



Louisiana

Germline Genetic Testing for Pancreatic Cancer Susceptibility Genes

Policy # 00706

Original Effective Date: 05/11/2020

Current Effective Date: 05/10/2021

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Genetic Testing for Hereditary Breast and or Ovarian Cancer is addressed separately in medical policy 00047 (genetic testing for BRCA1 and BRCA2 variants).

Note: Genetic Testing for Lynch Syndrome and Other Inherited Colon is addressed separately in medical policy 00190 (genetic testing for EPCAM, MMR, and STK11 variants).

Note: Genetic Testing for Li-Fraumeni Syndrome is addressed separately in medical policy 00424 (genetic testing for TP53 variants).

Note: Moderate Penetrance Variants Associated with Breast Cancer in Individuals at High Breast Cancer Risk is addressed separately in medical policy 00504 (genetic testing for ATM and PALB2).

Note: Genetic Testing for Familial Cutaneous Malignant Melanoma is addressed separately in medical policy 00206 (genetic testing for CDKN2A).

Note: Genetic Cancer Susceptibility Panels Using Next Generation Sequencing is addressed separately in medical policy 00382.

Note: Genetic Testing for Hereditary Pancreatitis is addressed separately in medical policy 00394.

When Services Are Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

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Based on review of available data, the Company may consider genetic testing for BRCA1, BRCA2, and PALB2 variants to guide selection for treatment with platinum-based chemotherapy in previously untreated patients with locally advanced or metastatic pancreatic cancer to be **eligible for coverage**.**

Based on review of available data, the Company may consider genetic testing for BRCA1 and BRCA2 variants to guide selection for treatment with olaparib (Lynparza) in patients with pancreatic cancer to be **eligible for coverage**.**

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers genetic testing for ATM, CDK2NA, EPCAM, MMR genes (MLH1, MSH2, MSH6, PMS2), STK11, and TP53 in patients with pancreatic cancer unless the individual meets criteria for testing as specified in another policy to be **investigational**.*

Based on review of available data, the Company considers genetic testing for ATM, BRCA1, BRCA2, CDK2NA, EPCAM, MMR genes (MLH1, MSH2, MSH6, PMS2), PALB2, STK11, and TP53 in asymptomatic individuals at high risk for hereditary pancreatic cancer unless the individual meets criteria for testing as specified in another policy to be **investigational**.*

Policy Guidelines

Testing At-Risk Relatives

Individuals are considered at high risk for hereditary pancreatic cancer if they have 2 close relatives with pancreatic adenocarcinoma where 1 is a first-degree relative, have 3 or more close relatives with pancreatic cancer, or have a history of hereditary pancreatitis.

For familial assessment, 1st-, 2nd-, and 3rd-degree relatives are blood relatives on the same side of the family (maternal or paternal).

- 1st-degree relatives are parents, siblings, and children.

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- 2nd-degree relatives are grandparents, aunts, uncles, nieces, nephews, grandchildren, and half-siblings.
- 3rd-degree relatives are great-grandparents, great-aunts, great-uncles, great-grandchildren, and first cousins.

At-risk relatives primarily refer to first-degree relatives. However, some judgment must be permitted, e.g., in the case of a small family pedigree, when extended family members may need to be included in the testing strategy.

Targeted Variant Testing

It is recommended that, when possible, initial genetic testing for variants associated with hereditary pancreatic cancer be performed in an affected family member so that testing in unaffected family members can focus on the pathogenic variant found in the affected family member. In unaffected family members of potential hereditary pancreatic cancer families, most test results will be negative and uninformative. Therefore, it is strongly recommended that an affected family member be tested first whenever possible to adequately interpret the test. Should a 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.

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.

Background/Overview

Pancreatic Cancer Epidemiology

Pancreatic cancer is the fourth leading cause of cancer death in the U.S., accounting for 7.8% of all cancer deaths in 2020. The disease has a poor prognosis, with only 10.0% of patients surviving to 5

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years. Five-year survival for localized pancreatic cancer is 39.4% but most symptomatic patients have advanced, incurable disease at diagnosis.

