

MEDICAL POLICY – 12.04.63

Use of Common Genetic Variants (Single Nucleotide Variants) to Predict Risk of Non-familial Breast Cancer

BCBSA Ref. Policy: 2.04.63

Effective Date: Dec. 1, 2017

Last Revised: Nov. 9, 2017

Replaces: 2.04.63


RELATED MEDICAL POLICIES:

12.04.93 Genetic Cancer Susceptibility Panels Using Next - Generation Sequencing

12.04.504 Genetic Testing for Hereditary Breast/ Ovarian Cancer Syndrome (BRCA1/BRCA2)

Select a hyperlink below to be directed to that section.

[POLICY CRITERIA](#) | [CODING](#) | [RELATED INFORMATION](#)
[EVIDENCE REVIEW](#) | [REFERENCES](#) | [HISTORY](#)

 Clicking this icon returns you to the hyperlinks menu above.

Introduction

A “single nucleotide variant” (SNV) is a change in a specific section of a person’s DNA. These changes may increase a person’s risk of developing breast cancer. Medical studies have not shown that doing genetic tests to look at these SNVs is effective and reliable in predicting a person’s chance of getting breast cancer. For this reason, testing for one or more SNVs to predict a person’s risk of getting breast cancer is considered unproven (investigational).

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Testing	Investigational
One or more single nucleotide variants (SNVs)	Testing for one or more single nucleotide variants (SNVs) to predict an individual's risk of breast cancer is considered investigational.
BREVA Genplus®	The BREVA Genplus® breast cancer risk test is considered investigational for all indications, including but not limited to use as a method of estimating an individual patient's risk for developing breast cancer.

Note: BRCA genetic testing should be used in those from high-risk families (see [Related Policies](#)).

Coding

Code	Description
CPT	
81479	Unlisted molecular pathology procedure
81599	Unlisted multianalyte assay with algorithmic analysis
84999	Unlisted chemistry procedure

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

Genetic Counseling

Experts recommend formal genetic counseling for patients who are at risk for inherited disorders and who wish to undergo genetic testing. Interpreting the results of genetic tests and understanding risk factors can be difficult for some patients. Genetic counseling helps individuals understand the impact of genetic testing, including the possible effects the test results could have on the individual or their family members. It should be noted that genetic



counseling may alter the utilization of genetic testing substantially and may reduce inappropriate testing. Further, genetic counseling should be performed by an individual with experience and expertise in genetic medicine and genetic testing methods.

Evidence Review

Description

A number of single nucleotide variants (SNVs), which are single base-pair variations in the DNA sequence of the genome, have been found to be associated with breast cancer and are common in the population but confer only small increases in the risk of getting breast cancer.

Commercially available assays test for several SNVs to predict an individual's risk of breast cancer relative to the general population. Some of these incorporate clinical information into risk prediction algorithms. The intent of this type of test is to identify subjects at increased risk who may benefit from more intensive surveillance.

Background

Gene Variants And Breast Cancer Risk

Rare, single-gene variants conferring a high risk of breast cancer have been linked to hereditary breast cancer syndromes. Examples are mutations in BRCA1 and BRCA2. These, and a few others, account for less than 25% of inherited breast cancer. Moderate risk alleles, such as variants in the CHEK2 gene, are also relatively rare and apparently explain very little of the genetic risk.

In contrast, several common SNVs associated with breast cancer have been identified primarily through genome-wide association studies (GWAS) of very large case-control populations. These alleles occur with high frequency in the general population, although the increased breast cancer risk associated with each is very small relative to the general population risk. Some have suggested that these common-risk SNVs could be combined for individualized risk prediction either alone or in combination with traditional predictors. Personalized breast cancer screening programs could then vary by the starting age and intensity of screening according to the person's risk. Along these lines, the American Cancer Society recommends that women at high risk (>20% lifetime risk) should undergo breast magnetic resonance imaging (MRI) and a mammogram every year, and those at moderately increased risk (15%-20% lifetime risk) should



talk with their doctors about the benefits and limitations of adding MRI screening to their yearly mammogram.¹

Clinical Genetic Tests

BREVAGenplus®

BREVAGenplus® (Phenogen Sciences, Charlotte, NC) evaluates breast cancer-associated SNVs identified in GWAS. The first-generation test, BREVA Gen, included 7 SNVs. In a 2015 report, the test included over 70 susceptibility SNVs.² Risk is calculated by combining individual SNV risks with the Gail model risk. BREVA Genplus® has been evaluated for use in African-American, white, and Hispanic patient samples age 35 years and older. BREVA Genplus® does not detect known high-risk mutations (eg, in BRCA). According to the BREVA Genplus® website, the test is not applicable to women who are already at high risk of breast cancer including those that have a personal or extensive family history of breast and/or ovarian cancer, LCIS [lobular carcinoma in situ], DCIS [ductal carcinoma in situ], AH [atypical hyperplasia] or have had prior thoracic RT [radiotherapy] under age 30. Any women with these risk factors are already at increased risk of breast cancer and should be screened and followed as such.³

Summary of Evidence

For individuals who are asymptomatic and have an average risk of breast cancer by clinical criteria who receive testing for common SNVs variants associated with a small increase in the risk of breast cancer, the evidence includes observational studies. Relevant outcomes are test accuracy and validity, morbid events, and quality of life. Information about analytic performance (reproducibility) of currently marketed tests is lacking. Clinical genetic tests may improve the predictive accuracy of currently used clinical risk predictors. However, the magnitude of improvement is small, and clinical significance is uncertain. Whether the potential harms of these tests due to false-negative and false-positive results are outweighed by the potential benefit associated with improved risk assessment is unknown. Evaluation of this technology is further complicated by the rapidly increasing numbers of SNVs associated with a small risk of breast cancer. Long-term prospective studies with large sample sizes are needed to determine the clinical validity and utility of SNV-based models for use in predicting breast cancer risk. The discrimination offered by the genetic factors currently known is insufficient to inform clinical practice. The evidence is insufficient to determine the effects of the technology on health outcomes.



Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this policy are listed in [Table 1](#).

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT02620852	Enabling a Paradigm Shift: A Preference-Tolerant RCT of Personalized vs. Annual Screening for Breast Cancer (WISDOM)	100,000	Dec 2020

NCT: national clinical trial.

