HEALTH PLANS
UNIVERSITY OF UTAH

Medical Policy

Genetic Testing for Breast and/or Ovarian Cancer Susceptibility (BRCA1/BRCA2)

Policy MP-033

Origination Date: 12/20/2018

Reviewed/Revised Date: 01/22/2026

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Disclaimer:

1. Policies are subject to change in accordance with State and Federal notice requirements.
2. Policies outline coverage determinations for U of U Health Plans Commercial, CHIP, Healthy U (Medicaid) and Health Choice Utah (Medicaid) plans. Refer to the "Policy" section for more information.
3. Services requiring prior-authorization may not be covered, if prior-authorization is not obtained.
4. This Medical Policy does not guarantee coverage or payment of the service. The service must be a benefit in the member's plan and the member must be eligible for coverage at the time of service. Additional payment guidelines may be applied that are not included in this policy.

Description:

Breast cancer is the second leading cause of cancer-related death among women, and ovarian cancer ranks fifth. An inherited predisposition to breast and ovarian cancer is known as **Hereditary Breast and Ovarian Cancer (HBOC) syndrome**, most commonly associated with pathogenic variants in the **BRCA1** and **BRCA2** genes. These genes encode tumor suppressor proteins involved in DNA repair; loss of function increases cancer susceptibility.

BRCA mutations are inherited in an autosomal dominant pattern through either parent. Genetic testing can identify individuals and families at increased cancer risk, allowing for targeted surveillance and risk-reducing interventions. Accordingly, BRCA mutation testing is recommended only for individuals with clinical or familial features associated with an increased likelihood of a pathogenic BRCA variant.

Policy Statement and Criteria

1. Commercial Plans/CHIP

U of U Health Plans covers genetic testing for BRCA1 and BRCA2 mutations in adult individuals at high risk for heritable breast and ovarian cancer syndromes when specific clinical coverage criteria are met:

Clinical criteria for coverage (Must meet any A-I):

A. Individual is from a family with a known BRCA1 or BRCA2 pathogenic/likely pathogenic variant, including such variants found on research testing (irrespective of degree of relatedness)

B. Personal history of breast cancer (includes invasive and ductal carcinoma in situ breast cancers), plus one or more of the following (i-v):

   i. Diagnosed with breast cancer ≤ age 45 years

   ii. Diagnosed with breast cancer between ages 46 to 50, with:

      a) An additional breast cancer primary at any age (two breast cancer primaries include bilateral [contralateral] disease or two or more clearly separate ipsilateral primary tumors diagnosed either synchronously or asynchronously), or

      b) ≥ 1 close blood relative* with breast cancer primary at any age, or

      c) ≥ 1 close blood relative* with high-grade prostate cancer (Gleason score ≥ 7), or

      d) An unknown or limited family history◊.

   iii. Diagnosed with breast cancer ≤ age 60 years, with:

      a) Triple-negative breast cancer

   iv. Diagnosed at any age with (a or b):

      a) ≥ 1 close blood relative* with:

         1. Breast cancer diagnosed ≤ age 50 years, or

         2. Ovarian carcinoma (includes fallopian tube and primary peritoneal cancers$^{\Delta}$), or

         3. Male breast cancer, or

         4. Metastatic prostate cancer (biopsy proven and/or with radiographic evidence, and includes distant metastasis and regional bed or nodes), or

         5. Pancreatic cancer.

      b) ≥ 2 additional diagnoses of breast cancer at any age in patient and/or in close blood relatives* (two breast cancer primaries include bilateral [contralateral]

disease or two or more clearly separate ipsilateral primary tumors diagnosed either synchronously or asynchronously).

v. Ashkenazi Jewish ancestry

C. Personal history of ovarian carcinoma (including fallopian tube and primary peritoneal cancers[Δ])

D. Personal history of male breast cancer

E. Personal history of pancreatic cancer[#]

F. Personal history of high-grade prostate cancer (Gleason score ≥ 7) at any age, with:

i. ≥ 1 close blood relative[*] with ovarian carcinoma, pancreatic cancer, or metastatic prostate cancer (biopsy proven and/or with radiographic evidence, and includes distant metastasis and regional bed or nodes), or

ii. ≥ 2 close blood relatives[*] with breast, or prostate cancer (any grade) at any age, or

iii. Ashkenazi Jewish ancestry[~].

