Geisinger Health Plan Policies and Procedure Manual

Policy: MP097

Section: Medical Benefit Policy

Subject: Genetic Testing for BRCA1, BRCA2 and PALB2 for Breast or Ovarian Cancer

Applicable line of business:

Commercial	**x**	**Medicaid**	**x**
Medicare	**x**	**ACA**	**x**
CHIP	**x**		

I. Policy: Genetic Testing for BRCA1, BRCA2 and PALB2 for Breast or Ovarian Cancer

II. Purpose/Objective:

To provide a policy of coverage regarding Genetic Testing for BRCA1, BRCA2 and PALB2 for Breast or Ovarian Cancer

III. Responsibility:

A. Medical Directors
B. Medical Management

IV. Required Definitions

1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than the department requiring/authoring the policy.
3. Devised – the date the policy was implemented.
4. Revised – the date of every revision to the policy, including typographical and grammatical changes.
5. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

Commercial

Geisinger Health Plan may refer collectively to health care coverage sponsors Geisinger Health Plan, Geisinger Quality Options, Inc., and Geisinger Indemnity Insurance Company, unless otherwise noted. Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization.

Medicare

Geisinger Gold Medicare Advantage HMO, PPO, and HMO D-SNP plans are offered by Geisinger Health Plan/Geisinger Indemnity Insurance Company, health plans with a Medicare contract. Continued enrollment in Geisinger Gold depends on contract renewal. Geisinger Health Plan/Geisinger Indemnity Insurance Company are part of Geisinger, an integrated health care delivery and coverage organization.

CHIP

Geisinger Health Plan Kids (GHP Kids) is a Children's Health Insurance Program (CHIP) offered by Geisinger Health Plan in conjunction with the Pennsylvania Department of Human Services (DHS). Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization.

Medicaid

Geisinger Health Plan Family (GHP Family) is a Medical Assistance (Medicaid) insurance program offered by Geisinger Health Plan in conjunction with the Pennsylvania Department of Human Services (DHS). Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization

V. Additional Definitions
Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
b. provided for the diagnosis, and the direct care and treatment of the Member's condition, illness disease or injury;
c. in accordance with current standards of good medical treatment practiced by the general medical community.
d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient.

Medicaid Business Segment
Medically Necessary — A service, item, procedure, or level of care that is necessary for the proper treatment or management of an illness, injury, or disability is one that:

- Will, or is reasonably expected to, prevent the onset of an illness, condition, injury or disability.
- Will, or is reasonably expected to, reduce or ameliorate the physical, mental or developmental effects of an illness, condition, injury or disability.
- Will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for Members of the same age

Triple negative breast cancer: a cancer negative for expression of estrogen and progesterone receptors, and for overexpression of HER2 receptors

Blood Relatives: NCCN defines blood relative as first- (parents, siblings and children), second- (grandparents, aunts, uncles, nieces and nephews, grandchildren and half-siblings), and third degree-relatives (great-grandparents, great-aunts, great uncles, great grandchildren and first cousins) on same side of family

DESCRIPTION:
Approximately 7-10% of all breast cancers,20-25% of all ovarian cancers, 10-17% of prostate cancers, and 5-10% of pancreas cancers can be attributed to a dominantly inherited susceptibility.

Multi-gene panel testing is the most cost-effective and accurate approach to characterize familial cancer risk. BRCA1 and BRCA2 testing alone is no longer the clinical standard of care. Mutations in BRCA1 and BRCA2 have been identified in up to 50% of the inherited forms of hereditary breast and ovarian cancers, however, additional high-and moderate-risk genes have been discovered that may (1) explain familial cancer risk, (2) provide future cancer risk information, or (3) direct targeted therapeutic options.

Disease-specific panels may change from year to year based on available evidence and technological advancements. Germline multigene panel testing (MGPT) for moderate and high-penetrance cancer susceptibility genes should ultimately include ATM, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, MLH1, MSH2, MSH6, PALB2, PTEN, STK11, TP53) and full duplication and deletion analysis (i.e., detection of large genomic rearrangements).