Practice Guidelines and Position Statements

National Comprehensive Cancer Network (NCCN)

Current guidelines from the NCCN identify the following limitations of multigene cancer panels: unknown significance of some variants, uncertain level of risk associated with most variants, and unclear guidance on risk management for carriers of some variants.⁸⁵

American Society of Clinical Oncology

For breast cancer risk assessment, the American Society of Clinical Oncology recommends the Gail model⁸⁶ or risk models for women with elevated risk based on family history (eg, Claus et al.⁸⁷ or Tyrer et al.^{88,89})

U.S. Preventive Services Task Force Recommendations

No U.S. Preventive Services Task Force recommendations for SNV testing either in conjunction with or without consideration of clinical factors to predict breast cancer risk have been identified.



Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

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 (CLIA). BREVA Genplus® (Phenogen Sciences, a subsidiary of Genetic Technologies, Melbourne, Australia) is available under the auspices of CLIA. Laboratories that offer laboratory-developed tests must be licensed by CLIA for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test. Under current regulations, CLIA requires that laboratories demonstrate the analytical validity of the tests they offer. However, there is no requirement for a test to demonstrate either clinical validity or clinical utility. Some states (eg, New York) have chosen to regulate direct-to-consumer (DTC) laboratories. Because these reviews are not public, the scientific standards applied are unknown.

References

1. American Cancer Society. Breast cancer: early detection, diagnosis, and staging topics - Can breast cancer be found early? (last medical review: 09/25/2014). <http://www.cancer.org/cancer/breastcancer/detailedguide/breast-cancer-detection> Accessed November 2017.
2. Allman R, Dite GS, Hopper JL, et al. SNPs and breast cancer risk prediction for African American and Hispanic women. *Breast Cancer Res Treat.* Dec 2015;154(3):583-589. PMID 26589314
3. Genetic Technologies. BREVA Genplus®. 2017; <http://brevagenplus.com> Accessed November 2017.
4. Mealiffe ME, Stokowski RP, Rhees BK, et al. Assessment of clinical validity of a breast cancer risk model combining genetic and clinical information. *J Natl Cancer Inst.* Nov 3 2010;102(21):1618-1627. PMID 20956782
5. Stacey SN, Manolescu A, Sulem P, et al. Common variants on chromosomes 2q35 and 16q12 confer susceptibility to estrogen receptor-positive breast cancer. *Nat Genet.* Jul 2007;39(7):865-869. PMID 17529974
6. Easton DF, Pooley KA, Dunning AM, et al. Genome-wide association study identifies novel breast cancer susceptibility loci. *Nature.* Jun 28 2007;447(7148):1087-1093. PMID 17529967



7. Hunter DJ, Kraft P, Jacobs KB, et al. A genome-wide association study identifies alleles in FGFR2 associated with risk of sporadic postmenopausal breast cancer. *Nat Genet.* Jul 2007;39(7):870-874. PMID 17529973
8. Thomas G, Jacobs KB, Kraft P, et al. A multistage genome-wide association study in breast cancer identifies two new risk alleles at 1p11.2 and 14q24.1 (RAD51L1). *Nat Genet.* May 2009;41(5):579-584. PMID 19330030
9. Stacey SN, Manolescu A, Sulem P, et al. Common variants on chromosome 5p12 confer susceptibility to estrogen receptor-positive breast cancer. *Nat Genet.* Jun 2008;40(6):703-706. PMID 18438407
10. Gold B, Kirchhoff T, Stefanov S, et al. Genome-wide association study provides evidence for a breast cancer risk locus at 6q22.33. *Proc Natl Acad Sci U S A.* Mar 18 2008;105(11):4340-4345. PMID 18326623
11. Ahmed S, Thomas G, Ghousaini M, et al. Newly discovered breast cancer susceptibility loci on 3p24 and 17q23.2. *Nat Genet.* May 2009;41(5):585-590. PMID 19330027
12. Zheng W, Long J, Gao YT, et al. Genome-wide association study identifies a new breast cancer susceptibility locus at 6q25.1. *Nat Genet.* Mar 2009;41(3):324-328. PMID 19219042
13. Garcia-Closas M, Hall P, Nevanlinna H, et al. Heterogeneity of breast cancer associations with five susceptibility loci by clinical and pathological characteristics. *PLoS Genet.* Apr 2008;4(4):e1000054. PMID 18437204
14. Beeghly-Fadiel A, Shu XO, Lu W, et al. Genetic variation in VEGF family genes and breast cancer risk: a report from the Shanghai Breast Cancer Genetics Study. *Cancer Epidemiol Biomarkers Prev.* Jan 2011;20(1):33-41. PMID 21119072
15. Cai Q, Wen W, Qu S, et al. Replication and functional genomic analyses of the breast cancer susceptibility locus at 6q25.1 generalize its importance in women of Chinese, Japanese, and European ancestry. *Cancer Res.* Feb 15 2011;71(4):1344-1355. PMID 21303983
16. Han W, Woo JH, Yu JH, et al. Common genetic variants associated with breast cancer in Korean women and differential susceptibility according to intrinsic subtype. *Cancer Epidemiol Biomarkers Prev.* May 2011;20(5):793-798. PMID 21415360
17. Jiang Y, Han J, Liu J, et al. Risk of genome-wide association study newly identified genetic variants for breast cancer in Chinese women of Heilongjiang Province. *Breast Cancer Res Treat.* Jul 2011;128(1):251-257. PMID 21197568
18. Mong FY, Kuo YL, Liu CW, et al. Association of gene polymorphisms in prolactin and its receptor with breast cancer risk in Taiwanese women. *Mol Biol Rep.* Oct 2011;38(7):4629-4636. PMID 21125332
19. Mukherjee N, Bhattacharya N, Sinha S, et al. Association of APC and MCC polymorphisms with increased breast cancer risk in an Indian population. *Int J Biol Markers.* Jan-Mar 2011;26(1):43-49. PMID 21279955
20. Ota I, Sakurai A, Toyoda Y, et al. Association between breast cancer risk and the wild-type allele of human ABC transporter ABCC11. *Anticancer Res.* Dec 2010;30(12):5189-5194. PMID 21187511
21. Ren J, Wu X, He W, et al. Lysyl oxidase 473 G>A polymorphism and breast cancer susceptibility in Chinese Han population. *DNA Cell Biol.* Feb 2011;30(2):111-116. PMID 20929399
22. Yu JC, Hsiung CN, Hsu HM, et al. Genetic variation in the genome-wide predicted estrogen response element-related sequences is associated with breast cancer development. *Breast Cancer Res.* Jan 31 2011;13(1):R13. PMID 21281495
23. Ma H, Li H, Jin G, et al. Genetic variants at 14q24.1 and breast cancer susceptibility: a fine-mapping study in Chinese women. *DNA Cell Biol.* Jun 2012;31(6):1114-1120. PMID 22313133
24. Dai J, Hu Z, Jiang Y, et al. Breast cancer risk assessment with five independent genetic variants and two risk factors in Chinese women. *Breast Cancer Res.* Jan 23 2012;14(1):R17. PMID 22269215
25. Long J, Cai Q, Sung H, et al. Genome-wide association study in east Asians identifies novel susceptibility loci for breast cancer. *PLoS Genet.* Feb 2012;8(2):e1002532. PMID 22383897
26. Huo D, Zheng Y, Ogundiran TO, et al. Evaluation of 19 susceptibility loci of breast cancer in women of African ancestry. *Carcinogenesis.* Apr 2012;33(4):835-840. PMID 22357627
27. McCarthy AM, Armstrong K, Handorf E, et al. Incremental impact of breast cancer SNP panel on risk classification in a screening population of white and African American women. *Breast Cancer Res Treat.* Apr 2013;138(3):889-898. PMID 23474973



