Genetic Testing for Lactase Insufficiency

Policy # 00370
Original Effective Date: 07/17/2013
Current Effective Date: 09/11/2023

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.

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 the use of targeted MCM6 -13910C>T variant analysis for the prediction of lactase insufficiency to be **investigational.***

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 was implemented for genetic testing medical evidence review updates 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

Experts recommend formal genetic counseling for individuals 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 individuals; 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

Lactase

The predominant carbohydrate in milk is the disaccharide, lactose, comprising the simple sugars, glucose, and galactose. The brush-border enzyme, lactase (also called lactase-phlorizin hydrolase),

hydrolyzes lactose into its monosaccharide components, which are absorbable by the intestinal mucosa. Except in rare instances of congenital hypolactasia, most infants can produce lactase, and enzyme levels are highest at birth. Sometime after weaning in most children, there is a decrease in lactase production through a multifactorial process that is regulated at the gene transcription level.

The decrease in lactase level varies significantly by ethnic group both in terms of the lowest level of lactase and time from weaning necessary to reach the nadir of lactase activity. By 2 to 12 years of age, 2 groups emerge: a group with insufficient levels of lactase activity (primary hypolactasia or lactase nonpersistence) and a group that retains the infant level of lactase activity through adulthood (lactase persistence). Ethnic groups with the highest prevalences of lactase insufficiency are Asian, Native American, and Black, with the lowest prevalences in people of northern European origin (see Table 1).

Table 1. Prevalence of Lactase Insufficiency by Ethnicity

Populations	**Percent Lactase Insufficient,[a] %**
Northern Europeans	2-15
American whites	6-22
Central Europeans	9-23
Northern Indians	20-30
Southern Indians	60-70
Hispanics	50-80
Ashkenazi Jews	60-80
Blacks	60-80
American Indians	80-100
Asians	95-100

Adapted from Sahi (1994).
[a] Identified through hydrogen breath test or lactose tolerance blood test.

Several terms are used to describe lactose malabsorption: lactase insufficiency, lactose malabsorption, and lactose intolerance. We discuss each below.

Lactase Insufficiency
Lactase insufficiency (lactase nonpersistence or primary hypolactasia) indicates that lactase activity is a fraction of the original infantile level. Direct measurement of lactase activity is tested biochemically through duodenal biopsy. Lactase insufficiency is highly correlated with the C/C genotype at -13910 in the lactase promoter region. In adults homozygous for the lactase persistence genotype (T/T), lactase levels are approximately 10 times higher than in those who are homozygous lactase insufficient (C/C); heterozygous persons (C/T) have intermediate lactase activity levels. In heterozygous people, symptoms of lactose intolerance may appear if the quantity of ingested lactose exceeds the maximum digestible by the reduced level of lactase.

Lactose Malabsorption
Lactose malabsorption indicates that a large portion of lactose cannot be absorbed in the small bowel and is delivered to the colon. Malabsorption is tested by hydrogen breath test (HBT) or lactose tolerance blood test.

Lactose Intolerance
Lactose intolerance indicates that lactose malabsorption causes gastrointestinal symptoms. There is no genetic test for lactose intolerance; demonstration of lactose intolerance requires individuals to self-report symptoms (see Table 2) after lactose ingestion. Diagnosis of lactose intolerance is highly susceptible to the placebo effect, and studies should conduct a blinded lactose challenge with an indistinguishable placebo. Jellema et al (2010) indicated in their meta-analysis that no specific complaint could predict lactose malabsorption; for common lactose intolerance symptoms, sensitivity and specificity ranged from 0% to 90% and 18% to 96%, respectively. Similarly, self-reported milk intolerance was inaccurate for predicting lactose malabsorption, with sensitivity and specificity ranging from 30% to 70% and 25% to 87%, respectively.