G. BRCA1 or BRCA2 pathogenic/likely pathogenic variant detected by tumor profiling on any tumor type in the absence of germline pathogenic/likely pathogenic variant analysis

H. Regardless of family history, some individuals with a BRCA-related cancer may benefit from genetic testing to determine eligibility for targeted treatment

I. An individual who does not meet the above criteria, but with ≥ 1 first- or second-degree blood[*] relative[+] meeting criteria A through H.

[*] Close blood relatives include: first-, second-, and third-degree relatives on same side of family.

[◊] Refer to applicable NCCN Guidelines (listed in the last paragraph of the rationale).

[Δ] BRCA-related ovarian cancers are associated with epithelial, non-mucinous histology. Lynch syndrome can be associated with both non-mucinous and mucinous epithelial tumors. Be attentive for clinical evidence of Lynch syndrome. Specific types of non-epithelial ovarian cancers and tumors can also be associated with other rare syndromes. Examples include an associate between sex-chord tumors with annular tubules and Peutz-Jeghers syndrome or Sertoli-Leydig tumors and DICER1-related disorders.

[#] Approximately 2%–5% of unselected cases of pancreatic adenocarcinoma will have a BRCA1 or BRCA2 pathogenic/likely pathogenic variant. However, the disease is highly lethal and the option to test the affected relative may not be available in the future. Thus, there may be significant benefit to family members in testing these patients near the time of diagnosis. In addition, increasing evidence suggests that identification of a BRCA1 or BRCA2 pathogenic/likely pathogenic variant may direct use of targeted therapies for patients with pancreatic cancer.

[+] This may be extended to an affected third-degree relative if related through two male relatives (e.g., paternal grandfather's mother or sister).

[~] Testing for Ashkenazi Jewish founder-specific pathogenic/likely pathogenic variant(s), should be performed first. Comprehensive genetic testing may be considered if ancestry also includes non-Ashkenazi Jewish relatives or if other BRCA-related criteria are met. Founder pathogenic/likely pathogenic variants exist in other populations.

Gleason Score: Table

GLEASON SCORES IN CATEGORICAL ORDER	
Gleason X	Gleason score cannot be determined
Gleason 6 or less	The tumor tissue is well differentiated, less aggressive and likely to grow more slowly
Gleason 7	The tumor tissue is moderately differentiated, moderately aggressive and likely to grow but may not spread quickly
Gleason 8-10	The tumor tissue is poorly differentiated or undifferentiated, highly aggressive and likely to grow faster and spread

U of U Health Plans does NOT cover BRCA1 and BRCA2 variant testing in minors as it is considered investigational.

U of U Health Plans COVERS BRCA testing in individuals with triple negative breast cancer being considered for PARP therapy as a medical benefit.

U of U Health Plans does not Cover Myriad Genetics *myRISK®*, Ambry Genetics *BreastNEXT™*, or similar hereditary breast/ovarian cancer specialty panels as they are considered investigational.

2. **Medicaid Plans**
   Coverage is determined by the State of Utah Medicaid program; if Utah State Medicaid has no published coverage position and InterQual criteria are not available, the U of U Health Plans Commercial criteria will apply. For the most up-to-date Medicaid policies and coverage, please visit their website at: https://medicaid.utah.gov/utah-medicaid-official-publications/ or the Utah Medicaid code Look-Up tool

   CPT/HCPCS codes covered by Utah State Medicaid may still require further evaluation to determine medical necessity for coverage.

