Medical Policy
Multitarget Polymerase Chain Reaction Testing for Diagnosis of Bacterial Vaginosis

Table of Contents
- Policy: Commercial
- Policy: Medicare
- Authorization Information
- Coding Information
- Description
- Policy History
- Information Pertaining to All Policies
- References

Policy Number: 711
BCBSA Reference Number: 2.04.127
NCD/LCD: NA

Related Policies
- Identification of Microorganisms Using Nucleic Acid Probe, #555

Policy
Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity
Medicare HMO BlueSM and Medicare PPO BlueSM Members

Multitarget polymerase chain reaction (PCR) testing for diagnosis of bacterial vaginosis is considered INVESTIGATIONAL.

Prior Authorization Information
Pre-service approval is required for all inpatient services for all products. See below for situations where prior authorization may be required or may not be required for outpatient services.
Yes indicates that prior authorization is required.
No indicates that prior authorization is not required.
N/A indicates that this service is primarily performed in an inpatient setting.

<table>
<thead>
<tr>
<th>Outpatient</th>
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<tr>
<td>Commercial Managed Care (HMO and POS)</td>
<td>This is not a covered service.</td>
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<td>Commercial PPO and Indemnity</td>
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<td>Medicare PPO BlueSM</td>
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CPT Codes / HCPCS Codes / ICD Codes
Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.
Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

**CPT codes**
There is no specific CPT code for this testing.

**Description**
BV is a condition caused by an imbalance in the normal bacteria vaginal flora. It is a common disorder, especially in women of reproductive age. While there is no single known etiologic agent, there is a shift in vaginal flora that involves a depletion of Lactobacillus species and overgrowth of other bacteria, including *G. vaginalis, Mycoplasma hominis, Peptostreptococcus, Mobiluncus species,* and various 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 in 2001 to 2004, the prevalence of BV among women ages 14 to 49 in the United States is 29%.1 BV is often confused with nonbacterial causes of vaginitis, including Candida (i.e., yeast infection, caused by a fungus) and Trichomonas (caused by a parasite).

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. Some women experience mild itching. In addition, BV may be a risk factor for conditions such as preterm delivery and spontaneous abortion in pregnant women, pelvic inflammatory disease, HIV and other sexually transmitted diseases. However, causality is difficult to demonstrate, especially in this type of situation where these associations may be spurious due to confounding, because both BV and HIV infection are related to multiple sexual partners. Because of potential risks during pregnancy, treatment of BV is indicated for symptomatic pregnant women. However, national organizations do not recommend routine screening for BV among pregnant women, and national guidelines do not address screening of nonpregnant women.

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. Probiotics, alone or in conjunction with antibiotics, are also used but their efficacy in improving cure rates or preventing recurrences is not well-characterized.

**Laboratory- and Examination-Based Methods of Diagnosis**
BV can be diagnosed in the primary care setting based on patient-reported symptoms, clinical findings during vaginal examination and analysis of vaginal discharge. Office-based analysis of vaginal discharge includes a wet mount preparation using saline, an odor (“whiff”) test to detect amines before or after the addition of 10% potassium hydroxide (KOH) and a test of the pH level. Clinical diagnosis generally involves applying the Amsel criteria, which requires 3 of the following 4 to be present in order for a diagnosis of BV to be confirmed:

- vaginal discharge that is homogeneous, thin and whitish gray discharge;
- presence of clue cells on microscopic examination. These 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;
- a fishy odor of vaginal discharge before or after addition of 10% KOH

In most cases of uncomplicated BV, clinical and microscopic examination of the discharge is sufficient to make a presumptive diagnosis using the Amsel criteria. For patients with a moderate to high probability of BV following clinical and microscopic exam, an empiric treatment trial can be prescribed. Patients who respond to empiric treatment do not require further workup.

A subset of women may require more definitive tests to determine whether BV is present. These include women with unusual or unexpected signs and symptoms and those in whom it is not possible to exclude...
other etiologies with certainty. In these cases, laboratory tests are available to assist with making a definitive diagnosis. Gram staining of vaginal discharge samples is the conventional laboratory method of BV diagnosis, and many experts consider it to be the criterion standard for diagnosing BV. Samples are analyzed using criteria such as the Nugent criteria, or a modified version by Ison and Hay.

