Analysis of Human DNA or RNA in Stool Samples as a Technique for Colorectal Cancer Screening

Policy # 00003
Original Effective Date: 08/25/2003
Current Effective Date: 06/01/2025

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.

When Services May Be 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.*

Based on review of available data, the Company may consider analysis of stool samples using the Cologuard multi-targeted stool deoxyribonucleic acid (DNA) test as a screening technique for colorectal cancer (CRC) at intervals of one test every one to three years to be **eligible for coverage.****

Patient Selection Criteria

Cologuard multi-targeted stool deoxyribonucleic acid (DNA) test as a screening technique for colorectal cancer (CRC) will be eligible for coverage in individuals meeting **ALL** of the following criteria:

- Age 45 to 85 years, **AND**
- Asymptomatic (no signs or symptoms of colorectal disease including but not limited to lower gastrointestinal pain, blood in stool, positive guaiac fecal occult blood test or fecal immunochemical test), **AND**
- At average risk of developing colorectal cancer ([CRC] no personal history of adenomatous polyps, colorectal cancer [CRC], or inflammatory bowel disease, including Crohn's disease and ulcerative colitis; no family history of colorectal cancers [CRCs], familial adenomatous polyposis, or hereditary nonpolyposis colorectal cancer [HNPCC]); **AND**
- Individual has not been screened by another colorectal cancer screening method within the last year.

Based on review of available data, the Company may consider analysis of stool samples using the ColoSense multi-target stool ribonucleic acid (RNA) test as a screening technique for colorectal cancer (CRC) at intervals of one test every three years to be **eligible for coverage.****

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Patient Selection Criteria

Colosense multi-target stool ribonucleic acid (RNA) test as a screening technique for colorectal cancer (CRC) will be eligible for coverage in individuals meeting **ALL** of the following criteria:

- Age 45 to 75 years, **AND**
- Asymptomatic (no signs or symptoms of colorectal disease including but not limited to lower gastrointestinal pain, blood in stool, positive guaiac fecal occult blood test or fecal immunochemical test), **AND**
- At average risk of developing CRC (no personal history of adenomatous polyps, CRC, or inflammatory bowel disease, including Crohn's disease and ulcerative colitis; no family history of CRCs, familial adenomatous polyposis, or hereditary nonpolyposis colorectal cancer [HNPCC]); **AND**
- Individual has not been screened by another colorectal cancer screening method within the last year.

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 deoxyribonucleic acid (DNA) or ribonucleic acid (RNA) analysis of stool samples as a screening technique for colorectal cancer (CRC) when patient selection criteria are not met or using any stool DNA or RNA test other than Cologuard or ColoSense to be **investigational.***

Background/Overview

Colorectal Cancer

Several cellular genetic alterations have been associated with colorectal cancer (CRC). In the proposed multistep model of carcinogenesis, the tumor suppressor gene *p53* and the proto-oncogene *KRAS* are most frequently altered. Variants in adenomatous polyposis coli genes and epigenetic markers (eg, hypermethylation of specific genes) have also been detected. CRC is also associated with DNA replication errors in microsatellite sequences (termed microsatellite instability) in patients with Lynch syndrome (formerly known as hereditary nonpolyposis CRC) and in subgroups of patients with sporadic colon carcinoma. Tumor-associated gene variants and epigenetic markers can be detected in exfoliated intestinal cells in stool specimens. Because cancer cells are shed into the stool, tests have been developed to detect these genetic alterations in the DNA from shed CRC cells isolated from stool samples.

Cologuard

Cologuard detects 3 independent categories of biomarkers: 1) epigenetic changes in the form of gene promoter region methylation (N-Myc Downstream-Regulated Gene 4 [NDRG4] and Bone Morphogenetic Protein 3 [BMP3]); 2) 7 specific gene mutations in V-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog [KRAS]; 3) non-DNA based, occult hemoglobin.

Cologuard Plus
Cologuard Plus expands the original Cologuard by incorporating a new molecular panel (methylated DNA markers ceramide synthase 4 gene [LASS4], leucine-rich repeat-containing protein 4 gene [LRRC4], serine–threonine protein phosphatase 2A 56-kDa regulatory subunit gamma isoform gene [PPP2R5C], and reference marker zinc finger DHHC-type containing 1 gene [ZDHHC1]. The goal of the additional biomarkers was to increase specificity without decreasing sensitivity compared to the original Cologuard.

