed in addition, 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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## ATM and/or CHEK2 Gene Testing

**ATM or CHEK2 Targeted Variant Analysis**

1. *ATM* or *CHEK2* targeted variant analysis for hereditary breast and/or ovarian cancer susceptibility is considered **medically necessary** when:
   - A. The member is 18 years or older, **and**
   - B. One of the following:
     - i. The member has a close relative with a known pathogenic or likely pathogenic variant in *ATM* or *CHEK2*, **or**
     - ii. A pathogenic or likely pathogenic variant in *ATM* or *CHEK2* was identified by tumor profiling in the member and germline analysis has not yet been performed.
2. *ATM* or *CHEK2* targeted variant analysis for hereditary breast and/or ovarian cancer susceptibility is considered **investigational** for all other indications.

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**ATM and/or CHEK2 Sequencing and/or Deletion/Duplication Analysis**

1. *ATM* and/or *CHEK2* sequencing and/or deletion/duplication analysis for hereditary breast and/or ovarian cancer susceptibility, as a stand-alone test, is considered **investigational**.
2. *ATM* mRNA sequencing analysis for the interpretation of variants of unknown significance, when billed in addition, 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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## Lynch Syndrome / Hereditary Nonpolyposis Colorectal Cancer (HNPCC) Testing

### MLH1, MSH2, MSH6, PMS2, or EPCAM Targeted Variant Analysis

1. *MLH1*, *MSH2*, *MSH6*, *PMS2*, or *EPCAM* targeted variant analysis for Lynch syndrome/HNPCC is considered **medically necessary** when:
    - A. The member has a blood relative with a known pathogenic or likely pathogenic variant in *MLH1*, *MSH2*, *MSH6*, *PMS2*, or *EPCAM*, **or**
    - B. A pathogenic or likely pathogenic variant in *MLH1*, *MSH2*, *MSH6*, *PMS2,* or *EPCAM* was identified by tumor profiling in the member and germline analysis has not yet been performed.
2. *MLH1*, *MSH2*, *MSH6*, *PMS2*, or *EPCAM* targeted variant analysis for Lynch syndrome/HNPCC is considered **investigational** for all other indications.

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### MLH1, MSH2, MSH6, PMS2, and/or EPCAM Sequencing and/or Deletion/Duplication Analysis

1. *MLH1*, *MSH2*, *MSH6*, *PMS2*, and/or *EPCAM* sequencing and/or duplication analysis for Lynch syndrome/HNPCC is considered **medically necessary** when:
    - A. The member has a Lynch syndrome-related cancer **and** the tumor shows evidence of mismatch repair (MMR) deficiency (either by microsatellite instability (MSI) or loss of MMR protein expression), **or**
    - B. The member has a diagnosis of a Lynch syndrome-related cancer, **and** any of the following:
        - i. Diagnosed before age 50, **or**
        - ii. Diagnosed at any age with an additional Lynch syndrome-related cancer, **or**
        - iii. Diagnosed at any age with one or more first- or second-degree relatives diagnosed before age 50 with a Lynch syndrome-related cancer, **or**
        - iv. Diagnosed at any age with two or more first- or second-degree relatives diagnosed at any age with a Lynch syndrome-related cancer, **or**
    - C. The member has a family history of **any** of the following:
        - i. One or more first-degree relatives diagnosed with colorectal or endometrial cancer before age 50, **or**
        - ii. One or more first-degree relatives diagnosed with colorectal or endometrial cancer and an additional Lynch syndrome-related cancer, **or**
        - iii. Two or more first- or second-degree relatives on the same side of the family diagnosed with a Lynch syndrome-related cancer, one of whom was diagnosed before age 50, **or**
        - iv. Three or more first- or second-degree relatives on the same side of the family diagnosed with a Lynch syndrome-related cancer, **or**
    - D. The member has a 5% or greater risk of having Lynch syndrome based on one of the following variant prediction models: MMRpro, PREMM5, MMRpredict, **or**
    - E. The member has a personal history of colorectal and/or endometrial cancer with a PREMM5 score of 2.5% or greater.
2. *MLH1*, *MSH2*, *MSH6*, *PMS2*, and/or *EPCAM* sequencing and/or duplication analysis for Lynch syndrome/HNPCC is considered **investigational** for all other indications.
3. *MLH1, MSH2, MSH6, PMS2,* and *EPCAM* mRNA sequencing analysis for the interpretation of variants of unknown significance, when billed in addition, 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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## BAP1-Tumor Predisposition Syndrome

### BAP1 Targeted Variant Analysis

1. *BAP1* targeted variant analysis for *BAP1*-tumor predisposition syndrome is considered **medically necessary** when:
    - A. The member has a close relative with a known pathogenic or likely pathogenic variant in *BAP1*, **or**
    - B. A pathogenic or likely pathogenic variant in *BAP1* was identified by tumor profiling in the member and germline analysis has not yet been performed.
2. *BAP1* targeted variant analysis for *BAP1*-tumor predisposition syndrome is considered **investigational** for all other indications.

