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MEDICAL POLICY – 2.04.127

Multitarget Polymerase Chain Reaction Testing for Diagnosis of Bacterial Vaginosis

BCBSA Ref. Policy:	2.04.127	
Effective Date:	Jun. 6, 2025	RELATED MEDICAL POLICIES:
Last Revised:	Feb. 11, 2025	None
Replaces:	N/A	

Select a hyperlink below to be directed to that section.

Clicking this icon returns you to the hyperlinks menu above.

Introduction

Bacterial vaginosis (BV) is a common vaginal infection that occurs when the natural balance of bacteria in the vagina is disrupted. It can cause symptoms like unusual discharge, odor, and discomfort. Traditional testing for diagnosis of BV look at bacteria under a microscope, but multitarget polymerase chain reaction (PCR) testing detects the DNA of bacteria linked to the condition. Multitarget PCR testing for BV is unproven (investigational). More studies are needed to see if this test improves health outcomes.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Procedure	Investigational
Multitarget polymerase chain reaction testing	**Multitarget polymerase chain reaction testing for the diagnosis of bacterial vaginosis is considered investigational.**

Coding

Code	Description
CPT	
0330U	Infectious agent detection by nucleic acid (DNA or RNA), vaginal pathogen panel, identification of 27 organisms, amplified probe technique, vaginal swab (used to report Bridge Women's Health Infectious Disease Detection Test)
0505U	Infectious disease (vaginal infection), identification of 32 pathogenic organisms, swab, real-time PCR, reported as positive or negative for each organism (used to report Vaginal Infection Testing, NxGen MDx LLC) (new code effective 10/01/24)
81513	Infectious disease, bacterial vaginosis, quantitative real-time amplification of RNA markers for Atopobium vaginae, Gardnerella vaginalis, and Lactobacillus species, utilizing vaginal-fluid specimens, algorithm reported as a positive or negative result for bacterial vaginosis
81514	Infectious disease, bacterial vaginosis and vaginitis, quantitative real-time amplification of DNA markers for Gardnerella vaginalis, Atopobium vaginae, Megasphaera type 1, Bacterial Vaginosis Associated Bacteria-2 (BVAB-2), and Lactobacillus species (L. crispatus and L. jensenii), utilizing vaginal-fluid specimens, algorithm reported as a positive or negative for high likelihood of bacterial vaginosis, includes separate detection of Trichomonas vaginalis and/or Candida species (C. albicans, C. tropicalis, C. parapsilosis, C. dubliniensis), Candida glabrata, Candida krusei, when reported
81515	Infectious disease, bacterial vaginosis and vaginitis, realtime PCR amplification of DNA markers for Atopobiumvaginae, Atopobium species, Megasphaera type 1, and Bacterial Vaginosis Associated Bacteria-2 (BVAB-2), utilizing vaginal-fluid specimens, algorithm reported as positive or negative for high likelihood of bacterial vaginosis, includes separate detection of Trichomonas vaginalis and Candida species (C. albicans, C. tropicalis, C. parapsilosis, C. dubliniensis), Candida glabrata/ Candida krusei, when reported (new code effective 01/01/25)

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

Definition of Terms

Amsel criteria are a set of four microscopic findings used to diagnose bacterial vaginosis of which three of the four following signs or symptoms need to be present:

- A thin vaginal discharge (gray, white, or yellow) consistent in appearance throughout
- A vaginal pH greater than 4.5
- Positive whiff test (a fishy odor is released when 10% potassium hydroxide is added to the vaginal discharge on the microscope slide)
- Clue cells (vaginal epithelial cells covered in bacteria) on wet mount microscopy

Nugent score is a Gram-stained scoring system of vaginal smears used for a quantitative concentration of bacteria

- **0-3**: Normal flora, or Lactobacillus-predominant vaginal microbiota (or negative for BV)
- **4-6:** Intermediate flora, or a mixed flora of Gardnerella. Vaginalis (indeterminate for BV)
- **7 10:** Bacterial vaginosis flora (positive for BV)

Evidence Review

Description

Bacterial vaginosis (BV) is a common medical condition resulting from an imbalance in the normal vaginal flora. Although the identification of *Gardnerella vaginalis* has traditionally been associated with BV, there is no single etiologic agent. Most cases are asymptomatic, and most symptomatic cases can be diagnosed using clinical and microscopic evaluation. Multitarget polymerase chain reaction (PCR) testing is proposed as an alternative to currently available laboratory tests to diagnose BV. This test may improve outcomes if it is a more accurate and reliable method to diagnose BV.

