BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Laboratory Testing for HIV Tropism

Policy #: 322
Latest Review Date: December 2024
Category: Laboratory

BACKGROUND:

Blue Advantage medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*
   - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
   - *Furnished in a setting appropriate to the patient's medical needs and condition;*
   - *Ordered and furnished by qualified personnel;*
   - *One that meets, but does not exceed, the patient's medical need; and*
   - *At least as beneficial as an existing and available medically appropriate alternative.*

**Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000, which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill Original Medicare for covered services that are related to clinical trials that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

POLICY:

Blue Advantage will treat HIV tropism testing with either the phenotypic assay or V3 population (via Sanger or V3 deep sequencing method) genotyping as a covered benefit for selecting patients for treatment with HIV co-receptor antagonists, such as maraviroc (Selzentry®), when there is an immediate plan to prescribe a co-receptor antagonist.

Blue Advantage will treat HIV tropism testing without immediate plans to prescribe HIV co-receptor antagonists such as maraviroc (Selzentry®) as a non-covered benefit.

Blue Advantage will treat repeat HIV tropism testing during co-receptor antagonist treatment or after failure with co-receptor antagonists as a non-covered benefit and as investigational.

Blue Advantage will treat HIV tropism testing to predict disease progression (irrespective of co-receptor antagonist treatment) as a non-covered benefit and as investigational.

Refer also to Blue Advantage medical policy *#264 HIV Genotyping and Phenotyping* for additional information.

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

DESCRIPTION OF PROCEDURE OR SERVICE:

HIV tropism testing can determine the predominant co-receptor protein used by the human immunodeficiency virus (HIV) to infect target cells. Tropism testing can help select patients for treatment with HIV co-receptor antagonists, such as maraviroc (Selzentry®), which selectively binds to the CCR5 co-receptor and thus is only effective for use against CCR5-tropic HIV-1.

HIV

The human immunodeficiency virus (HIV-1), which causes acquired immunodeficiency syndrome, uses co-receptor proteins (either CCR5 or CXCR4) on the surface of target cells to enter and infect the cells. The most commonly transmitted strains of HIV-1 bind to CCR5 and are said to have “tropism” for CCR5-expressing cells. Dual or mixed (D/M) tropic viruses can bind to either receptor type. CXCR4-tropic virus is associated with immunosuppression and later stages of disease. Co-receptor antagonists have been designed to interfere with the interaction between HIV-1 and its co-receptors.

HIV Co-receptor Antagonists

Maraviroc (Selzentry®) is a selective, slowly reversible, small-molecule antagonist of the interaction between human cell surface CCR5 and HIV-1 gp120, necessary for HIV-1 cell

infection. Blocking this interaction prevents CCR5-tropic HIV-1 entry into cells. CXCR4-tropic HIV-1 entry is not prevented. The currently-approved maraviroc (Selzentry®) label indicates that the drug is indicated for combination antiretroviral treatment for adults infected with only CCR5-tropic HIV-1, without discussion of the presence of viral replication.

Other HIV co-receptor antagonists are in the drug development pipeline, such as cenicriviroc (CVC) is a small-molecule antagonist of both CCR5 and CCR2, allowing it to function as an entry inhibitor which prevents the virus from entering into a human cell. The CCR2 receptor may have an anti-inflammatory effect. This drug has not received FDA approval for use in HIV.

Phenotype testing
The first method available and most widely recommended tropism testing is phenotype testing. Phenotypic resistance testing directly measures relative in vitro susceptibility to a drug. Trofile® is a phenotypic viral RNA assay that can identify CCR5 antagonist candidates. Commercially available HIV drug susceptibility and resistance tests include phenotypic tests (e.g., PhenoSense HIV, and Virco Antivirogram).