### BAP1 Sequencing and/or Deletion/Duplication Analysis

1. *BAP1* sequencing and/or deletion/duplication analysis for *BAP1*-tumor predisposition syndrome is considered **medically necessary** when:
    - A. The member has a personal history of:
        - i. Two or more of the following:

a) *BAP1*-inactivated melanocytic tumors (aka atypical spitz tumor), **or**
b) Uveal melanoma, **or**
c) Malignant mesothelioma, **or**
d) Renal cell carcinoma, **or**
e) Hepatocellular carcinoma, **or**
f) Cholangiocarcinoma, **or**
g) Meningioma, **or**

ii. One of the tumors/cancers listed in the criteria A.i., **and**
a) A cutaneous melanoma, **or**
b) A basal cell carcinoma, **or**

iii. One of the tumors/cancers listed in the criteria A.i., **and**
a) A first- or second-degree relative with any of the following tumors/cancers:
(a) *BAP1*-inactivated melanocytic tumors (aka atypical spitz tumor), **or**
(b) Uveal melanoma, **or**
(c) Malignant mesothelioma, **or**
(d) Renal cell carcinoma, **or**
(e) Hepatocellular carcinoma, **or**
(f) Cholangiocarcinoma, **or**
(g) Meningioma, **or**
(h) Cutaneous melanoma, **or**
(i) Basal cell carcinoma, **or**

iv. Both of the following:
a) A diagnosis of:
(a) Cutaneous melanoma, **or**
(b) Basal cell carcinoma, **and**
b) A first- or second-degree relative with any of the following tumors/cancer:
(a) *BAP1*-inactivated melanocytic tumors (aka atypical spitz tumor), **or**
(b) Uveal melanoma, **or**
(c) Malignant mesothelioma, **or**
(d) Renal cell carcinoma, **or**
(e) Hepatocellular carcinoma, **or**
(f) Cholangiocarcinoma, **or**
(g) Meningioma.

2. *BAP1* sequencing and/or deletion/duplication analysis for *BAP1*-tumor predisposition syndrome is considered **investigational** for all other indications.

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## Birt-Hogg-Dube Syndrome (BHDS)

### FLCN Targeted Variant Analysis

1. *FLCN* targeted variant analysis for Birt-Hogg-Dube syndrome (BHDS) is considered **medically necessary** when:
A. The member has a first- or second-degree relative with a known pathogenic or likely pathogenic variant in *FLCN*, **or**
B. A pathogenic or likely pathogenic variant in *FLCN* was identified by tumor profiling in the member and germline analysis has not yet been performed.
2. *FLCN* targeted variant analysis for Birt-Hogg-Dube syndrome (BHDS) is considered **investigational** for all other indications.

### FLCN Sequencing and/or Deletion/Duplication Analysis

1. *FLCN* sequencing and/or deletion/duplication analysis for Birt-Hogg-Dube syndrome (BHDS) is considered **medically necessary** when:
A. The member has a personal history of any of the following:
i. 5 or more fibrofolliculomas/trichodiscomas with at least one confirmed histologically, **or**
ii. Multiple lung cysts with no apparent cause, with or without pneumothorax, **or**
iii. Renal cancer diagnosed before 50 years of age, **or**
iv. Multifocal or bilateral renal cancer, **or**
v. Renal cancer of mixed chromophobe and oncocytic histology, **or**
vi. A first-degree relative with BHDS who has not yet had genetic testing, or the results of genetic testing are unknown.

2. *FLCN* sequencing and/or deletion/duplication analysis for Birt-Hogg-Dube syndrome (BHDS) is considered **investigational** for all other indications.

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## Cowden Syndrome (CS)/*PTEN* Hamartoma Tumor Syndrome (PHTS)

### PTEN Targeted Variant Analysis

1. *PTEN* targeted variant analysis for Cowden syndrome (CS)/PTEN hamartoma tumor syndrome (PHTS) is considered **medically necessary** when:
   - A. The member has a blood relative with a known pathogenic or likely pathogenic variant in *PTEN*, **or**
   - B. A pathogenic or likely pathogenic variant in *PTEN* was identified by tumor profiling in the member and germline analysis has not yet been performed.
2. *PTEN* targeted variant analysis for Cowden syndrome (CS)/PTEN hamartoma tumor syndrome (PHTS) is considered **investigational** for all other indications.

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### PTEN Sequencing and/or Deletion/Duplication Analysis

1. *PTEN* sequencing and/or deletion/duplication analysis for Cowden syndrome (CS)/PTEN hamartoma tumor syndrome (PHTS) is considered **medically necessary** when:
   - A. The member has a personal history of any of the following:
     - i. Bannayan Riley-Ruvalcaba syndrome (BRRS), **or**
     - ii. Adult Lhermitte-Duclos disease (LDD), defined as the presence of cerebellar dysplastic gangliocytoma, **or**
     - iii. Autism-spectrum disorder and macrocephaly, **or**
     - iv. At least 2 biopsy-proven trichilemmomas, **or**
   - B. The member meets clinical criteria for CS/PHTS:
     - i. Macrocephaly (greater than or equal to 97 percentile), **or**
     - ii. Lhermitte-Duclos disease, **or**
     - iii. Gastrointestinal hamartomas or ganglioneuromas, **and**
     - iv. At least two of the following:
       - a) Breast cancer, **or**
       - b) Endometrial cancer, **or**
       - c) Thyroid cancer (follicular), **or**
       - d) Macular pigmentation of the glans penis, **or**
       - e) Mucocutaneous lesions (one biopsy-proven trichilemmoma; multiple palmoplantar keratoses; multifocal or extensive oral mucosal papillomatosis; multiple cutaneous facial papules), **or**
   - C. The member has at least two of the following:
     - i. Breast cancer, **or**
     - ii. Endometrial cancer, **or**
     - iii. Thyroid cancer (follicular), **or**
     - iv. Multiple gastrointestinal hamartomas or ganglioneuromas, **or**
     - v. Macrocephaly (greater than or equal to 97 percentile), **or**
     - vi. Macular pigmentation of the glans penis, **or**
     - vii. Mucocutaneous lesions (one biopsy-proven trichilemmoma; multiple palmoplantar keratoses; multifocal or extensive oral mucosal papillomatosis; multiple cutaneous facial paules), **and**
     - viii. At least three of the following:
       - a) Autism Spectrum Disorder, **or**
       - b) Colon cancer, **or**
       - c) Esophageal glycogenic acanthosis (3 or more), **or**
       - d) Lipomas, **or**
       - e) Intellectual disability (i.e., IQ less than or equal to 75), **or**
       - f) Thyroid cancer (papillary or follicular variant of papillary thyroid cancer), **or**
       - g) Thyroid structural lesions (such as adenoma, multinodular goiter), **or**
       - h) Renal cell carcinoma, **or**
       - i) Single GI hamartoma or ganglioneuroma, **or**
       - j) Testicular lipomatosis, **or**
       - k) Vascular anomalies (including multiple intracranial developmental venous anomalies), **or**
   - D. The member has macrocephaly, **and**
     - i. Breast cancer, **or**
     - ii. Endometrial cancer, **or**