A limitation of both of the above diagnostic methods (ie, clinical diagnosis using Amsel criteria and laboratory diagnosis using Nugent, or Ison and Hay criteria) is that they have subjective components and therefore may be imprecise. Gram stain examination, moreover, is time-consuming and requires substantial training, and it 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.

Various commercial tests are also available to 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.

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

**Nucleic Acid Probes**
DNA probes have been developed and are now available to directly detect and quantify the bacteria in vaginal fluid samples. Bacterial DNA is extracted and amplified by PCR methods, using either universal or specific primers. Bacteria are then identified by characterizing their ribosomal DNA (rDNA) sequences. The specific target is typically the ribosomal subunit of the 16SrRNA gene, which is present in all bacteria. The 16SrRNA genes can be amplified by PCR using universal and/or specific primers. The amplified product is then quantified to give an assessment of how many microorganisms are present. In addition to being able to more accurately diagnose health conditions, use of these new techniques has resulted in the identification of previously unrecognized cultivation-resistant organisms in vaginal fluid.

**Proposed Multitarget PCR Test**
At least 1 commercially available product measures multiple organisms using PCR technology for the diagnosis of BV. This product, SureSwab (Quest Diagnostics) tests for Lactobacillus species, *G vaginalis*, *Atopobium vaginae*, and Megasphaera species. *A vaginae* is a bacterium species named in 1999 and subsequently, using molecular-based techniques, has been found to be more common in women with BV than women with normal flora.

The SureSwabTotal test involves obtaining vaginal swab specimens and extracting total DNA. Next, real-time PCR is used to quantitate the 4 types of bacteria. Results are reported as log cells per mL for each organism (concentrations of all lactobacilli species are reported together).

In addition, the company provides summary interpretive information based on the findings from all tests. Interpretive information accompanying test results classify findings into 1 of the following 3 categories:

- Not supportive of BV diagnosis:
  - Presence of Lacobacillus species, G. vaginalis levels <6.0 log cells/mL and absence of A. vaginae and Megasphaera species; or
  - Absence of Lactobacillus species, G. vaginalis levels <6.0 log cells/mL and absence of A. vaginae and Megasphaera species; or
  - Absence of all targeted organisms.

- Equivocal:
  - Presence of Lactobacillus species, plus G. vaginalis at least 6.0 log cells/mL and/or presence of A. vaginae and/or Megasphaera species.
Supportive of BV diagnosis:
- Presence of Lacobacillus species, G. vaginalis levels at least 6.0 log cells/mL and presence of A. vaginae and/or Megasphaera species.

Quest Diagnostics also offers a SureSwab bacterial vaginosis/vaginitis test that includes the bacterial vaginosis test, previously described, and tests for Trichomonas vaginalis and 4 Candidiasis species.

Summary
Bacterial vaginosis (BV) is a common medical condition resulting from an imbalance in the normal vaginal flora. Although 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 diagnosis BV. This test may improve outcomes if it is a more accurate and reliable method to diagnose BV, especially in symptomatic women with an indeterminate diagnosis.

No published evidence was available on the diagnostic accuracy of any commercially available multitarget PCR test compared with alternatives. There is some evidence that PCR tests for individual bacterial genera/species and combinations of these organisms may have high sensitivity and specificity for diagnosing BV, but it is not possible to determine the true diagnostic accuracy with certainty due to limited research. Moreover, approaches to using PCR in the various studies differ, and there no generally accepted cutoffs for the levels of novel species such as Atopobium vaginae. Furthermore, studies were not conducted with the most clinically relevant target population, symptomatic women with indeterminate diagnoses after standard workup.

There is also a lack of evidence on the clinical utility of PCR testing for BV, ie, studies showing that testing leads to better patient management decisions and/or better health outcomes. Studies of diagnostic accuracy alone are inadequate, especially because most symptomatic women can be diagnosed with a standard workup and/or a trial of empiric therapy. Screening asymptomatic women or screening of all pregnant women is not recommended by national organizations. Therefore, multitarget PCR tests for the diagnosis of for BV are considered investigational.

Policy History

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<td>New references added from BCBSA National medical policy.</td>
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<td>1/2016</td>
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Information Pertaining to All Blue Cross Blue Shield Medical Policies
Click on any of the following terms to access the relevant information:
- Medical Policy Terms of Use
- Managed Care Guidelines
- Indemnity/PPO Guidelines
- Clinical Exception Process
- Medical Technology Assessment Guidelines

References