Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 9/1/24**
(See policy history boxes for previous effective dates)

Title: Diagnosis of Vaginitis

Description/Background

Vaginitis is defined as inflammation of the vagina with symptoms of discharge, itching, and discomfort often due to a disruption of the vaginal microflora. The most common infections are bacterial vaginosis, Candida vulvovaginitis, and trichomoniasis (Sobel, 1999).[26] Other causes include vaginal atrophy in postmenopausal women, cervicitis, foreign body, irritants, and allergens (Sobel, 2023b).[27]

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.

Vulvovaginal candidiasis (VVC) is usually caused by Candida albicans but can occasionally be caused by other Candida species (CDC, 2021c).[28] It is the second most common cause of vaginitis symptoms (after BV) and accounts for approximately one-third of vaginitis cases (Sobel, 2023a; Workowski & Bolan, 2015).[29,21]

Trichomoniasis is caused by the flagellated protozoan Trichomonas vaginalis, which principally infects the squamous epithelium in the urogenital tract: vagina, urethra, and paraurethral glands (Kissinger, 2015; Sobel & Mitchell, 2023b).[30,31]

Historically, the diagnosis of vaginitis particularly BV was done with office based tests including microscopy, measurement of pH and the whiff test (amine detection) and culture when applicable. Vaginal culture is not an appropriate diagnostic method to identify BV because BV is not caused by the presence of a particular bacterial species. In the case of Trichomoniasis

culture is no longer favorable because it takes up to a week for results. For vulvovaginal candidiasis culture can be helpful for the diagnosis of complicated vulvovaginal candidiasis by identifying non albicans strains of candida. However, presently there are multiple nucleic acid amplification test (NAATs) available for the diagnosis of vaginitis. They are now an alternative method of diagnosis and have superior sensitivity and specificity for identification of involved organisms compared to office-based testing. More and more offices do not have access to microscopy, so NAATs have become a viable option.

An accurate diagnosis of vaginitis hinges on a proper evaluation. The physician must combine information from the history and physical examination with information obtained from a vaginal swab to make a diagnosis for the appropriate treatment. The gold standard for diagnosis of BV is Gram stain microscopy of vaginal secretions with Nugent scoring, but because of the skill and time needed, it is typically only used in research settings. Historically, in clinical practice, healthcare providers have had to rely on microscopy with Amsel criteria because it is a relatively fast way of diagnosing BV during an office visit despite its less diagnostic accuracy. The sensitivity and specificity of the Amsel criteria are 37%–70% and 94%–99%, respectively, compared with the Nugent score. The diagnosis of vulvovaginal candidiasis can also be made by visual examination of potassium hydroxide microscopy identifying the presence of yeast hyphae. Lastly, trichomonas can be diagnosed by visual examination of saline microscopy when motile flagellated protozoa are observed.

However, nowadays microscopy may not be readily available and physical exam may be prohibited. In this scenario a clinical diagnosis is subjective, and it is impossible to distinguish BV from other causes of vaginitis (i.e., candidiasis, trichomonas). However, with new information from molecular-based studies, there is increasingly more use of molecular techniques for the diagnosis of bacterial vaginitis. They can be performed by either clinician - or self-collected vaginal specimens with results available in <24 hours depending on the availability of the molecular diagnostic platform. Two of these assays are FDA cleared (BD Max Vaginal Panel and Aptima BV Assay) and have 90.5% sensitivity and 85.8 % specificity for BV diagnosis. The other three are laboratory-developed tests. The three laboratory-developed tests (NuSwabVG, OneSwab BV Panel PCR with Lactobacillus Profiling by qPCR, and SureSwab BV) must be internally validated before use for patient care yet have good sensitivity and specificity, like FDA-cleared assays.

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, and SureSwab BV) are laboratory-developed tests.

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

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.

Medical Policy Statement

The effectiveness and clinical utility of molecular testing to make a diagnosis of vaginitis have been established. It is a useful option when indicated.

Inclusionary and Exclusionary Guidelines

Inclusions:
The following molecular tests are considered established for the diagnosis of vaginitis:

- Nucleic Acid Amplification Test (NAAT), Polymerase Chain Reaction (PCR) testing, and Multitarget PCR (MT PCR) testing in symptomatic individuals.