iii. Thyroid cancer (follicular), **or**
iv. Multiple gastrointestinal hamartomas or ganglioneuromas, **or**
v. Macrocephaly (greater than or equal to 97 percentile), **or**
vi. Macular pigmentation of the glans penis, **or**
vii. Mucocutaneous lesions (One biopsy-proven trichilemmoma; multiple palmoplantar keratoses; multifocal or extensive oral mucosal papillomatosis; multiple cutaneous facial papules), **or**

E. The member has at least three of the following:
i. Breast cancer, **or**
ii. Endometrial cancer, **or**
iii. Thyroid cancer (follicular), **or**
iv. Multiple gastrointestinal hamartomas or ganglioneuromas, **or**
v. Macular pigmentation of the glans penis, **or**
vi. Mucocutaneous lesions (One biopsy-proven trichilemmoma; multiple palmoplantar keratoses; multifocal or extensive oral mucosal papillomatosis; multiple cutaneous facial papules), **or**
vii. The member has a close relative with a clinical diagnosis of CS/PHTS or BRRS for whom testing has not been performed, **or**

F. The member has both of the following:
i. Breast cancer, **or**
ii. Endometrial cancer, **or**
iii. Thyroid cancer (follicular), **or**
iv. Multiple gastrointestinal hamartomas or ganglioneuromas, **or**
v. Macrocephaly (greater than or equal to 97 percentile), **or**
vi. Macular pigmentation of the glans penis, **or**
vii. Mucocutaneous lesions (One biopsy-proven trichilemmoma; multiple palmoplantar keratoses; multifocal or extensive oral mucosal papillomatosis; multiple cutaneous facial papules), **and**
viii. At least three of the following:
a) Autism Spectrum Disorder, **or**
b) Colon cancer, **or**
c) Esophageal glycogenic acanthosis (3 or more), **or**
d) Lipomas, **or**
e) Intellectual disability (i.e., IQ less than or equal to 75), **or**
f) Thyroid cancer (papillary or follicular variant of papillary thyroid cancer), **or**
g) Thyroid structural lesions (such as adenoma, multinodular goiter), **or**
h) Renal cell carcinoma, **or**
i) Single GI hamartoma or ganglioneuroma, **or**
j) Testicular lipomatosis, **or**
k) Vascular anomalies (including multiple intracranial developmental venous anomalies), **or**

G. The member has at least four of the following:
i. Autism Spectrum Disorder, **or**
ii. Colon cancer, **or**
iii. Esophageal glycogenic acanthosis (3 or more), **or**
iv. Lipomas, **or**
v. Intellectual disability (i.e., IQ less than or equal to 75), **or**
vi. Thyroid cancer (papillary or follicular variant of papillary thyroid cancer), **or**
vii. Thyroid structural lesions (such as adenoma, multinodular goiter), **or**
viii. Renal cell carcinoma, **or**
ix. Single GI hamartoma or ganglioneuroma, **or**
x. Testicular lipomatosis, **or**
xi. Vascular anomalies (including multiple intracranial developmental venous anomalies), **or**

H. The member has a close relative with a clinical diagnosis of CS/PHTS or BRRS for whom testing has not been performed, **and**
i. The member has at least one of the following:
a) Breast cancer, **or**
b) Endometrial cancer, **or**
c) Thyroid cancer (follicular), **or**
d) Multiple gastrointestinal hamartomas or ganglioneuromas, **or**

e) Macrocephaly (greater than or equal to 97 percentile), **or**
f) Macular pigmentation of the glans penis, **or**
g) Mucocutaneous lesions (One biopsy-proven trichilemmoma; multiple palmoplantar keratoses; multifocal or extensive oral mucosal papillomatosis; multiple cutaneous facial papules), **or**

ii. At least two of the following:
a) Autism Spectrum Disorder, **or**
b) Colon cancer, **or**
c) Esophageal glycogenic acanthosis (3 or more), **or**
d) Lipomas, **or**
e) Intellectual disability (i.e., IQ less than or equal to 75), **or**
f) Thyroid cancer (papillary or follicular variant of papillary thyroid cancer), **or**
g) Thyroid structural lesions (such as adenoma, multinodular goiter), **or**
h) Renal cell carcinoma, **or**
i) Single GI hamartoma or ganglioneuroma, **or**
j) Testicular lipomatosis, **or**
k) Vascular anomalies (including multiple intracranial developmental venous anomalies).

2. *PTEN* sequencing and/or deletion/duplication analysis for Cowden syndrome (CS)/PTEN hamartoma tumor syndrome (PHTS) is considered **investigational** for all other indications**.**

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## Adenomatous Polyposis Conditions (Familial Adenomatous Polyposis Syndrome (FAP)/Attenuated FAP (AFAP) AND/OR *MUTYH*-Associated Polyposis Syndrome (MAP)

### *APC* AND/OR *MUTYH* Targeted Variant Analysis

1. *APC* and/or *MUTYH* targeted variant analysis for adenomatous polyposis testing is considered **medically necessary** when:
A. The member has a family history of a known pathogenic or likely pathogenic variant in *APC* or *MUTYH*, **or**
B. A pathogenic or likely pathogenic variant in *APC* or *MUTYH* was identified by tumor profiling in the member and germline analysis has not yet been performed.
2. *APC* and/or *MUTYH* targeted variant analysis for adenomatous polyposis conditions is considered **investigational** for all other indications.