Table 2. Symptoms of Lactose Intolerance

Symptoms	**Percent of Total Individuals Who Experience Symptoms, %**
Gut-related symptoms	

Abdominal pain	100
Gut distension	100
Borborygmi (stomach rumbling)	100
Flatulence	100
Diarrhea	70
Nausea	78
Vomiting	78
Constipation	30
Systemic symptoms	
Headache and lightheadedness	86
Loss of concentration and poor short-term memory	82
Muscle pain	71
Joint pain and/or swelling	71
Long-term fatigue	63
Allergy (eczema, pruritus, rhinitis, sinusitis, asthma)	40
Mouth ulcers	30
Heart arrhythmia	24
Increased frequency of micturition	<20
Sore throat	<20

Adapted from Matthews et al (2005).

Genetic Testing for Lactase Insufficiency

Policy # 00370
Original Effective Date: 07/17/2013
Current Effective Date: 09/11/2023

Symptoms
Lactase insufficiency is common, occurring in approximately 70% of persons after weaning. Lactase insufficiency results in lactose malabsorption, which may lead to symptoms of lactose intolerance such as abdominal pain, bloating, diarrhea, and increased flatulence, caused by bacterial fermentation of undigested lactose in the colon. However, demonstration of lactose malabsorption does not necessarily indicate that a person will be symptomatic. Factors that determine whether a person with lactose malabsorption will develop symptoms include the dose of lactose ingested; residual intestinal lactase activity; ingestion of food along with lactose; the ability of the colonic flora to ferment lactose; and individual sensitivity to the products of lactose fermentation. Because of these factors, the number of persons reporting symptoms of lactose intolerance is likely only a portion of those who are lactase insufficient. Also, lactose malabsorption may be secondary (secondary hypolactasia) to acquired conditions, such as small bowel bacterial overgrowth; infectious enteritis; mucosal damage due to celiac disease; inflammatory bowel disease; antibiotics; gastrointestinal surgery; short bowel syndrome; radiation enteritis; or other conditions that may lead to reduced lactase expression in the small intestine.

Clinical Diagnosis
Mucosal biopsy of the duodenum followed by biochemical lactase assay to directly measure lactase activity is the criterion standard for diagnosing lactase insufficiency. Although this approach also may exclude other causes of secondary lactose malabsorption, the utility is limited due to the invasiveness of the procedure and the patchy expression of lactase in the duodenum.

Two common alternatives to this direct method of measuring lactase activity are the HBT and the lactose tolerance blood test, which measure lactose malabsorption. Because lactose malabsorption is nearly always attributable to lactase insufficiency, insufficiency typically can be imputed from the assessment of lactose malabsorption.

The HBT measures by gas chromatography the amount of hydrogen exhaled for up to 3 hours after ingesting 25 to 50 g of lactose. Persons undergoing HBT are required to fast overnight and refrain from activities that may elevate breath hydrogen during testing. A rise in breath hydrogen of 0.31 to 2.5 mL/min is indicative of bacterial fermentation from malabsorbed lactose. A negative HBT can exclude lactose malabsorption as the cause of symptoms, and a positive result indicates that symptoms may be attributable to lactose ingestion. The following factors are associated with increased breath hydrogen and may cause false-positive results if present at the time of testing:

- Diabetes
- Small bowel disease (eg, celiac, giardiasis)
- Bacterial overgrowth
- Altered colon pH
- Antibiotic usage
- Probiotic usage
- Smoking
- Exercise
- Aspirin usage
- Colonic bacterial adaptation

The lactose tolerance blood test measures blood glucose increase over time with blood drawn at 15, 30, 60, and 90 minutes after ingesting a 25- to 50-g dose of lactose. A glucose increase of less than 20 mg/dL above an 8-hour fasting level indicates an abnormal test. The following factors are associated with increased blood sugar when undergoing a lactose tolerance test and may cause false-positive results:

- Diabetes
- Small bowel disease (eg, celiac, giardiasis)
- Thyroid disorders
- Motility disorders (stomach, small bowel)
- Bacterial overgrowth

