Genetic Cancer Susceptibility Panels Using Next-Generation Sequencing

Policy # 00382
Original Effective Date: 09/18/2013
Current Effective Date: 01/08/2024

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: Germline Genetic Testing for Hereditary Breast/Ovarian Cancer Syndrome and Other High-Risk Cancers (BRCA1, BRCA2, PALB2) is addressed separately in medical policy 00047.

Note: Genetic Testing for Lynch Syndrome and Other Inherited Colon Cancer Syndromes is addressed separately in medical policy 00190.

Note: Genetic Testing for Li-Fraumeni Syndrome is addressed separately in medical policy 00424.

Note: Germline Genetic Testing for Gene Variants Associated With Breast Cancer in Individuals at High Breast Cancer Risk (CHEK2, ATM, and BARD1) is addressed separately in medical policy 00504.

Note: Use of Common Genetic Variants (single nucleotide Variants) to Predict Risk of Nonfamilial Breast Cancer is addressed separately in medical policy 00268.

Note: Genetic Testing for PTEN Hamartoma Tumor Syndrome is addressed separately in medical policy 00417.

Note: Germline Genetic Testing for Pancreatic Cancer Susceptibility Genes is addressed separately in medical policy 00706.

Note: Genetic Testing for Familial Cutaneous Malignant Melanoma is addressed separately in medical policy 00206.

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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 general genetic cancer susceptibility panel testing to be **investigational;*** however, when the coverage criteria of other policies are met (see related policies above), then limited genetic cancer susceptibility panels including only the gene variants for which a given member qualifies may be considered to be **eligible for coverage.****

Policy Guidelines

Genetics Nomenclature Update

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

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

Table PG1. Nomenclature to Report on Variants Found in DNA

Previous	Updated	Definition
Mutation	Disease-associated variant	Disease-associated change in the DNA sequence
	Variant	Change in the DNA sequence

	Familial variant	Disease-associated variant identified in a proband for use in subsequent targeted genetic testing in first-degree relatives

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

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

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

Genetic Counseling

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

Background/Overview

Genetic Testing for Cancer Susceptibility

Genetic testing for cancer susceptibility may be approached by a focused method that involves testing for gene(s) that may be the cause of the heritable or familial cancer. Panel testing with next-generation sequencing (NGS) involves evaluating sequence variants in multiple genes at once.

Multiple commercial companies and medical center laboratories offer genetic testing panels that use NGS methods for hereditary cancers. Next-generation sequencing is 1 of several methods that use massively parallel platforms to allow the sequencing of large stretches of DNA. Panel testing is potentially associated with greater efficiencies in the evaluation of genetic diseases; however, it may provide information on genetic variants of uncertain clinical significance or findings that would not lead to changes in patient management.

Genes Included in Next-Generation Sequencing Panels
The following summarizes the function and disease association of major genes included in NGS panels. This summary is not comprehensive.

BRCA1 *and* BRCA2 *Variants*
BRCA1 and *BRCA2* germline variants are associated with hereditary breast and ovarian cancer syndrome, which is associated most strongly with increased susceptibility to breast cancer at an early age, bilateral breast cancer, male breast cancer, ovarian cancer, cancer of the fallopian tube, and primary peritoneal cancer. *BRCA1* and *BCRA2* variants are also associated with increased risk of other cancers, including prostate cancer, pancreatic cancer, gastrointestinal cancers, melanoma, and laryngeal cancer.

APC *Variants*
APC germline variants are associated with familial adenomatous polyposis (FAP) and attenuated FAP. Familial adenomatous polyposis is an autosomal dominant colon cancer predisposition syndrome characterized by hundreds to thousands of colorectal adenomatous polyps and accounts for about 1% of all colorectal cancers (CRCs).

ATM *Variants*
ATM is associated with the autosomal recessive condition ataxia-telangiectasia. This condition is characterized by progressive cerebellar ataxia with onset between the ages of 1 and 4 years, telangiectasias of the conjunctivae, oculomotor apraxia, immune defects, and cancer predisposition, particularly leukemia and lymphoma.

BARD1, BRIP1, MRE11A, NBN, RAD50, *and* RAD51C *Variants*
BARD1, *BRIP1*, *MRE11A*, *NBN*, *RAD50*, and *RAD51C* are genes in the Fanconi anemia/*BRCA* pathway. Variants in these genes are estimated to confer up to a 4-fold increase in the

risk of breast cancer. This pathway is also associated with a higher risk of ovarian cancer and, less often, pancreatic cancer.