Background

Bacterial Vaginosis

BV is a condition caused by an imbalance in the normal bacteria vaginal flora. It is common, especially in women of reproductive age. While there is no single known etiologic agent, there is a shift in vaginal flora that involves depletion of hydrogen peroxide-producing Lactobacillus species with a rise in vaginal pH and overgrowth of other bacteria, including Gardnerella vaginalis, *Mycoplasma hominis*, *Peptostreptococcus*, *Mobiluncus* species, and other anaerobic gram-negative rods.

Vaginal culture is not an appropriate diagnostic method to identify BV because BV is not caused by the presence of a particular bacterial species.

Various commercial tests provide rapid and accurate pH evaluation and amine detection. For example, automated devices that measure the volatile gases produced from vaginal samples and a colorimetric pH test are commercially available.

Nucleic acid probes of DNA fragments are available to detect and quantify specific bacteria in vaginal fluid samples. Polymerase chain reaction (PCR) methods extract and amplify the DNA fragments using either universal or specific primers. The result can be qualitative (to assess whether a specific microorganism is present) or quantitative (to assess how many microorganisms are present). The technology can be used to measure multiple organisms (e.g., those known to be associated with BV) at the same time and is commercially available as multitarget PCR testing.

Multitarget PCR Tests

Five quantitative multiplex PCR assays are available: BD Max (Becton Dickinson), Aptima BV (Hologic), NuSwab VG (LabCorp), OneSwab BV Panel PCR with Lactobacillus Profiling by qPCR (Medical Diagnostic Laboratories), and SureSwab BV (Quest Diagnostics). Also included is the, Bridge Women's Health Infectious Disease Detection test (Bridge Diagnostics) and the Vaginal Infection Testing from NxGen MDx LLC. (This list may not be all inclusive)

The SureSwab Total test involves obtaining vaginal swab specimens, extracting total DNA, and quantitating the 4 types of bacteria using PCR. Results are reported as log cells per milliliter for each organism and concentrations of all *Lactobacilli* species are reported together then classified into one of the following three categories: not supportive, equivocal, and supportive.

A classification of *not supportive* of BV diagnosis is based on:

- The presence of *Lactobacillus* species, *G. vaginalis* levels <6.0 log cells/mL, and absence of *Atopobium vaginae* and *Megasphaera* species; or
- The absence of *Lactobacillus* species, *G. vaginalis* levels <6.0 log cells/mL, and absence of *A. vaginae* and *Megasphaera* species; or
- The absence of all targeted organisms.

A classification of equivocal is based on:

- The presence of *Lactobacillus* species, plus *G. vaginalis*at least 6.0 log cells/mL, and/or the presence of *A. vaginae* and/or *Megasphaera* species.

A classification of supportive of BV diagnosis is based on the absence of *Lactobacillus* species, and presence of *G. vaginalis* levels of at least 6.0 log cells/mL, and the presence of *A. vaginae and*/or *Megasphaera* species.

The BD Max (Becton, Dickinson), tests for markers of BV and vaginitis. The test uses a similar process to that described for SureSwab. Vaginal swab specimens are collected, DNA is extracted, and real-time PCR is used to quantitate targeted organisms. Results of BV marker tests are not reported for individual organisms. Instead, qualitative BV results are reported as positive or negative for BV based on the relative quantity of the various organisms.

The Aptima BV Assay was cleared by the US Food and Drug Administration with the BD Max as the predicate device. The Aptima assay is a nucleic acid amplification test (NAAT) for detection and quantitation of ribosomal RNA.

