

MEDICAL POLICY

POLICY TITLE	MOLECULAR TESTING FOR GERMLINE VARIANTS ASSOCIATED WITH OVARIAN CANCER (BRIP1, RAD51C, RAD51D, NBN)
POLICY NUMBER	MP 2.377

CLINICAL BENEFIT	<input type="checkbox"/> MINIMIZE SAFETY RISK OR CONCERN. <input checked="" type="checkbox"/> MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. <input type="checkbox"/> ASSURE APPROPRIATE LEVEL OF CARE. <input type="checkbox"/> ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. <input type="checkbox"/> ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. <input type="checkbox"/> ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
Effective Date:	RETIRED 7/1/2026

POLICY

Testing for germline *BRIP1*, *RAD51C*, and *RAD51D* variants for ovarian cancer risk assessment in adults may be considered **medically necessary** when the following criteria are met:

- The individual has a diagnosis of epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer; AND
 - The individual has not previously been tested for these gene variants; AND
 - The individual is thought to be the most informative member of a family (proband) to have genetic testing (see Policy Guidelines); AND
 - The individual has closely related (first- and/or second-degree) relatives who are considering genetic testing for these gene variants to inform prophylactic decision-making or who have test results that cannot be fully interpreted without testing an affected relative; OR
- The individual has not been diagnosed with epithelial ovarian cancer; AND
 - The individual has any blood relative with a known pathogenic/likely pathogenic *BRIP1*, *RAD51C*, or *RAD51D* variant; OR
 - The individual has a first- or second-degree relative diagnosed with ovarian cancer^a

Testing for germline *NBN* variants for ovarian cancer risk assessment in adults is considered **investigational** as there is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

Testing for germline *BRIP1*, *RAD51C*, *RAD51D*, and *NBN* variants in individuals diagnosed with epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer to guide treatment of the diagnosed individual is considered **investigational** as there is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

Testing for germline *BRIP1*, *RAD51C*, and *RAD51D* variants in adults who do not meet the criteria above is considered **investigational** as there is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

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^a For familial assessment, first- and second-degree relatives are blood relatives on the same side of the family (maternal or paternal):

- First-degree relatives: parents, siblings, and children
- Second-degree relatives: grandparents, aunts, uncles, nieces, nephews, grandchildren, and half-siblings

POLICY GUIDELINES

Recommended Genetic Testing Strategies

Individuals who meet criteria for germline (not somatic) genetic testing as outlined in the policy statements should be tested for variants in *BRIP1*, *RAD51C*, and *RAD51D*. Recommended strategies are listed below.

- In individuals with a known familial germline *BRIP1*, *RAD51C*, or *RAD51D* variant, targeted testing for the specific variant is recommended.
- In individuals with an unknown familial germline *BRIP1*, *RAD51C*, or *RAD51D* variant:
 - To identify clinically significant variants, the National Comprehensive Cancer Network (NCCN) advises testing a relative who has early-onset disease, bilateral disease, or multiple primaries, because that individual has the highest likelihood of obtaining an informative, positive test result. This individual, the first-affected individual in a family who brings a genetic disorder to the attention of the medical community, is commonly referred to as the proband.
 - Testing undiagnosed, at-risk family members when a diagnosed relative is unavailable for testing, is unwilling to undergo testing, or is unwilling to share genetic testing results, should still be considered. However, indeterminate genetic testing results may be poorly understood by family members. Therefore, significant limitations of interpreting test results, including uninformative negative results or non-actionable variants of unknown significance (VUS), should be discussed.

This policy applies to testing for ovarian cancer risk assessment and does not address testing for autosomal recessive conditions associated with *BRIP1*, *RAD51C*, or *NBN*.

Germline genetic testing for *BRCA1*, *BRCA2*, and *PALB2* is addressed separately in **MP 2.211**.

Germline testing for Fanconi Anemia is addressed separately in **MP 2.362**.

Testing for *ATM* in the context of hereditary breast cancer is addressed separately in **MP 2.279**. NCCN recommends that *ATM* carriers at risk for epithelial ovarian cancer should be managed based on family history alone.

Mismatch repair genes associated with Lynch syndrome are addressed in **MP 5.013**.