Up to 12% of genomic tumor profiling or sequencing tests will reveal a germline pathogenic variant. some germline variants are highly predictive of response to specific cancer-directed therapies, such as poly-ADP ribose polymerase (PARP) inhibitors in patients with breast or ovarian cancer who have germline BRCA1/2 variants. Some reports suggest up to 50- 60% likelihood that when a BRCA sequencing variant is reported in any tumor type, it will be present in the germline.

Panel testing is considered medically necessary once per lifetime for persons who meet one or more National Comprehensive Cancer Network (NCCN) testing criteria for high-penetrance breast, ovarian, or pancreatic cancer susceptibility gene

INDICATIONS:
The Plan considers molecular susceptibility testing for hereditary breast and ovarian cancer (HBOC) via panel testing,medically necessary in **ANY** of the following indications:

NOTE: STAT testing of BRCA1, BRCA2, and PALB2 may be required in specific clinical scenarios for surgical or therapeutic decision making. Panel testing is considered medically necessary and will be approved for members undergoing this sequential testing.

Members with a personal history of an HBOC-related cancer, at any age, regardless of family history:

- Breast cancer (includes histologic subtypes: invasive lobular, invasive ductal, inflammatory, papillary, and DCIS. (LCIS excluded.)
- Ovarian, fallopian tube, primary peritoneal cancer
- Pancreatic adenocarcinoma
- Prostate adenocarcinoma

Members with any other type of malignancy where somatic (tumor-based) testing demonstrates a BRCA1 or BRCA2 variant within the tumor sample.

Members without a personal history of cancer, but with a family history of meeting ANY ONE of the following criteria:

1. A blood relative with a mutation in a known cancer susceptibility gene, OR.
2. A blood relative with a mutation in a hereditary cancer syndrome gene found on tumor testing who is unable to undergo germline testing, OR
3. At least one blood relative with a history of breast cancer diagnosed at 50 years or younger
4. At least one blood relative diagnosed with triple negative breast cancer OR bilateral breast cancer OR two separate breast primaries, at any age
5. At least one blood relative with any of the following cancers, diagnosed at any age:
    a. male breast cancer
    b. epithelial ovarian cancer, fallopian tube, or primary peritoneal cancer
    c. pancreatic adenocarcinoma
    d. prostate cancer (metastasis or high-grade diagnosis not required)
6. At least two close relatives on the same side of the family with any combination of breast, ovary, pancreas, or prostate cancers
7. At least 5% mutation probability using a validated risk tool (eg. Tyrer-Cuzick v8, BRCAPro, or CanRisk).
8. A reported history of Ashkenazi Jewish ancestry with at least one first or second-degree relative with an HBOC cancer (eg. breast, ovarian, pancreas, or prostate cancer) at any age.
9. The member has a personal or family history suggestive of a rare hereditary cancer syndrome that does not fall into the above criteria AND provider submits documentation of current NCCN criteria for evaluation.
   Examples: Li-Fraumeni syndrome (TP53), Peutz-Jeghers syndrome (STK11), or PTEN Hamartoma Tumor syndrome (aka Cowden syndrome, PTEN).
    a. Features suggestive of PHTS: macrocephaly, cerebellar tumors or adult Lhermitte-Duclose disease, autism spectrum disorder, intellectual disability, macular degeneration of the glans penis, one ganglioneuroma or at least two hamartomas of the GI tract, follicular thyroid cancer, breast cancer, endometrial cancer, or two or more trichilemmomas, oral papillomatosis, verrucous facial papules, or palmoplantar keratoses.
    b. Features suggestive of Li-Fraumeni syndrome: Close relative with acute lymphoblastic leukemia (ALL), soft tissue or bone sarcoma, CNS cancer, chorioid plexus carcinoma, rhabdomyosarcoma, or adrenocortical carcinoma.