Genetics and Pancreatic Cancer

Approximately 10%-15% of patients with pancreatic cancer are thought to have a hereditary susceptibility to the disease. Multiple genetic syndromes, including hereditary breast and ovarian cancer syndrome, are associated with an increased risk for pancreatic cancer. Five percent to 9% of pancreatic ductal adenocarcinomas (PDACs) develop in patients with a germline *BRCA* or *PALB2* variant, with higher rates observed in those with a family or personal history of pancreatic cancer or other *BRCA*-related malignancies. The incidence of germline *PALB2* variants in persons with PDAC is estimated to be between 0.6% and 2.1%.

Having a first-degree relative with pancreatic cancer increases an individual's risk of developing pancreatic cancer, and the degree of risk increases depending on the number of affected relatives (Table 1). Individuals are considered at high-risk for hereditary pancreatic cancer if they have 2 relatives with pancreatic cancer where 1 is a first-degree relative, have 3 or more relatives with pancreatic cancer or have a history of hereditary pancreatitis. In 80% of pancreatic cancer patients with a family history of pancreatic cancer, the genetic basis of the inherited predisposition is unknown.

Table 1. Family History and Pancreatic Cancer Risk

Number of First Degree Relatives (FDR) with Pancreatic Cancer	Increased Risk
1 affected FDR	4.6-fold
2 affected FDR	6.4-fold
3 affected FDR	32-fold

Sources: American Society of Clinical Oncology,² American College of Gastroenterology⁷
FDR: first-degree relative.

Germline genetic testing for pancreatic cancer susceptibility genes has several proposed purposes. In patients with pancreatic cancer, the purpose of genetic testing would be to guide treatment decisions (e.g., selection of platinum-based chemotherapy for first-line treatment, targeted treatment

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with a poly *ADP* ribose polymerase [PARP] inhibitor). In asymptomatic patients at high risk of pancreatic cancer (e.g., due to family history or other clinical factors), the purpose of genetic testing would be to inform decisions about surveillance for early detection of pancreatic cancer. Because the incidence of pancreatic cancer in the general population is low, with a lifetime risk of approximately 1.6%, screening is not recommended for patients who are not at high-risk, but patients with a family history of pancreatic cancer or a syndrome associated with increased risk of pancreatic cancer are potential targets for surveillance

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Testing for variants associated with pancreatic cancer is typically done by direct sequence analysis or next-generation sequencing. A number of laboratories offer to test for the relevant genes, either individually or as panels.

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). Lab Test X is available under the auspices of the CLIA. Laboratories that offer laboratory-developed tests must be licensed by the CLIA for high-complexity testing. To date, the U.S. Food and Drug Administration (FDA) has chosen not to require any regulatory review of this test.

In December 2019, the FDA approved olaparib (LYNPARZA, AstraZeneca Pharmaceuticals LP) for the maintenance treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated metastatic pancreatic adenocarcinoma, as detected by an FDA approved test, whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen. Also in 2019, BRACAnalysis CDx received expanded FDA approval for use as a companion diagnostic for Lynparza (olaparib) in pancreatic cancer patients.

Rationale/Source

Description

Pancreatic cancer is the fourth leading cause of cancer death in the United States, accounting for 7.8% of all cancer deaths in 2020. Multiple genetic syndromes are associated with an increased risk for pancreatic cancer, and approximately 10% to 15% of patients with pancreatic cancer are thought

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to have a hereditary susceptibility to the disease. Germline genetic testing for pancreatic cancer susceptibility genes is proposed to guide treatment decisions in patients with pancreatic cancer, and to inform decisions about surveillance in asymptomatic patients at high risk of pancreatic cancer.