Testing Undiagnosed, At-Risk Individuals

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In unaffected (i.e., undiagnosed), at-risk family members of potential *BRIP1*, *RAD51C*, or *RAD51D* variant families, most test results will be negative and uninformative. Therefore, it is strongly recommended that an *affected* (i.e., diagnosed) family member be tested first whenever possible to adequately interpret the test. Should a causative variant be found in an affected family member(s), DNA from an *unaffected* family member can be tested specifically for the same variant of the affected family member without having to sequence the entire gene. Interpreting test results for an *unaffected* family member without knowing the genetic status of the family may be possible in the case of a positive result for an established disease-associated variant but leads to difficulties in interpreting uninformative negative test results or VUS because the possibility of a causative variant is not ruled out (Himes et al [2019]; PMID 31199558). Non-actionable VUS are highly prevalent with multi-gene testing, which may be avoided with targeted testing for a known familial variant (Tung et al [2016]; PMID: 27296296).

Genetics Nomenclature Update

The Human Genome Variation Society nomenclature is used to report information on variants found in DNA and serves as an international standard in DNA diagnostics. It is being implemented for genetic testing medical evidence review updates starting in 2017 (see Table PG1). The Society's nomenclature is recommended by the Human Variome Project, the Human Genome Organization, and by the Human Genome Variation Society itself.

The American College of Medical Genetics and Genomics and the Association for Molecular Pathology standards and guidelines for interpretation of sequence variants represent expert opinion from both organizations, in addition to the College of American Pathologists. These recommendations primarily apply to genetic tests used in clinical laboratories, including genotyping, single genes, panels, exomes, and genomes. Table PG2 shows the recommended standard terminology - "pathogenic," "likely pathogenic," "uncertain significance," "likely benign," and "benign" - to describe variants identified that cause Mendelian disorders.

Table PG1. Nomenclature to Report on Variants Found in DNA

Previous	Updated	Definition
Mutation	Disease-associated variant	Disease-associated change in the DNA sequence
	Variant	Change in the DNA sequence
	Familial variant	Disease-associated variant identified in a proband for use in subsequent targeted genetic testing in first-degree relatives

Table PG2. ACMG-AMP Standards and Guidelines for Variant Classification

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Variant Classification	Definition
Pathogenic	Disease-causing change in the DNA sequence
Likely pathogenic	Likely disease-causing change in the DNA sequence
Variant of uncertain significance	Change in DNA sequence with uncertain effects on disease
Likely benign	Change in DNA sequence with uncertain effects on disease
Benign	Benign change in the DNA sequence

ACMG: American College of Medical Genetics and Genomics; AMP: Association for Molecular Pathology.

Genetic Counseling

Genetic counseling is primarily aimed at patients who are at risk for inherited disorders, and experts recommend formal genetic counseling in most cases when genetic testing for an inherited condition is considered. The interpretation of the results of genetic tests and the understanding of risk factors can be very difficult and complex. Therefore, genetic counseling will assist individuals in understanding the possible benefits and harms of genetic testing, including the possible impact of the information on the individual's family. Genetic counseling may alter the utilization of genetic testing substantially and may reduce inappropriate testing. Genetic counseling should be performed by an individual with experience and expertise in genetic medicine and genetic testing methods.

Cross-References:

MP 2.211 Germline Genetic Testing for Hereditary Breast/Ovarian Cancer Syndrome and other High-Risk Cancers (BRCA1, BRCA2, PALB2)

MP 2.279 Germline Genetic Testing for Gene Variants Associated with Breast Cancer in Individuals at High Breast Cancer Risk (CHEK2, ATM, and BARD1)

MP 2.325 Genetic Cancer Susceptibility Panels Using Next Generation Sequencing

MP 2.362 Genetic Testing for Fanconi Anemia

MP 2.393 Germline and Somatic Biomarker Testing (Including Liquid Biopsy) for Targeted Treatment in Breast Cancer (BRCA1, BRCA2, PIK3CA, Ki-67, RET, BRAF, ESR1, NTRK)

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MP 2.394 Germline and Somatic Biomarker Testing (Including Liquid Biopsy) for Targeted Treatment in Prostate Cancer (BRCA1/2, Homologous Recombination Repair Gene Alterations, NTRK Gene Fusion)
MP 2.395 Germline and Somatic Biomarker Testing (Including Liquid Biopsy) for Targeted Treatment in Ovarian Cancer (BRCA1, BRCA2, Homologous Recombination Deficiency, NTRK)
MP 5.013 Genetic Testing for Lynch Syndrome and Other Inherited Colon Cancer Syndromes

PRODUCT VARIATIONS

This policy is only applicable to certain programs and products administered by Capital Blue Cross and subject to benefit variations. Please see additional information below.