BMPR1A *and* SMAD4 *Variants*
BMPR1A and *SMAD4* are genes mutated in juvenile polyposis syndrome and account for 45% to 60% of cases. Juvenile polyposis syndrome is an autosomal dominant disorder that predisposes to the development of polyps in the gastrointestinal tract. Malignant transformation can occur, and the risk of gastrointestinal cancer has been estimated from 9% to 50%.

CHEK2 *Variants*
CHEK2 gene variants confer an increased risk of developing several different types of cancer, including breast, prostate, colon, thyroid, and kidney. *CHEK2* regulates the function of the BRCA1 protein in DNA repair and has been associated with familial breast cancers.

CDH1 *Variants*
CDH1 is a tumor suppressing gene located on chromosome 16q22.1 that encodes the cell-to-cell adhesion protein E-cadherin. Germline variants in the CDH1 gene have been associated with an increased risk of developing hereditary diffuse gastric cancer (DGC) and lobular breast cancer. A diagnosis of HDGC can be confirmed by genetic testing, although 20% to 40% of families with suspected HDGC do not have a CDH1 variant on genetic testing. Pathogenic CDH1 variants have been described in Māori families in New Zealand, and individuals of Maori ethnicity have a higher prevalence of diffuse-type gastric cancer than non-Maori New Zealanders. The estimated cumulative risk of gastric cancer for *CDH1* variant carriers by age 80 years is 70% for men and 56% for women. *CDH1* variants are associated with a lifetime risk of 39% to 52% of lobular breast cancer.

EPCAM, MLH1, MSH2, MSH6, *and* PMS2 *Variants*
EPCAM, *MLH1*, *MSH2*, *MSH6*, and *PMS2* are mismatch repair genes associated with Lynch syndrome (hereditary nonpolyposis CRC). Lynch syndrome is estimated to cause 2% to 5% of all colon cancers. Lynch syndrome is associated with a significantly increased risk of several types of cancer: colon cancer (60% to 80% lifetime risk), uterine/endometrial cancer (20% to 60% lifetime risk), gastric cancer (11% to 19% lifetime risk), and ovarian cancer (4% to 13% lifetime risk). The risks of other types of cancer, including the small intestine, hepatobiliary tract, upper urinary tract, and brain, are also elevated.

MUTYH *Variants*
MUTYH germline variants are associated with an autosomal recessive form of hereditary polyposis. It has been reported that 33% and 57% of patients with clinical FAP and attenuated FAP, respectively, who are negative for variants in the *APC* gene, have *MUTYH* variants.

PALB2 *Variants*
PALB2 germline variants are associated with an increased risk of pancreatic and breast cancer. Familial pancreatic and/or breast cancer due to *PALB2* variants are inherited in an autosomal dominant pattern.

PTEN *Variants*
PTEN variants are associated with *PTEN* hamartoma tumor syndrome (PHTS), which includes Cowden syndrome (CS), Bannayan-Riley-Ruvalcaba syndrome, and Proteus syndrome. Cowden syndrome is characterized by a high risk of developing tumors of the thyroid, breast, and endometrium. Affected persons have a lifetime risk of up to 50% for breast cancer, 10% for thyroid cancer, and 5% to 10% for endometrial cancer.

STK11 Variants
STK11 germline variants are associated with Peutz-Jeghers syndrome, an autosomal dominant disorder, with a 57% to 81% risk of developing cancer by age 70, of which gastrointestinal and breast cancers are the most common.

TP53 *Variants*
TP53 variants are associated with Li-Fraumeni syndrome. People with *TP53* variants have a 50% risk of developing any of the associated cancers by age 30 and a lifetime risk up to 90%, including sarcomas, breast cancer, brain tumors, and adrenal gland cancers.

NF1 *Variants*
The *NF1* gene encodes a negative regulator in the *ras* signal transduction pathway. Variants in the *NF1* gene have been associated with neurofibromatosis type 1, juvenile myelomonocytic leukemia, and Watson syndrome.

RAD51D *Variants*
RAD51D germline variants are associated with familial breast and ovarian cancers.