Exclusions:

- All other molecular tests not meeting criteria above are considered experimental and investigational.

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

81513	81514	87510	87511	87512	87480
87481	87482	87660	87661	0352U	

Other codes (investigational, not medically necessary, etc.):

0455U

Note: Individual policy criteria determine the coverage status of the CPT/HCPCS code(s) on this policy. Codes listed in this policy may have different coverage positions (such as established or experimental/investigational) in other medical policies.

Rationale

Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.

Individuals with Signs or Symptoms of Bacterial Vaginosis

Clinical Context and Test Purpose

The purpose of multitarget polymerase chain reaction (PCR) testing in patients who have signs or symptoms of bacterial vaginosis (BV) is as a replacement to current diagnostic strategies so that appropriate treatment is selected and patient outcomes are improved.

This review evaluates whether multimarker PCR testing improves health outcomes compared with standard diagnostic tests. These tests have been proposed as a replacement for standard diagnostic tests such as Amsel criteria and Nugent score.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with signs or symptoms of BV. 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 Lactobacillus species and overgrowth of other bacteria, including *Gardnerella vaginalis*, *Mycoplasma hominis*, *Peptostreptococcus*, *Mobiluncus* species, and other anaerobic gram-negative rods. Prevalence of the condition is high, and it is asymptomatic in most cases. According to data from a nationally representative sample of women surveyed from 2001 to 2004, the prevalence of BV among women ages 14 to 49 years in the U. S. was 29%.[1] BV may be confused with nonbacterial causes of vaginitis, including *candidiasis* and *trichomoniasis*.

When symptomatic, BV is associated with characteristic signs and symptoms. The most common sign of BV is an abnormal grayish-white vaginal discharge, generally with an unpleasant, often “fishy” smell in association with mild itching or irritation.

BV resolves spontaneously in a high percentage of women, treatment for symptomatic BV is usually a course of oral antibiotics, either metronidazole or clindamycin. Antibiotic treatment results in a high rate of remission of symptoms, but recurrences are common within the first year after treatment.

Interventions

The intervention of interest is a multitarget PCR test for BV. Nucleic acid probes of DNA fragments are available to detect and quantify the bacteria in vaginal fluid samples. Bacterial DNA is extracted and amplified by PCR methods, 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 (eg, those known to be associated with BV) at the same time and is commercially available as multitarget PCR testing.

Comparators

The comparators of interest are standard diagnostic approaches such as clinical examination and microscopic examination of vaginal specimens.

Gram staining of vaginal discharge samples is the conventional microscopic method of BV diagnosis and requires preparation and analysis of the specimen in the laboratory setting. It remains the historical research criterion standard for diagnosing BV. Gram-stained samples are analyzed using the Nugent criteria or a modified version by Ison and Hay.

For the Nugent criteria, levels of 3 types of bacteria (*Lactobacillus, Gardnerella/Bacteroides*, and *Mobiluncus)* in vaginal discharge samples are estimated. Levels of *Lactobacillus* and *Gardnerella/Bacteroides* are rated on a scale from 0 to 4 based on the number of cells per field magnified at 100 times, and levels of *Mobiluncus* are rated on a scale from 0 to 2. A composite score is calculated by summing the 3 subscores, as listed in Table 1.

Table 1. Nugent Criteria

Criterion	Scoring Range
Not consistent with BV	Score of 0-3; or score of 4-6 with clue cells not present
Consistent with BV	Score of 4-6 with clue cells present; or score of at least 7

Some clinicians include a third, middle category in Nugent scoring, with a total score of 0 to 3 considered normal, 4 to 6 as intermediate/equivocal, and 7 to 10 as definite BV. BV: bacterial vaginosis.

Table 2 summarizes the simplified Ison and Hay criteria.

Table 2. Ison and Hay Criteria

Criterion	Scoring Range
Grade 1 (normal)	*Lactobacillus* morphotypes predominate
Grade 2 (intermediate)	Flora are mixed with some *Lactobacillus* morphotypes and some *Gardnerella* or *Mobiluncus* morphotypes are present
Grade 3 (bacterial vaginosis)	*Gardnerella* and/or *Mobiluncus* morphotypes predominate; *lactobacilli* morphotypes are few or absent

Table 3 summarizes the Amsel criteria.