### *APC* AND/OR *MUTYH* Sequencing and/or Deletion/Duplication Analysis

1. *APC* sequencing and/or deletion/duplication analysis and/or *MUTYH* sequencing and/or deletion/duplication analysis for adenomatous polyposis conditions is considered **medically necessary** when:
A. The member has a history of any of the following:
i. 10 or more cumulative adenomas, **or**
ii. Congenital hypertrophy of the retinal pigment epithelium (CHRPE), **or**
iii. Desmoid tumor, **or**
iv. Hepatoblastoma, **or**
v. Cribriform-morular variant of papillary thyroid cancer, **or**
vi. 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, **or**
vii. Duodenal cancer, **or**
viii. Duodenal adenomas.
2. *APC* sequencing and/or deletion/duplication analysis and/or *MUTYH* sequencing and/or deletion/duplication analysis for adenomatous polyposis conditions is considered **investigational** for all other indications.
3. *APC* mRNA sequencing analysis for the interpretation of variants of unknown significance, when billed in addition, 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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## Familial Atypical Multiple Mole Melanoma (FAMMM) Syndrome

### CDKN2A Targeted Variant Analysis

1. *CDKN2A* targeted variant analysis for familial atypical multiple mole melanoma (FAMMM) syndrome, also known as melanoma-pancreatic cancer syndrome, is considered **medically necessary** when:
   A. The member has a close relative with a known pathogenic or likely pathogenic variant in *CDKN2A*, **or**
   B. A *CDKN2A* pathogenic or likely pathogenic variant was identified by tumor profiling in the member and germline analysis has not yet been performed.
2. *CDKN2A* targeted variant analysis for familial atypical multiple mole melanoma (FAMMM) syndrome, also known as melanoma-pancreatic cancer syndrome is considered **investigational** for all other indications.

**CDKN2A Sequencing and/or Deletion/Duplication Analysis**

1. *CDKN2A* sequencing and/or deletion/duplication analysis for familial atypical multiple mole melanoma (FAMMM) syndrome, also known as melanoma-pancreatic cancer syndrome, is considered **medically necessary** when:
   A. The member has had 3 or more invasive cutaneous melanomas, **or**
   B. The member has had pancreatic adenocarcinoma, **or**
   C. The member has had at least one cutaneous melanoma, **and**
      i. The member has at least two close relatives with pancreatic cancer or cutaneous melanoma on the same side of the family.
2. CDKN2A sequencing and/or deletion/duplication analysis for familial atypical multiple mole melanoma (FAMMM) syndrome, also known as melanoma-pancreatic cancer syndrome is considered Investigational for all other indications.

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## Hereditary Diffuse Cancer (aka, Signet Ring Cell Gastric Cancer):

**CDH1 Targeted Variant Analysis**

1. *CDH1* targeted variant analysis for Hereditary Diffuse Gastric Cancer (aka, Signet Ring Cell Gastric Cancer) is considered **medically necessary** when:
   A. The member is 18 years or older, **and**
   B. One of the following:
      i. The member has a close relative with a known pathogenic or likely pathogenic variant in *CDH1*, **or**
      ii. A pathogenic or likely pathogenic variant in *CDH1* was identified by tumor profiling in the member and germline analysis has not yet been performed.
2. *CDH1* targeted variant analysis for Hereditary Diffuse Gastric Cancer (aka, Signet Ring Cell Gastric Cancer) is considered **investigational** for all other indications.

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**CDH1 Sequencing and/or Deletion/Duplication Analysis**

1. *CDH1* sequencing and/or deletion/duplication analysis for Hereditary Diffuse Gastric Cancer (aka, Signet Ring Cell Gastric Cancer) is considered **medically necessary** when:
   A. The member is 18 years or older, **and**
   B. The member meets at least one of the following criteria:
      i. Diffuse gastric cancer diagnosed before age 50 years, **or**
      ii. Diffuse gastric cancer diagnosed at any age in a member with Maori ancestry, **or**
      iii. Diffuse gastric cancer diagnosed at any age in a member with a personal or family history of cleft lip/cleft palate, **or**
      iv. Bilateral lobular breast cancer diagnoses before age 70 years, **or**
      v. Personal or family history of diffuse gastric cancer and lobular breast cancer, one diagnosed before age 70 years, **or**
      vi. Two cases of gastric cancer in the family, at least one of which is a confirmed case of diffuse gastric cancer, diagnosed at any age, **or**
      vii. Two cases of lobular breast cancer in family members before 50 years of age.
2. *CDH1* sequencing and/or deletion/duplication analysis for Hereditary Diffuse Gastric Cancer (aka, Signet Ring Cell Gastric Cancer) is considered **investigational** for all other indications.

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## Juvenile Polyposis Syndrome (JPS)

**SMAD4 or BMPR1A Targeted Variant Analysis**

1. *SMAD4* and/or *BMPR1A* targeted variant analysis for juvenile polyposis syndrome (JPS) is considered **medically necessary** when:
   A. The member has a blood relative with a known pathogenic or likely pathogenic variant in *SMAD4* and/or *BMPR1A*, **or**
   B. A pathogenic or likely pathogenic variant in *SMAD4* and/or *BMPR1A* was identified by tumor profiling in the member and germline analysis has not yet been performed.