Medical Diagnostics Laboratory offers a Bacterial Vaginosis Panel. Markers are assessed using real-time PCR and *Lactobacillus* is profiled using quantitative PCR. GenPath Diagnostics also offers a bacterial vaginosis test.

The NuSwab Select BV test (Laboratory Corporation of America) uses semiquantitative PCR analysis of three predictive marker organisms of vaginal dysbiosis to generate a total score that is associated with the presence or absence of BV. In this test system, samples with a total score of 0 to 1 are considered negative for BV, samples with a score of 3 to 6 are positive for BV, and samples with a score of 2 are indeterminate for BV.

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Summary of Evidence

In individuals who have signs or symptoms of BV who receive multitarget PCR testing, the evidence includes several prospective studies on technical performance and diagnostic accuracy. Relevant outcomes are test validity, symptoms, and change in disease status. Several studies have evaluated the diagnostic accuracy of multitarget PCR tests for BV, including 5 studies evaluating commercially available tests. The studies found sensitivities between 84% and 95% and specificities between 85% and 97% compared with standard methods of diagnosis. Most studies used a combination of the Amsel criteria and Nugent scoring as the reference standard. There is a lack of direct evidence on the clinical utility of PCR testing for BV (i.e., studies showing that testing leads to better patient management decisions and/or better health outcomes than current approaches). Moreover, a chain of evidence does not currently support multitarget testing because most symptomatic individuals can be diagnosed with a standard workup. The evidence is insufficient to determine that the technology results in an improvement in the net health outcomes

Ongoing and Unpublished Clinical Trials

A search of **ClinicalTrials.gov** in November 2024 did not identify any ongoing or unpublished trials that would likely influence this review.

Practice Guidelines and Position Statements

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

Guidelines or position statements will be considered for inclusion if they were issued by, or jointly by, a US professional society, an international society with US representation, or the 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 College of Obstetricians and Gynecologists

Published in 2012 and reaffirmed in 2018, the American College of Obstetricians and Gynecologists (ACOG) has produced a Practice Bulletin on the prediction of preterm birth. The Bulletin stated that BV testing is not recommended as a screening strategy in asymptomatic pregnant women at increased risk of preterm birth.[23,]

Published in 2020, the ACOG has issued a Practice Bulletin on vaginitis in nonpregnant individuals.[24,] The Bulletin made the following recommendations on the initial evaluation of individuals with symptoms of vaginitis, citing CDC guidelines:

"A complete medical history, physical examination of the vulva and vagina, and clinical testing of vaginal discharge (i.e., pH testing, a potassium hydroxide "whiff test," and microscopy) are recommended for the initial evaluation of individuals with vaginitis symptoms."

The Bulletin noted that single-swab multiplex PCR testing "may be a promising alternative to microscopy," but that its clinical utility is still under evaluation.

Centers for Disease Control and Prevention

In 2021, the Centers for Disease Control and Prevention updated its guidelines on sexually transmitted infections.[25,] Regarding the diagnosis of bacterial vaginosis (BV), the guidelines stated:

"BV can be diagnosed by....clinical criteria (i.e., Amsel's Diagnostic Criteria) or by determining the Nugent score from a vaginal Gram stain. Vaginal Gram stain, considered the reference standard laboratory method for diagnosing BV, is used to determine the relative concentration of lactobacilli ..."

The guidelines state that multiplex PCR assays are available, but noted that traditional methods of BV diagnosis, including the Amsel criteria, Nugent score, and the Affirm VP III assay, remain useful for diagnosing symptomatic BV because of their lower cost and ability to provide a rapid diagnosis. The guidelines also stated that BV nucleic acid amplification tests should be used among symptomatic women only (e.g., women with vaginal discharge, odor, or itch) because their accuracy is not well defined for asymptomatic women.

US Preventive Services Task Force Recommendations

The USPSTF (2020) recommendations on screening for BV in pregnancy[26] have stated that:

"The USPSTF recommends against screening for bacterial vaginosis in pregnant persons who are not at increased risk for preterm delivery." (Grade D recommendation)

"The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for bacterial vaginosis in pregnant persons who are at increased risk for preterm delivery." (I statement)

Medicare National Coverage

There is no national coverage determination.