Table 3. Amsel Criteria

Criterion
Thin, homogenous vaginal discharge
Vaginal pH greater than 4.5
Positive whiff test (fishy amine odor when 10 percent potassium hydroxide solution is added)
At least 20 percent clue cells

In clinical practice, bacterial vaginosis is diagnosed by the presence of three out of four Amsel criteria [2]

In practice, the diagnosis of BV can be made based on the presence of at least 3 Amsel criteria (characteristic vaginal discharge, elevated pH, clue cells, fishy odor),[2] which is simple and has a sensitivity of over 90% and specificity of 77% compared with Gram stain.[3]

More specifically, vaginal discharge is characterized as homogeneous, thin, and whitish-gray; clue cells are squamous epithelial cells that normally have a sharply defined cell border but in BV, have bacteria adherent to their surfaces and appear to be “peppered” with bacteria; pH of vaginal fluid greater than 4.5; and a “fishy” odor of vaginal discharge before or after addition of potassium hydroxide 10%.

Both comparator diagnostic methods (ie, clinical diagnosis using the Amsel criteria and laboratory diagnosis using Nugentor Ison and Hay criteria) [4,5] have subjective components and, therefore, may be imprecise. Moreover, Gram stain examination is time-consuming, requires substantial training, and it is difficult to determine an appropriate clinical response for intermediate scores. The 2 methods of diagnosis can also be used in combination to increase diagnostic accuracy.

Outcomes

The primary outcomes of interest are test validity, symptom resolution, and cure rate (absence of symptoms and normal vaginal flora).

Study Selection Criteria

For the evaluation of the clinical validity of the tests, studies that met the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores)
- Included a suitable reference standard (Amsel, Nugent, or Hay/Ison criteria)
- Patient/sample clinical characteristics were described
- Patient/sample selection criteria were described
- Included a validation cohort separate from the development cohort.

A publication by Hilbert et al (2016), funded through Medical Diagnostics Laboratory and evaluating markers in that laboratory’s BV Panel, and Gaspar et al (2019) were not selected because they did not include a validation cohort independent of the development cohort.[6] Thompson et al (2020) was not included because it did not include a suitable reference standard.[7] Other publications were not included because they analyzed data previously reported in Gaydos et al (2017).[8,9]

Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

There are no published studies on the diagnostic accuracy of the SureSwab test or the GenPath test, but the information is available on the diagnostic accuracy of the BD Max test, the Aptima BV test, and the NuSwab offered by LabCorp.

The characteristics of the studies are shown in Table 4 and the results are shown in Table 5. The studies are briefly described following the tables.

Table 4. Characteristics of Clinical Validity Studies Assessing BV Tests

Study	Study Population	Design	Reference Standard	Threshold for Positive Index Test	Timing of Reference and Index Tests	Blinding of Assessors
BD Max						
Aguirre-Quiñonero (2019)[10,]	Women ≥ 14 years old with or without symptoms in Spain; median age, 39 years; 5% pregnant	Prospective, unclear whether consecutive, single-center	Combination of Hay's criteria, the presence of clue cells, and a predominant growth of G. vaginalis; independent scoring by 2 microbiologists	NR	Simultaneous	Yes
van den Munckhof (2019)[11,]	Women with symptoms of BV visiting a single outpatient clinic in the Netherlands between January and July 2015 and additional asymptomatic women from the same clinic; mean age, 34 years; majority of 'European origin'	Prospective, unclear whether consecutive, single-center	Microbiota analysis	≤47% relative abundance of Lactobacillus and mainly anaerobes	Simultaneous	Yes
FDA decision Summary [12]; Gaydos (2017) [8]	Women with symptoms of BV or vaginitis; samples collected in 2015; 53% African American; 25% white; age range, 18-29 y	Prospective, consecutive, multicenter	Nugent score; indeterminate by Nugent diagnosed with Amsel criteria	Automatic reporting based on algorithmic analysis of molecular DNA detection of lactobacilli and bacteria associated with BV	Simultaneous	Yes