28. Schoeps A, Rudolph A, Seibold P, et al. Identification of new genetic susceptibility loci for breast cancer through consideration of gene-environment interactions. *Genet Epidemiol.* Jan 2014;38(1):84-93. PMID 24248812
29. Nickels S, Truong T, Hein R, et al. Evidence of gene-environment interactions between common breast cancer susceptibility loci and established environmental risk factors. *PLoS Genet.* 2013;9(3):e1003284. PMID 23544014
30. Pei J, Li F, Wang B. Single nucleotide polymorphism 6q25.1 rs2046210 and increased risk of breast cancer. *Tumour Biol.* Dec 2013;34(6):4073-4079. PMID 23888322
31. Wu X, Xu QQ, Guo L, et al. Quantitative assessment of the association between rs2046210 at 6q25.1 and breast cancer risk. *PLoS One.* 2013;8(6):e65206. PMID 23785413
32. Liu JJ, Liu JL, Zhang X, et al. A meta-analysis of the association of glutathione S-transferase P1 gene polymorphism with the susceptibility of breast cancer. *Mol Biol Rep.* Apr 2013;40(4):3203-3212. PMID 23334471
33. Zheng W, Zhang B, Cai Q, et al. Common genetic determinants of breast-cancer risk in East Asian women: a collaborative study of 23 637 breast cancer cases and 25 579 controls. *Hum Mol Genet.* Jun 15 2013;22(12):2539-2550. PMID 23535825
34. Yao S, Graham K, Shen J, et al. Genetic variants in microRNAs and breast cancer risk in African American and European American women. *Breast Cancer Res Treat.* Oct 2013;141(3):447-459. PMID 24062209
35. Zhou ZC, Wang J, Cai ZH, et al. Association between vitamin D receptor gene Cdx2 polymorphism and breast cancer susceptibility. *Tumour Biol.* Dec 2013;34(6):3437-3441. PMID 23821301
36. Chen QH, Wang QB, Zhang B. Ethnicity modifies the association between functional microRNA polymorphisms and breast cancer risk: a HuGE meta-analysis. *Tumour Biol.* Jan 2014;35(1):529-543. PMID 23982873
37. Xu Q, He CY, Liu JW, et al. Pre-miR-27a rs895819A/G polymorphisms in cancer: a meta-analysis. *PLoS One.* Jun 2013;8(6):e65208. PMID 23762318
38. Zhong S, Chen Z, Xu J, et al. Pre-mir-27a rs895819 polymorphism and cancer risk: a meta-analysis. *Mol Biol Rep.* Apr 2013;40(4):3181-3186. PMID 23266669
39. Fan C, Chen C, Wu D. The association between common genetic variant of microRNA-499 and cancer susceptibility: a meta-analysis. *Mol Biol Rep.* Apr 2013;40(4):3389-3394. PMID 23271127
40. Michailidou K, Hall P, Gonzalez-Neira A, et al. Large-scale genotyping identifies 41 new loci associated with breast cancer risk. *Nat Genet.* Apr 2013;45(4):353-361. PMID 23535729
41. Siddiq A, Couch FJ, Chen GK, et al. A meta-analysis of genome-wide association studies of breast cancer identifies two novel susceptibility loci at 6q14 and 20q11. *Hum Mol Genet.* Dec 15 2012;21(24):5373-5384. PMID 22976474
42. Garcia-Closas M, Couch FJ, Lindstrom S, et al. Genome-wide association studies identify four ER negative-specific breast cancer risk loci. *Nat Genet.* Apr 2013;45(4):392-398. PMID 23535733
43. Milne RL, Herranz J, Michailidou K, et al. A large-scale assessment of two-way SNP interactions in breast cancer susceptibility using 46 450 cases and 42 461 controls from the Breast Cancer Association Consortium. *Hum Mol Genet.* Apr 1 2014;23(7):1934-1946. PMID 24242184
44. Joshi AD, Lindstrom S, Husing A, et al. Additive interactions between susceptibility single-nucleotide polymorphisms identified in genome-wide association studies and breast cancer risk factors in the Breast and Prostate Cancer Cohort Consortium. *Am J Epidemiol.* Nov 15 2014;180(10):1018-1027. PMID 25255808
45. Gu C, Zhou L, Yu J. Quantitative assessment of 2q35-rs13387042 polymorphism and hormone receptor status with breast cancer risk. *PLoS One.* Jul 2013;8(7):e66979. PMID 23894282
46. Gong WF, Zhong JH, Xiang BD, et al. Single nucleotide polymorphism 8q24 rs13281615 and risk of breast cancer: meta-analysis of more than 100,000 cases. *PLoS One.* 2013;8(4):e60108. PMID 23565189
47. Milne RL, Burwinkel B, Michailidou K, et al. Common non-synonymous SNPs associated with breast cancer susceptibility: findings from the Breast Cancer Association Consortium. *Hum Mol Genet.* Nov 15 2014;23(22):6096-6111. PMID 24943594