Molecular Diagnosis

Enattah et al (2002) identified the first DNA variant to control transcription of lactase. This variant (MCM6 -13910C>T) is located in a noncoding region of the MCM6 gene that is upstream of the lactase gene (LCT). The less common T allele has been associated with lactase persistence and has demonstrated an autosomal dominant pattern of inheritance. This variant is thought to be related to the domestication of animals during the last 10,000 to 12,000 years, and persons with the C/C genotype have been shown to be associated strongly with a lactase insufficiency phenotype in whites. Other variants in the same MCM6 regulatory region are associated with other ethnic groups (eg, Africans, Arabs), but prevalence varies geographically and, to date, no commercially available testing kits have incorporated these variants.

Prometheus's *Lacto*TYPE®‡ is a commercially available polymerase chain reaction-based test that assesses the most common lactase nonpersistence variant (*MCM6* -13910C>T) in individuals with suspected lactose intolerance. Fulgent Clinical Diagnostics Lab also offers *MCM6* sequencing as well as deletion and duplication analysis using next-generation sequencing. Demonstration of the C/C genotype can be used as indirect evidence of lactase insufficiency and lactose malabsorption.

Treatment
The goal of treatment should be to ensure adequate nutrition for skeletal health. For individuals with lactase insufficiency, dietary adjustment to restrict the consumption of foods containing lactose is the principal form of therapy. However, even lactose maldigesters can usually tolerate small amounts of lactose (12 g/d) with no or minimal symptoms. Lactase enzyme preparations are available for symptom relief but may not be effective in all individuals.

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 this test.

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.

Genetic testing of adults with suspected lactase insufficiency is proposed as an alternative to current diagnostic practices, which include hydrogen breath test, lactose tolerance blood test, and intestinal biopsy.

Genetic Testing for Lactase Insufficiency

Policy # 00370
Original Effective Date: 07/17/2013
Current Effective Date: 09/11/2023

Summary of Evidence
For individuals with suspected lactase insufficiency who receive targeted testing for the *MCM6* -13910C>T variant, the evidence includes genotype-phenotype studies and a meta-analysis. Relevant outcomes are symptoms, morbid events, functional outcomes, health status measures, and quality of life. Studies have demonstrated a high correlation between the -13910C>T single nucleotide variant upstream of the gene encoding the enzyme lactase, and lactase insufficiency in persons of European ancestry. Studies in white populations have reported a high degree of agreement for the diagnosis of lactase insufficiency between genotyping and both hydrogen breath test and lactose tolerance blood test. However, there is no current treatment for lactase insufficiency, and management involves dietary restriction and palliation of lactose intolerance symptoms. Therefore, an empirical diagnosis of lactose intolerance in the absence of confirmation by hydrogen breath test, lactose tolerance blood test, or genotyping, followed by treatment with dietary restriction of lactose, is suitable. Currently, the evidence does not support the conclusion that assessment of the genetic etiology of lactose intolerance would affect clinical management or improve clinical outcomes. The evidence is insufficient 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.

No guidelines or statements were identified.

U.S. Preventive Services Task Force Recommendations
Not applicable.

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.

Genetic Testing for Lactase Insufficiency

Policy # 00370
Original Effective Date: 07/17/2013
Current Effective Date: 09/11/2023

Ongoing and Unpublished Clinical Trials
A search of ClinicalTrials.gov in March 2023 did not identify any ongoing or unpublished trials that would likely influence this review.