FEP PPO: Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at: <https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies>.

DESCRIPTION/BACKGROUND

Ovarian Cancer and Genetics

In 2024, it is estimated that there will be 19,680 new diagnosed cases of ovarian cancer (OC) and that an estimated 12,740 women will die from their disease. Over 95% of OC are derived from epithelial cells. High-grade serous epithelial ovarian carcinoma, fallopian tube carcinoma, and primary peritoneal carcinomas are thus considered a single clinical entity (i.e., epithelial OC [EOC]) due to their shared pathologic behavior and treatment. Based upon data from the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) Program, approximately 1.1% of women in the United States will be diagnosed with OC in their lifetime.

Due to the limited benefit of presymptomatic screening for OC, identifying women at high risk of the disease who may benefit from prophylactic risk-reducing surgery is critically important. Approximately 70% of women are diagnosed with late-stage disease, resulting in a 5-year relative survival rate of 29% compared to 92% for early-stage disease. It is estimated that more than 20% of women diagnosed with OC have a hereditary predisposition to the disease, harboring loss-of-function (LoF) mutations in cancer-related genes. Most of the identified germline mutations in OC occur in the highly penetrant BRCA1 and BRCA2 genes which regulate DNA repair. It is estimated that high penetrance variants in BRCA1 and BRCA2 genes account for ~27% of familial OC cases. Mutations in these genes result in homologous recombination deficiency (HRD), which has been targeted with platinum-based chemotherapy and poly (ADP-ribose) polymerase (PARP) inhibitors. Other mechanisms of HRD lead to a phenotype known as BRCAness and include germline and somatic mutations in genes related to homologous recombination, epigenetic modifications, and EMSY amplification or overexpression. Homologous recombination-related genes with a documented association with

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OC risk include BRIP1, RAD51C, and RAD51D, and may represent the most important OC predisposition genes after BRCA1/2. Hereditary OC risk may also be influenced by mismatch repair genes and variants in PALB2. BRIP1, RAD51C, and RAD51D, and the mismatch repair genes are estimated to contribute to 10% of hereditary OC cases.⁵ Approximately 60% of the familial relative risk in OC is unexplained. Risk estimates may be higher in patients with a family history of OC or a family history of a specific gene variant.

Penetrance of Pathogenic Variants

Penetrance is the risk conferred by a pathogenic variant or the proportion of individuals with the variant expected to develop cancer. For example, a woman's lifetime risk for developing OC is roughly 36% to 63% for *BRCA1* carriers and 10% to 27% for *BRCA2* carriers. Penetrance can be modified by environmental factors and by family history, which is an important modifier for low and moderate penetrance genes. Moreover, specific pathogenic variants within a gene may confer somewhat different risks.

There is no consensus on how to calculate lifetime risk. Cumulative lifetime risk (CLTR) may be calculated as a multiple of the US SEER Program estimates of 'ever' developing cancer combined with the average relative risk for the gene variant in question. Other experts may calculate risk of cancer development by a defined age, which is often described as lifetime penetrance. Others describe the remaining lifetime risk (LTR) as the CLTR remaining after an individual reaches a particular age. The lack of a consensus for defining LTR may confound guidelines based on this measurement. It is also important to note that the risk threshold separating moderate-penetrance from high-penetrance genes is defined arbitrarily. Average relative risks may not account for individual risk modifications due to genetic and non-genetic factors.

Determining Variant Pathogenicity

Determining the pathogenicity of variants in a more commonly detected cancer susceptibility gene (e.g., founder sequence mutations) is generally straightforward because associations are repeatedly observed. For uncommonly identified variants, such as those found in a few individuals or families, defining pathogenicity can be more difficult. For example, predicting the pathogenicity of previously unidentified variants typically requires in silico (computational) analysis predicting protein structure/function, evolutionary conservation, and splice site prediction. The approach to defining pathogenicity is clearly outlined in standards and reporting guidelines. Still, distinctions between a VUS and a pathogenic one from different laboratories may not always be identical.