Genotype testing
Tropism testing is based on sequencing the third variable (V3) loop of the HIV glycoprotein 120 gene, because the V3 loop interacts with the HIV co-receptor, and mutations in V3 are associated with measurable changes in HIV tropism. Genotypic resistance testing depends on the ability to interpret such sequence data. Tropism assignment is derived from the sequence data using a bio-informatic algorithm such as geno2pheno. The geno2pheno system has been designed to support the interpretation of sequence data resulting from genotypic resistance tests. Commercially available HIV drug susceptibility and resistance tests include genotypic tests (e.g., ABI Gene Sequencing; TrueGene HIV Genotyping GeneKit; HIV-1 GeneSeek Test; Murex LiPA HIV-1 RT; ViroSeq Genotyping System, and Affymetrix GeneChip HIV PRT Assay).

KEY POINTS:

This policy was updated with the literature available through December 6, 2024.

Summary of Evidence
For individuals who have HIV infection who are being considered for HIV co-receptor antagonist therapy who receive HIV tropism testing, the evidence includes RCTs. Relevant outcomes are overall survival, disease-specific survival, morbid events, quality of life, hospitalizations, medication use, and treatment-related morbidity. RCTs on treatment-naive and treatment-experienced HIV-infected patients have provided evidence that selection of candidates for HIV co-receptor antagonist therapy using HIV tropism testing results in higher rates of treatment success compared with HIV co-receptor antagonist therapy without HIV tropism testing. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with HIV infection receiving HIV co-receptor antagonist therapy or who have failed co-receptor antagonist therapy who receive HIV tropism testing, the evidence includes

post hoc analysis of RCTs and observational studies. Relevant outcomes are overall survival, disease-specific survival, morbid events, quality of life, hospitalizations, medication use, and treatment-related mortality and morbidity. Current evidence does not indicate improved outcomes with additional tropism monitoring during treatment. The evidence is insufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with HIV infection who are undergoing tests to predict disease progression who receive HIV tropism testing, the evidence includes observational studies. Relevant outcomes are overall survival, disease-specific survival, morbid events, quality of life, hospitalizations, and medication use. Current evidence is inconsistent in proving if HIV tropism testing independently predicts disease progression among HIV-infected patients. The evidence is insufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Practice Guidelines and Position Statements
HIV Medicine Association of the Infectious Disease society of North America
The HIV Medicine Association of the Infectious Disease Society of North America released updated guidelines on the on the management of persons infected with HIV in 2020. These guidelines state that tropism testing should be performed if the use of a CCR5 antagonist is being considered (strong recommendation, high quality evidence). The guidelines also state that "routine tropism testing is not recommended prior to initiation of other regimens because of cost and lack of demonstrated benefit." The guidelines do not specify the preferred method of tropism testing.

European Consensus Group
The European Consensus Group on clinical management of tropism testing states that tropism testing is indicated for patients who fail treatment or have unacceptable toxicity and a CCR5 inhibitor is being considered. In the absence of evidence, the group provides no guidance regarding tropism testing for newly diagnosed patients whose immediate treatment plan does not include a CCR5 inhibitor. In the absence of adequate data, the group could provide no guidance regarding the question of testing treatment-naïve patients prior to the start of a regimen not including a CCR5 inhibitor, in anticipation of need for a fast change to a CCR5 inhibitor due to the toxicity of the initial treatment regimen. For patients with a plasma HIV RNA load >1,000 copies/mL, tropism testing can be done by Trofile® or by population genotypic analysis of the V3 loop, indicating for both a moderate level of evidence based on well-designed, nonrandomized trials or cohort studies with long-term clinical outcomes. For patients with a plasma HIV RNA load <1,000 copies/mL, genotyping is the preferred method.