Therapeutic companion testing:

BRCA/PALB2 testing using an FDA-approved companion diagnostic is considered medically necessary when the following criteria are met:

- The member has a diagnosis of cancer; and
- The specific therapeutic is FDA- approved and treatment eligibility is dependent upon BRCA1/2 or PALB2 testing

PALB2 mutation testing:

The Plan considers full sequence analysis molecular testing for PALB2 mutation to be medically necessary when **ALL** of the following are met:

- The member is 18 years of age or older
- Member has met criteria for BRCA1/2 analysis;
- Member tested negative for BRCA1/2

The Plan considers known familial mutation analysis for PALB2 mutation to be medically necessary when ALL of the following are met:

- The member is 18 years of age or older
- A mutation in PALB2 has been identified in 1st, 2nd, or 3rd degree relative(s)

Genetic testing is appropriate only when offered in a setting where a licensed or certified genetic counselor* or adequately trained health care professional is able to provide appropriate pre- and post-test genetic counseling, and medical necessity is supported by ALL of the following criteria:

1. The information is needed to adequately assess risk in the member; **and**
2. The information will be used in the immediate care plan of the member; **and**
3. Pedigree analysis establishes that the insured individual is in a high risk group for the disease; **or**
4. Clinical presentation of symptomology is evident and diagnosis cannot be established with conventional evaluation testing.

*A genetic counselor is considered by the Plan to be qualified if the following are met:

- M.S. or Ph.D. degree from a genetic counseling program approved/ certified by the American Board of Genetic Counseling or the American Board of Medical Genetics

or

- Board certified or board qualified/eligible in the orderly process of obtaining board certification by the American Board of Genetic Counseling or American Board of Medical Genetics

and

- Proof of current competence and demonstrated ability (minimum of two years recent and continual experience within the past three years).

EXCLUSIONS:

- Genetic testing for BRCA1 or BRCA2 mutations on those less than 18 years of age is considered **experimental, investigational, and unproven.**
- Testing of unaffected individuals with no significant family history of cancer or no known genetic mutations in the family is considered **not medically necessary**
- Genetic testing to assess the risk breast or prostate cancer in men without breast cancer is considered **experimental, investigational, and unproven.**
- The use of CHECK2 testing is considered **experimental, investigational, and unproven.**
- The use of direct-to-consumer testing for hereditary breast and/or ovarian cancer (e.g., 23 and Me) is **experimental, investigational, or unproven**. These tests have not been validated for clinical use and have a substantial error rate. They are not able to provide information that is appropriate for medical management and are therefore **NOT COVERED**.

PROCESS:

The Plan will utilize available published, peer reviewed medical literature, independent technology assessment program reports and/or review by the Geisinger Clinic Technology Assessment Committee to evaluate the following criteria when assessing the validity and efficacy of a specific genetic test:

- The analytical power of a test determined by its sensitivity and specificity is established.
- There is evidence of defined outcome measures that permits conclusions concerning the effect on health outcomes.
- The net health outcomes benefit of the test as compared to established alternatives is evaluated if applicable.
- The availability of test to membership is evaluated.
- The appropriate governmental and/or professional regulatory body approval is established.
- The test result will influence the treatment or alter the management of the insured individual medical care plan
- The test result has the capability to confirm a diagnosis when conventional medical evaluation is equivocal.

Note: A complete description of the process by which a given technology or service is evaluated and determined to be experimental, investigational or unproven is outlined in MP 15 - Experimental Investigational or Unproven Services or Treatment.

Medicaid Business Segment:

Any requests for services, that do not meet criteria set in the PARP, may be evaluated on a case by case basis.

CODING ASSOCIATED WITH: Genetic Testing for BRCA1 or BRCA2 for Breast or Ovarian Cancer

The following codes are included below for informational purposes and may not be all inclusive. Inclusion of a procedure or device code(s) does not constitute or imply coverage nor does it imply or guarantee provider reimbursement. Coverage is determined by the member specific benefit plan document and any applicable laws regarding coverage of specific services. Please note that per Medicare coverage rules, only specific CPT/HCPCS Codes may be covered for the Medicare Business Segment. Please consult the CMS website at www.cms.gov ***or the local Medicare Administrative Carrier (MAC) for more information on Medicare coverage and coding requirements.***

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

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) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis

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

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

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

81211 BRCA1, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and common duplication/deletion variants in BRCA1 (ie, exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-20 del 26kb, exon 22 del 510bp, exon