Genes Associated with a Moderate-to-High Penetrance of Ovarian Cancer

BRIP1 Gene

The *BRIP1* (*BRCA1* interaction protein C-terminal helicase 1) gene, also known as *FANCI*, is located at 17q23.2 and encodes a protein which binds to BRCT repeats in *BRCA1* via a nuclear localization signal in its helicase domain to facilitate DNA repair. Biallelic germline mutations result in Fanconi anemia, which is also seen in *BRCA2* germline mutations. *BRIP1*-inactivating

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truncating and frameshift mutations have been associated with an increased risk of OC. Ovarian tumors from heterozygous carriers of the c.1702_1703del mutation showed loss of the wildtype allele, suggesting behavior typical of a classical tumor suppressor gene.

RAD51 Genes

The RAD51 paralogs, *RAD51C* and *RAD51D*, are involved in the FA-*BRCA1/2* homologous recombination pathway. Biallelic missense mutations in the *RAD51C* gene are associated with a Fanconi anemia-like phenotype. These mutations are rare and are associated with an increased risk of OC as well as a potential increased risk of triple-negative breast cancer.

NBN Gene

The *NBN* gene encodes the nibrin protein, which is mapped within a critical region for Nijmegen breakage syndrome (NBS) on chromosome 8q21. The encoded protein, also known as p95, is a member of the MRE11/RAD50 double-strand break repair complex and is implicated in cell cycle checkpoint functions and cellular responses to ionizing radiation.

Identifying Women at Risk of an Inherited Susceptibility to Ovarian Cancer

Risk factors for OC include older age, early menarche or late menopause, family history of disease, genetic factors, nulliparity, endometriosis, and exposure to asbestos. Risk assessed through family history is dependent on the number and closeness of affected relatives, the age at which cancer developed, and if other cancers occurred (e.g., breast). For women without OC, the probability of detecting a pathogenic variant can be estimated from a detailed multigenerational pedigree (e.g., Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm), screening tools (e.g., BRCAPRO), or by referring to guidelines that define specific family history criteria (see Supplemental Information Section on Practice Guidelines and Position Statements). For women with OC, family history also affects the likelihood of carrying a pathogenic variant.

Regulatory Status

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. *BRIP1*, *RAD51C*, *RAD51D*, and *NBN* testing are available under the auspices of the Clinical Laboratory Improvement Amendments. Laboratories offering to test and voluntarily list are available through the National Center for Biotechnology Genetic Testing Registry. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of these tests.

Customized next-generation sequencing panels provide simultaneous analysis of multiple cancer predisposition genes and typically include both moderate- and high-penetrance genes.

Myriad Genetic Laboratories offers the myRisk® Hereditary Cancer multi-gene panel test which includes 35 genes. Testing for OC risk includes analysis of *BRCA1*, *BRCA2*, *MLH1*, *MSH2*, *MSH6*, *PMS2*, *EPCAM*, *TP53*, *STK11*, *PALB2*, *BRIP1*, *RAD51C*, and *RAD51D* genes.

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Ambry Genetics offers the BRCANext-Expanded® panel which includes 23 genes associated with risk of gynecologic cancer, including *BRIP1*, *RAD51C*, and *RAD51D*. Testing for *NBN* is also included in this panel.