Clinical Rationale

According to the National Cancer Institute (NCI) BRCA mutations increase a woman's lifetime risk of developing breast and/or ovarian cancer. Approximately 12% of women in the general population will develop breast cancer and 1.3% will develop ovarian cancer during their lifetime. By way of comparison, an estimated 72% of women who inherit the BRCA1 mutation and 69% who inherit the BRCA2 mutation will develop breast cancer by the age of 80. Then by the first 20 years after the first diagnosis it is estimated that about 40% of those women with BRCA1 and 26% with BRCA2 will develop cancer in the other breast. As far as ovarian cancer, it is estimated that 44% of women that have the BRCA1 mutation and 17% that have the BRCA2 mutation will develop ovarian cancer by the age of 80. The NCI agrees with the USPSTF's recommendations for BRCA testing.

The U.S. Preventative Services Task Force (USPSTF) is currently of updating the 2013 topic of BRCA1 and BRCA2 genetic testing. As for now, their recommendations are to use one of the many screening tools

used to identify family history in women who have had family members that have been diagnosed with breast, ovarian, tubal or peritoneal cancer and may be at an increased risk of having a mutation in breast cancer susceptibility genes (i.e. BRCA1 and BRCA2). If the screening comes back positive the woman should have genetic counseling and then determine if BRCA testing is warranted. If the women does not have a family history of an associated increased risk, the USPSTF does not recommend genetic counseling or BRCA testing. These recommendations do not apply to men, although some male members may be identified during testing.

Looking at cost and health benefits, Kwon et al. used a simulation model in 2010 to evaluate six populations of women younger than 50 with breast cancer. Nearly 10% of women with breast cancer who are younger than age 50 have BRCA mutations. Most of the BRCA-positive women do not have personal or family histories of breast or ovarian cancer and are not of Ashkenazi Jewish ancestry. The results concluded that testing women with triple negative breast cancers who were younger than 50 years for BRCA mutations should be adopted into current guidelines for genetic testing.

In a 2011 cohort study of germline and somatic BRCA1 and BRCA2 mutations in 77 unselected Triple Negative Breast Cancer (TNBC) patients (Gonzalez-Angulo et al), 15 (19.5%) had *BRCA* mutations. Out of the 15 patients, 12 had BRCA1 (1 of them somatic) and 3 had BRCA2. Median age was 51 years (27-83 years). The authors recommend that genetic testing should be discussed with TNBC patients, and it should be noted that TNBC patients with BRCA mutations have a significantly lower risk of relapse.

In a 2018 UpToDate® article on triple negative breast cancer (TNBC), BRCA testing is recommended in the metastatic stage, in that a better strategy for therapy may be determined depending on prior treatment history and the mutation status. If patients have advanced TNBC with germline BRCA mutations and have been previously treated with chemo in the adjuvant, neoadjuvant or metastatic disease setting, UpToDate experts suggest polyadenosine diphosphate-ribose polymerase (PARP)—an oral inhibitor—for treatment. If the patient has advanced TNBC, is chemo naïve and a BRCA carrier, initial treatment should consist of chemo and either a taxane or a platinum agent.

A 2012 clinical database review (Stadler et al) evaluated Breast Cancer (BC) probands in the Ashkenazi Jewish (AJ) population to determine if a BRCA mutation was harbored in those who had a family history of pancreatic cancer. Of the 211 AJ BC probands identified, 30 (14.2%) harbored a mutation, of those, 14 (47%) of the mutations were in BRCA1 and 16 (53%) were in BRCA2. Patients diagnosed with BC at age

≤ 50 years were found to have a higher BRCA1/2 mutation prevalence than probands with BC who were diagnosed at age > 50 years (21.1% vs 6.9%). In patients with first, second, or third-degree relatives with pancreatic cancer, mutation prevalence was 15.4%, 15.3% and 8.6%, respectively. In conclusion, it appears that BRCA1 and BRCA2 mutations are observed with nearly equal distribution in AJ breast-pancreas cancer families, suggesting that both genes are associated with pancreatic cancer risk. However, a family history of pancreatic cancer, at least in this population, was found to have limited effect on mutation prevalence.