Regulatory Status

Two assays are FDA cleared (BD Max and Aptima BV), and 3 (NuSwab VG, OneSwab BV Panel PCR with Lactobacillus Profiling by qPCR, SureSwab BV are laboratory-developed tests. Other laboratory developed tests may include the Vaginosis Test from NxGen MDx LLC) and the Bridge Women's Health Infectious Disease Detection test (Bridge Diagnostics).

Several of the manufacturers of the BV tests also have extensions that include other causes of vaginitis such as *Trichomonas vaginalis* and *Candidiasis* species. For example, the BD Vaginal Panel was cleared in March 2023 with the BD Max as the predicate device. It is intended to aid in the diagnosis of vaginal infections in individuals with a clinical presentation consistent with bacterial vaginosis, vulvovaginal candidiasis and trichomoniasis, as well as the Xpert Xpress MVP (Cepheid).[1]

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 Act (CLIA). Laboratories that offer laboratory-developed tests must be licensed by the CLIA for high-complexity testing.

References

1. Food and Drug Administration. BD Vaginal Panel. 510(k) K223653. **https://www.accessdata.fda.gov/cdrh_docs/pdf22/K223653.pdf**. Accessed January 15, 2025.
2. Allsworth JE, Peipert JF. Prevalence of bacterial vaginosis: 2001-2004 National Health and Nutrition Examination Survey data. Obstet Gynecol. Jan 2007; 109(1): 114-20. PMID 17197596
3. Amsel R, Totten PA, Spiegel CA, et al. Nonspecific vaginitis. Diagnostic criteria and microbial and epidemiologic associations. Am J Med. Jan 1983; 74(1): 14-22. PMID 6600371
4. Landers DV, Wiesenfeld HC, Heine RP, et al. Predictive value of the clinical diagnosis of lower genital tract infection in women. Am J Obstet Gynecol. Apr 2004; 190(4): 1004-10. PMID 15118630
5. Nugent RP, Krohn MA, Hillier SL. Reliability of diagnosing bacterial vaginosis is improved by a standardized method of gram stain interpretation. J Clin Microbiol. Feb 1991; 29(2): 297-301. PMID 1706728
6. Ison CA, Hay PE. Validation of a simplified grading of Gram stained vaginal smears for use in genitourinary medicine clinics. Sex Transm Infect. Dec 2002; 78(6): 413-5. PMID 12473800
7. Hilbert DW, Smith WL, Chadwick SG, et al. Development and Validation of a Highly Accurate Quantitative Real-Time PCR Assay for Diagnosis of Bacterial Vaginosis. J Clin Microbiol. Apr 2016; 54(4): 1017-24. PMID 26818677
8. Thompson A, Timm K, Borders N, et al. Diagnostic performance of two molecular assays for the detection of vaginitis in symptomatic women. Eur J Clin Microbiol Infect Dis. Jan 2020; 39(1): 39-44. PMID 31502121
9. Broache M, Cammarata CL, Stonebraker E, et al. Performance of a Vaginal Panel Assay Compared With the Clinical Diagnosis of Vaginitis. Obstet Gynecol. Dec 01 2021; 138(6): 853-859. PMID 34736269
10. Gaydos CA, Beqaj S, Schwebke JR, et al. Clinical Validation of a Test for the Diagnosis of Vaginitis. Obstet Gynecol. Jul 2017; 130(1): 181-189. PMID 28594779
11. Schwebke JR, Gaydos CA, Nyirjesy P, et al. Diagnostic Performance of a Molecular Test versus Clinician Assessment of Vaginitis. J Clin Microbiol. Jun 2018; 56(6). PMID 29643195
12. Aguirre-Quiñonero A, Castillo-Sedano IS, Calvo-Muro F, et al. Accuracy of the BD MAX™ vaginal panel in the diagnosis of infectious vaginitis. Eur J Clin Microbiol Infect Dis. May 2019; 38(5): 877-882. PMID 30685805
13. van den Munckhof EHA, van Sitter RL, Boers KE, et al. Comparison of Amsel criteria, Nugent score, culture and two CE-IVD marked quantitative real-time PCRs with microbiota analysis for the diagnosis of bacterial vaginosis. Eur J Clin Microbiol Infect Dis. May 2019; 38(5): 959-966. PMID 30903536
14. Food and Drug Administration. Evaluation of Automatic Class III Designation For BD Max Vaginal Panel: Decision Summary. 2016; **https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN160001.pdf**. Accessed January 15, 2025.
15. Cartwright CP, Pherson AJ, Harris AB, et al. Multicenter study establishing the clinical validity of a nucleic-acid amplification-based assay for the diagnosis of bacterial vaginosis. Diagn Microbiol Infect Dis. Nov 2018; 92(3): 173-178. PMID 29937222
16. Cartwright CP, Lembke BD, Ramachandran K, et al. Development and validation of a semiquantitative, multitarget PCR assay for diagnosis of bacterial vaginosis. J Clin Microbiol. Jul 2012; 50(7): 2321-9. PMID 22535982
17. Schwebke JR, Taylor SN, Ackerman R, et al. Clinical Validation of the Aptima Bacterial Vaginosis and Aptima Candida/Trichomonas Vaginitis Assays: Results from a Prospective Multicenter Clinical Study. J Clin Microbiol. Jan 28 2020; 58(2). PMID 31748322
18. Richter SS, Otiso J, Goje OJ, et al. Prospective Evaluation of Molecular Assays for Diagnosis of Vaginitis. J Clin Microbiol. Dec 23 2019; 58(1). PMID 31694966
19. Kusters JG, Reuland EA, Bouter S, et al. A multiplex real-time PCR assay for routine diagnosis of bacterial vaginosis. Eur J Clin Microbiol Infect Dis. Sep 2015; 34(9): 1779-85. PMID 26143346
20. Rumyantseva TA, Bellen G, Romanuk TN, et al. Utility of microscopic techniques and quantitative real-time polymerase chain reaction for the diagnosis of vaginal microflora alterations. J Low Genit Tract Dis. Apr 2015; 19(2): 124-8. PMID 25023332