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

81213 BRCA1, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; uncommon duplication/deletion variants

81214 BRCA1 (breast cancer 1) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and common duplication/deletion variants (ie, exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-20 del 26kb, exon 22 del 510bp, exon 8-9 del 7.1kb)

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

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

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

81307 PALB2 (PARTNER AND LOCALIZER OF BRCA2) (EG, BREAST AND PANCREATIC CANCER) GENE ANALYSIS; FULL GENE SEQUENCE

81308 PALB2 (PARTNER AND LOCALIZER OF BRCA2) (EG, BREAST AND PANCREATIC CANCER) GENE ANALYSIS; KNOWN FAMILIAL VARIANT

81432 Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence analysis panel, must include sequencing of at least 14 genes, including ATM, BRCA1, BRCA2, BRIP1, CDH1, MLH1, MSH2, MSH6, NBN, PALB2, PTEN, RAD51C, STK11, and TP53 **(Requires PE for Medicaid)**

81433 Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); duplication/deletion analysis panel, must include analyses for BRCA1, BRCA2, MLH1, MSH2, and STK11 **(Requires PE for Medicaid)**

81403 PALB2 known familial mutation analysis

81406 PALB2 sequencing

81308 PALB2 (Partner and Localizer of BRAC2)(eg, breast and pancreatic cancer) gene analysis, known family variant

0102U Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer), genomic sequence analysis panel utilizing a combination of NGS, Sanger, MLPA, and array CGH, with mRNA analytics to resolve variants of unknown significance when indicated (17 genes [sequencing and deletion/duplication])

0103U Hereditary ovarian cancer (e.g., hereditary ovarian cancer, hereditary endometrial cancer), genomic sequence analysis panel utilizing a combination of NGS, Sanger, MLPA, and array CGH, with mRNA analytics to resolve variants of unknown significance when indicated (24 genes [sequencing and deletion/duplication], EPCAM [deletion/duplication only])

0129U Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer), genomic sequence analysis and deletion/duplication analysis panel (ATM, BRCA1, BRCA2,

CDH1, CHEK2, PALB2, PTEN, and TP53)
0138U BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) mRNA sequence analysis
0172U Oncology (solid tumor as indicated by the label), somatic mutation analysis of BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) and analysis of homologous recombination deficiency pathways, DNA, formalin-fixed paraffin-embedded tissue, algorithm quantifying tumor genomic instability score

LINE OF BUSINESS:
Eligibility and contract specific benefits, limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy. For Medicare, applicable LCD's and NCD's will supercede this policy. For PA Medicaid Business segment, this policy applies as written.

REFERENCES:
Brekelmans CTM, Seynaeve C, et. al., "Effectiveness of Breast Cancer Surveillance in BRCA 1 / 2 Gene Mutation Carriers and Women With High Familial Risk", *Journal of Clinical Oncology*, 19(4):924-930, 15 Feb. 2001.

Martin AM, Blackwood MA, et. al., "Germline Mutations in BRCA1 and BRCA2 in Breast-Ovarian Families From a Breast Cancer Risk Evaluation Clinic", *Journal of Clinical Oncology*, 19(8):2247-2253, 15 April 2001.

Issacs CJD, Peshkin BN, "Genetic Testing for Breast Cancer – Who Should be Tested and What To Do With the Results", *Medscape Oncology* 1(4), 1998. http://www.oncology.medscape.com

Shattuck-Eidens D, Oliphant A, et.al., "BRCA1 Sequence Analysis in Women at High Risk for Susceptibility Mutations. Risk factor Analysis and Implications for Genetic Testing", *JAMA* 278(15):1242-1250. 15 Oct. 1997.

Gayther SA, deFoy KAF, Harrington P, Pharoah P, Dunsmuir WD, Edwards SM, Gillett C. et al. The frequency of germ-line mutations in the breast cancer predisposition genes BRCA1 and BRCA2 in Familial Prostate Cancer. Cancer Research 15 August 2000; 60:4513-4518.

Sinclair CS, Berry R, Schnaid D, Thibodeau SN, Couch FJ. BRCA1 and BRCA2 have a limited role in familial prostate cancer. Cancer Research 1 March 2000;60:1371-1375.