Petrucelli et al published a study in 2016 regarding the HBOC syndrome and its association with BRCA1 and BRCA2 mutations. This study characterized the increased risk for female and male breast cancer, ovarian cancer and other cancers such as prostate, pancreatic and melanoma. The study determined the exact cancer risk depends on whether HBOC is caused by BRCA1 or 2. The diagnosis is established in a proband by the identification of a heterozygous germline pathogenic variant in BRCA1 or 2 on molecular genetic testing. Treatment could include bilateral mastectomy because of elevated rate of ipsilateral and contralateral breast cancer for surgical treatment. Ovarian and other cancers are treated similar to that of sporadic cancers. Prevention may include prophylactic bilateral mastectomy, prophylactic

oophorectomy, and chemoprevention (e.g., tamoxifen) for breast cancer; however, these have not been assessed in high-risk women by randomized trials. Surveillance for women include a combination of monthly self-breast exams, annual or semiannual clinical breast exams, annual mammograms, and breast MRIs. Annual transvaginal ultrasounds and CA-125 concentration may be used beginning at age 35 for ovarian cancer, although in detecting early-stage ovarian cancer either in high or average risk women, this screening has not been effective. For men with breast cancer risk, screening should begin at age 35 with self-breast exams and annual clinical exams, prostate cancer risk screening should start at age 45.

A 2017 study (Kolor et al) summarized medical claims for BRCA testing among women aged 18-64 with employer-sponsored healthcare and the resulting interventions between 2009 and 2014. During the study period, BRCA testing increased by 2.3 times in metropolitan, and by 3 times in non-metropolitan areas. The percentage of women who were less likely to receive an MRI of the breast in non-metropolitan areas was 8.2% vs. 10.3% in metropolitan area and mammography in non-metro 11.5% vs. 13.8% in metro. Preventive services received within 90 days of testing also varied between these regions. Receiving genetic counseling before or after testing, increased over the study period from 5.3% to 8% in metropolitan areas and from 3.8% to 5.2% in non-metropolitan areas. After the implementation of the USPSTF guidelines and the availability of BRCA counseling and testing under the Affordable Care Act in September of 2010 the differences between the groups declined, the authors indicate that these implementations may have influenced the increase in testing and the reduction in variances between the two groups. Comparable to the estimated prevalence of BRCA mutations in the general U.S. population, the study's highest rate of BRCA testing was 332.5 women per 100,000 women aged 44-54. It should be noted that to minimize potential bias, this study did not include Ashkenazi Jewish women as they have a greater risk of carrying BRCA mutations and are highly populated in metropolitan areas.

Due to the lack of guidelines for genetic counseling and testing in the pediatric population, Druker et al. arranged an expert consensus of recommendations in 2017 for the testing and surveillance of pediatric cancers from the 2016 American Association for Cancer Research (AACR) Childhood Cancer Predisposition Workshop. When to refer patients to pediatric cancer genetics clinics, pretest counseling, informed consent and assent for cancer genetic testing of children, test selection and timing of testing, posttest counseling, and psychosocial aspects of cancer surveillance for children with hereditary cancer syndromes were all included in the consensus. The following recommendations were provided: The child and family should be referred to genetic counseling at the time the tumor is diagnosed or germline genetic testing is being considered; the clinician should consider clinical presentation and family history to determine whether to order a test for a familial variant or a broader panel; if a family pathogenic variant is known, the test should only be for that variant (if possible use the same lab that identified the mutation in the initial family member); when the patient’s presentation clearly fits a specific syndrome, only the gene(s) for that specific syndrome should be tested; if a patient presents with symptoms that may be explained by multiple syndromes, a multi-gene hereditary cancer panel may be considered; however, this also increases the chance of second findings which may cause additional challenges; and finally, for those with multi-system phenotypes, negative multigene panel results and wanting to participate in research, whole exome or genome sequencing should be considered. It should be noted however, that there are inconsistent findings with whole exome or genome sequencing. The authors concluded that the clinician should confirm the test ordered includes the gene(s) of interest and has been well validated; and understands the lab's reinterpretation practices, costs, turnaround times, and policies regarding data sharing.