NuSwab						
Cartwright (2018)[13]	Women with symptoms of vaginitis or BV; samples collected in 2016-2017; 34% African American, 38% white, age range, 18-49 y	Prospective, multicenter	Nugent score; indeterminate by Nugent diagnosed with Amsel criteria	Score of 3-6 indicates presence of BV	Simultaneous	Yes
Cartwright (2012)[14]; validation cohort	Women evaluated at 3 clinics in Alabama in 2011; 87% African American, 13% (50/402) white	Prospective, selection criteria not described	Nugent score; indeterminate by Nugent diagnosed with Amsel criteria	Score of 3-6 indicates presence of BV	Simultaneous	Yes
Aptima BV						
Schwebke (2020)[15]	Women ≥ 14 years old with symptoms of vaginitis evaluated at 21 US sites between June and October 2018; 50.2% African American, 22% white; mean age, 35.3 years	Prospective, multicenter	Nugent consensus score, indeterminate by Nugent diagnosed with modified Amsel criteria	Nugent score ≥ 7 indicates presence of BV	Simultaneous	Yes
Richter (2019)[16]	Women with symptoms of vaginitis evaluated at Cleveland Clinic between May and December 2018	Prospective, selection criteria not described, single-center	Nugent score; indeterminate by Nugent diagnosed with ≥2 Amsel criteria	Nugent score ≥ 7 indicates presence of BV	Simultaneous	**Yes**

BV: bacterial vaginosis; FDA: U.S. Food and Drug Administration; NR: not reported.

Table 5. Results of Clinical Validity Studies Assessing BV Tests

Study	Initial N	Final N	Excluded Samples	Prevalence of Condition, %	Clinical Validity (95% Confidence Interval), %			
					Sensitivity	Specificity	PPV	NPV
BD Max								
Aguirre-Quiñonero (2019)[10]	1000	1000	13 results were reported to be invalidated; unclear how these were coded for analysis	19.3	89.8 (85.0 to 93.1)	96.5 (95.1 to 97.6)	86.9 (81.9 to 90.7)	97.3 (96.0 to 98.2)
van den Munckhof (2019)[11]	80 women; designed for 2 visits per	115 for either visit; 63 in visit 1	14 women did not attend visit 2; data from 31 visits excluded because of insufficient sample volume or	31				

	women		indeterminate outcome by at least 1 of the methods					
Amsel criteria, Visit 1					70.8 (50.8 to 85.1)	92.3 (79.7 to 97.4)	85.0 (64.0 to 94.8)	83.7 (70.0 to 91.9)
Nugent score, Visit 1					70.8 (50.8 to 85.1)	100 (91.0 to 100)	100 (81.6 to 100)	84.8 (71.8 to 92.4)
BD Max, Visit 1					66.7 (46.7 to 82.0)	97.4 (86.8 to 99.6)	94.1 (73.0 to 99.0)	82.6 (69.3 to 90.9)
FDA decision summary[12]; Gaydos (2017)[8]	1763	1559[a] 1582[b]	Protocol issues: withdrawn (13), informed consent process incorrect (7), asymptomatic patient enrolled (2), and >1 specimen obtained for same patient (1) TPI: reference standard results not compliant with protocol (130); index test not compliant with protocol (8); index test results not reported (71)	56	90.5 (88.3 to 92.2)[a] 90.7 (88.6 to 92.5)[b]	85.8 (83.0 to 88.3)[a] 84.5 (81.6 to 87.0)[b]	89.0 (NR)[a] 88.1 (NR)[b]	87.7 (NR)[a] 87.8 (NR)[b]
NuSwab								
Cartwright (2018)[13]	1595	1484	Incomplete testing (16); test indeterminate (95)	34	96 (94 to 98)	90 (88 to 92)	83 (81 to 86)	98 (97 to 99)
Cartwright (2012)[14]; validation cohort	227	213	Indeterminate (14)	49	99 (NR)	91 (NR)	NR	NR
Aptima BV								