2. *SMAD4* and/or *BMPR1A* targeted variant analysis for juvenile polyposis syndrome (JPS) is considered **investigational** for all other indications.

**SMAD4 and/or BMPR1A Sequencing and/or Deletion/Duplication Analysis**

1. *SMAD4* and/or *BMPR1A* sequencing and/or deletion/duplication analysis for juvenile polyposis syndrome (JPS) is considered **medically necessary** when:
   - A. The member has 5 or more juvenile polyps in the colon, **or**
   - B. The member has multiple juvenile polyps throughout the gastrointestinal tract, **or**
   - C. The member has a family history of JPS.
2. *SMAD4* and/or *BMPR1A* sequencing and/or deletion/duplication analysis for juvenile polyposis syndrome (JPS) is considered **investigational** for all other indications.

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## Hereditary Leiomyomatosis and Renal Cell Cancer (HLRCC)

**FH Targeted Variant Analysis**

1. *FH* targeted variant analysis for hereditary leiomyomatosis and renal cell cancer (HLRCC) is considered **medically necessary** when:
   - A. The member has a first- or second-degree relative with a known pathogenic or likely pathogenic variant in *FH*, **or**
   - B. A pathogenic or likely pathogenic variant in *FH* was identified by tumor profiling in the member and germline analysis has not yet been performed.
2. *FH* targeted variant analysis for hereditary leiomyomatosis and renal cell cancer (HLRCC) is considered **investigational** for all other indications.

**FH Sequencing and/or Deletion/Duplication Analysis**

1. *FH* sequencing and/or deletion/duplication analysis for hereditary leiomyomatosis and renal cell cancer (HLRCC) is considered **medically necessary** when:
   - A. The member is 18 years or older, **and**
   - B. The member has at least one of the following:
     - i. Cutaneous leiomyomata, **or**
     - ii. Uterine leiomyomata (uterine fibroids), **or**
     - iii. Renal cell carcinoma.
2. *FH* sequencing and/or deletion/duplication analysis for hereditary leiomyomatosis and renal cell cancer (HLRCC) is considered **investigational** for all other indications.

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## Li-Fraumeni Syndrome (LFS)

**TP53 Targeted Variant Analysis**

1. *TP53* targeted variant analysis for Li-Fraumeni syndrome (LFS) is considered **medically necessary** when:
   - A. The member has a close relative with a known pathogenic or likely pathogenic variant in *TP53*, **or**
   - B. A pathogenic or likely pathogenic variant in *TP53* was identified by tumor profiling in the member and germline analysis has not yet been performed.
2. *TP53* targeted variant analysis for Li-Fraumeni syndrome (LFS) is considered **investigational** for all other indications.

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**TP53 Sequencing and/or Deletion/Duplication Analysis**

1. *TP53* sequencing and/or deletion/duplication analysis for Li-Fraumeni syndrome (LFS) is considered **medically necessary** when:
   - A. The member was diagnosed with breast cancer before 31 years of age, **or**
   - B. The member has a personal or family history of pediatric hypodiploid acute lymphoblastic leukemia, **or**
   - C. The member was diagnosed with a sarcoma before 45 years of age, **and**
     - i. The member has a first-degree relative diagnosed with any cancer before 45 years of age, **and**
     - ii. At least one of the following:
       - a) The member has an additional first- or second-degree relative diagnosed with any cancer before 45 years of age, **or**
       - b) The member has an additional first- or second-degree relative diagnosed with sarcoma at any age, **or**
   - D. The member was diagnosed with any of the following at any age:
     - i. Adrenocortical carcinoma, **or**
     - ii. Choroid plexus carcinoma, **or**
     - iii. Rhabdomyosarcoma of embryonal anaplastic subtype, **or**

E. The member was diagnosed with any of the following tumors from the LFS tumor spectrum before 46 years of age:
   i. Soft tissue sarcoma, **or**
   ii. Osteosarcoma, **or**
   iii. Central nervous system tumor, **or**
   iv. Breast cancer, **or**
   v. Adrenocortical carcinoma, **and**
      a) The member has had a second tumor from the LFS tumor spectrum (except breast cancer if the initial cancer was breast cancer), **or**
      b) The member has a first- or second-degree relative with a tumor from the LFS tumor spectrum before 56 years of age (except breast cancer if the member had breast cancer), **or**
      c) The member has a first- or second-degree relative with a history of multiple primary tumors at any age.

2. *TP53* sequencing and/or deletion/duplication analysis for Li-Fraumeni syndrome (LFS) is considered **investigational** for all other indications**.**

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## Multiple Endocrine Neoplasia Type 1 (MEN1)

### ***MEN1*** **Targeted Variant Analysis**

1. *MEN1* targeted variant analysis for multiple endocrine neoplasia type 1 (MEN1) is considered **medically necessary** when:
   A. The member has a close relative with a known pathogenic or likely pathogenic variant in *MEN1*, **or**
   B. A pathogenic or likely pathogenic variant in *MEN1* was identified by tumor profiling in the member and germline analysis has not yet been performed.
2. *MEN1* targeted variant analysis for multiple endocrine neoplasia type 1 (MEN1) is considered **investigational** for all other indications.