American College of Medical Genetics (ACMG). Statement on population screening for BRCA-1 mutation in Ashkenazi Jewish women. Bethesda, MD: ACMG; 1996. Available at: http://www.acmg.net/resources/policies/pol-002.asp.

Frank TS, Deffenbaugh AM, Reid JE, Hulick M, Ward BE, Ligenfelter B, Gumpper KL, Scholl T, Tavtigian SV, Pruss DR, and Critchfield GC. Clinical Characteristics of individuals with germ line mutations in BRCA1 and BRCA2: Analysis of 10,000 individuals. J Clin Oncol 2002;20:1480-1490.

James PA, Doherty R, Harris M, Mukesh BN, Milner A, Young MA, Scott C. Optimal selection of individuals for BRCA mutation testing: A comparison of available methods. J Clin Oncol 2006;24:707-715.

CHEK2 Breast Cancer Case-Control Consortium. CHEK2*1100delC and susceptibility to breast cancer: a collaborative analysis involving 10,860 breast cancer cases and 9,065 controls from 10 studies. Am J Hum Genet 2004 Jun;74(6):1175-82.

Meijers-Heijboer H, et al. Low-penetrance susceptibility to breast cancer due to CHEK2(*)1100delC in noncarriers of BRCA1 or BRCA2 mutations. Nat Genet. 2002 May;31(1):55-9.

Narod SA and Lynch HT. CHEK2 mutation and hereditary breast cancer. J Clin Oncol 2007 Jan 1;25(1):6-7.

Oldenburg RA, et al. The CHEK2*1100delC variant acts as a breast cancer risk modifier in non-BRCA1/BRCA2 multiple-case families. Cancer Res 2003 Dec 1;63(23):8153-7.

Walsh T, et al. Spectrum of mutations in BRCA1, BRCA2, CHEK2, and TP53 in families at high risk of breast cancer. JAMA 2006 Mar 22;295(12):1379-88.

National Cancer Institute (NCI) US National Institute of Health (NIH). Genetics of breast and ovarian cancer (PDQ). http://www.cancer.gov/cancertopics/pdq/genetics/breast-and-ovarian/HealthProfessional/page1

Liede A, Karlan BY, Narod SA. Cancer risks for male carriers of germline mutations in BRCA1 or BRCA2: a review of the literature. J Clin Oncol. 2004;22(4):735-742.

Tai YC, Domchek S, et al. Breast cancer risk among male BRCA1 and BRCA2 mutation carriers. J Nat Cancer Inst. 2007;99(23):1811–1814.

Mohamed HD, Apffelstaedt JP. Counseling for male BRCA mutation carriers: a review. Breast 2008;17(5):441-450.

Weischer, M, Bojesen, SE, Ellervik, C, Tybjaerg-Hansen, A, Nordestgaard, BG. CHEK2*1100delC genotyping for clinical assessment of breast cancer risk: meta-analyses of 26,000 patient cases and 27,000 controls. J Clin Oncol. 2008 Feb 1;26(4):542-8.

Offit, K, Garber, JE. Time to check CHEK2 in families with breast cancer? J Clin Oncol. 2008 Feb 1;26(4):519-20.

Myszka, A, Karpinski, P, Slezak, R, et al. Irrelevance of CHEK2 variants to diagnosis of breast/ovarian cancer predisposition in Polish cohort. J Appl Genet. 2011 May;52(2):185-91.

Zhang, B, Beeghly-Fadiel, A, Long, J, Zheng, W. Genetic variants associated with breast-cancer risk: comprehensive research synopsis, meta-analysis, and epidemiological evidence. Lancet Oncol. 2011 May;12(5):477-88.

Peng, S, Lu, B, Ruan, W, Zhu, Y, Sheng, H, Lai, M. Genetic polymorphisms and breast cancer risk: evidence from meta-analyses, pooled analyses, and genome-wide association studies. Breast Cancer Res Treat. 2011 Jun;127(2):309-24.

Judkins T, Rosenthal E, Arnell C, et al. Clinical significance of large rearrangements in BRCA1 and BRCA2. Cancer. 2012;118(21):5210-5216.

