Diagnosis of Vaginitis

Policy Number: AHS – M2057 – Diagnosis of Vaginitis	Prior Policy Name and Number, as applicable: AHS – M2057 – Diagnosis of Vaginitis including Multi-target PCR Testing
Effective Date: 09/01/2024	

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I. Policy Description

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). Other causes include vaginal atrophy in postmenopausal women, cervicitis, foreign body, irritants, and allergens (Sobel, 2023b).

Bacterial vaginosis (BV) is characterized by a shift in microbial species from the normally dominant hydrogen-peroxide producing *Lactobacillus* species to *Gardnerella vaginalis* and anaerobic commensals (Eschenbach et al., 1989; Hill, 1993; Lamont et al., 2011; Ling et al., 2010; Sobel, 2023a).

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

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).

II. Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request. Specifications pertaining to Medicare and Medicaid can be found in the "Applicable State and Federal Regulations" section of this policy document.

1) For individuals with symptoms of vaginitis, testing of pH, testing for the presence of amines, saline wet mount, hydrogen peroxide (KOH) wet mount, and microscopic examination of vaginal fluids **MEETS COVERAGE CRITERIA**.

2) For individuals with symptoms of vaginitis, direct probe DNA-based identification of *Gardnerella*, *Trichomonas*, and *Candida* (e.g., BD Affirm™ VPIII) **MEETS COVERAGE CRITERIA**.

3) For individuals with clinical signs and symptoms of vaginitis but with negative findings on wet-mount preparations and a normal pH test, vaginal cultures for *Candida* species for the diagnosis of vulvovaginal candidiasis **MEET COVERAGE CRITERIA**.

4) For individuals with symptoms of vaginitis, measurement of sialidase activity in vaginal fluid for the diagnosis of bacterial vaginosis **MEETS COVERAGE CRITERIA**.

5) For individuals with symptoms of vaginitis, nucleic acid amplification testing (NAAT) or polymerase chain reaction (PCR)-based identification of *Trichomonas vaginalis* **MEETS COVERAGE CRITERIA**.

6) For individuals with risk factors for trichomoniasis (new or multiple partners; history of sexually transmitted infections (STIs), especially HIV; exchange of sex for payment; incarceration; injection drug use), screening for *Trichomonas* **MEETS COVERAGE CRITERIA**.

7) For individuals with complicated vulvovaginal candidiasis (VVC), polymerase chain reaction (PCR) based identification of *Candida* to confirm clinical diagnosis and identify non-albicans *Candida* **MEETS COVERAGE CRITERIA**.

8) For individuals with symptoms of bacterial vaginosis (BV), NAAT specific to the diagnosis of BV (e.g., Aptima® BV; OneSwab® BV Panel PCR with Lactobacillus Profiling by qPCR; SureSwab® Advanced BV, TMA) and single or multitarget PCR testing for the diagnosis of BV **MEETS COVERAGE CRITERIA**.

9) NAAT panel testing designed to detect more than one type of vaginitis (VVC, BV, and/or trichomoniasis; e.g., BD MAX™ Vaginal Panel, NuSwab® VG, Xpert® Xpress MVP) **MEETS COVERAGE CRITERIA**.

10) For asymptomatic individuals, including asymptomatic pregnant individuals at an average or high risk for premature labor, screening for trichomoniasis and bacterial vaginosis **DOES NOT MEET COVERAGE CRITERIA**.

The following does not meet coverage criteria due to a lack of available published scientific literature confirming that the test(s) is/are required and beneficial for the diagnosis and treatment of an individual's illness.

11) For individuals with symptoms of vaginitis, rapid identification of *Trichomonas* by enzyme immunoassay **DOES NOT MEET COVERAGE CRITERIA**.

12) Testing for microorganisms involved in vaginal flora imbalance and/or infertility using molecular-based panel testing **DOES NOT MEET COVERAGE CRITERIA**.

13) All other tests for vaginitis not addressed above **DO NOT MEET COVERAGE CRITERIA**.