RATIONALE

SUMMARY OF EVIDENCE

For individuals without diagnosed epithelial ovarian cancer (EOC) and in a family at risk of developing EOC who receive germline genetic testing for genes associated with hereditary OC (i.e., *BRIP1*, *RAD51C*, and *RAD51D*), the evidence includes studies of clinical validity and studies of OC risk, including meta-analyses. Relevant outcomes are overall survival (OS), disease-specific survival, and test validity. Evidence supporting clinical validity was obtained from numerous studies reporting relative risk (RR) or odds ratio (OR) and 4 studies provided penetrance estimates. Study designs included family-based case-control and population- or multicenter-based case-control. The number of P/LP variants identified in association studies ranged from 10 to 36, 11 to 44, and 8 to 13 for *BRIP1*, *RAD51C*, and *RAD51D*, respectively. The RR for OC associated with *BRIP1* ranged from 3 to 19, with population-based study reporting the 2 highest and lowest values. The RR for OC associated with *RAD51C* ranged from 3 to 6, with a family-based study reporting the highest value. The RR for OC associated with *RAD51D* ranged from 5 to 12, with family- and population-based studies reporting the highest values. Evidence of preventative interventions in women with *BRIP1*, *RAD51C*, and *RAD51D* variants is indirect, relying on studies of high-risk women and *BRCA* carriers. These interventions include chemoprevention with oral contraceptives and risk-reducing oophorectomy and RRSO. Given the penetrance of *BRIP1*, *RAD51C*, and *RAD51D* variants, the outcomes following risk-reducing oophorectomy and RRSO examined in women with a family history consistent with hereditary OC (including *BRCA1* and *BRCA2* carriers) can be applied to women with *BRIP1*, *RAD51C*, and *RAD51D* variants, with the benefit-to-risk balance affected by penetrance. In women at high-risk of hereditary OC who would consider risk-reducing interventions, identifying a *BRIP1*, *RAD51C*, or *RAD51D* variant provides a more precise estimated risk of developing OC compared to family history alone and can offer women a more accurate understanding of benefits and potential harms of any intervention. Additionally, RRSO may provide an opportunity for occult gynecologic cancer detection in high-risk *BRCA*-negative women. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals without diagnosed EOC and in a family at risk of developing EOC who receive germline genetic testing for *NBN* gene variants, the evidence includes studies of clinical validity and studies of OC risk, including a meta-analysis. Relevant outcomes are OS, disease-specific survival, and test validity. *NBN* variants have been associated with a 2- to 3.5-fold increased risk of OC across studies. However, a significantly increased frequency of *NBN* mutations has not been consistently observed in cases versus controls and penetrance estimates have not been reported. Accordingly, national guidelines have not recommended risk-reducing interventions for *NBN* carriers at this time due to insufficient data to define risk and recommend managing

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these individuals based on family history alone. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals without diagnosed EOC and in a family at risk of developing EOC who are considering prophylactic surgery who receive germline genetic testing of first- and/or second-degree relative(s) with a personal history of EOC for genes associated with hereditary OC (i.e., *BRIP1*, *RAD51C*, and *RAD51D*) to guide prophylactic decision-making or interpretation of test results in the undiagnosed, at-risk family member, the evidence on the use of preventative interventions is indirect, relying on studies of at-risk women and *BRCA* carriers. Relevant outcomes are OS, disease-specific survival, and test validity. Evidence of preventative interventions in women with *BRIP1*, *RAD51C*, and *RAD51D* variants is indirect, relying on studies of high-risk women and *BRCA* carriers. Preventative interventions include chemoprevention with oral contraceptives and risk-reducing oophorectomy and RRSO. Given the penetrance of *BRIP1*, *RAD51C*, and *RAD51D* variants, the outcomes following risk-reducing oophorectomy and RRSO examined in women with a family history consistent with hereditary OC (including *BRCA1* and *BRCA2* carriers) can be applied to women with *BRIP1*, *RAD51C*, and *RAD51D* variants, with the benefit-to-risk balance affected by penetrance. In women at risk of hereditary OC who are considering prophylactic surgery, genetic testing of first- and/or second-degree relative(s) with a personal history of EOC to identify a familial *BRIP1*, *RAD51C*, or *RAD51D* germline variant provides a more precise estimated risk of developing OC compared to family history alone and reduces the incidence of uninformative negative test results or non-actionable variants of unknown significance. Identification of and targeted testing for a known familial variant can offer women a more accurate understanding of benefits and potential harms of prophylactic surgery and is a testing strategy supported by national guidelines. Testing a relative with early-onset disease, bilateral disease, or multiple primaries is recommended, as that individual has the highest likelihood of obtaining an informative, positive test result. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals without diagnosed EOC and in a family at risk of developing EOC who are considering prophylactic surgery who receive germline genetic testing of first- and/or second-degree relative(s) with a personal history of EOC for *NBN* gene variants to guide prophylactic decision-making or interpretation of test results in the undiagnosed, at-risk family member, direct evidence is lacking. Relevant outcomes are OS, disease-specific survival, and test validity. National guidelines have not recommended prophylactic surgery due to insufficient data to establish absolute risk estimates. Given that the clinical validity of *NBN* germline variant testing has not been established, a chain of evidence cannot be constructed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with diagnosed OC who receive germline genetic testing for genes associated with hereditary OC (i.e., *BRIP1*, *RAD51C*, *RAD51D*, and *NBN*) to guide treatment decisions in the individual with diagnosed EOC, the evidence includes studies of variant prevalence and studies of OC risk. Relevant outcomes are OS, disease-specific survival, and test validity. Direct evidence for the clinical utility of genetic testing for *BRIP1*, *RAD51C*, *RAD51D*,