48. Lin WY, Brock IW, Connley D, et al. Associations of ATR and CHEK1 single nucleotide polymorphisms with breast cancer. *PLoS One*. Jul 2013;8(7):e68578. PMID 23844225
49. Bodelon C, Malone KE, Johnson LG, et al. Common sequence variants in chemokine-related genes and risk of breast cancer in post-menopausal women. *Int J Mol Epidemiol Genet*. Nov 2013;4(4):218-227. PMID 24319537
50. He XF, Wei W, Li SX, et al. Association between the COMT Val158Met polymorphism and breast cancer risk: a meta-analysis of 30,199 cases and 38,922 controls. *Mol Biol Rep*. Jun 2012;39(6):6811-6823. PMID 22297695
51. Dai ZJ, Shao YP, Ma XB, et al. Association of the three common SNPs of cyclooxygenase-2 gene (rs20417, rs689466, and rs5275) with the susceptibility of breast cancer: an updated meta-analysis involving 34,590 subjects. *Dis Markers*. 2014;2014:484729. PMID 25214704
52. Tang L, Xu J, Wei F, et al. Association of STXBP4/COX11 rs6504950 (G>A) polymorphism with breast cancer risk: evidence from 17,960 cases and 22,713 controls. *Arch Med Res*. Jul 2012;43(5):383-388. PMID 22863968
53. He XF, Wei W, Liu ZZ, et al. Association between the CYP1A1 T3801C polymorphism and risk of cancer: evidence from 268 case-control studies. *Gene*. Oct 24 2014;534(2):324-344. PMID 24513335
54. Tian Z, Li YL, Zhao L, et al. Role of CYP1A2 1F polymorphism in cancer risk: evidence from a meta-analysis of 46 case-control studies. *Gene*. Jul 25 2013;524(2):168-174. PMID 23628800
55. Pineda B, Garcia-Perez MA, Cano A, et al. Associations between aromatase CYP19 rs10046 polymorphism and breast cancer risk: from a case-control to a meta-analysis of 20,098 subjects. *PLoS One*. 2013;8(1):e53902. PMID 23342035
56. Agarwal D, Pineda S, Michailidou K, et al. FGF receptor genes and breast cancer susceptibility: results from the Breast Cancer Association Consortium. *Br J Cancer*. Feb 18 2014;110(4):1088-1100. PMID 24548884
57. Yu Z, Liu Q, Huang C, et al. The interleukin 10 -819C/T polymorphism and cancer risk: a HuGE review and meta-analysis of 73 studies including 15,942 cases and 22,336 controls. *OMICS*. Apr 2013;17(4):200-214. PMID 23574339
58. Zhang H, Wang A, Ma H, et al. Association between insulin receptor substrate 1 Gly972Arg polymorphism and cancer risk. *Tumour Biol*. Oct 2013;34(5):2929-2936. PMID 23708959
59. Zheng Q, Ye J, Wu H, et al. Association between mitogen-activated protein kinase kinase kinase 1 polymorphisms and breast cancer susceptibility: a meta-analysis of 20 case-control studies. *PLoS One*. Mar 2014;9(3):e90771. PMID 24595411
60. Gao J, Kang AJ, Lin S, et al. Association between MDM2 rs 2279744 polymorphism and breast cancer susceptibility: a meta-analysis based on 9,788 cases and 11,195 controls. *Ther Clin Risk Manag*. May 2014;10:269-277. PMID 24790452
61. Wang Z, Wang T, Bian J. Association between MDR1 C3435T polymorphism and risk of breast cancer. *Gene*. Dec 10 2013;532(1):94-99. PMID 24070710
62. Zhong S, Xu J, Li W, et al. Methionine synthase A2756G polymorphism and breast cancer risk: an up-to-date meta-analysis. *Gene*. Sep 25 2013;527(2):510-515. PMID 23845785
63. Saadat M. Paraoxonase 1 genetic polymorphisms and susceptibility to breast cancer: a meta-analysis. *Cancer Epidemiol*. Apr 2012;36(2):e101-103. PMID 22133529
64. Qin K, Wu C, Wu X. Two nonsynonymous polymorphisms (F31I and V57I) of the STK15 gene and breast cancer risk: a meta-analysis based on 5966 cases and 7609 controls. *J Int Med Res*. Aug 2013;41(4):956-963. PMID 23803310
65. Chen J, Yuan T, Liu M, et al. Association between TCF7L2 gene polymorphism and cancer risk: a meta-analysis. *PLoS One*. Aug 2013;8(8):e71730. PMID 23951231
66. Perna L, Butterbach K, Haug U, et al. Vitamin D receptor genotype rs731236 (Taq1) and breast cancer prognosis. *Cancer Epidemiol Biomarkers Prev*. Mar 2013;22(3):437-442. PMID 23300018
67. Zhang K, Song L. Association between vitamin D receptor gene polymorphisms and breast cancer risk: a meta-analysis of 39 studies. *PLoS One*. Apr 2014;9(4):e96125. PMID 24769568
68. Li J, Ju Y. Association between the functional polymorphism of vascular endothelial growth factor gene and breast cancer: a meta-analysis. *Iran J Med Sci*. Jan 2015;40(1):2-12. PMID 25649829