References

1. Suchy FJ, Brannon PM, Carpenter TO, et al. National Institutes of Health Consensus Development Conference: lactose intolerance and health. Ann Intern Med. Jun 15 2010; 152(12): 792-6. PMID 20404261
2. Matthews SB, Waud JP, Roberts AG, et al. Systemic lactose intolerance: a new perspective on an old problem. Postgrad Med J. Mar 2005; 81(953): 167-73. PMID 15749792
3. Shaukat A, Levitt MD, Taylor BC, et al. Systematic review: effective management strategies for lactose intolerance. Ann Intern Med. Jun 15 2010; 152(12): 797-803. PMID 20404262
4. Sahi T. Genetics and epidemiology of adult-type hypolactasia. Scand J Gastroenterol Suppl. 1994; 202: 7-20. PMID 8042019
5. Wilt TJ, Shaukat A, Shamliyan T, et al. Lactose intolerance and health. Evid Rep Technol Assess (Full Rep). Feb 2010; (192): 1-410. PMID 20629478
6. Misselwitz B, Pohl D, Fruhauf H, et al. Lactose malabsorption and intolerance: pathogenesis, diagnosis and treatment. United European Gastroenterol J. Jun 2013; 1(3): 151-9. PMID 24917953
7. Jellema P, Schellevis FG, van der Windt DA, et al. Lactose malabsorption and intolerance: a systematic review on the diagnostic value of gastrointestinal symptoms and self-reported milk intolerance. QJM. Aug 2010; 103(8): 555-72. PMID 20522486
8. Haberkorn BC, Ermens AA, Koeken A, et al. Improving diagnosis of adult-type hypolactasia in patients with abdominal complaints. Clin Chem Lab Med. Sep 21 2011; 50(1): 119-23. PMID 21936609
9. Hogenauer C, Hammer HF, Mellitzer K, et al. Evaluation of a new DNA test compared with the lactose hydrogen breath test for the diagnosis of lactase non-persistence. Eur J Gastroenterol Hepatol. Mar 2005; 17(3): 371-6. PMID 15716664
10. Enattah NS, Sahi T, Savilahti E, et al. Identification of a variant associated with adult-type hypolactasia. Nat Genet. Feb 2002; 30(2): 233-7. PMID 11788828
11. Raz M, Sharon Y, Yerushalmi B, et al. Frequency of LCT-13910C/T and LCT-22018G/A single nucleotide polymorphisms associated with adult-type hypolactasia/lactase persistence among Israelis of different ethnic groups. Gene. Apr 25 2013; 519(1): 67-70. PMID 23415628

12. Enko D, Rezanka E, Stolba R, et al. Lactose malabsorption testing in daily clinical practice: a critical retrospective analysis and comparison of the hydrogen/methane breath test and genetic test (c/t-13910 polymorphism) results. Gastroenterol Res Pract. 2014; 2014: 464382. PMID 24829570
13. Di Stefano M, Terulla V, Tana P, et al. Genetic test for lactase non-persistence and hydrogen breath test: is genotype better than phenotype to diagnose lactose malabsorption?. Dig Liver Dis. Jul 2009; 41(7): 474-9. PMID 19010095
14. Eadala P, Matthews SB, Waud JP, et al. Association of lactose sensitivity with inflammatory bowel disease--demonstrated by analysis of genetic polymorphism, breath gases and symptoms. Aliment Pharmacol Ther. Oct 2011; 34(7): 735-46. PMID 21815901
15. Mendoza Torres E, Varela Prieto LL, Villarreal Camacho JL, et al. Diagnosis of adult-type hypolactasia/lactase persistence: genotyping of single nucleotide polymorphism (SNP C/T-13910) is not consistent with breath test in Colombian Caribbean population. Arq Gastroenterol. Jan-Mar 2012; 49(1): 5-8. PMID 22481679
16. Santonocito C, Scapaticci M, Guarino D, et al. Lactose intolerance genetic testing: is it useful as routine screening? Results on 1426 south-central Italy patients. Clin Chim Acta. Jan 15 2015; 439: 14-7. PMID 25281930
17. Gugatschka M, Dobnig H, Fahrleitner-Pammer A, et al. Molecularly-defined lactose malabsorption, milk consumption and anthropometric differences in adult males. QJM. Dec 2005; 98(12): 857-63. PMID 16299058
18. Buning C, Genschel J, Jurga J, et al. Introducing genetic testing for adult-type hypolactasia. Digestion. 2005; 71(4): 245-50. PMID 16024930
19. Bulhoes AC, Goldani HA, Oliveira FS, et al. Correlation between lactose absorption and the C/T-13910 and G/A-22018 mutations of the lactase-phlorizin hydrolase (LCT) gene in adult-type hypolactasia. Braz J Med Biol Res. Nov 2007; 40(11): 1441-6. PMID 17934640
20. Schirru E, Corona V, Usai-Satta P, et al. Genetic testing improves the diagnosis of adult type hypolactasia in the Mediterranean population of Sardinia. Eur J Clin Nutr. Oct 2007; 61(10): 1220-5. PMID 17311063
21. Bernardes-Silva CF, Pereira AC, de Fatima Alves da Mota G, et al. Lactase persistence/non-persistence variants, C/T_13910 and G/A_22018, as a diagnostic tool for lactose intolerance in IBS patients. Clin Chim Acta. Nov-Dec 2007; 386(1-2): 7-11. PMID 17706627
22. Szilagyi A, Malolepszy P, Hamard E, et al. Comparison of a real-time polymerase chain reaction assay for lactase genetic polymorphism with standard indirect tests for lactose maldigestion. Clin Gastroenterol Hepatol. Feb 2007; 5(2): 192-6. PMID 16876487