Department of Health and Human Services (DHHS)
In 2018, the United States Department of Health and Human Services published guidelines for the use of antiretroviral agents in adults and adolescents living with HIV. They recommend the use of co-receptor tropism assays (including a phenotypic tropism assay) in clinical practice as follows:

A co-receptor tropism assay should be performed whenever the use of a CCR5 co-receptor antagonist is being considered (Level of Evidence AI);

Co-receptor tropism testing is also recommended for patients who exhibit virologic failure on a CCR5 antagonist (Level of Evidence BIII);

A phenotypic tropism assay is preferred to determine HIV-1 co-receptor usage (Level of Evidence A1);

A proviral DNA tropism assay can be utilized for patients with undetectable HIV-1 RNA when CCR5 antagonist is considered for use in a new regimen (e.g., as part of a regimen switch or simplification) (Level of Evidence BII).

Note:
Rating of Recommendations: A = Strong; B = Moderate; C = Optional;

Rating of Evidence: I = data from randomized controlled trials; II = data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = expert opinion.

Infectious Diseases Society of America
In 2020, The Infectious Diseases Society of America published guidelines that state "tropism testing should be done before starting any CCR5 antagonist. Also, patients who exhibit virologic failure while taking a CCR5 antagonist may also be considered for tropism testing".

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

KEY WORDS:
Maraviroc (Selzentry, Pfizer), Trofile (Monogram Biosciences, South San Francisco, CA) assay, SensiTrop assay, HIV-1 Coreceptor Tropism, Tropism testing, Genotypic tropism testing, tropism assay, V3 genotyping, HIV V3, ESTA, antiretroviral drug resistance testing

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

The FDA-approved full prescribing information for maraviroc (Selzentry®) states that "Tropism testing must be conducted with a highly sensitive and specific tropism assay that has demonstrated the ability to identify patients appropriate for [maraviroc (Selzentry®)] use."

Currently-available HIV tropism tests are performed as laboratory developed tests (LDTs). Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; LDTs must meet the general regulatory standards of the Clinical Laboratories Improvement Act (CLIA). HIV tropism tests are is available under the auspices of the Clinical

Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the FDA has chosen not to require any regulatory review of this test.

BENEFIT APPLICATION:

Coverage is subject to member's specific benefits. Group-specific policy will supersede this policy when applicable.

CURRENT CODING:

CPT Codes:

87999	Unlisted microbiology procedure

REFERENCES:

1. Aberg JA, Gallant JE, Ghanem KG et al. Primary care guidelines for the management of persons infected with HIV: 2013 update by the HIV Medicine Association of the Infectious Diseases Society of America. Clin Infect Dis 2014; 58(1):1-10.
2. Almeida FJ, Zaparoli MS, Moreira DH, et al. Association of X4 tropism with disease progression in antiretroviral-treated children and adolescents living with HIV/AIDS in Sao Paulo, Brazil. Braz J Infect Dis. May-Jun 2014; 18(3):300-307.
3. Archer J, Weber J, Henry K et al. Use of four next-generation sequencing platforms to determine HIV-1 coreceptor tropism. PloS One 2012; 7(11):e49602.
4. Aves T, Tambe J, Siemieniuk RA, Mbuagbaw L. Antiretroviral resistance testing in HIV-positive people. Cochrane Database Syst Rev. 2018 Nov 9; 11(11):CD006495.
5. Bartlett AD, MaCartney MJ, Conibear TC, et al. The utility of different bioinformatics algorithms for genotypic HIV-1 tropism testing in a large clinical cohort with multiple subtypes. AIDS. Jul 17 2014; 28(11):1611-1617.
6. Beerenwinkel N, Däumer M, Oette M, et al. Geno2pheno: Estimating phenotypic drug resistance from HIV-1 genotypes. Nucleic Acids Res. 2003; 31(13):3850-3855.
7. Brown J, Burger H, Weiser B, et al. A genotypic HIV-1 proviral DNA coreceptor tropism assay: characterization in viremic subjects. AIDS Res Ther. 2014; 11:14.
8. Cardona L, Ana G, Luisa B et al. Thrombus formation on a left atrial appendage closure device. Circulation 2011; 124(14):1595-6.
9. Casadella M, Cozzi-Lepri A, Phillips A, et al. Plasma HIV-1 Tropism and the Risk of Short-Term Clinical Progression to AIDS or Death. PLoS One. 2017; 12(1):e0166613.
10. Castagna A, Monno L, Carta S, et al. Switch of predicted HIV-1 tropism in treated subjects and its association with disease progression. Medicine (Baltimore). Nov 2016; 95(44):e5222