### ***MEN1*** **Sequencing and/or Deletion/Duplication Analysis**

1. *MEN1* sequencing and/or deletion/duplication analysis for multiple endocrine neoplasia type 1 (MEN1) is considered **medically necessary** when:
   A. The member has a personal history of at least **two** of the following:
      i. Duodenal/pancreatic neuroendocrine tumor, **or**
      ii. Primary hyperparathyroidism, **or**
      iii. Pituitary adenoma, **or**
      iv. Foregut (bronchial, thymic, or gastric) carcinoid, **or**
   B. The member has a personal history of one of the above, **and**
      i. The member has a close relative with at least one of the above.
2. *MEN1* sequencing and/or deletion/duplication analysis for multiple endocrine neoplasia type 1 (MEN1) is considered **investigational** for all other indications**.**

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## Multiple Endocrine Neoplasia Type 2 (MEN2)

### ***RET*** **Targeted Variant Analysis**

1. *RET* targeted variant analysis for multiple endocrine neoplasia type 2 (MEN2) is considered **medically necessary** when:
   A. The member has a close relative with a known pathogenic or likely pathogenic variant in *RET*, **or**
   B. A pathogenic or likely pathogenic variant in *RET* was identified by tumor profiling in the member and germline analysis has not yet been performed.
2. *RET* targeted variant analysis for multiple endocrine neoplasia type 2 (MEN2) is considered **investigational** for all other indications.

### ***RET*** **Sequencing and/or Deletion/Duplication Analysis**

1. *RET* sequencing and/or deletion/duplication analysis for multiple endocrine neoplasia type 2 (MEN2) is considered **medically necessary** when:
   A. The member has a diagnosis of any of the following:
      i. Medullary thyroid cancer, **or**
      ii. Adrenal pheochromocytoma, **or**
      iii. Parathyroid adenoma or hyperplasia, **or**
   B. The member has a first-degree relative that meets at least one of the above criteria, **and**
      i. The relative has not previously undergone *RET* sequencing and/or deletion duplication analysis.
2. *RET* sequencing and/or deletion/duplication analysis for multiple endocrine neoplasia type 2 (MEN2) is considered **investigational** for all other indications.

## Nevoid Basal Cell Carcinoma Syndrome (NBCCS) (akd Gorlin syndrome)

### *PTCH1* or *SUFU* Targeted Variant Analysis

1. *PTCH1* or *SUFU* targeted variant analysis for nevoid basal cell carcinoma syndrome (NBCCS), also known as Gorlin syndrome, is considered **medically necessary** when:
   - A. The member has a close relative with a known pathogenic or likely pathogenic variant in *PTCH1* or *SUFU*, **or**
   - B. A pathogenic or likely pathogenic variant in *PTCH1* or *SUFU* was identified by tumor profiling in the member and germline analysis has not yet been performed.
2. *PTCH1* or *SUFU* targeted variant analysis for nevoid basal cell carcinoma syndrome (NBCCS), also known as Gorlin syndrome, is considered **investigational** for all other indications.

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### *PTCH1* and *SUFU* Sequencing and/or Deletion/Duplication Analysis

1. *PTCH1* and *SUFU* sequencing and/or deletion/duplication analysis for nevoid basal cell carcinoma syndrome (NBCCS), also known as Gorlin syndrome, is considered **medically necessary** when:
   - A. The member has a personal history of:
     - i. At least two of the following:
       - a) Lamellar calcification of the falx, **or**
       - b) Jaw keratocyst, **or**
       - c) Palmar/plantar pits (2 or more), **or**
       - d) Multiple basal cell carcinomas (more than 5 in lifetime) or a basal cell carcinoma diagnosed before 30 years of age, **or**
       - e) A first-degree relative with NBCCS, **and**
     - ii. At least one of the following:
       - a) Childhood medulloblastoma, **or**
       - b) Lympho-mesenteric or pleural cysts, **or**
       - c) Macrocephaly (OFC greater than 97th centile), **or**
       - d) Cleft lip/palate, **or**
       - e) Vertebral/rib anomalies (bifid/splayed/extra ribs; bifid vertebrae), **or**
       - f) Pre- or post-axial polydactyly, **or**
       - g) Ovarian fibromas, **or**
       - h) Cardiac fibromas, **or**
       - i) Ocular anomalies (examples: cataract, pigmentary changes of the retinal epithelium, developmental defects), **or**
   - B. The member has a personal history of:
     - i. At least one of the following:
       - a) Lamellar calcification of the falx, **or**
       - b) Jaw keratocyst, **or**
       - c) Palmar/plantar pits (2 or more), **or**
       - d) Multiple basal cell carcinomas (more than 5 in lifetime) or a basal cell carcinoma diagnosed before 30 years of age, **or**
       - e) A first-degree relative with NBCCS, **and**
     - ii. At least three of the following:
       - a) Childhood medulloblastoma, **or**
       - b) Lympho-mesenteric or pleural cysts, **or**
       - c) Macrocephaly (OFC greater than 97th centile), **or**
       - d) Cleft lip/palate, **or**
       - e) Vertebral/rib anomalies (bifid/splayed/extra ribs; bifid vertebrae), **or**
       - f) Pre- or post-axial polydactyly, **or**
       - g) Ovarian fibromas, **or**
       - h) Cardiac fibromas, **or**
       - i) Ocular anomalies (examples: cataract, pigmentary changes of the retinal epithelium, developmental defects).
2. *PTCH1* and *SUFU* sequencing and/or deletion/duplication analysis is considered **investigational** for all other indications.

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## Hereditary Paraganglioma/Pheochromocytoma Syndrome (PGL/PCC)

### *MAX*, *SDHA*, *SDHAF2*, *SDHB*, *SDHC*, *SDHD*, or *TMEM127* Targeted Variant Analysis

1. *MAX*, *SDHA*, *SDHAF2*, *SDHB*, *SDHC*, *SDHD*, or *TMEM127* targeted variant analysis for hereditary paraganglioma/pheochromocytoma syndrome (PGL/PCC) is considered **medically necessary** when:
   - A. The member has a close relative with a known pathogenic or likely pathogenic variant in *MAX*, *SDHA*, *SDHAF2*, *SDHB*, *SDHC*, *SDHD*, or *TMEM127*, **or**

B. A pathogenic or likely pathogenic variant in *MAX*, *SDHA*, *SDHAF2*, *SDHB*, *SDHC*, *SDHD*, or *TMEM127* was identified by tumor profiling in the member and germline analysis has not yet been performed.