Summary of Evidence

For individuals who have pancreatic cancer who receive testing for a *BRCA1*, *BRCA2*, or *PALB2* variant to guide selection for first-line treatment, the evidence includes observational studies. Multiple observational studies have demonstrated that testing patients with pancreatic cancer can identify individuals with *BRCA1*, *BRCA2*, and *PALB2* variants, including among those who do not have a family history of pancreatic cancer. Observational studies have reported a survival advantage when patients with a *BRCA* or *PALB2* variant were treated with platinum-based chemotherapy regimens compared to non-platinum-based regimens. Although these studies are limited by their small sample sizes and retrospective designs, the consistency and magnitude of benefit across studies suggests that genetic testing for these variants to aid in treatments decisions is a reasonable approach. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have pancreatic cancer who receive testing for a *BRCA1* or *BRCA2* variant to guide selection for targeted treatment, the evidence includes observational studies and 1 randomized controlled trial. Multiple observational studies have demonstrated that testing patients with pancreatic cancer can identify individuals with *BRCA1* or *BRCA2* variants, including among those who do not have a family history of pancreatic cancer. A placebo-controlled trial of olaparib as maintenance therapy in patients with germline *BRCA1* or *BRCA2* variants and metastatic pancreatic cancer found longer progression-free survival with olaparib (7.4 months vs. 3.8 months; hazard ratio 0.53; 95% confidence interval 0.35 to 0.82; $P=0.04$). The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with pancreatic cancer who receive genetic testing for *ATM*, *CDK2NA*, *EPCAM*, *MMR* genes (*MLH1*, *MSH2*, *MSH6*, *PMS2*), *STK11*, and *TP53* to guide treatment, the evidence includes observational studies. Relevant outcomes are overall survival, disease-specific survival, test accuracy, and test validity. Multiple observational studies have demonstrated that testing patients with pancreatic cancer can identify individuals with disease-associated variants, including among those who do not have a family history of the disease. However, there is no direct evidence comparing health outcomes in patients tested or not tested for a variant. Additionally, there are no

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targeted treatments for pancreatic cancer based on these genes, and management changes that would result from testing these genes are unclear. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are asymptomatic and at high risk for hereditary pancreatic cancer who receive testing for genes associated with hereditary pancreatic cancer, the evidence includes observational studies. There is no direct evidence comparing health outcomes in patients tested or not tested for a variant. There is indirect evidence from 1 comparative observational study of high-risk patients under surveillance that the risk of progression to pancreatic cancer is higher among individuals with a known pathogenic variant than in patients identified as at-risk based on family history alone. There is also evidence from prospective observational studies that surveillance of high-risk individuals can identify pancreatic cancer and precursor lesions. In 1 analysis of 76 high-risk individuals under surveillance, survival was better in those who had surgery due to detection of either low- or high-risk neoplastic precursor lesions (n=71) compared to those who had advanced to unresectable disease (n=5). Although observational studies have demonstrated that surveillance can identify pancreatic cancer and precursor lesions in asymptomatic individuals, it is not possible to conclude from this body of evidence that surveillance improves survival. Longer survival time observed in individuals undergoing surveillance could be due to earlier identification of the disease (downstaging) and not the effects of early intervention and treatment. Additionally, evidence is too limited to determine if selecting patients for surveillance based on genetic testing leads to better outcomes than using criteria such as family history alone. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

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American College of Gastroenterology

In 2015, the American College of Gastroenterology Clinical Guideline on Genetic Testing and Management of Hereditary Gastrointestinal Cancer Syndromes includes the following recommendations on genetic testing for pancreatic cancer:

- Individuals should be considered to be at risk for familial pancreatic adenocarcinoma if they (i) have a known genetic syndrome associated with pancreatic cancer, including hereditary breast-ovarian cancer syndrome, familial atypical multiple melanoma, and mole syndrome, PJS, LS, or other gene mutations associated with an increased risk of pancreatic adenocarcinoma; or (ii) have 2 relatives with pancreatic adenocarcinoma, where 1 is a first-degree relative; (iii) have 3 or more relatives with pancreatic cancer; or (iv) have a history of hereditary pancreatitis.
- Genetic testing of patients with suspected familial pancreatic cancer should include analysis of BRCA1/2, CDKN2A, PALB2, and ATM. Evaluation for PJS, LS, and hereditary pancreatitis-associated genes should be considered if other component personal and/or family history criteria are met for the syndrome.

