Genetic Testing – Inherited Cancer Predisposition

I. Policy

University Health Alliance (UHA) will reimburse for Inherited Cancer Predisposition genetic testing when such testing is determined to be medically necessary and when testing meets the medical criteria guidelines (subject to limitations and exclusions) indicated below. Within the additional limitations of this policy, only genetic testing that is for the purpose of treating a medical condition is covered.

Refer to separate UHA policies for Genetic Testing for Hereditary Breast and/or Ovarian Cancer and for Lynch Related Syndromes.

II. Criteria/Guidelines

A. Genetic testing is covered (subject to Limitations/Exclusions and Administrative Guidelines) when all of the following criteria are met:

1. There must be a reasonable expectation based on family history, pedigree analysis, risk factors, and/or symptomatology that a genetically inherited condition exists and the individual displays clinical features or is at direct risk of inheriting the mutation in question based on family history or ethnic background

2. The genotypes to be detected by a genetic test must be shown by scientifically valid methods to be associated with the occurrence of the disease, and the analytical and clinical validity of the test must be established.

3. The clinical utility of the test must be established (e.g., test results will influence decisions concerning disease treatment or prevention).
   a. Clinical utility refers to the ability of genetic test results, either positive or negative, to provide information that is of value in the clinical setting. The development of genetic tests that can diagnose or predict disease occurrence has far outpaced the development of interventions to treat, ameliorate, or prevent those same diseases. In the absence of such interventions, the benefits of testing are limited, and in fact, can cause psychological harm.
   b. Specifically for positive test results, interventions could involve instituting treatments or surveillance measures, making decisions concerning future conception, or avoiding harmful treatments.
   c. Negative test results can have clinical utility in avoidance of unnecessary treatments or surveillance

B. Oncologic Genetic testing is covered (subject to Limitations/Exclusions and Administrative Guidelines) when the above criteria are met the patient has a cancer or a strong suspicion of cancer for the following:

1. Hereditary Diffuse Gastric Syndrome (CDH1 gene)
   a. The evaluation should include a detailed three-generation family pedigree,
   b. Histopathological confirmation of DGC diagnoses and/or
   c. Precursor lesions (in situ or pagetoid spreading of signet ring cells)

2. Medullary thyroid carcinoma (MEN2)
a. Patient has a first-degree relatives with proven hereditary MTC; or
b. Patient is a parent whose infant or young children have the classic phenotype of MEN2B; or
c. Patient has CLA (cutaneous lichen amyloidosis) and

d. Infants or young children with Hirschsprung's Disease (HD) and exon 10 RET germline mutations, and adults with MEN2A and exon 10 mutations who have symptoms suggestive of HD

3. Retinoblastoma
   a. After history, physical examination, pedigree analysis, genetic counseling, completion of appropriate conventional diagnostic studies, a definitive diagnosis is unclear and genetic testing would provide needed information

4. Multiple Endocrine Neoplasia Type 1/MENIN
   a. Individuals have a personal history of two of the three main MEN1 related cancers (islet cell pancreatic, parathyroid (hyperplasia) and/or pituitary adenoma; or
   b. Unaffected individuals who have family history of a documented MEN 1 gene mutation in a first or second degree relative

5. Von-Hippel-Lindau (VHL)
   a. Members who have one or more characteristic lesions with or without family history; or
   b. Unaffected individuals who have a family history of a documented VHL gene mutation

6. Pancreatic cancer syndrome
   a. Individual has a personal history of pancreatic cancer; or
   b. Unaffected individuals with a first or second degree relative with a documented BRCA2 mutation; or
   c. Unaffected individuals with two or more first degree relatives with pancreatic cancer; or
   d. Unaffected individuals with two or more second degree relatives with pancreatic cancer, one of whom developed it at an early age (under the age 50)

7. Thyroid (RET proto-oncogene point mutations)
   a. Asymptomatic patients of well-characterized families with defined RET gene mutations; or
   b. Members of families known to be affected by inherited medullary thyroid carcinoma but not previously evaluated for RET mutations; or
   c. Members with apparently sporadic medullary thyroid carcinoma; or
   d. Patients with first-degree relatives with apparently sporadic medullary thyroid carcinoma