11. Ceresola ER, Nozza S, Sampaolo M, et al. Performance of commonly used genotypic assays and comparison with phenotypic assays of HIV-1 coreceptor tropism in acutely HIV-1-infected patients. J Antimicrob Chemother. May 2015; 70(5):1391-1395.
12. Cooper DA, Heera J, Goodrich J et al. Maraviroc versus efavirenz, both in combination with zidovudine-lamivudine, for the treatment of antiretroviral-naive subjects with CCR5-tropic HIV-1 infection. J Infect Dis 2010; 201(6):803-13.
13. Daar ES, Kesler KL, Petropoulos CJ et al. Baseline HIV type 1 coreceptor tropism predicts disease progression. Clin Infect Dis 2007; 45(5):643-9.
14. Diez-Fuertes F, Delgado E, Vega Y et al. Improvement of HIV-1 coreceptor tropism prediction by employing selected nucleotide positions of the env gene in a Bayesian network classifier. J Antimicrob Chemother 2013; 68(7):1471-85.
15. Fatkenheuer G, Nelson M, Lazzarin A, et al. Subgroup analyses of maraviroc in previously treated R5 HIV-1 infection. NEJM, October 2008; 359(14): 1441-1455.
16. Fontdevila MC, Cozzi-Lepri A, Phillips A, et al. Plasma HIV-1 tropism and risk of short-term clinical progression to AIDS or death. J Int AIDS Soc. 2014; 17(4 Suppl 3):19685.
17. Gibert CL. Treatment Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents: An Update. Fed Pract. 2016 Apr; 33(Suppl 3):31S-36S.
18. Gibson RM, Meyer AM, Winner D, et al. Sensitive deep-sequencing-based HIV-1 genotyping assay to simultaneously determine susceptibility to protease, reverse transcriptase, integrase, and maturation inhibitors, as well as HIV-1 coreceptor tropism. Antimicrob Agents Chemother. 2014; 58(4):2167-2185.
19. Gonzalez-Serna A, McGovern RA, Harrigan PR et al. Correlation of the virological response to short-term Maraviroc monotherapy with standard and deep sequencing-based genotypic tropism methods. Antimicrob Agents Chemother 2012; 56(3):1202-07.
20. Gulick RM, Fatkenheuer G, Burnside R et al. Five-Year Safety Evaluation of Maraviroc in HIV-1- Infected Treatment-Experienced Patients. J Acquir Immune Defic Syndr 2014; 65(1):78-81.
21. Hardy WD, Gulick RM, Mayer H et al. Two-year safety and virologic efficacy of maraviroc in treatment-experienced patients with CCR5-tropic HIV-1 infection: 96-week combined analysis of MOTIVATE 1 and 2. J Acquir Immune Defic Syndr 2010; 55(5):558-64.
22. Heera J, Valluri S, Craig C, et al. First prospective comparison of genotypic vs phenotypic tropism assays in predicting virologic responses to Maraviroc (MVC) in a phase 3 study: MODERN. J Int AIDS Soc. 2014;17(4 Suppl 3):19519
23. Heera, J., Valluri, S. R., Craig, C., Fang, A., Thomas, N., Meyer, R. D., Lewis, M. E., van der Ryst, E., & Demarest, J. (2019). First prospective comparison of genotypic versus phenotypic tropism assays in predicting virologic responses to maraviroc in a phase 3 study. The new microbiologica, 42(2), 101–107.
24. Huang W, Toma J, Stawiski E et al. Characterization of human immunodeficiency virus type 1 populations containing CXCR4-using variants from recently infected individuals. AIDS Res Hum Retroviruses 2009; 25(8):795-802.