69. He Y, Zhang Y, Jin C, et al. Impact of XRCC2 Arg188His polymorphism on cancer susceptibility: a meta-analysis. *PLoS One*. Mar 2014;9(3):e91202. PMID 24621646
70. He XF, Wei W, Su J, et al. Association between the XRCC3 polymorphisms and breast cancer risk: meta-analysis based on case-control studies. *Mol Biol Rep*. May 2012;39(5):5125-5134. PMID 22161248
71. Pharoah PD, Antoniou AC, Easton DF, et al. Polygenes, risk prediction, and targeted prevention of breast cancer. *N Engl J Med*. Jun 26 2008;358(26):2796-2803. PMID 18579814
72. Reeves GK, Travis RC, Green J, et al. Incidence of breast cancer and its subtypes in relation to individual and multiple low-penetrance genetic susceptibility loci. *JAMA*. Jul 28 2010;304(4):426-434. PMID 20664043
73. Sakoda LC, Jorgenson E, Witte JS. Turning of COGS moves forward findings for hormonally mediated cancers. *Nat Genet*. Apr 2013;45(4):345-348. PMID 23535722
74. Hunter DJ, Altshuler D, Rader DJ. From Darwin's finches to canaries in the coal mine--mining the genome for new biology. *N Engl J Med*. Jun 26 2008;358(26):2760-2763. PMID 18579810
75. Dite GS, Mahmoodi M, Bickerstaffe A, et al. Using SNP genotypes to improve the discrimination of a simple breast cancer risk prediction model. *Breast Cancer Res Treat*. Jun 2013;139(3):887-896. PMID 23774992
76. Mavaddat N, Pharoah PD, Michailidou K, et al. Prediction of breast cancer risk based on profiling with common genetic variants. *J Natl Cancer Inst*. May 2015;107(5):dju036. PMID 25855707
77. Zheng W, Wen W, Gao YT, et al. Genetic and clinical predictors for breast cancer risk assessment and stratification among Chinese women. *J Natl Cancer Inst*. Jul 7 2010;102(13):972-981. PMID 20484103
78. Campa D, Kaaks R, Le Marchand L, et al. Interactions between genetic variants and breast cancer risk factors in the Breast and Prostate Cancer Cohort Consortium. *J Natl Cancer Inst*. Aug 17 2011;103(16):1252-1263. PMID 21791674
79. Wacholder S, Hartge P, Prentice R, et al. Performance of common genetic variants in breast-cancer risk models. *N Engl J Med*. Mar 18 2010;362(11):986-993. PMID 20237344
80. Darabi H, Czene K, Zhao W, et al. Breast cancer risk prediction and individualised screening based on common genetic variation and breast density measurement. *Breast Cancer Res*. Feb 7 2012;14(1):R25. PMID 22314178
81. Armstrong K, Handorf EA, Chen J, et al. Breast cancer risk prediction and mammography biopsy decisions: a model-based study. *Am J Prev Med*. Jan 2013;44(1):15-22. PMID 23253645
82. Cuzick J, Brentnall AR, Segal C, et al. Impact of a panel of 88 single nucleotide polymorphisms on the risk of breast cancer in high-risk women: results from two randomized tamoxifen prevention trials. *J Clin Oncol*. Mar 2017;35(7):743-750. PMID 28029312
83. Bloss CS, Schork NJ, Topol EJ. Effect of direct-to-consumer genomewide profiling to assess disease risk. *N Engl J Med*. Feb 10 2011;364(6):524-534. PMID 21226570
84. McCarthy A, Keller B, Kontos D, et al. The use of the Gail model, body mass index and SNPs to predict breast cancer among women with abnormal (BI-RADS 4) mammograms. *Breast Cancer Res*. Jan 8 2015;17(1):1. PMID 25567532
85. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology: genetic/familial high-risk assessment: breast and ovarian. Version 2.2017. http://www.nccn.org/professionals/physician_gls/pdf/genetics_screening.pdf Accessed November 2017.
86. National Cancer Institute. Breast cancer risk assessment tool. <http://www.cancer.gov/bcrisktool/> Accessed November 2017.
87. Claus EB, Risch N, Thompson WD. Autosomal dominant inheritance of early-onset breast cancer. Implications for risk prediction. *Cancer*. Feb 1 1994;73(3):643-651. PMID 8299086
88. Tyrer J, Duffy SW, Cuzick J. A breast cancer prediction model incorporating familial and personal risk factors. *Stat Med*. Apr 15 2004;23(7):1111-1130. PMID 15057881
89. Visvanathan K, Hurley P, Bantug E, et al. Use of pharmacologic interventions for breast cancer risk reduction: American Society of Clinical Oncology clinical practice guideline. *J Clin Oncol*. Aug 10 2013;31(23):2942-2962. PMID 23835710



History

Date	Comments
07/12/11	Add to Pathology/Laboratory Section - New medical policy with literature search through March 2011; considered investigational. ICD-10 codes included.
05/24/12	Policy renumbered to 12.04.63 (previously 2.04.63) and reassigned to new Genetic Testing category.
07/20/12	Replace policy. Policy updated with literature search, references 12, 13, 19-22, 27-30 added. No change to policy statement.
10/10/12	Update Coding Section – ICD-10 codes are now effective 10/01/2014.
01/11/13	Effective 1/1/13, CPT codes 81200 – 81479 will be used for lab testing; these replace codes 83891 – 83912 which are deleted effective 12/31/12.
05/14/13	Update Related Policies. Add 12.04.91.
07/24/13	Replace policy. Policy updated with literature search through April 9, 2013; references 23-33 added. No change to policy statement.
10/17/13	Update Related Policies. Change title to 12.04.57.
11/21/13	Update Related Policies. Add 12.04.93.
01/16/14	Update Related Policies. Change title to 12.04.504.
06/09/14	Annual Review. Policy updated with literature review through March 18, 2014. Policy combined with Policy No. 12.04.57 (Non-BRCA Breast Cancer Risk Assessment [eg, OncoVue®]) and title changed to “Use of Common Genetic Variants (SNPs) to Predict Risk of Nonfamilial Breast Cancer;”; references 1-2, 6-8, 34-45, 48-50, 52-53, 56-64, 66-67, 69-70, 74, and 96 added. Investigational policy statement for OncoVue® and BREVAGen® modified to indicate investigational for all indications.
07/23/14	Update Related Policies. Remove 12.04.91.
06/17/15	Annual Review. Policy updated with literature review through March 3, 2015. References 1, 2, 49, 52, 56, 65, 72, 73, 76, 108 added; references 1 and 4-5 deleted. Policy statements unchanged.
12/01/16	Annual review, approved November 8, 2016. Policy updated with literature review; reference 113 added. Added code 81479. Policy statements unchanged.
09/22/17	Policy moved into new format. No changes to policy statement.
12/01/17	Annual Review, approved November 9, 2017. Policy updated with literature review through August 2017; references 2, 76, and 82 added; some references removed; “polymorphisms” changed to “variants” throughout policy. OncoVue removed from



Date	Comments
	policy; it is no longer commercially available. Policy statements unchanged.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2017 Premera All Rights Reserved.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.



Discrimination is Against the Law

Premera Blue Cross complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. Premera does not exclude people or treat them differently because of race, color, national origin, age, disability or sex.

Premera:

- Provides free aids and services to people with disabilities to communicate effectively with us, such as:
 - Qualified sign language interpreters
 - Written information in other formats (large print, audio, accessible electronic formats, other formats)
- Provides free language services to people whose primary language is not English, such as:
 - Qualified interpreters
 - Information written in other languages

If you need these services, contact the Civil Rights Coordinator.

If you believe that Premera has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with:

Civil Rights Coordinator - Complaints and Appeals
PO Box 91102, Seattle, WA 98111
Toll free 855-332-4535, Fax 425-918-5592, TTY 800-842-5357
Email AppealsDepartmentInquiries@Premera.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at <https://ocrportal.hhs.gov/ocr/portal/lobby.jsf>, or by mail or phone at: U.S. Department of Health and Human Services
200 Independence Avenue SW, Room 509F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)
Complaint forms are available at <http://www.hhs.gov/ocr/office/file/index.html>.

Getting Help in Other Languages

This Notice has Important Information. This notice may have important information about your application or coverage through Premera Blue Cross. There may be key dates in this notice. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost. Call 800-722-1471 (TTY: 800-842-5357).