2. *MAX*, *SDHA*, *SDHAF2*, *SDHB*, *SDHC*, *SDHD*, or *TMEM127* targeted variant analysis for hereditary paraganglioma/pheochromocytoma syndrome (PGL/PCC) is considered **investigational** for all other indications.

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***MAX*, *SDHA*, *SDHAF2*, *SDHB*, *SDHC*, *SDHD*, and *TMEM127* Sequencing and/or Deletion/Duplication Analysis**

1. *MAX*, *SDHA*, *SDHAF2*, *SDHB*, *SDHC*, *SDHD*, and *TMEM127* sequencing and/or deletion/duplication analysis for hereditary paraganglioma/pheochromocytoma syndrome (PGL/PCC) is considered **medically necessary** when:
   A. The member has a diagnosis of one or more of the following:
      i. Pheochromocytoma, **or**
      ii. Paraganglioma, **or**
      iii. Clear cell renal cell cancer, **or**
      iv. Gastrointestinal stromal tumor (GIST), **or**
   B. The member has a close relative with paraganglioma or pheochromocytoma.
2. *MAX*, *SDHA*, *SDHAF2*, *SDHB*, *SDHC*, *SDHD*, and *TMEM127* sequencing and/or deletion/duplication for hereditary paraganglioma/pheochromocytoma syndrome (PGL/PCC) is considered **investigational** for all other indications.

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## Peutz-Jeghers Syndrome (PJS)

***STK11* Targeted Variant Analysis**

1. *STK11* targeted variant analysis for Peutz-Jeghers syndrome is considered **medically necessary** when:
   A. The member has a blood relative with a known pathogenic or likely pathogenic variant in *STK11*, **or**
   B. A pathogenic or likely pathogenic variant in *STK11* was identified by tumor profiling in the member and germline analysis has not yet been performed.
2. *STK11* targeted variant analysis for Peutz-Jeghers syndrome is considered **investigational** for all other indications.

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***STK11* Sequencing and/or Deletion/Duplication Analysis**

1. *STK11* sequencing and/or deletion/duplication analysis for Peutz-Jeghers syndrome (PJS) is considered **medically necessary** when:
   A. The member has at least two histologically confirmed Peutz-Jeghers-type hamartomatous polyps of the GI tract, **or**
   B. The member has mucocutaneous pigmentation of the mouth, lips, nose, eyes, genitalia, or fingers, **or**
   C. The member has a family history of PJS.
2. *STK11* sequencing and/or deletion/duplication analysis for Peutz-Jeghers syndrome is considered **investigational** for all other indications.

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## Retinoblastoma

***RB1* Targeted Variant Analysis**

1. *RB1* targeted variant analysis for retinoblastoma is considered **medically necessary** when:
   A. The member has a close relative with a known pathogenic or likely pathogenic variant in *RB1*, **or**
   B. A pathogenic or likely pathogenic variant in *RB1* was identified by tumor profiling in the member and germline analysis has not yet been performed.
2. *RB1* targeted variant analysis for retinoblastoma is considered **investigational** for all other indications.

***RB1* Sequencing and/or Deletion/Duplication Analysis**

1. *RB1* sequencing and/or deletion/duplication analysis for retinoblastoma is considered **medically necessary** when:
   A. The member has a diagnosis of retinoblastoma in one or both eyes, **or**
   B. The member has a close relative with retinoblastoma in one or both eyes.
2. *RB1* sequencing and/or deletion/duplication analysis for retinoblastoma is considered **investigational** for all other indications.

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## Von Hippel-Lindau Syndrome (VHL)

***VHL* Targeted Variant Analysis**

1. *VHL* targeted variant analysis for Von Hippel-Lindau syndrome is considered **medically necessary** when:
   A. The member has a first- or second-degree relative with a known pathogenic or likely pathogenic variant in *VHL*, **or**
   B. A pathogenic or likely pathogenic variant in *VHL* was identified by tumor profiling in the member and germline analysis has not yet been performed.
2. *VHL* targeted variant analysis for Von Hippel-Lindau syndrome is considered **investigational** for all other indications.

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***VHL* Sequencing and/or Deletion/Duplication Analysis**

1. *VHL* sequencing and/or deletion/duplication analysis for Von Hippel-Lindau syndrome is considered **medically necessary** when:
   A. The member has a diagnosis of one or more of the following:
      i. Hemangioblastoma of the retina, spine, or brain, **or**
      ii. Renal cell carcinoma diagnosed before age 40 years, **or**
      iii. Multiple and/or bilateral renal cell carcinoma diagnosed at any age, **or**
      iv. Pheochromocytoma or paraganglioma (in abdomen, thorax, or neck), **or**
      v. Retinal angiomas, **or**
      vi. Endolymphatic sac tumor, **or**
      vii. Epididymal or adnexal papillary cystadenoma, **or**
      viii. Pancreatic serous cystadenoma, **or**
      ix. Pancreatic neuroendocrine tumors, **or**
      x. Multiple renal, pancreatic or hepatic cysts
2. *VHL* sequencing and/or deletion/duplication analysis for Von Hippel-Lindau syndrome is considered **investigational** for all other indications**.**