Colosense
ColoSense evaluates 8 stool-derived eukaryotic ribonucleic acid (seRNA) markers [(Glyceraldehyde-3-Phosphate Dehydrogenase (GAPDH), Aminoacylase 1 (ACY1), Amphiregulin (AREG), TNF Receptor Superfamily Member 10B (TNFRSF10B), Cadherin 1 (CDH1), Egl-9 Family Hypoxia Inducible Factor 2 (EGLN2), Ki-ras2 Kirsten rat sarcoma viral oncogene homolog (KRAS), Suppressor of Mothers against Decapentaplegic (SMAD) Family Member 4 (SMAD4)] and an occult hemoglobin assay result fecal immunochemical test (FIT)/iFOBT. A single ColoSense result is provided based on combined results of the RNA markers, hemoglobin, and smoking status.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Table 1. FDA Approved Colorectal Cancer Screening Tests Evaluating DNA or RNA in Stool Samples

Device	Manufacturer	Original Date Approved	Pivotal study	Original PMA number	PAS identifier(s)	Indication(s)
Cologuard™‡	Exact Sciences Corporation	Aug 2014	NCT01260168	P130017	P130017 S029/ PAS001; clinicaltrials.gov registry not listed	'intended for the qualitative detection of colorectal neoplasia associated DNA markers and for the presence of occult hemoglobin in human stool. A positive result may indicate the presence of colorectal cancer (CRC) or

						advanced adenoma (AA) and should be followed by diagnostic colonoscopy. Cologuard is indicated to screen adults of either sex, 45 years or older, who are at typical average-risk for CRC. Cologuard is not a replacement for diagnostic colonoscopy or surveillance colonoscopy in high risk individuals.'
Cologuard Plus™‡	Exact Sciences Corporation	Oct 2024	NCT04144738	P230043	NA	'intended for the detection of colorectal neoplasia-associated DNA markers and for the presence of occult hemoglobin in human stool. The Cologuard Plus test is performed on samples collected using the Cologuard Plus Collection Kit. A positive result may indicate the

						presence of colorectal cancer (CRC) or advanced precancerous lesions (APL) and should be followed by colonoscopy. The Cologuard Plus test is indicated to screen adults 45 years or older, who are at average risk for CRC. The Cologuard Plus test is not a replacement for diagnostic colonoscopy or surveillance colonoscopy in high-risk individuals.'
ColoSense®‡	Geneoscopy, Inc	May 2024	NCT04739722	P230001	P230001 / PAS001; NCT04739722	'intended for the detection of colorectal neoplasia associated RNA markers and for the presence of occult hemoglobin in human stool. ColoSense is for use with the ColoSense Collection Kit, the ColoSense

						Test Kit, the ColoSense Software, and the following instruments: Polymedco Immunochemical Fecal Occult Blood Test (iFOBT) Analyzer; bioMerieux EMAG Nucleic Acid Extraction System; and Bio-Rad QXDx Droplet Digital Polymerase Chain Reaction (ddPCR) System. ColoSense is a single-site test performed at Geneoscopy, Inc. A positive ColoSense result may indicate the presence of colorectal cancer (CRC), advanced adenomas (AA) or serrated precancerous lesions (SPL) and should be followed by a colonoscopy. ColoSense is indicated as a screening test for adults, 45 years

						of age or older, who are at average-risk for developing CRC. ColoSense is not a replacement for diagnostic colonoscopy or surveillance colonoscopy in high-risk individuals.

PMA: Premarket Approval; PAS: Post-approval Study

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 regulations, other plan medical policies, and accredited national guidelines.

Description

Detection of DNA or RNA abnormalities associated with colorectal cancer (CRC) in stool samples has been proposed as a screening test for CRC. This technology is another potential alternative to currently available screening approaches such as fecal occult blood testing, fecal immunochemical testing (FIT), and colonoscopy. The currently available stool tests combine FIT and DNA or RNA analysis and are referred to as FIT-DNA or FIT-RNA in this review, though other publications use terms such as stool DNA (sDNA)-FIT, multitarget stool DNA (mt-sDNA) or multitarget stool RNA (mt-sRNA) test.