23. Kerber M, Oberkanins C, Kriegshauser G, et al. Hydrogen breath testing versus LCT genotyping for the diagnosis of lactose intolerance: a matter of age?. Clin Chim Acta. Aug 2007; 383(1-2): 91-6. PMID 17574225
24. Mattar R, Monteiro Mdo S, Villares CA, et al. Single nucleotide polymorphism C/T(-13910), located upstream of the lactase gene, associated with adult-type hypolactasia: validation for clinical practice. Clin Biochem. May 2008; 41(7-8): 628-30. PMID 18237552
25. Krawczyk M, Wolska M, Schwartz S, et al. Concordance of genetic and breath tests for lactose intolerance in a tertiary referral centre. J Gastrointestin Liver Dis. Jun 2008; 17(2): 135-9. PMID 18568133
26. Mottes M, Belpinati F, Milani M, et al. Genetic testing for adult-type hypolactasia in Italian families. Clin Chem Lab Med. 2008; 46(7): 980-4. PMID 18605960
27. Waud JP, Matthews SB, Campbell AK. Measurement of breath hydrogen and methane, together with lactase genotype, defines the current best practice for investigation of lactose sensitivity. Ann Clin Biochem. Jan 2008; 45(Pt 1): 50-8. PMID 18275674
28. Nagy D, Bogacsi-Szabo E, Varkonyi A, et al. Prevalence of adult-type hypolactasia as diagnosed with genetic and lactose hydrogen breath tests in Hungarians. Eur J Clin Nutr. Jul 2009; 63(7): 909-12. PMID 19156157
29. Szilagyi A, Shrier I, Chong G, et al. Lack of effect of lactose digestion status on baseline fecal micoflora. Can J Gastroenterol. Nov 2009; 23(11): 753-9. PMID 19893771
30. Babu J, Kumar S, Babu P, et al. Frequency of lactose malabsorption among healthy southern and northern Indian populations by genetic analysis and lactose hydrogen breath and tolerance tests. Am J Clin Nutr. Jan 2010; 91(1): 140-6. PMID 19889824
31. Pohl D, Savarino E, Hersberger M, et al. Excellent agreement between genetic and hydrogen breath tests for lactase deficiency and the role of extended symptom assessment. Br J Nutr. Sep 2010; 104(6): 900-7. PMID 20398434
32. Morales E, Azocar L, Maul X, et al. The European lactase persistence genotype determines the lactase persistence state and correlates with gastrointestinal symptoms in the Hispanic and Amerindian Chilean population: a case-control and population-based study. BMJ Open. Jul 29 2011; 1(1): e000125. PMID 22021768
33. Nilsson TK, Johansson CA. A novel method for diagnosis of adult hypolactasia by genotyping of the -13910 C/T polymorphism with Pyrosequencing technology. Scand J Gastroenterol. Mar 2004; 39(3): 287-90. PMID 15074401
34. Ridefelt P, Hakansson LD. Lactose intolerance: lactose tolerance test versus genotyping. Scand J Gastroenterol. Jul 2005; 40(7): 822-6. PMID 16109658