CDK4 *Variants*
Cyclin-dependent kinase-4 is a protein-serine kinase involved in cell cycle regulation. Variants in the *CDK4* gene are associated with a variety of cancers, particularly cutaneous melanoma.

CDKN2A *Variants*
The *CDKN2A* gene encodes proteins that act as multiple tumor suppressors through their involvement in 2 cell cycle regulatory pathways: the p53 pathway and the RB1 pathway. Variants or deletions in *CDKN2A* are frequently found in multiple types of tumor cells. Germline variants in *CDKN2A* have been associated with the risk of melanoma, along with pancreatic and central nervous system cancers.

RET *Variants*
RET encodes a receptor tyrosine kinase; variants in this gene are associated with multiple endocrine neoplasia syndromes (types IIA and IIB) and medullary thyroid carcinoma.

SDHA, SDHB, SDHC, SDHD, *and* SDHAF2 *Variants*
SDHA, *SDHB*, *SDHC*, *SDHD*, and *SDHAF2* gene products are involved in the assembly and function of a component of the mitochondrial respiratory chain. Germline variants in these genes are associated with the development of paragangliomas, pheochromocytomas, gastrointestinal stromal tumors, and a *PTEN*-negative Cowden-like syndrome.

***TMEM127* Variants**
TMEM127 germline variants are associated with the risk of pheochromocytomas.

VHL *Variants*
VHL germline variants are associated with Hippel-Lindau syndrome, an autosomal dominant familial cancer syndrome. This syndrome is associated with various malignant and benign tumors, including central nervous system tumors, renal cancers, pheochromocytomas, and pancreatic neuroendocrine tumors.

FH *Variants*
FH variants are associated with renal cell and uterine cancers.

FLCN *Variants*
FLCN acts as a tumor suppressor gene; variants in this gene are associated with the autosomal dominant Birt-Hogg-Dube syndrome, which is characterized by hair follicle hamartomas, kidney tumors, and CRC.

MET *Variants*
MET is a proto-oncogene that acts as the hepatocyte growth factor receptor. *MET* variants are associated with hepatocellular carcinoma and papillary renal cell carcinoma.

MITF *Variants*
Microphthalmia-associated transcription factor (encoded by the *MITF* gene) is a transcription factor involved in melanocyte differentiation. *MITF* variants lead to several auditory-pigmentary syndromes, including Waardenburg syndrome type 2 and Tietze syndrome. *MITF* variants are also associated with melanoma and renal cell carcinoma.

TSC1 *Variants*
TSC1 and *TSC2* encode the proteins hamartin and tuberin, which are involved in cell growth, differentiation, and proliferation. Variants in these genes are associated with the development of tuberous sclerosis complex, an autosomal dominant syndrome characterized by skin abnormalities, developmental delay, seizures, and multiple types of cancers, including central nervous system tumors, renal tumors (including angiomyolipomas, renal cell carcinomas), and cardiac rhabdomyomas.

XRCC2 *Variants*
XRCC2 encodes proteins thought to be related to the RAD51 protein product that is involved in DNA double-stranded breaks. Variants may be associated with Fanconi anemia and breast cancer.

FANCC *Variants*
FANCC is 1 of several DNA repair genes that mutate in Fanconi anemia, which is characterized by bone marrow failure and a high predisposition to multiple types of cancer.

AXIN2 *Variants*
AXIN2 variants are associated with FAP syndrome, although the phenotypes associated with *AXIN2* variants do not appear to be well-characterized.

Hereditary Cancer and Cancer Syndromes

Genetic testing for breast and ovarian cancer syndromes is evaluated in separate policies.

Genetic testing for Li-Fraumeni syndrome is evaluated in a separate policy.

Cowden syndrome is a part of PHTS and is the only PHTS disorder associated with a documented predisposition to malignancies. Genetic testing for CS is evaluated in a separate policy.

Genetic testing for hereditary colon cancer syndromes is addressed in a separate policy.

Genetic testing for familial pancreatic testing is evaluated in a separate policy.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

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). 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 has chosen not to require any regulatory review of these tests.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Commercially available cancer susceptibility gene panels can test for multiple variants associated with a specific type of cancer or can include variants associated with a wide variety of cancers. Some of these variants are associated with inherited cancer syndromes. The cancer type(s), as well as a cancer history involving multiple family members, increase the clinical concern for the presence of a heritable genetic variant. It has been proposed that variant testing using next-generation sequencing

(NGS) technology to analyze multiple genes at once (panel testing) can optimize genetic testing in these individuals compared with sequencing single genes.

