FEP Medical Policy Manual

FEP 2.04.127 Multitarget Polymerase Chain Reaction Testing for Diagnosis of Bacterial Vaginosis

Effective Policy Date: April 1, 2021

Original Policy Date: December 2014

Related Policies:

2.04.10 - Identification of Microorganisms Using Nucleic Acid Probes

Multitarget Polymerase Chain Reaction Testing for Diagnosis of Bacterial Vaginosis

Description

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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.

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 (eg, those known to be associated with BV) at the same time and is commercially available as multitarget PCR testing.

(Evidence review 2.04.10 addresses the use of nucleic acid probes to detect other microorganisms of clinical significance. This policy includes identification of *G. vaginalis* which is a single microorganism associated with BV.)

Proposed Multitarget PCR Tests

The SureSwab Total (Quest Diagnostics) 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 1 of the following 3 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 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 presence of *A. vaginae and*/or *Megasphaera* species.

Another product, 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 U.S. 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 3 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.

Several of the manufacturers of the BV tests also have extensions that include other causes of vaginitis such as *Trichomonas vaginalis* and *Candidiasis* species.

OBJECTIVE

The objective of this evidence review is to evaluate whether the technical performance, diagnostic accuracy, and clinical utility of multitarget polymerase chain reaction testing improve net health outcomes in patients with signs or symptoms of BV.

POLICY STATEMENT

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

POLICY GUIDELINES

None

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

FDA REGULATORY STATUS

In October 2016, the U.S. Food and Drug Administration completed a review of a de novo request for classification of the BD Max™ Vaginal Panel (Becton, Dickinson). The test was granted class II designation, marketing authorization, and is indicated for the direct detection of DNA targets from bacteria associated with bacterial vaginosis (DEN160001). In 2019, the Aptima BV Assay (Hologic, Inc.) received 510(k) clearance (K190452) with the BD Max as the predicate device. Product code: PQA, NSU, PMN.

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.

RATIONALE

Summary of Evidence

In individuals who have signs or symptoms of bacterial vaginosis (BV) who receive multitarget polymerase chain reaction (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 (ie, 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 women 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.

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 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 2015, the Centers for Disease Control and Prevention updated its guidelines on sexually transmitted diseases.[21.] Regarding the diagnosis of bacterial vaginosis (BV), the guidelines stated:

"BV can be diagnosed by....clinical criteria (i.e., Amsel"s Diagnostic Criteria) or Gram stain. A Gram stain (considered the gold standard laboratory method for diagnosing BV) is used to determine the relative concentration of lactobacilli ... PCR [polymerase chain reaction] has been used in research settings for the detection of ... organisms associated with BV, but evaluation of its clinical utility is still underway. Detection of specific organisms might be predictive of BV by PCR. Additional validation is needed...."

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.[22.]

Published in 2020, the ACOG has issued a Practice Bulletin on vaginitis in nonpregnant patients.[23.] The Bulletin made the following recommendations on the initial evaluation of patients with symptoms of vaginitis, citing CDC guidelines:

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

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.[24.] 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."

U.S. Preventive Services Task Force Recommendations

The USPSTF (2020) recommendations on screening for BV in pregnancy[25] 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. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

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POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

Date	Action	Description
December 2014	New policy	Policy created with literature review. Multitarget polymerase chain reaction (PCR) testing for diagnosis of bacterial vaginosis is considered investigational.
March 2019	Replace policy	Policy updated with literature review through October 1, 2018; references 3- 7, 9-10 and 15-16 added; reference 18 updated. Policy statement unchanged.
March 2020	Replace policy	Policy updated with literature review through October 18, 2019; references added. Policy statement unchanged.
March 2021	Replace policy	Policy updated with literature review through September 21, 2020; references added. Policy statement unchanged.