Schwebke (2020)[15]	1519	1413[a] 1405[b]	Ineligibility (17); test not evaluable (58); test not available (26); indeterminate score could not be resolved (1)	49.5	95.0 (93.1 to 96.4)[a] 97.3 (95.8 to 98.2)[b]	89.6 (87.1 to 91.6)[a] 85.8 (83.1 to 88.2)[b]	95.6 (93.9 to 96.9)[a] 93.3 (91.4 to 94.9)[b]	95.9 (94.1 to 97.2)[a] 97.7 (96.3 to 98.7)[b]
Richter (2019)[16]	111	111	-	40.5	84.4 (70.9 to 92.6)	86.3 (75.9 to 92.9)	80.9 (67.2 to 89.8)	89.1 (78.8 to 94.9)

BV: bacterial vaginosis; FDA: U.S. Food and Drug Administration; NPV: negative predictive value; NR: not reported; PPV: positive predictive value; TPI: test performance issues. a Clinician. b Self.

BD Max Test

The U.S. Food and Drug Administration (FDA) decision summary and Gaydos et al (2017) for the BD Max test includes a description of a prospective clinical diagnostic accuracy study.[12,8] The study included 1,763 women with symptoms of BV or vaginitis. Both clinician-collected and self-collected vaginal swabs were obtained and were analyzed independently. A total of 1,559 (88%) clinician-detected and 1582 (90%) self-detected samples were available for analysis.

Aguirre-Quiñonero et al (2019) describes the results of the BD MAX in 1000 vaginal swabs from women ≥ 14 years old(median age, 33 years) presenting with or without symptoms from a single-institution in Spain.[10] Consistent with the inclusion of asymptomatic women, the prevalence of BD was lower in this study at 19%.

van den Munckhof (2019) compared BD MAX to Amsel and Nugent with microbiota analysis as a reference standard in 60 symptomatic women and 20 women treated for other reasons from a single-institution in the Netherlands.[11] Samples were collected at 2 visits approximately 4 weeks apart. It is unclear what treatments women received between the visits. The performance characteristics for samples collected at visit 1 are included in Table 4. The authors used microbiota analysis as the reference standard and therefore performance characteristics of BD MAX may not be comparable to other studies. The confidence intervals for the performance characteristics of Amsel and BD MAX were highly overlapping

NuSwab

Cartwright et al (2012) published data on a multitarget semiquantitative PCR test including 3 organisms: *Atopobiumvaginae*, *Megasphaera* type 1, and *BVAB2*.[14] The investigators used separate samples for the development and validation phases and compared the diagnostic accuracy of the multitarget panel with an accepted reference standard. The patient population consisted of 402 women presenting at a clinic for sexually transmitted infections (n=299) or a personal health clinic (n=103). Samples from 169 women were included in the development phase, of which 108 (64%)were positive for BV and 61 (36%) were negative for BV. In the validation phase, the multitarget PCR test was assessed using an additional 227 samples. Results were similar in Cartwright et al (2018), which reported on a multicenter study of1579 women of whom 538 were positive and 1041 were negative for BV.[13] In this publication, the authors proposed an α-diversity score generated from next-generation sequencing that could be used to resolve discordant PCR and Nugent/Amsel results.

Aptima BV
Schwebke et al (2020) compared the Aptima BV assay (Hologic, Inc.) to Nugent score as reference standard in 1,417symptomatic women.[15] Both clinician- and patient-collected swabs were assessed. Clinicians utilized modified Amsel criteria for the resolution of indeterminate Nugent scores. Performance characteristics for evaluable samples are included in Table 4.

Richter et al (2019) compared the accuracy of testing with Aptima BV, Hologic Analyte Specific Reagent, and the direct-probe BD Affirm test to Nugent score as the reference standard in 111 symptomatic women.[16] Modified Amsel criteria were used for the resolution of indeterminate Nugent scores. Performance characteristics for the commercially-marketed nucleic acid amplification Aptima BV test are included in Table 4.

Section Summary: Clinically Valid
Several studies have evaluated the diagnostic accuracy of multitarget PCR tests for BV, including 5 studies evaluating commercially available tests. The studies found sensitivities of 84% to 95% and specificities of 85% to 97%, compared with a reference standard combination of the Amsel criteria and Nugent or Hay score. Several studies generally included symptomatic women; 2 studies included symptomatic and asymptomatic women.