አማርኛ (Amharic):

ይህ ማስታወቂያ አስፈላጊ መረጃ ይዟል። ይህ ማስታወቂያ ስለ ማመልከቻዎ ወይም የ Premera Blue Cross ሽፋን አስፈላጊ መረጃ ሊኖረው ይችላል። በዚህ ማስታወቂያ ውስጥ ቁልፍ ቀዳጅ ሊኖሩ ይችላሉ። የጤና ሽፋንዎን ለመጠበቅና በአስፋፈል እርዳታ ለማግኘት በተውሰኑ የጊዜ ገደቦች እርምጃ መውሰድ ይገባዎት ይሆናል። ይህን መረጃ እንዲያገኙ እና የለምንም ክፍያ በቋንቋዎ እርዳታ እንዲያገኙ መሰታ አለዎት። በስልክ ቁጥር 800-722-1471 (TTY: 800-842-5357) ይደውሉ።

العربية (Arabic):

يحتوي هذا الإشعار على معلومات هامة. قد يحوي هذا الإشعار معلومات مهمة بخصوص طلبك أو التغطية التي تزيد الحصول عليها من خلال Premera Blue Cross. قد تكون هناك تواريخ مهمة في هذا الإشعار. وقد تحتاج لاتخاذ إجراء في تاريخ معينه للحفاظ على تغطيتك الصحية أو المساعدة في دفع التكاليف. يحق لك الحصول على هذه المعلومات والمساعدة بلغتك دون تكبد أية تكلفة. اتصل بـ 800-722-1471 (TTY: 800-842-5357)

中文 (Chinese):

本通知有重要的訊息。本通知可能有關於您透過 Premera Blue Cross 提交的申請或保險的重要訊息。本通知內可能有重要日期。您可能需要在截止日期之前採取行動，以保留您的健康保險或者費用補貼。您有權利免費以您的母語得到本訊息和幫助。請撥電話 800-722-1471 (TTY: 800-842-5357)。

Oromoo (Cushite):

Beeksisni kun odeeffannoo barbaachisaa qaba. Beeksisti kun sagantaa yookan karaa Premera Blue Cross tiin tajaajila keessan ilaalchisee odeeffannoo barbaachisaa qabaachuu danda'a. Guyyaawwan murteessaa ta'an beeksisa kana keessatti ilaalaa. Tarii kaffaltiidhaan deeggaramuuf yookan tajaajila fayyaa keessaniif guyyaa dhumaa irratti wanti raawwattan jiraachuu danda'a. Kaffaltii irraa bilisa haala ta'een afaan keessaniin odeeffannoo argachuu fi deeggarsa argachuuf mirga ni qabaattu. Lakkoofsa bilbilaa 800-722-1471 (TTY: 800-842-5357) tii bilbilaa.

Français (French):

Cet avis a d'importantes informations. Cet avis peut avoir d'importantes informations sur votre demande ou la couverture par l'intermédiaire de Premera Blue Cross. Le présent avis peut contenir des dates clés. Vous devez peut-être prendre des mesures par certains délais pour maintenir votre couverture de santé ou d'aide avec les coûts. Vous avez le droit d'obtenir cette information et de l'aide dans votre langue à aucun coût. Appelez le 800-722-1471 (TTY: 800-842-5357).

Kreyòl ayisyen (Creole):

Avi sila a gen Enfòmasyon Enpòtan ladann. Avi sila a kapab genyen enfòmasyon enpòtan konsènan aplikasyon w lan oswa konsènan kouvèti asirans lan atravè Premera Blue Cross. Kapab genyen dat ki enpòtan nan avi sila a. Ou ka gen pou pran kèk aksyon avan sèten dat limit pou ka kenbe kouvèti asirans sante w la oswa pou yo ka ede w avèk depans yo. Se dwa w pou resewva enfòmasyon sa a ak asistans nan lang ou pale a, san ou pa gen pou peye pou sa. Rele nan 800-722-1471 (TTY: 800-842-5357).

Deutsche (German):

Diese Benachrichtigung enthält wichtige Informationen. Diese Benachrichtigung enthält unter Umständen wichtige Informationen bezüglich Ihres Antrags auf Krankenversicherungsschutz durch Premera Blue Cross. Suchen Sie nach eventuellen wichtigen Terminen in dieser Benachrichtigung. Sie könnten bis zu bestimmten Stichtagen handeln müssen, um Ihren Krankenversicherungsschutz oder Hilfe mit den Kosten zu behalten. Sie haben das Recht, kostenlose Hilfe und Informationen in Ihrer Sprache zu erhalten. Rufen Sie an unter 800-722-1471 (TTY: 800-842-5357).

Hmoob (Hmong):

Tsawb ntawv tshaj xo no muaj cov ntshiab lus tseem ceeb. Tej zaum tsawb ntawv tshaj xo no muaj cov ntshiab lus tseem ceeb txog koj daim ntawv thov kev pab los yog koj qhov kev pab cuam hnuv ntawm Premera Blue Cross. Tej zaum muaj cov hnuv tseem ceeb uas sau rau hauv daim ntawv no. Tej zaum koj kuj yuav tau ua qee yam uas pab kom koj ua tsis pub dhau cov caij nyoog uas teev tseg rau hauv daim ntawv no mas koj thiaj yuav tau txais kev pab cuam kho mob los yog kev pab them tej nqi kho mob ntawd. Koj muaj cai kom lawv muab cov ntshiab lus no uas tau muab sau ua koj hom lus pub dawb rau koj. Hu rau 800-722-1471 (TTY: 800-842-5357).

Iloko (Ilocano):

Daytoy a Pakdaar ket naglaon iti Napateg nga Impormasion. Daytoy a pakdaar mabalin nga adda ket naglaon iti napateg nga impormasion maipanggep iti aplikasyonyo wenna coverage babaen iti Premera Blue Cross. Daytoy ket mabalin dagiti importante a petsa iti daytoy a pakdaar. Mabalin nga adda rumbeng nga aramidenyo nga addang sakbay dagiti partikular a naituding nga aldaw tapno mapagtalinaedyo ti coverage ti salun-atyto wenna tulong kadagiti gastos. Adda karbenganyo a mangala iti daytoy nga impormasion ken tulong iti bukodyo a pagsasao nga awan ti bayadanyo. Tumawag iti numero nga 800-722-1471 (TTY: 800-842-5357).