25. IOM (Institute of Medicine). 2011. Clinical Practice Guidelines We Can Trust. Washington, DC: The National Academies Press.
26. Kagan RM, Johnson EP, Siaw M et al. A genotypic test for HIV-1 tropism combining Sanger sequencing with ultradeep sequencing predicts virologic response in treatment-experienced patients. PloS One 2012; 7(9):e46334.
27. Kanters S, Vitoria M, Doherty M, et al. Comparative efficacy and safety of first-line antiretroviral therapy for the treatment of HIV infection: a systematic review and network meta-analysis. Lancet HIV. 2016; 3(11):e510-e520.
28. Kaplan SS, Mounzer KC. Antiretroviral therapy in HIV-infected patients with multidrug-resistant virus: applying the guidelines to practice. AIDS Patient Care STDS. 2008; 22(12):931-940.
29. Lin NH, Kuritzkes DR. Tropism testing in the clinical management of HIV-1 infection. Curr Opin HIV AIDS. 2009; 4(6):481-487.
30. Low AJ, Swenson LC and Harrigan PR. HIV coreceptor phenotyping in the clinical setting. AIDS Rev, Jul-Sept 2008; 10(3): 143-151.
31. Misbah M, Roy G, Shahid M, et al. Comparative analysis of drug resistance mutations in the human immunodeficiency virus reverse transcriptase gene in patients who are non-responsive, responsive and naive to antiretroviral therapy. Arch Virol. 2016; 161(5):1101-1113.
32. Mortier V, Dauwe K, Vancoillie L, et al. Frequency and predictors of HIV-1 co-receptor switch in treatment naive patients. PLoS One. 2013; 8(11):e80259.
33. Moyle GJ, Wildfire A, Mandalia S, et al. Epidemiology and predictive factors for chemokine receptor use in HIV-1 infection. J Infect Dis 2005; 191(6):866-72.
34. Nanfack AJ, Takou D, Fokam J, et al. HIV-1 drug susceptibility to potential second- and third-line antiretroviral regimens among Cameroonian patients: Evidence from a cross-sectional design. Curr HIV Res. 2017; 15(1):66-73.
35. Perez-Olmeda M, Alcami J. Determination of HIV tropism and its use in the clinical practice. Expert Rev Anti Infect Ther. 2013; 11(12):1291-1302.
36. Pfizer, Inc. Selzentry TM, (maroviroc) prescribing information. 2009; www.accessdata.fda.gov/drugsatfda_docs/label/2009/022128s002lbl.pdf. Accessed January 6, 2022.
37. Poveda E, Paredes R, Moreno S et al. Update on clinical and methodological recommendations for genotypic determination of HIV tropism to guide the usage of CCR5 antagonists. AIDS Reviews 2012; 14(3):208-17.
38. Raymond S, Maillard A, Amiel C, et al. Virological failure of patients on maraviroc-based antiretroviral therapy. J Antimicrob Chemother. Feb 2015; 70(6):1858-1864.
39. Reeves JD, Coakley E, Petropoulos CJ et al. An enhanced-sensitivity Trofile HIV coreceptor tropism assay for selecting patients for therapy with entry inhibitors targeting CCR5: A review of analytical and clinical studies. J Viral Entry 2009; 3:94-102.
40. Saag M, Goodrich J, Fatkenheuer G et al. A double-blind, placebo-controlled trial of maraviroc in treatment-experienced patients infected with non-R5 HIV-1. J Infect Dis 2009; 199(11):1638-47.