Summary of Evidence

For individuals who are asymptomatic and at average risk of colorectal cancer (CRC) who receive fecal immunochemical testing (FIT)-DNA, the evidence includes screening studies comparing the original and next-generation version of the FIT-DNA (using colonoscopy as the reference standard) to FIT alone, 2 systematic reviews of screening studies, and modeling studies. Relevant outcomes are overall survival and disease-specific survival. The screening studies have reported that both the original and the next-generation FIT-DNA tests have higher sensitivity and lower specificity than FIT. There are no studies directly assessing health outcomes such as overall survival or disease-specific survival. The screening interval for the test has not been confirmed nor is there evidence on the adherence of the test at a recommended screening interval. Effective screening for CRC requires a screening program with established screening intervals and appropriate follow-up for positive tests.

Clinical utility of FIT-DNA is based on modeling studies. These studies have demonstrated that the diagnostic characteristics of FIT-DNA are consistent with decreases in CRC mortality that are in the range of other accepted modalities. FIT-DNA every 3 years is less effective than most other accepted screening strategies, while FIT-DNA every year is close to the efficacy of colonoscopy every 10 years. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are asymptomatic and at average risk of colorectal cancer (CRC) who receive fecal immunochemical testing (FIT)-RNA, the evidence includes a screening study comparing the FIT-RNA (using colonoscopy as the reference standard) to FIT alone. Relevant outcomes are overall survival and disease-specific survival. The screening study reported that the FIT-RNA test has higher sensitivity and lower specificity than FIT. There are no studies directly assessing health outcomes such as overall survival or disease-specific survival. The screening interval for the test has not been confirmed nor is there evidence on the adherence of the test at a recommended screening interval. Effective screening for CRC requires a screening program with established screening intervals and appropriate follow-up for positive tests. Clinical utility of FIT-RNA is based on the similar performance characteristics of FIT-RNA compared to FIT-DNA so that FIT-DNA modeling studies are also of relevance for FIT-RNA. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information

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.

National Comprehensive Cancer Network

The National Comprehensive Cancer Network (NCCN) guideline (v.1.2024) for colorectal cancer (CRC) screening includes the use of fecal immunochemical testing (FIT)-DNA to screen patients with an average risk for colon cancer. Following a negative test, the recommendation is to rescreen with any modality in 3 years. Use of FIT-DNA is not described for the screening of high-risk individuals. Follow-up colonoscopy is recommended within 9 months after a positive test.

Multi-Society Task Force on Colorectal Cancer

A U.S. Multi-Society task force representing the American College of Gastroenterology, the American Gastroenterological Association (AGA), and the American Society for Gastrointestinal Endoscopy (2017) provided recommendations for CRC screening. The recommended first-tier tests for individuals with average risk were colonoscopy every 10 years, and for individuals who decline colonoscopy, annual FIT. Recommended second-tier tests in patients who declined the first-tier tests were computed tomography colonography every 5 years, FIT-DNA every 3 years, or flexible

sigmoidoscopy every 5 to 10 years. Capsule colonoscopy was listed as a third-tier test. The task force recommended, "[computed tomography] colonography every 5 years or FIT-fecal DNA every 3 years (strong recommendation, low-quality evidence), or flexible sigmoidoscopy every 5-10 years (strong recommendation, high-quality evidence) in patients who refuse colonoscopy and FIT." In 2022, a focused update to the 2017 CRC screening recommendations from the task force was published that addressed the age to begin and stop CRC screening in average-risk individuals. The task force now suggests CRC screening in average-risk individuals aged 45 to 49 years. Unchanged from 2017 are the following recommendations: a) offer CRC screening to all average-risk individuals aged 50 to 75 years, b) consider starting or continuing screening for individuals aged 76 to 85 years on an individualized basis (depending on patient and disease factors), and c) screening is not recommended after age 85 years.

American Cancer Society
In 2018, the American Cancer Society updated its guidelines for CRC screening for average-risk adults. Regular screening with either a structural examination (ie, colonoscopy) or a high-sensitivity stool-based test is recommended to start in adults who are age 45 years and older (qualified recommendation) or who are age 50 years and older (strong recommendation). Recommendations for screening with stool-based tests include FIT repeated every year, high-sensitivity guaiac-based fecal occult blood test repeated every year, or multitarget stool DNA test repeated every 3 years.