III. Table of Terminology

Term	Definition
AAFP	American Academy of Family Physicians
ACOG	American College of Obstetrics and Gynaecology
ASM	American Society for Microbiology
AV	Aerobic vaginitis
BV	Bacterial vaginosis
BVAB	BV associated bacteria
CDC	Centers for Disease Control and Prevention
CLIA	Clinical Laboratory Improvement Amendments
CMS	Centers for Medicare and Medicaid
DNA	Deoxyribose nucleic acid
DOS	Date of service
HIV	Human Immunodeficiency Virus
IDSA	Infectious Diseases Society of America
LDTs	Laboratory developed tests
MDL	Medical Diagnostic Laboratories
NAAT	Nucleic acid amplification testing
NPV	Negative predictive value
OADS	Office of the Associate Director for Science
PCR	Polymerase chain reaction
PMNs	Polymorphonuclear cells
PPV	Positive predictive value
RTPCR	Real-time polymerase chain reaction
SOGC	Society Of Obstetricians and Gynaecologists of Canada
STDs	Sexually transmitted diseases
TMA	Transcription-mediated amplification
TV	Trichomonas vaginalis
USPSTF	U.S. Preventive Services Task Force
VVC	Vulvovaginal candidiasis

IV. Scientific Background

Vaginitis is characterized by several symptoms including odor, itching, abnormal vaginal discharge, burning and irritation; this inflammatory ailment is considered the most common gynecologic diagnosis in primary care as most women experience vaginitis at least once in their lives (Paladine & Desai, 2018). A diagnosis of vaginitis can be given based on a combination of symptoms, physical examination, and office or laboratory-based testing methods.

The squamous epithelium of the vagina in premenopausal women is rich in glycogen, a substrate for lactobacilli, which create an acidic vaginal environment (pH 4.0 to 4.5). This acidity helps maintain the normal vaginal flora and inhibits growth of pathogenic organisms. Disruption of the normal ecosystem by menstrual cycle, sexual activity, contraceptive, pregnancy, foreign bodies, estrogen level, sexually transmitted diseases, and use of hygienic products or antibiotics can lead to development of vaginitis. Bacterial vaginosis (BV), vulvovaginal candidiasis (VVC), and trichomoniasis are the three most common infections responsible for vaginitis. Other causes include: vaginal atrophy in postmenopausal women, cervicitis, foreign body, irritants and allergens (Sobel, 2023b).

Bacterial vaginosis is caused by an imbalance of naturally occurring vaginal bacteria, characterized by both a change in the most common type of bacteria present, along with an increase in the total number of bacteria present. Normal vaginal microbiota is dominated by the species *Lactobacilli*, which are known to produce hydrogen peroxide and lactic acid, which help to keep the acidic vaginal environment below pH 4.5 (Jones, 2019; Kairys & Garg, 2023). Though the origin of vaginal bacterial infections is still unclear, it is believed that most of such infections are the result of another bacteria, *Gardnerella vaginalis,* creating a biofilm which allows opportunistic bacteria to grow within the vagina, causing a decrease in the *Lactobacilli* and subsequent disruption of the pH of the system. An entire host of etiologic organisms have been identified as possible instigators and exacerbators, including *Atopobium vaginae*, *Megasphaera* phylotype 1 and 2, *Leptotrichia aminionii*, *Mobiluncus spp*, *Prevotella spp*, *Mycoplasma hominis*, *Bacteroides spp*, *Sneathia*, and BV-associated bacteria (BVAB) 1, 2, and 3, though as aforementioned the causative mechanism and the interaction between these species are still uncertain (Jones, 2019).

Laboratory documentation of the etiology of vaginitis is important before initiating therapy, given the nonspecific nature and considerable overlap of the symptoms (Anderson et al., 2004; Ellis et al., 2001; Landers et al., 2004). Diagnostic testing enables targeted treatment, increases therapeutic compliance, and increases the likelihood of partner notification (Sobel, 2023b; Workowski & Bolan, 2015).

Measurement of vaginal pH is the primary initial finding that drives the diagnostic. The pH of the normal vaginal secretions in premenopausal women with relatively high estrogen levels is 4.0 to 4.5. The pH of normal vaginal secretions in premenarchal and postmenopausal women in whom estrogen levels are low is ≥4.7. An elevated pH in a premenopausal woman suggests infections, such as BV (pH>4.5) or trichomoniasis (pH 5 to 6) and helps to exclude *Candida* vulvovaginitis (pH 4 to 4.5). Vaginal pH may also be altered by lubricating gels, semen, douches, intravaginal medications and in pregnant women, leakage of amniotic fluid (Anderson et al., 2004; Sobel, 2023b).