Summary of Evidence
For individuals who have a personal and/or family history suggesting an inherited cancer syndrome who receive expanded gene panel testing, the evidence includes reports describing the diagnostic yield of expanded gene panels. Relevant outcomes are overall survival, disease-specific survival, and test validity. Studies of gene panel testing for genetic cancer risk assessment have reported primarily on the frequency with which variants are identified. The rates of variants of uncertain significance for gene panels are significant and increase in proportion with panel size, reaching nearly 50% for large gene panels. Variants included in these panels are associated with varying levels of risk of developing cancer. Published data on clinical utility are lacking, and it is unknown whether the use of these panels improves health outcomes. Only some variants included on panels are associated with a high risk of developing a well-defined cancer syndrome for which there are established clinical management guidelines. Many expanded panels include genetic variants considered to be of moderate or low penetrance, and clinical management recommendations for these genes are not well-defined. The lack of clinical management pathways for variants of uncertain clinical significance increases the potential for harm. 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.

American Society of Clinical Oncology

In 2015, the American Society of Clinical Oncology (ASCO) issued a policy statement on genetic and genomic testing for cancer susceptibility. The update addressed the application of next-generation sequencing (NGS) and confirmed that panel testing may also identify variants in genes associated with moderate or low cancer risks, variants in high-penetrance genes that would not have been evaluated based on the presenting personal or family history, and variants of uncertain significance in a substantial proportion of patient cases. Further, the statement indicated there is little consensus as to which genes should be included on panels for cancer susceptibility testing.

In 2020, ASCO published a guideline on germline and somatic tumor testing in epithelial ovarian cancer. Based on a systematic review of evidence and expert panel input, ASCO recommended that women with epithelial ovarian cancer should be offered germline testing for *BRCA1/2* and other specified ovarian susceptibility genes with a multi-gene panel. It was considered more practical to evaluate a minimum of the 10 genes that have been associated with inherited risk of ovarian cancer in a panel in comparison to testing *BRCA1 and BRCA2* alone.

National Comprehensive Cancer Network

Breast and Ovarian Cancers

National Comprehensive Cancer Network (NCCN) guidelines on genetic/familial high-risk assessment for breast, ovarian cancers, and/or pancreatic cancer (v1.2024) include the following on multi-gene testing:

- "An individual's personal and/or family history may be explained by more than one inherited cancer syndrome; thus, phenotype-directed testing based on personal and family history through a tailored multi-gene panel test is often more efficient and cost-effective and increases the yield of detecting a pathogenic/likely pathogenic variant in a gene that will impact medical management for the individual or their family members with increased risk.
- There may also be a role for multi-gene testing in individuals who have tested negative for a single syndrome, but whose personal or family history remains suggestive of an inherited susceptibility.
- Some individuals may carry pathogenic/likely pathogenic germline variants in more than one cancer susceptibility gene..."

The NCCN defines a "tailored" multi-gene panel test as a "disease-focused multi-gene panel of clinically actionable cancer susceptibility genes, in contrast to large multi-gene panels of uncertain or unknown clinical relevance." The NCCN cautions that multi-gene panels may include moderate-risk genes that have limited data on the degree of cancer risk and no clear guidelines on risk management. As more genes are tested, the likelihood of finding variants of uncertain significance increases. Multi-gene panel testing also increases the likelihood of finding pathogenic/likely pathogenic variants without clear significance.

Colorectal Cancer
The NCCN guidelines on genetic/familial high-risk assessment for colorectal cancer (v1.2023) state that “when more than one gene can explain an inherited cancer syndrome, multi-gene testing is more efficient than single-gene testing, or sequential single syndrome testing" and “there is also a role for multi-gene testing in individuals who have tested negative (indeterminate) for a single syndrome, but whose personal or family history remains strongly suggestive of an inherited susceptibility." However, the NCCN cautioned about the increased likelihood of finding variants of uncertain significance, which increases with the number of genes included in the panel, and that gene panels can include moderate-risk genes that may not be clinically actionable.