American College of Physicians
In 2023, the American College of Physicians (ACP) released updated guidance on screening for CRC in asymptomatic, average-risk adults. The ACP stated that "Clinicians should not use stool DNA, computed tomography colonography, capsule endoscopy, urine, or serum screening tests for colorectal cancer". A guidance statement of approved tests is as follows: "Clinicians should select among a fecal immunochemical or high-sensitivity guaiac fecal occult blood test every 2 years, colonoscopy every 10 years, or flexible sigmoidoscopy every 10 years plus a fecal immunochemical test every 2 years as a screening test for colorectal cancer".

American Gastroenterological Association
In 2022, the AGA published a clinical practice update commentary that reviewed the evidence on noninvasive CRC screening options. Similar to the U.S. Multi-Society task force, the ACG recommends FIT-DNA every 3 years as an average-risk option for CRC screening. The commentary compares this recommendation to that of the U.S. Preventive Services Task Force (USPSTF), which recommends FIT-DNA every 1 to 3 years.

In 2023, the AGA published a clinical practice update reviewing risk stratification for CRC screening and post-polypectomy surveillance. Similar to other guidelines, the following best practice advice was provided: "Screening options for individuals at average risk for CRC should include colonoscopy, fecal immunochemical test (FIT), flexible sigmoidoscopy plus FIT, multitarget stool DNA test, and computed tomography colonography, based on availability and individual preference."

U.S. Preventive Services Task Force Recommendations

In 2021, the U.S. Preventive Services Task Force published updated recommendations for CRC screening in asymptomatic, average risk adults (defined as no prior diagnosis of CRC, adenomatous polyps, or inflammatory bowel disease; no personal diagnosis or family history of known genetic disorders that predispose them to a high lifetime risk of CRC [such as Lynch syndrome or familial adenomatous polyposis]). The USPSTF recommended universal screening for average risk adults aged 45 to 49 years (B recommendation) and for adults aged 50 to 75 years (A recommendation). For adults aged 76 to 85 years, the USPSTF recommends selective screening due to the small magnitude of net benefit (C Recommendation). The USPSTF reviewed evidence for 6 screening strategies, including FIT-DNA. They do not recommend one screening strategy over another, and noted the lack of direct evidence on clinical outcomes when comparing screening strategies. Clinical considerations noted for FIT-DNA testing appear in Table 2.

Table 2. U.S. Preventative Services Task Force Considerations for Fecal Immunochemical-DNA Testing

Recommended screening interval	Efficacy	Other considerations
1 to 3 years	• Improved sensitivity compared with FIT per 1-time application of screening test • Specificity is lower than that of FIT, resulting in more false-positive results, more follow-up colonoscopies, and more associated adverse events per FIT-DNA screening test compared with per FIT test • Modeling suggests that screening every 3 years does not provide a favorable balance of benefits and harms compared with other	• Harms from screening with FIT-DNA arise from colonoscopy to follow-up abnormal FIT-DNA results • Can be done with a single stool sample but involves collecting an entire bowel movement • Requires good adherence over multiple rounds of testing • Does not require bowel preparation, anesthesia or sedation, or transportation to and from the screening examination (test is performed at home)

	stool-based screening options (annual FIT or FIT-DNA every 1 or 2 years) • Insufficient evidence about appropriate longitudinal follow-up of abnormal findings after a negative follow-up colonoscopy • No direct evidence evaluating the effect of FIT-DNA on colorectal cancer mortality	

FIT: fecal immunochemical testing.

Medicare National Coverage

In 2014, a Centers for Medicare & Medicaid Services decision memo indicated Medicare Part B will cover the Cologuard test once every 3 years for beneficiaries who meet all of the following criteria:

- "Age 50 to 85 years, and
- Asymptomatic (no signs or symptoms of colorectal disease including but not limited to lower gastrointestinal pain, blood in stool, positive guaiac fecal occult blood test or fecal immunochemical test), and
- At average risk of developing colorectal cancer (no personal history of adenomatous polyps, colorectal cancer, or inflammatory bowel disease, including Crohn's Disease and ulcerative colitis; no family history of colorectal cancers or adenomatous polyps, familial adenomatous polyposis, or hereditary nonpolyposis colorectal cancer)."