In a 2018 UpToDate article on "Genetic Testing", experts found that more than 35% of pediatric medical conditions are due to genetic issues. Most genetic testing is only included when the findings of the test will affect the current management of the child. The testing of children for adult-onset genetic conditions, that would have no current impact on a child's care or prognosis, raises additional issues such as the patient and family being burdened rather than empowered by the results. The American Society of Human Genetics (ASHG) released a position statement in 2015 regarding the testing of children. The UpToDate experts agree with the following ASHG recommendations:

1. Unless there is a clinical intervention appropriate in childhood, parents should be encouraged to defer predictive or pre-dispositional testing for adult-onset conditions until adulthood or at least until the child is an older adolescent who can participate in decision making in a relatively mature manner.
2. Based on clinical presentation, targeted gene panels or single gene testing should be tested initially, then if those tests are not definitive whole exome or whole genome sequencing may be used. The first approach reduces the possibility of secondary findings.
3. Unless there is clear medical benefit that outweighs potential harms, discovery of misattribution of parentage from genetic testing should not be disclosed.
4. Adolescents should have the opportunity to discuss concerns of genetic testing and related disorders. A separate conversation that discusses other aspects of informed consent in adolescent health care should be performed as well.

In 2015, Hayes reported on the BRACAnalysis® Rearrangement Test™ (BART). BART was introduced to the market as a refinement of the BRCA genetic tests and was used to detect rare, large rearrangements of DNA in the BRCA1 and BRCA2 genes which were previously undetected by standard genetic testing. Myriad now includes BART testing as part of the Comprehensive BRACAnalysis test. Hayes conducted a search strategy that backdated to 1996 and found only 3 studies that evaluated BART specifically. NCCN guidelines recommend testing for large genomic rearrangements in individuals meeting criteria for HBOC as part of BRCA1/2 comprehensive testing, however, they do not define a specific test or mention BART specifically. Hayes was unable to perform a Genetic Test Evaluation (GTE) health technology assessment based on the insufficient published evidence; and therefore, cannot recommend BART for use until further studies demonstrate its efficacy with analytical validity, clinical validity, and clinical utility.

The U.S. Food and Drug Administration (FDA) approved the first direct-to-consumer (DTC) test to market the Personal Genome Service® Genetic Health Risk (GHR) Report for BRCA1 and BRCA2 (Selected Variants) by 23andMe® on March 6, 2018. The test uses saliva to detect three specific BRCA gene mutations out of thousands, which are mostly prevalent in people from the Ashkenazi Jewish decent, that are not the most common in the general population. The FDA states that health care professionals or consumers should not make any decisions for treatment using the results of this test. If concerns are raised from test results, individuals should see their physicians, have confirmatory testing, and seek genetic counseling.

With regard to pre- and post-test genetic counseling, the Society of Gynecology Oncology (SGO) and the American College of Obstetricians and Gynecologists (ACOG) published a joint statement in the ACOG Practice Bulletin #182 in September 2017. This document replaced the previous Practice Bulletin #103 published in April 2009. These new guidelines recommend the following: Genetic Counseling for all women who have ovarian epithelial cancer and for individuals who have a personal or family history of breast or ovarian cancer. ACOG and SGO have issued guidance on what risk factors should be included

when collecting an individual's family history of cancer assessment. If counseling suggests the presence of an inherited cancer syndrome to which genetic testing will likely influence medical management that option should be offered to the individual. If the individual agrees, the next phase is to see if that individual meets criteria for genetic testing. To give a little background on BRCA genes, the phrase "two-hit hypothesis" describes how an individual may develop cancer. The BRCA genes are actually tumor suppressor genes, which encode proteins that assist in DNA repair. Hereditary breast and ovarian cancer (HBOC) syndrome are inherited from either the mother or the father with one defective allele from either side; however, they have a second functional allele. If the second allele becomes non-functional because of somatic mutation, cancer may develop. BRCA1 and BRCA2 germline mutations are estimated to cause approximately 4.5% breast cancer cases and 9% to 24% of epithelial cancer cases. According to ACOG, approximately 39-46% of women harboring the BRCA1 mutation have a risk of developing ovarian, primary peritoneal, and/or fallopian tube cancer by the age of 70; 10% to 27% carrying the BRCA2 mutation have the risk of developing ovarian cancer. Ovarian cancer associated with BRCA1/BRCA2 mutations is usually high grade and has a distinct histologic phenotype that is predominantly endometrioid or serous. Mutations in the BRCA genes have also been associated with other types of cancer such as melanoma, prostate, pancreatic, and potentially uterine cancer.