American Society of Clinical Oncology

In 2019, an American Society of Clinical Oncology (ASCO) opinion statement addressed the identification and management of patients and family members with a possible predisposition to pancreatic adenocarcinoma and made the following recommendations:

- PCO 1.2 Individuals with a family history of pancreatic cancer affecting 2 first-degree relatives meet the criteria for familial pancreatic cancer. Individuals whose family history meets criteria for familial pancreatic cancer, those with 3e or more diagnoses of pancreatic cancer in the same side of the family, and individuals meeting criteria for other genetic syndromes associated with increased risk for pancreatic cancer have an increased risk for pancreatic cancer and are candidates for genetic testing (Type: informal consensus; benefits outweigh harms; Strength of statement: strong).
- PCO 1.3 Genetic risk evaluation should be conducted in conjunction with health care providers familiar with the diagnosis and management of hereditary cancer syndromes to determine the most appropriate testing strategy and discuss implications of the findings for family members. Germline genetic testing for patients with pancreatic cancer should be offered in the context of shared decision making. (Type: informal consensus; benefits outweigh harms; Strength of statement: strong).

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- PCO 2.1 All patients diagnosed with pancreatic adenocarcinoma should undergo an assessment of risk for hereditary syndromes known to be associated with an increased risk for pancreatic adenocarcinoma. Assessment of risk includes obtaining a personal cancer history and family history of cancers in first- and second-degree relatives. However, recent data demonstrate that many individuals who develop pancreatic cancer in the setting of genetic predisposition lack clinical features or family cancer history typically associated with the corresponding hereditary syndrome. Therefore, germline genetic testing may be discussed with patients with a personal history of pancreatic cancer, even if family history is unremarkable (Type: informal consensus; benefits outweigh harms; Strength of statement: strong).

In 2020, ASCO published a guideline update on recommendations for second-line therapy options for metastatic pancreatic cancer. In patients who have a germline BRCA1 or BRCA2 mutation and who have received first-line platinum based chemotherapy without disease progression for at least 16 weeks, options for continued treatment include chemotherapy or the PARP inhibitor olaparib.

International Cancer of the Pancreas Screening Consortium

In 2020, the International Cancer of the Pancreas Screening Consortium published an updated consensus document on the management of patients with increased risk for familial pancreatic cancer. The panel recommended pancreatic cancer surveillance performed in a research setting for the following individuals:

- All patients with Peutz-Jeghers syndrome (carriers of a germline *LKB1/STK11* gene mutation)
- All carriers of a germline *CDKN2A* mutation
- Carriers of a germline *BRCA2*, *BRCA1*, *PALB2*, *ATM*, *MLH1*, *MSH2*, or *MSH6* gene mutation with at least 1 affected first-degree blood relative
- Individuals who have at least 1 first-degree relative with pancreatic cancer who in turn also has a first-degree relative with pancreatic cancer (familial pancreatic cancer kindred)

The preferred surveillance tests are endoscopic ultrasound and magnetic resonance imaging (MRI). The recommended age to initiate surveillance depends on an individual's gene mutation status and family history, but no earlier than age 50 or 10 years earlier than the youngest relative with pancreatic cancer. There was no consensus on the age to end surveillance.

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National Comprehensive Cancer Network

Two National Comprehensive Cancer Network (NCCN) guidelines address germline genetic testing in individuals with or at high risk for pancreatic cancer.

The Guidelines on Genetic/Familial High-risk Assessment: Breast, Ovarian, and Pancreatic (v.2.2021) recommend germline testing for all individuals with exocrine pancreatic cancer, and specify that testing of first-degree relatives should only be done only if it is impossible to test the individual who has pancreatic cancer.