As noted in the Centers for Medicare & Medicaid Services decision memo, the optimal screening interval for Cologuard is unknown. In the interim, Centers for Medicare & Medicaid Services has indicated it will cover Cologuard every 3 years as previously specified and would reevaluate the screening interval after the FDA post-approval study is completed.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and 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
Ongoing			
NCT04739722[a]	Multitarget Stool RNA Test (ColoSense) for Colorectal Cancer Screening	14,263	Jan 2024
NCT04124406[a]	Voyage: Real-World Impact of the Multi-target Stool DNA Test on CRC Screening and Mortality	150,000	Dec 2029
NCT04336397	Randomized Controlled Trial of the Stool DNA Test to Improve Colorectal Cancer Screening Among Alaska Native People	1,540	Sept 2024
Unpublished			
NCT02419716[a]	A Longitudinal Study of Cologuard in an Average Risk Population Assessing a 3 Year Test Interval	2,404	Mar 2020

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

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08/19/2003	Medical Policy Committee review
08/25/2003	Managed Care Advisory Council approval
08/03/2005	Medical Director review
08/16/2005	Medical Policy Committee review. No change to coverage eligibility.
08/24/2005	Managed Care Advisory Council approval
07/07/2006	Format revision, including addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged.
05/02/2007	Medical Director review
05/23/2007	Medical Policy Committee approval. Coverage eligibility unchanged.
05/07/2009	Medical Director review
05/20/2009	Medical Policy Committee approval. Coverage eligibility unchanged.
05/06/2010	Medical Director review
06/16/2010	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/01/2011	Coding review
05/05/2011	Medical Director review
05/18/2011	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/03/2012	Medical Policy Committee review
05/16/2012	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/04/2013	Coding updated
05/02/2013	Medical Director review
05/22/2013	Medical Policy Implementation Committee approval. No change to coverage.
03/06/2014	Medical Policy Committee review
03/19/2014	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2015	Coding updated
04/02/2015	Medical Policy Committee review
04/20/2015	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/03/2015	Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
01/01/2016	Coding update: CPT code added
04/07/2016	Medical Policy Committee review

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04/20/2016	Medical Policy Implementation Committee approval. Added coverage statement for Cologuard testing every three years in patients meeting criteria.
11/03/2016	Medical Policy Committee review
11/16/2016	Medical Policy Implementation Committee approval. Adenomatous polyps removed from family history criteria. New reference added.
01/01/2017	Coding update: Removing ICD-9 Diagnosis codes
11/02/2017	Medical Policy Committee review
11/15/2017	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/28/2018	Coding update
11/08/2018	Medical Policy Committee review
11/21/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Coding section removed.
11/07/2019	Medical Policy Committee review
11/13/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/02/2020	Medical Policy Committee review
04/08/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/01/2021	Medical Policy Committee review
04/14/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/02/2021	Medical Policy Committee review
12/08/2021	Medical Policy Implementation Committee approval. Policy updated to comply with USPSTF guidelines to "Screen all asymptomatic adults aged 45 to 85 years for colorectal cancer."
12/01/2022	Medical Policy Committee review
12/14/2022	Medical Policy Implementation Committee approval. No change to coverage. Minor editorial refinements to policy statements; intent unchanged.
12/07/2023	Medical Policy Committee review
12/13/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/05/2024	Medical Policy Committee review
12/11/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/06/2025	Medical Policy Committee review
03/12/2025	Medical Policy Implementation Committee approval. Title changed from "Analysis of Human DNA in Stool Samples as a Technique for Colorectal Cancer Screening" to "Analysis of Human DNA or RNA in Stool Samples as a Technique for Colorectal Cancer Screening". Cologuard multi-targeted stool DNA test as a screening technique for colorectal cancer criteria added for an individual that has not been screened by another colorectal cancer screening method within the last

year. Added the ColoSense multitargeted stool RNA screening test for colorectal cancer coverage with criteria. Added RNA and ColoSense to the investigational statement for when criteria are not met.

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2024 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	0421U
HCPCS	NA
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.

**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.

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.