41. Saag M, Heera J, Goodrich J, et al. Reanalysis of the MERIT study with the enhanced Trofile® assay (MERIT-ES). Program and abstracts of the 48th Annual ICAAC/IDSA 46th Annual Meeting; October 25-28, 2008; Washington, DC. Abstract H1232a.
42. Saliou A, Delobel P, Dubois M et al. Concordance between two phenotypic assays and ultradeep pyrosequencing for determining HIV-1 tropism. Antimicrob Agents Chemother 2011; 55(6):2831-6.
43. Sanchez V, Masia M, Robledano C et al. Performance of genotypic algorithms for predicting HIV-1 tropism measured against the enhanced-sensitivity Trofile coreceptor tropism assay. J Clin Microbiol 2010; 48(11):4135-9.
44. Saracino A, Bruno G, Scudeller L, et al. Does HIV-1 co-receptor tropism correlate with fibrosis progression in HIV/HCV co-infected patients? J Clin Virol. Mar 2014; 59(3):167-171.
45. Strang AL, Cameron J, Booth CL et al. Genotypic prediction of viral co-receptor tropism: correlation with enhanced Trofile. 15th Annual Conference of the British HIV Association 1-3 April 2009, Liverpool, UK: Abstract P95.
46. Svicher V, Alteri C, Montano M, et al. Genotypic testing on HIV-1 DNA as a tool to assess HIV-1 co-receptor usage in clinical practice: results from the DIVA study group. Infection. Feb 2014; 42(1):61-71.
47. Svicher V, Alteri C, Montano M, et al. Performance of genotypic tropism testing on proviral DNA in clinical practice: results from the DIVA study group. New Microbiol. Jan 2012; 35(1):17-25.
48. Swenson LC, Mo T, Dong WW et al. Deep sequencing to infer HIV-1 co-receptor usage: application to three clinical trials of maraviroc in treatment-experienced patients. J Infect Dis 2011; 203(2):237-45.
49. Swenson LC, Moores A, Low AJ et al. Improved detection of CXCR4-using HIV by V3 genotyping: application of population-based and "deep" sequencing to plasma RNA and proviral DNA. J Acquir Immune Defic Syndr 2010; 54(5):506-10.
50. Trinh L, Han D, Huang W, et al. Technical validation of an enhanced sensitivity Trofile HIV coreceptor tropism assay for selecting patients for therapy with entry inhibitors targeting CCR5. Antivir Ther. 2008; 13(Suppl. 3):A128 (abstract no. 118)
51. Tsibris AM, Korber B, Arnaout R et al. Quantitative deep sequencing reveals dynamic HIV-1 escape and large population shifts during CCR5 antagonist therapy in vivo. PLoS One 2009; 4(5):e5683.
52. Vandekerckhove LP, Wensing AM, Kaiser R et al. European guidelines on the clinical management of HIV-1 tropism testing. Lancet Infect Dis 2011; 11(5):394-407.
53. Visseaux B, Charpentier C, Rouard C, et al. HIV-2 X4 tropism is associated with lower CD4+ cell count in treatment-experienced patients. AIDS. Sep 10 2014; 28(14):2160-2162.
54. Wilkin TJ, Goetz MB, Leduc R et al. Reanalysis of coreceptor tropism in HIV-1-infected adults using a phenotypic assay with enhanced sensitivity. Clin Infect Dis 2011; 52(7):925-8.

55. Wilkin TJ, Gulick RM. CCR5 Antagonism in HIV Infection: Current Concepts and Future Opportunities. Annu Rev Med 2012; 63:81-93.

POLICY HISTORY:

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Medical Policy Group, January 2019
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Medical Policy Group, December 2022: Reviewed by consensus. No new published peer-reviewed literature available that would alter the coverage statement in this policy.
Medical Policy Group, December 2023: Reviewed by consensus. No new published peer-reviewed literature available that would alter the coverage statement in this policy.
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Medical Policy Group, December 2024: Reviewed by consensus. No new published peer-reviewed literature available that would alter the coverage statement in this policy.