The Guideline on Treatment of Pancreatic Adenocarcinoma (v.1.2021) recommends germline testing for any patient with confirmed pancreatic cancer using comprehensive gene panels for hereditary cancer syndromes. The guideline specifies the following genes as those typically tested for pancreatic cancer risk: ATM, BRCA1, BRCA2, CDKN2A, most Lynch syndrome genes (MLH1, MSH2, MSH6, EPCAM), PALB2, STK11, and TP53. For patients with locally advanced disease, preferred first-line therapy regimens include gemcitabine + cisplatin for patients with BRCA1/2 or PALB2 variants. For patients with metastatic disease who have received previous platinum-based chemotherapy, olaparib is preferred only for patients with germline BRCA 1/2 variants.

Genetic counseling is recommended for patients who test positive for a pathogenic variant, or for patients with a positive family history of pancreatic cancer, regardless of test results. The guidelines also recommend genetic counseling for patients who test positive for a pathogenic variant or for patients with a positive family history of pancreatic cancer, regardless of variant status.

U.S. Preventive Services Task Force Recommendation

The 2019 U.S. Preventive Services Task Force recommendation on screening for pancreatic cancer applies to asymptomatic adults not known to be at high-risk of pancreatic cancer. The recommendation does not apply to persons at high-risk of pancreatic cancer due to an inherited genetic syndrome or due to a history of hereditary pancreatic cancer.

Medicare National Coverage

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

Ongoing and Unpublished Clinical Trials

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Some currently unpublished trials that might influence this review are listed in Table 2.

Table 2. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
<i>Ongoing</i>			
NCT03140670	A Phase 2, Open Label Study of Rucaparib in Patients With Advanced Pancreatic Cancer and a Known Deleterious Germline or Somatic BRCA or PALB2 Mutation	50	Jun 2022
NCT02790944 ^a	Utilizing a Multi-gene Testing Approach to Identify Hereditary Pancreatic Cancer in Consecutive Cases Unselected for Family History	300	May 2021
NCT03060720	Systematic Hereditary Pancreatic Cancer Risk Assessment and Implications for Personalized Therapy	375	Feb 2022
NCT00835133	Biospecimen Resource for Familial Pancreas Research, a Data and Tissue Registry (Also Known as a Bio-repository, Bio-bank, Data and Tissue Database, Data and Tissue Bank, Etc.) to Help Advance Research in Familial Pancreas Disease	4,000	Sep 2022
NCT02206360	Observational Study to Analyze the Outcomes of Subjects Who - Based Upon Their Sufficiently Elevated Risk for the Development of Pancreatic Adenocarcinoma- Elect to Undergo Early Detection Testing	100	Mar 2024
NCT00526578	Pancreatic Cancer Genetic Epidemiology (PACGENE) Study	4,770	Jun 2025

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NCT: national clinical trial.

^a Denotes industry-sponsored or cosponsored trial.

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Louisiana

Germline Genetic Testing for Pancreatic Cancer Susceptibility Genes

Policy # 00706

Original Effective Date: 05/11/2020

Current Effective Date: 05/10/2021

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Policy History

Original Effective Date: 05/11/2020

Current Effective Date: 05/10/2021

04/02/2020 Medical Policy Committee review

04/08/2020 Medical Policy Implementation Committee approval. New policy.

04/01/2021 Medical Policy Committee review

04/14/2021 Medical Policy Implementation Committee approval. New indication and eligible for coverage statement added for BRCA1, BRCA2, and PALB2 variant testing to select first-line treatment with platinum chemotherapy. PALB2 testing removed from indication 3. Indication 4 (genetic testing in asymptomatic individuals) unchanged. Title changed to "Germline Genetic Testing for Pancreatic Cancer Susceptibility Genes."

Next Scheduled Review Date: 04/2022

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2020 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	0129U, 81162, 81163, 81164, 81165, 81166, 81167, 81201, 81212, 81215, 81216, 81217, 81288, 81292, 81293, 81294, 81295, 81298, 81299, 81300, 81317, 81318, 81319, 81403, 81404, 81405, 81406, 81432, 81433, 81435, 81436, 81445, 81455
HCPCS	No codes
ICD-10 Diagnosis	C25.0-C25.9, Z12.89, Z15.09, Z80.0, Z85.07

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or

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diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

****Medically Necessary (or “Medical Necessity”)** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

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