Clinically Useful
A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

Direct Evidence
Direct evidence of clinical utility is provided by studies comparing health outcomes for patients managed with and without the test. Preferred evidence comes from randomized controlled trials.

Chain of Evidence
Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Diagnostic accuracy studies have found that multitarget PCR tests for BV have a sensitivity ranging from approximately 90% to 95% and specificity ranging from approximately 85% to 90% compared with a reference standard combining Amsel criteria and Nugent score. The studies have not reported the concurrent measurement of the diagnostic accuracy of Amsel criteria alone.

Section Summary: Clinically Useful
A useful test provides information to make a clinical management decision that improves the net health outcome. To improve the net health outcome, the multitarget PCR tests should either improve diagnostic accuracy (sensitivity, specificity) or have similar diagnostic accuracy with improvements in other health outcomes such as patient burden or timeliness of diagnosis.

An accurate diagnosis of vaginitis hinges on a proper evaluation. The physician must combine information from the history and physical examination with information obtained from a vaginal swab to make a diagnosis for the appropriate treatment. The gold standard for diagnosis of BV

is Gram stain microscopy of vaginal secretions with Nugent scoring, but because of the skill and time needed, it is typically only used in research settings. Historically, in clinical practice, healthcare providers have had to rely on microscopy with Amsel criteria because it is a relatively fast way of diagnosing BV during an office visit despite its less diagnostic accuracy. The sensitivity and specificity of the Amsel criteria are 37%–70% and 94%–99%, respectively, compared with the Nugent score. The diagnosis of vulvovaginal candidiasis can also be made by visual examination of potassium hydroxide microscopy identifying the presence of yeast hyphae. Lastly, trichomonas can be diagnosed by visual examination of saline microscopy when motile flagellated protozoa are observed.

However, nowadays microscopy may not be readily available and physical exam may be prohibited. In this scenario a clinical diagnosis is subjective, and it is impossible to distinguish BV from other causes of vaginitis (i.e., candidiasis, trichomonas). However, with new information from molecular-based studies, there is increasingly more use of molecular techniques for the diagnosis of vaginitis. They can be performed on either by clinician or self-collected vaginal specimens with results available in <24 hours depending on the availability of the molecular diagnostic platform.

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. 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. However, the NAAT are noninferior options that have demonstrated clinical utility and validity. The evidence available is sufficient to determine that the technology results in an improvement in the net health outcomes.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

The purpose of the remaining sections in Supplemental Information is to provide reference material regarding existing practice guidelines and position statements, U.S. Preventive Services Task Force Recommendations and Medicare National Coverage Decisions and registered, ongoing clinical trials. Inclusion in the Supplemental Information does not imply endorsement and information may not necessarily be used in formulating the evidence review conclusions.

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.

Centers for Disease Control and Prevention

In 2021, the Centers for Disease Control and Prevention updated its guidelines on sexually transmitted infections.[1] 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 (eg, women with vaginal discharge, odor, or itch) because their accuracy is not well defined for asymptomatic women.

American College of Obstetricians and Gynecologists

Published in 2020 and reaffirmed in 2022, the ACOG guidelines state given the limited diagnostic accuracy of microscopy, use of newer FDA-approved commercially available diagnostic tests may offer a needed option to improve diagnosis. Per the updated ACOG guidance, these tests may be considered when microscopy is not available. These new diagnostic tests use molecular markers of BV to detect specific bacterial nucleic acids. Two main types of commercial molecular assays for diagnosing BV are available in the United States–direct DNA probe and nucleic acid amplification assays.[22]

Table 6. Updated recommendations for diagnosis of bacterial vaginosis (Level A evidence *)

Recommendation	Alternative recommended treatments
Use Amsel clinical criteria or Gram stain with Nugent scoring	FDA-approved commercial tests

*Level A, based on good and consistent scientific evidence

National Institute for Health and Care Excellence

The National Institute for Health and Care Excellence (NICE; 2008) updated its clinical guideline on antenatal care for uncomplicated pregnancies in 2019.[23] Regarding the screening of asymptomatic bacterial vaginosis, the guidelines stated:

"Pregnant women should not be offered routine screening for bacterial vaginosis because the evidence suggests that the identification and treatment of asymptomatic bacterial vaginosis does not lower the risk of preterm birth and other adverse reproductive outcomes."