## Definitions

1. **Close relatives** include first, second, and third-degree **blood** relatives on the same side of the family:
   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
2. **Breast cancer**: Term that applies to patients with invasive cancer or ductal carcinoma in situ (DCIS).
3. **High risk breast cancer for olaparib therapy** is defined as:
   A. Triple negative breast cancer treated with either:
      i. Adjuvant chemotherapy with axillary node-positive disease or an invasive primary tumor greater than or equal to 2 cm on pathology analysis, **or**
      ii. Neoadjuvant chemotherapy with residual invasive breast cancer in the breast or resected lymph nodes, **or**
   B. Hormone receptor positive disease treated with either:
      i. Adjuvant chemotherapy with four or more positive pathologically confirmed lymph nodes, **or**
      ii. Neoadjuvant chemotherapy which did not have a complete pathologic response, with a CPS+CG score [pre-treatment clinical (CS) and post-treatment pathological stage (PS), estrogen-receptor status (E) and grade (G)] of 3 or higher.
4. **Juvenile polyps**: Polyps associated with Juvenile Polyposis Syndrome. These polyps are exophytic and eroded. They typically contain the following: marked edema and inflammation within the lamina propria, cystic glands filled with thick mucin, and some degree of smooth muscle proliferation.
5. **Maori ancestry**: Describes individuals who are of indigenous New Zealand ethnic background.
6. **High-risk-prostate cancer**: Defined by NCCN as an individual who has no very-high-risk features but has exactly one of the following high-risk features:
   A. cT3a, **or**
   B. Grade Group 4 or Grade Group 5, **or**
   C. PSA greater than 20ng/ml
7. **Very-high-risk prostate cancer**: Defined by NCCN as an individual who has at least one of the following:
   A. CT3b-cT4
   B. Primary Gleason pattern 5
   C. 2 or 3 high-risk features

D. Greater than 4 cores with Grade Group 4 or 5

8. **Adenomatous polyposis**: Conditions that cause multiple adenomas (i.e., benign polyps) in the gastrointestinal tract.

9. **Lynch syndrome-related cancer**: Defined as any of the following cancer types: colorectal, endometrial, gastric, ovarian, pancreatic, ureter and renal pelvic, brain (usually glioblastoma), biliary tract, small intestinal, sebaceous adenoma, sebaceous carcinoma, or keratoacanthoma.

## Products

This information is for most, but not all, HealthPartners plans. Please read your plan documents to see if your plan has limits or will not cover some items. If there is a difference between this general information and your plan documents, your plan documents will be used to determine your coverage. These coverage criteria do not apply to Medicare Products. For more information regarding Medicare coverage criteria or for a copy of a Medicare coverage policy, contact Member Services at 952-883-7272 or 1-877-778-8384.

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## References


1. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. Version 3.2024. https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf.
2. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Genetic/Familial High-Risk Assessment: Colorectal. Version 2.2023. 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. Released March 14, 2017.
4. Owens DK, Davidson KW, Krist AH, et al. Risk Assessment, Genetic Counseling, and Genetic Testing for BRCA -Related Cancer: US Preventive Services Task Force Recommendation Statement. JAMA - J Am Med Assoc. 2019; 322(7):652-665. doi:10.1001/jama.2019.10987
5. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Cutaneous Melanoma. Version 2.2024. https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf.
6. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Neuroendocrine and Adrenal Tumors. Version 2.2024. https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf.
7. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Gastric Cancer. Version 3.2024. https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf.
8. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Kidney Cancer. Version 1.2025. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf.
9. Skalet AH, Gombos DS, Gallie BL, et al. Screening Children at Risk for Retinoblastoma: Consensus Report from the American Association of Ophthalmic Oncologists and Pathologists. Ophthalmology. 2018; 125(3):453-458. doi: 10.1016/j.ophtha.2017.09.001
10. Sattler EC, Steinlein OK. Birt-Hogg-Dube Syndrome. 2006 Feb 27 [Updated 2020 Jan 30]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1522/
11. Hereditary Cancer Syndromes and Risk Assessment: ACOG COMMITTEE OPINION, Number 793. Obstet Gynecol. 2019; 134(6): e143-e149. doi:10.1097/AOG.0000000000003562
12. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines on Oncology: Uveal Melanoma. Version 1.2024. https://www.nccn.org/professionals/physician_gls/pdf/uveal.pdf
13. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines on Oncology: Mesothelioma: Pleural. Version 1.2024. https://www.nccn.org/professionals/physician_gls/pdf/meso_pleural.pdf
14. Pilarski R, Carlo M, Cebulla C, and Abdel-Rahman M. BAP1 Tumor Predisposition Syndrome. 2016 Oct 13 [Updated 2022 Mar 24]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK390611/
15. Evans DG, Farndon PA. Nevoid Basal Cell Carcinoma Syndrome. 2002 Jun 20 [Updated 2024 Feb 22]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1151/
16. Else T, Greenberg S, Fishbein L. Hereditary Paraganglioma-Pheochromocytoma Syndromes. 2008 May 21 [Updated 2023 September 21]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1548/
17. Eng C. and Plitt, G. Multiple Endocrine Neoplasia Type 2. 1999 Sep 27 [Updated 2023 Aug 10]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1257/
18. Kamihara J, Schultz KA, Rana H. FH Tumor Predisposition Syndrome. 2006 Jul 31. [Updated 2020 Aug 13]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1252/

19. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Ampullary Adenocarcinoma. Version 2.2024.
20. Swetter SM, Tsao H, Bichakjian CK, et al. Guidelines of care for the management of primary cutaneous melanoma. J Am Acad Dermatol. 2019;80(1):208-250. doi: 10.1016/j.jaad.2018.08.055
21. Bedrosian I, Somerfield MR, Achatz MI, et al. Germline Testing in Patients With Breast Cancer: ASCO-Society of Surgical Oncology Guideline. J Clin Oncol. 2024;42(5):584-604. doi:10.1200/JCO.23.02225