American Society of Clinical Oncology (ASCO). Policy statement update: Genetic testing for cancer susceptibility. 03/01/03. http://www.asco.org/asco/downloads/GeneticTesting.pdf

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Breast Cancer Risk Reduction. Version 1.2023

Theriault RL, Carlson RW, Allred DC, et al. Breast Cancer. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. Version 2.2016.

Mitra AV, Bancroft EK, Barbachano Y, et al. Targeted prostate cancer screening in men with mutations in BRCA1 and BRCA2 detects aggressive prostate cancer: preliminary analysis of the results of the IMPACT study. BJU Int. 2011 Jan;107(1):28-39

Rebbeck TR, Mitra N, Wan F, et al. Association of type and location of BRCA1 and BRCA2 mutations with risk of breast and ovarian cancer. JAMA. 2015 Apr 7;313(13):1347-61.

Moyer VA. Risk Assessment, Genetic Counseling, and Genetic Testing for BRCA-Related Cancer in Women: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2014;160(4):271-281.

Gallagher DJ, Gaudet MM, Pal P, et al. Germline BRCA mutations denote a clinicopathologic subset of prostate cancer. Clin Cancer Res. 2010 Apr 1;16(7):2115-21.

Heemskerk-Gerritsen BA, Seynaeve C, van Asperen CJ, et al. Breast cancer risk after salpingo-oophorectomy in healthy BRCA1/2 mutation carriers: revisiting the evidence for risk reduction. J Natl Cancer Inst. 2015 Mar 18;107(5).

Noh JM, Choi DH, Baek H, et al. Associations between BRCA Mutations in High-Risk Breast Cancer Patients and Familial Cancers Other than Breast or Ovary. J Breast Cancer. 2012 Sep;15(3):283-7.

Daly MB, Pilarski R, Berry M, et al. NCCN guidelines insights: genetic/familial high-risk assessment: breast and ovarian, version 2.2017. J Natl Comp Cancer 2017; 15:9–20.

Hayes. GTE Overview. Breast Cancer Susceptibility 1 and 2 (BRCA1/2) Gene Testing for Hereditary Breast and Ovarian Cancer (HBOC) for Familial Breast and Ovarian Cancer. July 20, 2015.

Daly MB, Axilbund JE, Buys SS, et al. Genetic/Familial High Risk Assessment: Breast and Ovarian. National Comprehensive Cancer Network clinical practice guidelines in oncology. Version 2.2016.

Peshkin, BN., Isaacs, C. Overview of hereditary breast and ovarian cancer syndromes. UpToDate, 2016.

Peshkin, BN., Isaacs, C. Genetic counseling and testing for hereditary breast and ovarian cancer. UpToDate, 2016.

Hayes GTE Report. The Clinical Utility of Genetic Testing for Hereditary Breast and Ovarian Cancer in Patients with no Personal History of Cancer and a Suggestive Family History. December 2016.

Levy-Lahad E, Catane R, et al. Founder BRCA1 and BRCA2 mutations in Ashkenazi Jews in Israel: frequency and differential penetrance in ovarian cancer and in breast-ovarian cancer families. Am J Hum Genet. 1997 May; 60(5): 1059–1067.

Abeliovich D, Kaduri L, et al. The founder mutations 185delAG and 5382insC in BRCA1 and 6174delT in BRCA2 appear in 60% of ovarian cancer and 30% of early-onset breast cancer patients among Ashkenazi women. Am J Hum Genet. 1997 Mar;60(3):505-14.

Satagopan JM, Offit K, et al. The lifetime risks of breast cancer in Ashkenazi Jewish carriers of BRCA1 and BRCA2 mutations. Cancer Epidemiol Biomarkers Prev. 2001 May;10(5):467-73.

Spannuth WA, Thaker PH, Sood AK. Concomitant BRCA1 and BRCA2 gene mutations in an Ashkenazi Jewish Woman with primary breast and ovarian cancer. AJOG 2007;196(4):e6-e9.

Walsh T, Mandell JB, et al. Genetic Predisposition to Breast Cancer Due to Mutations Other Than BRCA1 and BRCA2 Founder Alleles Among Ashkenazi Jewish Women. JAMA Oncol. 2017;3(12):1647-1653.