Italiano (Italian):

Questo avviso contiene informazioni importanti. Questo avviso può contenere informazioni importanti sulla tua domanda o copertura attraverso Premera Blue Cross. Potrebbero esserci date chiave in questo avviso. Potrebbe essere necessario un tuo intervento entro una scadenza determinata per consentirti di mantenere la tua copertura o sovvenzione. Hai il diritto di ottenere queste informazioni e assistenza nella tua lingua gratuitamente. Chiama 800-722-1471 (TTY: 800-842-5357).

日本語 (Japanese):

この通知には重要な情報が含まれています。この通知には、Premera Blue Cross の申請または補償範囲に関する重要な情報が含まれている場合があります。この通知に記載されている可能性がある重要な日付をご確認ください。健康保険や有料サポートを維持するには、特定の期日までに行動を取らなければならない場合があります。ご希望の言語による情報とサポートが無料で提供されます。800-722-1471 (TTY: 800-842-5357)までお電話ください。

한국어 (Korean):

본 통지서에는 중요한 정보가 들어 있습니다. 즉 이 통지서는 귀하의 신청에 관하여 그리고 Premera Blue Cross 를 통한 커버리지에 관한 정보를 포함하고 있을 수 있습니다. 본 통지서에는 핵심이 되는 날짜들이 있을 수 있습니다. 귀하의 건강 커버리지를 계속 유지하거나 비용을 절감하기 위해서 일정한 마감일까지 조치를 취해야 할 필요가 있을 수 있습니다. 귀하의 이러한 정보와 도움을 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 800-722-1471 (TTY: 800-842-5357) 로 전화하십시오.

ລາວ (Lao):

ແຈ້ງການນີ້ມີຂໍ້ມູນສໍາຄັນ. ແຈ້ງການນີ້ອາດຈະມີຂໍ້ມູນສໍາຄັນກ່ຽວກັບຄໍາຮ້ອງສະໝັກ ຫຼື ຄວາມຄົມຄອງປະກັນໄພຂອງທ່ານຜ່ານ Premera Blue Cross. ອາດຈະມີວັນທີ່ສໍາຄັນໃນແຈ້ງການນີ້. ທ່ານອາດຈະຈຳເປັນຕ້ອງດໍາເນີນການຕາມກຳນົດ ເວລາສະເພາະເພື່ອຮັກສາຄວາມຄົມຄອງປະກັນສະພາບ ຫຼື ຄວາມຊ່ວຍເຫຼືອເວັ້ນເວີ້ ຄ່າໃຊ້ຈ່າຍຂອງທ່ານໄດ້. ທ່ານມີສິດໄດ້ຮັບຂໍ້ມູນນີ້ ແລະ ຄວາມຊ່ວຍເຫຼືອເປັນພາສາຂອງທ່ານໂດຍບໍ່ເສຍຄ່າ. ໃຫ້ໃບທາ 800-722-1471 (TTY: 800-842-5357).

ភាសាខ្មែរ (Khmer):

សេចក្តីជូនដំណឹងនេះមានព័ត៌មានយ៉ាងសំខាន់។ សេចក្តីជូនដំណឹងនេះប្រហែលជាមានព័ត៌មានយ៉ាងសំខាន់អំពីទម្រង់បែបបទ ឬការរៀបចំរបស់អ្នកកាមរយ: Premera Blue Cross ។ ប្រហែលជាមាន កាលបរិច្ឆេទសំខាន់នៅក្នុងសេចក្តីជូនដំណឹងនេះ។ អ្នកប្រហែលជាត្រូវការបញ្ជាក់សមត្ថភាព ដល់កិច្ចការផ្ទៃក្នុងដូចជា ធានា ដើម្បីនឹងរក្សាទុកការធានារ៉ាប់រងអនុលោមតាមរបស់អ្នក ឬប្រាក់ជំនួយចេញថ្លៃ។ អ្នកមានសិទ្ធិទទួលបានព័ត៌មាននេះ និងជំនួយនៅក្នុងភាសារបស់អ្នកដោយមិនអស់លុយឡើយ។ សូមទូរស័ព្ទ 800-722-1471 (TTY: 800-842-5357)។

ਪੰਜਾਬੀ (Punjabi):

ਇਸ ਨੋਟਿਸ ਵਿਚ ਖਾਸ ਜਾਣਕਾਰੀ ਹੈ. ਇਸ ਨੋਟਿਸ ਵਿਚ Premera Blue Cross ਵਲੋਂ ਤੁਹਾਡੀ ਕਵਰੇਜ ਅਤੇ ਅਰਜੀ ਬਾਰੇ ਮਹੱਤਵਪੂਰਨ ਜਾਣਕਾਰੀ ਹੋ ਸਕਦੀ ਹੈ . ਇਸ ਨੋਟਿਸ ਨਵ ਖਾਸ ਤਾਰੀਖਾਂ ਹੋ ਸਕਦੀਆਂ ਹਨ. ਜੇਕਰ ਤੁਸੀਂ ਜਸਰਤ ਕਵਰੇਜ ਰਿੱਖਣੀ ਹੋਵੇ ਜਾਂ ਓਸ ਦੀ ਲਾਗਤ ਜਵਿੱਚ ਮਦਦ ਦੇ ਇਕੱਠ ਹੋ ਤਾਂ ਤੁਹਾਨੂੰ ਅੰਤਮ ਤਾਰੀਖ ਤੋਂ ਪਹਿਲਾਂ ਢੁੱਝ ਖਾਸ ਕਰਮ ਚੁੱਕਣ ਦੀ ਲੋੜ ਹੋ ਸਕਦੀ ਹੈ ,ਤੁਹਾਨੂੰ ਮੁਫਤ ਵਿੱਚ ਤੋਂ ਅਪਣੀ ਭਾਸ਼ਾ ਵਿੱਚ ਜਾਣਕਾਰੀ ਅਤੇ ਮਦਦ ਪ੍ਰਾਪਤ ਕਰਨ ਦਾ ਅਧਿਕਾਰ ਹੈ ,ਕਾਲ 800-722-1471 (TTY: 800-842-5357).

فارسی (Farsi):

این اعلامیه حاوی اطلاعات مهم میباشد. این اعلامیه ممکن است حاوی اطلاعات مهم درباره فرم تقاضا و یا پوشش بیمه ای شما از طریق Premera Blue Cross باشد. به تاریخ های مهم در این اعلامیه توجه نمایید. شما ممکن است برای حفظ پوشش بیمه تان یا کمک در پرداخت هزینه های درمانی تان، به تاریخ های مشخصی برای انجام کارهای خاصی احتیاج داشته باشید. شما حق این را دارید که این اطلاعات و کمک را به زبان خود به طور رایگان دریافت نمایید. برای کسب اطلاعات با شماره 800-722-1471 (کلیران TTY تماس باشماره 800-842-5357) تماس برقرار نمایید.