8. Breast cancer (see below and see also policy for Genetic Testing for Hereditary Breast and/or Ovarian Cancer)

9. Lynch Syndrome/Colorectal Cancer (see policy for Genetic Testing for Lynch Syndrome and Other Inherited Colon Cancer Syndromes)

10. Gene expression assays for determining the prognosis of stage II or III colon cancer following surgery are not covered as they are not known to be effective in improving health outcomes.
C. A pre-test genetic risk assessment by a properly certified genetic specialist (requiring prior authorization) has been performed and is concurrent with the test request.

   1. Certified genetic specialists are:
      a. Board-certified medical geneticist (MD)
      b. Board-certified clinical geneticist (PhD)
      c. Board-certified genetic counselor (MS and/or CGC)
      d. Licensed advanced practice registered nurse in genetics (APRN)

D. Breast cancer gene expression assay (i.e., Oncotype DX, EndoPredict, the Breast Cancer Index, Prosigna) is considered medically appropriate if ALL of the following are met:

   1. Newly diagnosed carcinoma of breast and ALL of the following:
      a. Primary, invasive breast cancer in women
      b. Unilateral tumor
      c. ANY ONE of the following:
         i. When 21-gene RT-PCR assay is NOT used, individual must be node negative (lymph nodes with micrometastases [less than 2 mm in size] are considered node negative)
         ii. When 21-gene RT-PCR assay is used, individual may be ANY ONE of the following:
            • Node negative (lymph nodes with micrometastases [less than 2 mm in size] are considered node negative)
            • Node positive (up to three positive axillary nodes in a post-menopausal woman)
         iii. Estrogen receptor positive or progesterone receptor positive
         iv. Human epidermal growth factor receptor 2 (HER2) negative
         v. Tumor size is ONE of the following:
            • 0.6 to 1 cm with moderate or poor differentiation
            • 0.6 to 1 cm with ONE of the following:
               o Angiolymphatic invasion
               o High histologic grade
               o High nuclear grade
            • Larger than 1 cm
   2. Individual will receive adjuvant endocrine therapy (e.g., tamoxifen, aromatase inhibitors)
   3. Test is ordered within six months of diagnosis
   4. Outcome of testing will guide decision-making regarding adjuvant chemotherapy

D. Within the limitations above, genetic testing is covered for National Comprehensive Cancer Network level 1 or 2A recommended tests.

**NOTE:**

This UHA payment policy is a guide to coverage, the need for prior authorization and other administrative directives. It is not meant to provide instruction in the practice of medicine and it should not deter a provider from expressing his/her judgment.
Even though this payment policy may indicate that a particular service or supply is considered covered, specific provider contract terms and/or member individual benefit plans may apply, and this policy is not a guarantee of payment. UHA reserves the right to apply this payment policy to all UHA companies and subsidiaries.

UHA understands that opinions about and approaches to clinical problems may vary. Questions concerning medical necessity (see Hawaii Revised Statutes §432E-1.4) are welcome. A provider may request that UHA reconsider the application of the medical necessity criteria in light of any supporting documentation.

## III. Limitations/Exclusions

A. Genetic testing is not covered for the following:
   1. Family members of subscribers, who themselves are not subscribers, are not covered;
   2. Members are not covered if the results of the genetic testing are for the benefit of family members who are not covered by UHA;
   3. Genetic testing is not covered in the absence of associated signs, symptoms or complaints;
   4. Home Genetic testing is not covered
   5. Chemoresistance and chemosensitivity; (e.g., CEMEX) are not covered.
   6. UGT1A1 Molecular Assay (Invader) are not covered;
   7. Pathfinder (Genetic fingerprinting/DNA fingerprinting) and any other genetic expressing test not supported by NCCN are not covered.

B. Genetic testing for cancer susceptibility using panels of genes (with or without next generation sequencing) is not covered because it is not known to be effective in improving health outcomes. However, individual components of a panel may be considered medically necessary as noted in this policy.