There are several challenging aspects to the diagnosis of the etiology of vaginitis based on clinical symptoms. Vaginitis is a global term for nonspecific syndrome and must be narrowed down to the distinct causative factors. Traditional methods have included microscopy, pH testing, amine 'whiff' test, and the Amsel criteria, depending on the suspected etiology. However, physicians may find in-office microscopy to be unavailable, time-consuming, and/or inconclusive in achieving a diagnosis – some estimates hold that misdiagnosis of vulvovaginitis approaches 50% (Brown & Drexler, 2020). As another confounding factor, coinfections are common in vaginitis,

adding difficulty in diagnosis of the three most common organisms if there is mixed vaginitis or coinfection (Sobel, 2023b).

Even though studies have shown that PCR methods have a higher specificity and sensitivity than culture and shorter turn-around time in identifying *Candida* (Diba et al., 2012; Mahmoudi Rad et al., 2012; Tabrizi et al., 2006; Weissenbacher et al., 2009), their use may be adding to clinical non-specificity. Tabrizi et al. (2006) reported that PCR "detected four additional *Candida albicans*, three *Candida parapsilosis* and one *Candida tropicalis* when compared with culture. All but one case additionally detected by PCR were found in patients with no VVC symptoms (Tabrizi et al., 2006)." These data support the earlier findings by Giraldo et al. (2000) where, unlike culture testing, "*Candida* was identified by PCR in a similar proportion of patients with previous recurrent vulvovaginal candidiasis (30%) and in controls (28.8%)." Taken together, these studies indicate that, even though PCR is more sensitive than culture, it may be identifying cases of *Candida* in asymptomatic women that are clinically irrelevant.

Overall, microscopy has lower sensitivities and negative predictive values for BV, candidiasis, and trichomoniasis, and yeast when compared to NAAT and culture, respectively (Sobel, 2023b). The use of established molecular diagnostic tests as an alternative to traditional methods is an opportunity to improve the diagnosis and management of vaginitis; NAAT tests have already improved detection of trichomoniasis (Sobel, 2023b).

Proprietary Tests

DNA hybridization probe tests

As previously stated, microscopy, rather than bacterial culture, is the standard of care for diagnosing BV, and commercially available tests are available in the absence of microscopy but are not widely used. A study of 176 women using the Affirm VP III test (a DNA hybridization probe test that identifies high concentrations of *G. vaginalis*) reported comparable results to wet mount examination with no false positives and only three false negatives for *T. vaginalis,* and three false positives and four false negatives for *G. vaginalis* (Briselden & Hillier, 1994). This test "takes less than one hour to perform and is the best option when findings on physical examination suggest BV… but microscopy cannot be performed to look for clue cells (Sobel, 2023a)."

Trichomoniasis

The OSOM *Trichomonas vaginalis* (TV) Rapid Test by Sekisui Diagnostics is "an antigen-detection test that uses immunochromatographic capillary flow dipstick technology that can be performed at the POC [point of care]"(CDC, 2022). The diagnostic accuracy of the OSOM TV Rapid assay was tested against the common laboratory-based Anyplex II STI-7 Detection in a South African cross-sectional study; all irregular results were further tested with the Fast Track Diagnostics (FTD) STD9 assay (Garrett et al., 2019). Vaginal swabs from 247 women were tested for this study. "The sensitivity and specificity of OSOM TV were 75.0% (45.0-100) and 100% (100-100)", respectively, showing a very high specificity and lower sensitivity (Garrett et al., 2019).

Bacterial Vaginosis tests

AMPLISwab™

The AMPLISwab™ by MedLabs is a comprehensive test created to assess the different organisms responsible for a variety of female genital tract infections, including causative pathogens for cervicitis, nongonococcal urethritis, pelvic inflammatory disease and infertility, sexually transmitted infections, and vaginitis (e.g., bacterial vaginosis, candidiasis and trichomoniasis). The test requires one swab to test for 23 total organisms, broken down into four categories (seven yeast, 12 bacteria and one reference bacteria, one parasite, and two types of herpes viruses), employing testing methodologies such as automated DNA/RNA extraction, transcription-mediated amplification (Schwebke et al.), and real-time polymerase chain reaction (RT-PCR) for the quantification of select organisms implicated in bacterial vaginosis (MedLabs, 2015).