Polskie (Polish):

To ogłoszenie może zawierać ważne informacje. To ogłoszenie może zawierać ważne informacje odnośnie Państwa wniosku lub zakresu świadczeń poprzez Premera Blue Cross. Prosimy zwrócić uwagę na kluczowe daty, które mogą być zawarte w tym ogłoszeniu aby nie przekroczyć terminów w przypadku utrzymania polisy ubezpieczeniowej lub pomocy związanej z kosztami. Macie Państwo prawo do bezpłatnej informacji we własnym języku. Zadzwońcie pod 800-722-1471 (TTY: 800-842-5357).

Português (Portuguese):

Este aviso contém informações importantes. Este aviso poderá conter informações importantes a respeito de sua aplicação ou cobertura por meio do Premera Blue Cross. Poderão existir datas importantes neste aviso. Talvez seja necessário que você tome providências dentro de determinados prazos para manter sua cobertura de saúde ou ajuda de custos. Você tem o direito de obter esta informação e ajuda em seu idioma e sem custos. Ligue para 800-722-1471 (TTY: 800-842-5357).

Română (Romanian):

Prezenta notificare conține informații importante. Această notificare poate conține informații importante privind cererea sau acoperirea asigurării dumneavoastră de sănătate prin Premera Blue Cross. Pot exista date cheie în această notificare. Este posibil să fie nevoie să acționați până la anumite termene limită pentru a vă menține acoperirea asigurării de sănătate sau asistența provizorie la costuri. Aveți dreptul de a obține gratuit aceste informații și ajutor în limba dumneavoastră. Sunați la 800-722-1471 (TTY: 800-842-5357).

Русский (Russian):

Настоящее уведомление содержит важную информацию. Это уведомление может содержать важную информацию о вашем заявлении или страховом покрытии через Premera Blue Cross. В настоящем уведомлении могут быть указаны ключевые даты. Вам, возможно, потребуется принять меры к определенным предельным срокам для сохранения страхового покрытия или помощи с расходами. Вы имеете право на бесплатное получение этой информации и помощь на вашем языке. Звоните по телефону 800-722-1471 (TTY: 800-842-5357).

Fa'asamoa (Samoan):

Atonu ua iai i lenei fa'asilasilaga ni fa'amatalaga e sili ona taua e tatau ona e malamalama i ai. O lenei fa'asilasilaga o se fesoasoani e fa'amatala atili i ai i le tulaga o le polokalame, Premera Blue Cross, ua e tau fia maua atu i ai. Fa'amolemole, ia e iloilo fa'alelei i aso fa'apitoa olo'o iai i lenei fa'asilasilaga taua. Masalo o le'a iai ni feau e tatau ona e faia ao le'i aulia le aso ua ta'ua i lenei fa'asilasilaga ina ia e iai pea ma maua fesoasoani mai ai i le polokalame a le Malo olo'o e iai i ai. Olo'o iai iate oe le aia tatau e maua atu i lenei fa'asilasilaga ma lenei fa'matalaga i legagana e te malamalama i ai aunoa ma se togiga tupe. Vili atu i le telefoni 800-722-1471 (TTY: 800-842-5357).

Español (Spanish):

Este Aviso contiene información importante. Es posible que este aviso contenga información importante acerca de su solicitud o cobertura a través de Premera Blue Cross. Es posible que haya fechas clave en este aviso. Es posible que deba tomar alguna medida antes de determinadas fechas para mantener su cobertura médica o ayuda con los costos. Usted tiene derecho a recibir esta información y ayuda en su idioma sin costo alguno. Llame al 800-722-1471 (TTY: 800-842-5357).

Tagalog (Tagalog):

Ang Paunawa na ito ay naglalaman ng mahalagang impormasyon tungkol sa iyong aplikasyon o pagsakop sa pamamagitan ng Premera Blue Cross. Maaaring may mga mahalagang petsa dito sa paunawa. Maaring mangailangan ka na magsagawa ng hakbang sa ilang mga itinakdang panahon upang mapanatili ang iyong pagsakop sa kalusugan o tulong na walang gastos. May karapatan ka na makakuha ng ganiitong impormasyon at tulong sa iyong wika ng walang gastos. Tumawag sa 800-722-1471 (TTY: 800-842-5357).

ไทย (Thai):

ประกาศนี้มีข้อมูลสำคัญ ประกาศนี้อาจมีข้อมูลที่สำคัญเกี่ยวกับกาการสมัครหรือขอบเขตประกันสุขภาพของคุณผ่าน Premera Blue Cross และอาจมีกำหนดการในประกาศนี้ คุณอาจจะต้องดำเนินการภายในกำหนดระยะเวลาที่แน่นอนเพื่อจะรักษาการประกันสุขภาพของคุณหรือการช่วยเหลือที่มีค่าใช้จ่าย คุณมีสิทธิที่จะได้รับข้อมูลและความช่วยเหลือในภาษาของคุณโดยไม่มีค่าใช้จ่าย โทร 800-722-1471 (TTY: 800-842-5357)

Український (Ukrainian):

Це повідомлення містить важливу інформацію. Це повідомлення може містити важливу інформацію про Ваше звернення щодо страховального покриття через Premera Blue Cross. Зверніть увагу на ключові дати, які можуть бути вказані у цьому повідомленні. Існує імовірність того, що Вам треба буде здійснити певні кроки у конкретні кінцеві строки для того, щоб зберегти Ваше медичне страхування або отримати фінансову допомогу. У Вас є право на отримання цієї інформації та допомоги безкоштовно на Вашій рідній мові. Дзвоніть за номером телефону 800-722-1471 (TTY: 800-842-5357).

Tiếng Việt (Vietnamese):

Thông báo này cung cấp thông tin quan trọng. Thông báo này có thông tin quan trọng về đơn xin tham gia hoặc hợp đồng bảo hiểm của quý vị qua chương trình Premera Blue Cross. Xin xem ngày quan trọng trong thông báo này. Quý vị có thể phải thực hiện theo thông báo đúng trong thời hạn để duy trì bảo hiểm sức khỏe hoặc được trợ giúp thêm về chi phí. Quý vị có quyền được biết thông tin này và được trợ giúp bằng ngôn ngữ của mình miễn phí. Xin gọi số 800-722-1471 (TTY: 800-842-5357).