C. For a known deleterious mutation, UHA will only cover a targeted single site analysis genetic test not a full analysis (i.e., testing for the mutation that has been identified in the family).

D. Most genetic tests are performed once per life time but neuro-oncologic therapies may warrant repeat testing and coverage based on current national clinical practices and guidelines.

E. Laboratories that conduct genetic testing must be CLIA certified.

F. Because of the rapidly evolving field of genetic testing, this policy does not address every genetic test available. All other conditions not mentioned in this policy will be reviewed based on medical necessity and the policy criteria.

## IV. Administrative Guidelines

A. Prior authorization is required for the necessary pre-test genetic risk assessment.

B. Prior authorization is required for genetic testing: oncology.

C. In addition to other required information, Prior Authorization must specify how the results of the genetic test will impact the clinical management of the patient in terms of improving health outcomes.

D. To request prior authorization, please submit via UHA’s online portal. If a login has not been established, you may contact UHA at 808-532-4000 to establish one.

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<tr>
<th>CPT Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>81206</td>
<td>BCR/ABL1 (t(9;22)) (e.g., chronic myelogenous leukemia) translocation analysis; major</td>
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breakpoint, qualitative or quantitative
81207 BCR/ABL1 (t(9;22)) (e.g., chronic myelogenous leukemia) translocation analysis; minor breakpoint, qualitative or quantitative
81208 BCR/ABL1 (t(9;22)) (e.g., chronic myelogenous leukemia) translocation analysis; other breakpoint, qualitative or quantitative
88230 Tissue culture for non-neoplastic disorders; lymphocyte
88233 Tissue culture for non-neoplastic disorders; skin or other solid tissue biopsy
88237 Tissue culture for neoplastic disorders; bone marrow, blood cells
88240 Cryopreservation, freezing and storage of cells, each cell line
88241 Thawing and expansion of frozen cells, each aliquot
88245 Chromosome analysis for breakage syndromes; baseline Sister Chromatid Exchange (SCE), 20-25 cells
88248 Chromosome analysis for breakage syndromes; baseline breakage, score 50-100 cells, count 20 cells, 2 karyotypes (e.g., for ataxia telangiectasia, Fanconi anemia, fragile X)
88249 Chromosome analysis for breakage syndromes; score 100 cells, clastogen stress (e.g., diepoxybutane, mitomycin C, ionizing radiation, UV radiation)
88261 Chromosome analysis; count 5 cells, 1 karyotype, with banding
88262 Chromosome analysis; count 15-20 cells, 2 karyotypes, with banding
88263 Chromosome analysis; count 45 cells for mosaicism, 2 karyotypes, with banding
88264 Chromosome analysis; analyze 20-25 cells
88271 Molecular cytogenetics; DNA probe, each (e.g., FISH)
88272 Molecular cytogenetics; chromosomal in situ hybridization, analyze 3-5 cells (e.g., for derivatives and markers)
88273 Molecular cytogenetics; chromosomal in situ hybridization, analyze 10-30 cells (e.g., for microdeletions)
88274 Molecular cytogenetics; interphase in situ hybridization, analyze 25-99 cells
88275 Molecular cytogenetics; interphase in situ hybridization, analyze 100-300 cells
88280 Chromosome analysis; additional karyotypes, each study
88283 Chromosome analysis; additional specialized banding technique (e.g., NOR, C-banding)
88285 Chromosome analysis; additional cells counted, each study
88289 Chromosome analysis; additional high resolution study
88291 Cytogenetics and molecular cytogenetics, interpretation and report

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<tr>
<td>S3840</td>
<td>DNA analysis for germline mutations of the RET proto-oncogene for susceptibility to multiple endocrine neoplasia type 2</td>
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<tr>
<td>S3841</td>
<td>Genetic testing for retinoblastoma</td>
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V. Policy History

Policy Number: MPP-0058-120301
Current Effective Date: 07/03/2019
Original Document Effective Date: 03/01/2012
Previous Revision Dates: 02/12/2018, 06/12/2018
PAC Approved Date: 03/01/2012
Previous Policy Title: Genetic Testing – Oncology