Ongoing and Unpublished Clinical Trials

A search of ClinicalTrials.gov in November 2022 did not identify any ongoing or unpublished trials that would likely influence this review.

U.S. Preventive Services Task Force Recommendations
The USPSTF (2020) recommendations on screening for BV in pregnancy [24] 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)

Government Regulations

National:
There is no national coverage determination on this testing.

Local:
There is no local coverage determination on this testing.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

Identification of Microorganisms Using Nucleic Acid Probes

References

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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through April 3, 2024, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
9/1/21	N/A		Joint policy established – policy was tabled at June 2021 JUMP.
9/1/23	6/26/23		• New existing policy – policy was tabled at June 17, 2021 JUMP. Need additional offline discussion re: code reimbursement and direction for policy. • Jump policy status changed from E/I to EST. • Jump policy diverge from BCBSA policy – 2.04.127 – Multitarget Polymerase Chain Reaction Testing for Diagnosis of Bacterial Vaginosis. BCBSA states: Multitarget polymerase chain reaction testing for the diagnosis of bacterial vaginosis is considered investigational. BCBSA updated policy on 12/8/22. • This policy will replace the IMP policy " Diagnosis of Vaginitis (including Bacterial Vaginosis, Trichomonas and Candidiasis) using Multi-target PCR Testing". • Vendor: Avalon – policy status aligns with Avalon policy – M2057 – Diagnosis of Vaginitis including Multi-target PCR Testing • Added code 0352U as E/I - in alignment with Avalon's code update Q1 CAB policy executive summary located in the Prism portal. Post JUMP changes/comments: Note: Avalon states in their Q1 CAB policy executive summary located in the Prism portal that BD Max vaginal panel which uses CPT code 81514 does not meet coverage criteria. They also state NuSwab VG which also tests for Chlamydia (87491) and

			Gonorrhea (87591) does not meet coverage criteria. Avalon's rationale for not covering these tests are due to the NAAT panel testing is designed to detect more than one type of vaginitis. Nu Swab VG in particular utilizes CPT code 87798 and 87801. However; we cover individual organisms to identify causes of vaginitis and sexually transmitted infections by nucleic acid probe technology with exception to 87798 and 87801 (which we have as E/I in a related policy Identification of Microorganisms Using Nucleic Acid Probes). Therefore a variance may need to be created with Avalon. (ky)
9/1/24	6/11/24		• Routine maintenance • Moved code 0352U from E/I to EST – this is in alignment with Avalon policy – M2057 – Diagnosis of Vaginitis Redlined version dated 3/6/24. This JUMP policy already covers code CPT code 81514 for the BD MAX™ Vaginal Panel. The FDA has determined the Cepheid Xpert® Xpress MVP code 0352U and the BD MAX™ Vaginal Panel 81514 to be substantially equivalent which supports equivalent coverage in this policy. • Added PLA code 0455U as E/I effective 7/1/24 per code update. • Updated the MPS, Inclusions and Exclusions section. • Title changed **from** Diagnosis of Vaginitis (including Bacterial Vaginosis, Trichomonas and Candidiasis) using Multi-target PCR Testing **to** Diagnosis of Vaginitis.

			• Vendor Managed: Avalon policy – M2057 – Diagnosis of Vaginitis Redlined version dated: 3/6/24 (ky)

Next Review Date: 2nd Qtr, 2025

Pre-Consolidation Medical Policy History

Original Policy Date	Comments
BCN:	Revised:
BCBSM:	Revised:

BLUE CARE NETWORK BENEFIT COVERAGE POLICY: DIAGNOSIS OF VAGINITIS

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered; criteria apply.
BCNA (Medicare Advantage)	Refer to the Medicare information under the Government Regulations section of this policy.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate, and certificate riders.

- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.