Pilié PG, Johnson AM, Hanson KL, et al. Germline genetic variants in men with prostate cancer and one or more additional cancers. Cancer. 2017 Oct 15;123(20):3925-3932

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Breast Cancer. Version 3.2023

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Genetic/familial high-risk assessment: Breast, Ovarian, Pancreatic and Prostate. V2.2025

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Genetic/familial high-risk assessment: Colorectal. v2.2022

Rahman N, Seal S, Thompson D, et al. PALB2, which encodes a BRCA2interacting protein, is a breast cancer susceptibility gene. Nat Genet. 2007;39(2):165-167

Antoniou AC, Casedi S et al. Breast-Cancer Risk in Families with Mutations in PALB2. NEJM 2014; 371(6): 497–506.

Kluska A, Balabas A, Piatkowska M, et al. PALB2 mutations in BRCA 1/2 mutation negative breast and ovarian cancer patients from Poland. BMC Medical Genomics. 2017; 10:14

Piffer A, Luporsi E, Mathelin C. PALB2, a major susceptibility gene for breast cancer. Gynecol Obstet Fertil Senol. 2018 Nov;46(10-11):701-705.

Boonen RACM, Rodrigue A, et al. Functional analysis of genetic variants in the high-risk breast cancer susceptibility gene PALB2. Nat Commun. 2019; 10: 5296.

Pilarski R. The role of BRCA testing in hereditary pancreatic and prostate cancer families. Am Soc Clin Oncol Educ Book 2019 Jan;39:79-86.

MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer L38972

Hu C, Hart SN, Gnanaolivu H, et al. A Population-Based Study of Genes Previously Implicated in Breast Cancer. N Engl J Med. 2021 Feb 4;384(5):440-451.

Konstantinopoulos PA, Norquist B, Lacchetti C, et al. Germline and Somatic Tumor Testing in Epithelial Ovarian Cancer: ASCO Guideline. J Clin Oncol. 2020 Apr 10;38(11):1222-1245.

Nicolosi P, Ledet E, Yang S, et al. Prevalence of Germline Variants in Prostate Cancer and Implications for Current Genetic Testing Guidelines. JAMA Oncol. 2019;5(4):523–528.

PA Dept. of Human Services Managed Care Operations Memorandum Technology Assessment Group OPS # 10/2023-013

A.B. No.290, 2023. Amendment to P.L.682, No.284, "Insurance Company Law Of 1921, The." Accessed on 3/1/24 at: https://www.legis.state.pa.us/CFDOCS/Legis/PN/Public/btCheck.cfm?txtType=PDF&sessYr=2023&sessInd=0&billBody=S&billTyp=B&billNbr=0008&pn=0290

Forman A, Sotelo J. Tumor-Based Genetic Testing and Familial Cancer Risk. Cold Spring Harb Perspect Med. 2020;10(8):a036590. Published 2020 Aug 3.

Bolze A, Cirulli ET, Hajek C, Schnell Blitstein JM, Grzymski JJ. The Potential of Genetics in Identifying Women at Lower Risk of Breast Cancer. JAMA Oncol. 2024 Feb 1;10(2):236-239. PMID: 38153744.

This policy will be revised as necessary and reviewed no less than annually.

Devised: 9/25/98

Revised: 6/17/99; 6/27/03, 7/23/04; 6/20/05;6/06 (removed prior auth); 6/07 (revised criteria); 7/08; 7/09 (add'l exclusion); 12/09 (revised criteria); 12/10 (revised criteria); 6/11 (clarified criteria for males); 1/13 (added triple negative criteria); 7/13(removed BART testing indications) , 4/14(updated criteria); 4/16 (revised criteria); 3/17(revised criteria); 5/18 (added criteria related to known variants) 3/19 (revised pancreatic and prostate cancer criteria); 2/20 (add PALB2 criteria); 3/23 (revise criteria based on NCCN updates), 3/24 (revise Indications); 3/25 (revise Indications)

Reviewed: 4/15, 3/18, 3/21, 3/22

CMS UM Oversight Committee Approval: 12/23, 5/24, 4/25