Aptima® BV

The Aptima® Assay by Hologic is a NAAT that identifies BV. "NAAT detects 3x more mixed infections cases than clinical diagnosis with wet mount and Amsel's criteria" (Hologic, 2024b). The Aptima BV Assay is a NAAT that utilizes real time transcription-mediated amplification (Schwebke et al., 2020) for the detection and quantification of ribosomal RNA from BV-associated bacteria: *Lactobacillus* (*L. gasseri*, *L. crispatus*, and *L. jensenii*), *Gardnerella vaginalis*, and *Atopobium vaginae*. "The assay reports a qualitative result for BV and does not report results for individual organisms. The assay is intended to aid in the diagnosis of BV on the automated Panther system using clinician-collected and patient-collected vaginal swab specimens from females with a clinical presentation consistent with vaginitis and/or vaginosis" (FDA, 2019a).

OneSwab®

OneSwab® by Medical Diagnostic Laboratories (MDL) uses real-time PCR and qPCR to output a graphical representation of the relative concentrations of the microbial flora. The Bacterial Vaginosis (with *Lactobacillus* profiling) qPCR test results are then reported in a text based and graphical format. The graphic format includes a representation of the results of all the quantitative tests included in the panel. The relative ratios of DNA species in the give sample in proportion to one another reflect the relative concentrations of different bacteria in vaginal specimens. According to the website, the panel includes assays to detect *Gardnerella vaginalis* and *Atopobium vaginae,* which are established BV organisms. NAAT is 95% sensitive and 99% specific for these organisms. In addition, two new assays to detect *Megasphaera* species and *Bacterial Vaginosis-Associated Bacterium 2* (BVAB2) are included in the Bacterial Vaginosis (with *Lactobacillus* profiling) panel. According to MDL, using NAAT to detect either of these two organisms is up to 99% sensitive and 94% specific for the diagnosis of BV when compared to Amsel Criteria and Nugent Score (MDLabs, 2022). Of note, the sensitivity and specificity just described are for the use of NAAT in detecting these microorganisms, as reported by Fredricks et al. (2007), and are not necessarily the sensitivity and specificity of the MDL *OneSwab®* for BV.

SureSwab® Advanced Bacterial Vaginosis (BV), TMA

The SureSwab® (Quest Diagnostics, Inc.) Advanced Bacterial Vaginosis (BV), TMA uses real time TMA to screen for microorganisms involved in BV vaginal flora imbalances, including *Lactobacillus* species, *Atopobium vaginae*, and *Gardnerella vaginalis* from a single vaginal swab. It reports a qualitative result for BV and does not report results for individual organisms. The swab can be collected either by a physician or the patient (Quest, 2022a).

OSOM® BVBlue®

The *OSOM® BVBlue®* chromogenic diagnostic point-of-care test is a CLIA-waived test with a reported 10 minute read time. The test detects "elevated vaginal fluid sialidase activity, an enzyme produced by bacterial pathogens associated with bacterial vaginosis including *Gardnerella, Bacteroides, Prevotella,* and *Mobiluncus*. 92.8% sensitive, 98% specific versus Gram Stain with a 1-minute hands-on-time, and instant color change provides clear easy-to-read results" (Diagnostics, 2023).

Combination panel tests for Vaginitis/Vaginosis

Aptima® CV/TV

Aptima® CV/TV assays are NAAT tests that identify "vulvovaginal candidiasis (Candida vaginitis or CV) and Trichomoniasis (Trichomonas vaginalis or TV) in symptomatic women from one vaginal sample. NAAT detects 3x more mixed infections cases than clinical diagnosis with wet mount and Amsel's criteria. These tests detect and qualitatively report results for the following organisms: *Candida* species group (*C. albicans, C. tropicalis, C. parapsilosis, C. dubliniensis*), *Candida glabrata*, *Trichomonas vaginalis*" (Hologic, 2024b).

SureSwab®

SureSwab® Advanced Vaginitis, TMA is a test for "vaginitis, including bacterial vaginosis, vulvovaginal candidiasis (*Candidiasis* species), and trichomoniasis (*Trichomonas vaginalis*) (Quest, 2022c). In an even more expansive combination test package, Quest offers a "SureSwab® Advanced Vaginitis Plus, TMA" assay which, in addition to detecting organisms associated with BV, trichomoniasis, and candidiasis, also detects *Chlamydia trachomatis* and *Neisseria gonorrhoeae* (Quest, 2022b).

BD MAX™ Vaginal Panel

The BD MAX™ Vaginal Panel is "an automated qualitative *in vitro* diagnostic test for the direct detection of DNA targets from bacteria associated with BV (qualitative results reported based on detection and quantitation of targeted organism markers), *Candida* species associated with vulvovaginal candidiasis, and *Trichomonas vaginalis* from vaginal swabs in patients who are symptomatic for vaginitis/vaginosis. The test utilizes real-time PCR for the amplification of specific DNA targets and utilizes fluorogenic target-specific hybridization probes to detect and differentiate DNA" (FDA, 2016).