The American Society of Clinical Oncology (ASCO) recommended in 2003 that genetic testing be offered when three factors are at play: (1) the individual has personal or family history features suggestive of a genetic cancer susceptibility condition, (2) the test can be adequately interpreted, and (3) the results will aid in diagnosis or influence the medical or surgical management of the patient or family member at hereditary risk of cancer. A 2010 update of this statement recommended "genetic tests with uncertain clinical utility, including genomic risk assessment, be administered in the context of clinical trials."

National Comprehensive Cancer Network's (NCCN) 2025 Recommendations:
TESTING CRITERIA FOR HIGH-PENETRANCE BREAST CANCER SUSCEPTIBILITY GENES (Specifically BRCA1, BRCA2, CDH1, PALB2, PTEN, STK11, and TP53):

1. Individuals with any blood relative with a known pathogenic/likely pathogenic variant in a cancer susceptibility gene
2. Individuals meeting the criteria below but tested negative with previous limited testing (e.g., single gene and/or absent deletion duplication analysis) interested in pursuing multi-gene testing
3. To aid in systemic therapy and surgical decision making
4. Individual who meets Li-Fraumeni syndrome (LFS) testing criteria (CRIT-7) or Cowden syndrome (CS)/PTEN hamartoma tumor syndrome (PHTS) testing criteria (CRIT-8) or Lynch syndrome (LS) NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal
5. Personal history of breast cancer with specific features:
    a. Diagnosed at or before age 50 y; or
    b. Diagnosed at any age:
        - Treatment indications:
            - To aid in systemic treatment decisions using PARP inhibitors for breast cancer in the metastatic setting
            - To aid in adjuvant treatment decision making with olaparib for high-risk, l HER2-negative breast cancer
        - Pathology/histology

    - Triple-negative breast cancer;
    - Multiple primary breast cancers (synchronous or metachronous);
    - Lobular breast cancer with personal or family history of gastric cancer;
  - Male breast cancer
  - Ashkenazi Jewish ancestry;
  - Family history:
    - ≥1 close blood relative with any:
    - Breast cancer at age ≤ 50 years,
    - Ovarian cancer (including fallopian tube cancer or peritoneal cancer)
    - Pancreatic
    - Prostate cancer with metastatic, or high- or very-high-risk group;
    - ≥ 3 diagnoses of breast and/or prostate cancer (any grade) on the same side of the family including the patient with breast cancer

6. Family history criteria:
   a. Individual unaffected or affected but does not meet the criteria above
   b. Individual with first- or second-degree blood relative meeting any of the criteria listed above (except unaffected individuals whose relatives meet criteria only for systemic therapy decision-making).
   c. Individual who has a probability >5% of a BRCA1/2 P/LP variant based on prior probability models (e.g., Tyrer-Cuzick, BRCAPro, CanRisk).

Applicable Coding

CPT Codes

Covered as preventive in appropriate population

81162 BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis (i.e., detection of large gene rearrangements)

81163 BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis

81164 BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full duplication/ deletion analysis (i.e., detection of large gene rearrangements)

81215 BRCA1 (breast cancer 1) (e.g., hereditary breast and ovarian cancer) gene analysis; known familial variant

81217 BRCA2 (breast cancer 2) (e.g., hereditary breast and ovarian cancer) gene analysis; known familial variant

Covered as medical benefit in appropriate population

81162 BRCA1, BRCA2 (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis

81165 BRCA1 (BRCA1, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis

81166 BRCA1 (BRCA1, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (i.e., detection of large gene rearrangements)

81167 BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (i.e., detection of large gene rearrangements)

81212 BRCA1, BRCA2 (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; 185delAG, 5385insC, 6174delT variants

81216 BRCA2 (breast cancer 2) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis

HCPCS Codes

G0452 Molecular pathology procedure; physician interpretation and report

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