Collaborative Group of the Americas on Inherited Gastrointestinal Cancer
In 2020, the Collaborative Group of the Americas on Inherited Gastrointestinal Cancer published a position statement on multi-gene panel testing for patients with colorectal cancer and/or polyposis. Recommendations were based on the evidence, professional society recommendations endorsing testing of a given gene, and opinion of the expert panel. The group noted the variability in genes included in commercially available panels, and recommended that multi-gene panels include a minimum of 11 specific genes associated with defective mismatch repair (Lynch syndrome) and polyposis syndromes. Additional genes to be considered had low to moderately increased risk, had limited data of colorectal cancer risk, or causation for colorectal cancer was not proven.

U.S. Preventive Services Task Force Recommendations
The **U.S. Preventive Services Task Force (2019) has** recommended that primary care providers screen women with a personal or family history of breast, ovarian, tubal, or peritoneal cancer or who have an ancestry associated with *BRCA1/2* gene mutations with an appropriate brief familial risk assessment tool. Women with positive screening results should receive genetic counseling and if

indicated after counseling, *BRCA* testing (grade B recommendation). The use of genetic cancer susceptibility panels was not specifically mentioned.

Medicare National Coverage
In January 2020, the Centers for Medicare and Medicaid Services (CMS) determined that NGS is covered for patients with breast or ovarian cancer when the diagnostic test is performed in a Clinical Laboratory Improvement Amendments (CLIA)-certified laboratory AND the test has approval or clearance by the U.S. Food and Drug Administration (CAG-00450R).

CMS states that local Medicare carriers may determine coverage of NGS for management of the patient for any cancer diagnosis with a clinical indication and risk factor for germline testing of hereditary cancers when performed in a CLIA-certified laboratory.

Ongoing and Unpublished Clinical Trials
Some currently ongoing and unpublished trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT05681416	Prostate Cancer Prevention Clinic for Men With Risk of Familial Prostate Cancer	300	Feb 2027
Unpublished			
NCT03688204	Clinical Implementation of a Polygenic Risk Score (PRS) for Breast Cancer: Impact on Risk Estimates, Management Recommendations, Clinical Outcomes, and Patient Perception	118	Nov 2020

NCT: national clinical trial.

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09/05/2013	Medical Policy Committee review
09/18/2013	Medical Policy Implementation Committee approval. New policy.
09/04/2014	Medical Policy Committee review
09/17/2014	Medical Policy Implementation Committee approval. No change to coverage.
01/01/2015	Coding Update
09/03/2015	Medical Policy Committee review
09/23/2015	Medical Policy Implementation Committee approval. No change to coverage.
09/08/2016	Medical Policy Committee review
09/21/2016	Medical Policy Implementation Committee approval. No change to coverage.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
12/07/2017	Medical Policy Committee review
12/20/2017	Medical Policy Implementation Committee approval. No change to coverage.
12/06/2018	Medical Policy Committee review
12/19/2018	Medical Policy Implementation Committee approval. No change to coverage. Added policy guidelines.
06/17/2019	Coding update
12/05/2019	Medical Policy Committee review
12/11/2019	Medical Policy Implementation Committee approval. No change to coverage. Coding update
12/03/2020	Medical Policy Committee review
12/09/2020	Medical Policy Implementation Committee approval. No change to coverage.
12/02/2021	Medical Policy Committee review
12/08/2021	Medical Policy Implementation Committee approval. Investigational statement reworded.
03/08/2022	Coding Update
03/25/2022	Coding Update
04/13/2022	Coding Update
12/01/2022	Medical Policy Committee review
12/14/2022	Medical Policy Implementation Committee approval. No change to coverage. Senate bill review.

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12/07/2023 Medical Policy Committee review
12/13/2023 Medical Policy Implementation Committee approval. No change to coverage.
Next Scheduled Review Date: 12/2024

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 2022 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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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	81437, 81438, 81442, 81479 Delete codes effective 01/01/2023: 0049U, 81162, 81163, 81164, 81165, 81166, 81167, 81201, 81202, 81203, 81206, 81207, 81208, 81210, 81212, 81215, 81216, 81217, 81235, 81270, 81275, 81276, 81287, 81292, 81293, 81294, 81295, 81296, 81297, 81298, 81299, 81300, 81309, 81317, 81318, 81319, 81321, 81322, 81323, 81345, 81432, 81433, 81443, 81455
HCPCS	No codes
ICD-10 Diagnosis	All related diagnoses

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

‡ 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.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.