21. Rumyantseva T, Shipitsyna E, Guschin A, et al. Evaluation and subsequent optimizations of the quantitative AmpliSens Florocenosis/Bacterial vaginosis-FRT multiplex real-time PCR assay for diagnosis of bacterial vaginosis. APMIS. Dec 2016; 124(12): 1099-1108. PMID 27714844

22. van der Veer C, van Houdt R, van Dam A, et al. Accuracy of a commercial multiplex PCR for the diagnosis of bacterial vaginosis. J Med Microbiol. Sep 2018; 67(9): 1265-1270. PMID 29985123

23. Committee on Practice Bulletins—Obstetrics, The American College of Obstetricians and Gynecologists. Practice bulletin no. 130: prediction and prevention of preterm birth. Obstet Gynecol. Oct 2012; 120(4): 964-73. PMID 22996126

24. Vaginitis in Nonpregnant Patients: ACOG Practice Bulletin, Number 215. Obstet Gynecol. Jan 2020; 135(1): e1-e17. PMID 31856123

25. Workowski KA, Bachmann LH, Chan PA, et al. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm Rep. Jul 23 2021; 70(4): 1-187. PMID 34292926

26. US Preventive Services Task Force. Bacterial Vaginosis in Pregnancy to Prevent Preterm Delivery: Screening. 2020; **Recommendation: Bacterial Vaginosis in Pregnant Persons to Prevent Preterm Delivery: Screening | United States Preventive Services Taskforce**. Accessed January 15, 2025.

History

Date	Comments
03/01/25	New policy, approved February 11, 2025, effective for dates of service on or after June 6, 2025, following 90-day provider notification. Policy updated with literature review through November 12, 2024. Multitarget polymerase chain reaction testing for the diagnosis of bacterial vaginosis is considered investigational. Added CPT codes 81513-81515, 0330U and 0505U to include all codes used for PCR BV testing.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.