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and *NBN* variants in individuals with OC was not identified. Due to the standard surgical management of OC patients, the clinical utility of *BRIP1*, *RAD51C*, *RAD51D*, and *NBN* variant testing to inform therapy was reviewed. In studies evaluating HRD assays in *BRCA* wild-type patients, an overlapping therapeutic benefit was found between deficient/high loss-of-heterozygosity and proficient/low loss-of-heterozygosity tumors and results were not stratified by non-*BRCA* HRD genes. The use of *BRIP1*, *RAD51C*, *RAD51D*, and *NBN* variant status to guide maintenance and recurrence therapy continues to be elucidated in the clinical trial setting. In contrast to undiagnosed women at high familial risk of OC, women diagnosed with OC who undergo testing for *BRIP1*, *RAD51C*, *RAD51D*, and *NBN* variants do not yield clinically actionable results. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

DEFINITIONS

N/A

DISCLAIMER

Capital Blue Cross' medical policies are used to determine coverage for specific medical technologies, procedures, equipment, and services. These medical policies do not constitute medical advice and are subject to change as required by law or applicable clinical evidence from independent treatment guidelines. Treating providers are solely responsible for medical advice and treatment of members. These policies are not a guarantee of coverage or payment. Payment of claims is subject to a determination regarding the member's benefit program and eligibility on the date of service, and a determination that the services are medically necessary and appropriate. Final processing of a claim is based upon the terms of contract that applies to the members' benefit program, including benefit limitations and exclusions. If a provider or a member has a question concerning this medical policy, please contact Capital Blue Cross' Provider Services or Member Services.

CODING INFORMATION

Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Investigational when used for testing *BRIP1*, *RAD51C*, and *RAD51D* variants:

Procedure Codes							
0102U	0103U	0134U	81432				

Covered when medically necessary when used for testing *BRIP1*, *RAD51C*, and *RAD51D* variants:

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Procedure Codes							
81479							

ICD-10-CM Diagnosis Code	Description
C48.0	Malignant neoplasm of retroperitoneum
C48.1	Malignant neoplasm of specified parts of peritoneum
C48.2	Malignant neoplasm of peritoneum, unspecified
C48.8	Malignant neoplasm of overlapping sites of retroperitoneum
C56.1	Malignant neoplasm of right ovary
C56.2	Malignant neoplasm of left ovary
C56.3	Malignant neoplasm of bilateral ovaries
C56.9	Malignant neoplasm of unspecified ovary
C57.00	Malignant neoplasm of unspecified fallopian tube
C57.01	Malignant neoplasm of right fallopian tube
C57.02	Malignant neoplasm of left fallopian tube
C57.8	Malignant neoplasm of overlapping sites of female genital organs
Z80.41	Family history of malignant neoplasm of ovary
Z80.49	Family history of malignant neoplasm of other genital organs
Z80.8	Family history of malignant neoplasm of other organs or systems
Z85.4A	Personal history of malignant neoplasm of fallopian tube(s)
Z86.00A	Personal history of in-situ neoplasm of the fallopian tube(s)

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POLICY HISTORY

MP 2.377	New Policy. Adopting BCBSA policy. Medically necessary criteria for <i>BRIP1</i> , <i>RAD51C</i> , and <i>RAD51D</i> variants. Effective 05/01/2021
	11/19/2021 Minor Review. Updated criteria per BCBSA that individual can have a diagnosis of epithelial ovarian and related cancers. Testing to guide treatment for diagnosed individual is INV. Added NCCN statement. Updated policy guidelines, FEP, and background. Added CPT and ICD-10 codes to policy.
	12/30/2022 Minor Review. Added NBN investigational statement. Title change. Updated cross-references, background, rationale, coding table and references.
	12/22/2023 Retirement Review. Policy has been combined with MP 2.211
	06/07/2024 Administrative Update. Added 0475U. Eff date 07/01/2024
	01/14/2025 Minor Review. Bringing out of retirement.
	06/25/2025 Administrative Update. Removed Benefit Variations Section and updated Disclaimer.
	09/03/2025 Administrative Update. Added ICD10 Codes Z85.4A & Z86.00A Eff date 10/01/2025
	12/04/2025 Administrative Update. Removed codes 0131U, 0132U & 0135U eff 01/01/2026
	03/05/2026 Retirement Review. Service to be managed by the vendor Evicore.

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Association. Communications issued by Capital Blue Cross in its capacity as administrator of programs and provider relations for all companies.

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