35. Rasinpera H, Savilahti E, Enattah NS, et al. A genetic test which can be used to diagnose adult-type hypolactasia in children. Gut. Nov 2004; 53(11): 1571-6. PMID 15479673
36. Kuchay RA, Thapa BR, Mahmood A, et al. Effect of C/T -13910 cis-acting regulatory variant on expression and activity of lactase in Indian children and its implication for early genetic screening of adult-type hypolactasia. Clin Chim Acta. Oct 09 2011; 412(21-22): 1924-30. PMID 21763294
37. Mattar R, Basile-Filho A, Kemp R, et al. Comparison of Quick Lactose Intolerance Test in duodenal biopsies of dyspeptic patients with single nucleotide polymorphism LCT-13910C T associated with primary hypolactasia/lactase-persistence. Acta Cir Bras. 2013; 28 Suppl 1: 77-82. PMID 23381829
38. Marton A, Xue X, Szilagyi A. Meta-analysis: the diagnostic accuracy of lactose breath hydrogen or lactose tolerance tests for predicting the North European lactase polymorphism C/T-13910. Aliment Pharmacol Ther. Feb 2012; 35(4): 429-40. PMID 22211845
39. Arroyo MA, Lopes A, Piatto V, et al. Perspectives for early genetic screening of lactose intolerance: - 13910C/T polymorphism tracking in the MCM6 gene. Open Biol J. 2010;3:66-71. https://benthamopen.com/contents/pdf/TOBIOJ/TOBIOJ-3-66.pdf.

Policy History

Original Effective Date: 07/17/2013
Current Effective Date: 09/11/2023

06/27/2013	Medical Policy Committee review
07/17/2013	Medical Policy Implementation Committee approval. New policy.
07/10/2014	Medical Policy Committee review
07/16/2014	Medical Policy Implementation Committee approval. No change to coverage.
06/25/2015	Medical Policy Committee review
07/15/2015	Medical Policy Implementation Committee approval. No change to coverage.
06/30/2016	Medical Policy Committee review
07/20/2016	Medical Policy Implementation Committee approval. No change to coverage.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
07/06/2017	Medical Policy Committee review
07/19/2017	Medical Policy Implementation Committee approval. No change to coverage.
07/05/2018	Medical Policy Committee review

Genetic Testing for Lactase Insufficiency

Policy # 00370
Original Effective Date: 07/17/2013
Current Effective Date: 09/11/2023

07/11/2018	Medical Policy Implementation Committee approval. Coverage statement reworded.
07/03/2019	Medical Policy Committee review
07/18/2019	Medical Policy Implementation Committee approval. No change to coverage.
07/02/2020	Medical Policy Committee review
07/08/2020	Medical Policy Implementation Committee approval. No change to coverage.
07/01/2021	Medical Policy Committee review
07/14/2021	Medical Policy Implementation Committee approval. No change to coverage.
08/04/2022	Medical Policy Committee review
08/10/2022	Medical Policy Implementation Committee approval. No change to coverage.
08/03/2023	Medical Policy Committee review
08/09/2023	Medical Policy Implementation Committee approval. No change to coverage.

Next Scheduled Review Date: 08/2024

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.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

Genetic Testing for Lactase Insufficiency

Policy # 00370
Original Effective Date: 07/17/2013
Current Effective Date: 09/11/2023

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	81400
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.

**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: 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.

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.