Analytical Validity

Microscopic examination of normal vaginal discharge reveals a predominance of squamous epithelial cells, rare polymorphonuclear leukocytes (PMNs), and *Lactobacillus* species. The

primary goal of the examination is to look for candidal buds or hyphae, motile trichomonads, epithelial cells studded with adherent coccobacilli (clue cells), and increased numbers of PMNs (Sobel, 2023b). The microscopic evaluation of BV is usually based on Amsel criteria (Amsel et al., 1983). Amsel criteria state that the presence of at least three out of the following four criteria are indicative of a BV diagnosis: increased homogeneous thin vaginal discharge, pH secretion > 4.5, amine odor when potassium hydroxide 10% solution is added to a vaginal secretion sample, and the presence of clue cells in wet preparations (Amsel et al., 1983). If clinical criteria are used to define infection, then reported sensitivity may range from 62 to 100 percent (Spiegel, 1991). Using Gram's stain as the standard for diagnosing BV, the sensitivity of Amsel criteria for diagnosis of BV is over 90 percent and specificity is 77 percent (Landers et al., 2004). The Nugent score is also available as a Gram staining scoring system to diagnose BV based on vaginal swab samples (Amegashie et al., 2017). Because BV represents complex changes in the vaginal flora, vaginal culture has **no** role in diagnosis. If microscopy is not available, commercial diagnostic testing methods (e.g., rapid antigen and nucleic acid amplification tests) are used for confirming the clinical suspicion of BV. Polymerase chain reaction (PCR)-based assays to quantify BV-associated bacteria (Cartwright et al., 2012; Menard et al., 2008) have good sensitivity and specificity compared with standard clinical tests (Dumonceaux et al., 2009; Menard et al., 2010). However, they are expensive and of limited utility (Sobel, 2023a).

Trichomoniasis can be diagnosed by the presence of motile trichomonads on wet mount, but it is identified in only 60 to 70 percent of culture-confirmed cases. Culture on Diamond's medium was considered the gold standard method for diagnosing a *T. vaginalis* infection (Workowski & Bolan, 2015); however, nucleic acid amplification tests (Baron et al., 2013) have become the accepted gold standard for the diagnosis of *T. vaginalis*. One study found the sensitivities for *T. vaginalis* using wet mount, culture, rapid antigen testing, and transcription-mediated amplification testing were 65, 96, 90, and 98 percent, respectively (Huppert et al., 2007). Coexistence of *T. vaginalis* and BV pathogens is common, with coinfection rates of 60 to 80 percent (Sobel & Mitchell, 2023b; Sobel et al., 2013).

Microscopy is negative in up to 50 percent of patients with culture-confirmed VVC (Sobel, 1985). Since there are no reliable point of care tests for *Candida* available in the United States (Abbott, 1995; Chatwani et al., 2007; Dan et al., 2010; Hopwood et al., 1985; Marot-Leblond et al., 2009; Matsui et al., 2009), culture must be obtained. PCR methods have high sensitivity and specificity and a shorter turn-around time than culture (Diba et al., 2012; Mahmoudi Rad et al., 2012; Tabrizi et al., 2006; Weissenbacher et al., 2009), but they are costly and offer no proven benefit over culture in symptomatic women (Sobel & Mitchell, 2023a).

Lynch et al. (2019) collected vaginal swabs from 93 women in a cross-sectional study; results from microscopy were compared to two molecular approaches (a qPCR assay with a BV interpretive algorithm and a microbiome profiling test of the 16S rRNA gene produced by Illumina) (Lynch et al., 2019). Results show that “Microscopy plus BV Nugent score had 76% overall agreement with the qPCR plus BV interpretive algorithm method”; further, “Microscopic identification of *Candida* versus that by qPCR had 94% agreement (9 positive, 78 negative) (Lynch et al., 2019).” The qPCR assays gave additional information regarding the types of bacteria present, and the 16S microbiome analysis identified differentiating patterns between BV, aerobic vaginitis (AV), and *Lactobacillus* type infections.

Cartwright et al. (2018) have published data regarding the clinical validity of a PCR-based assay for the detection of BV. This multicenter study included 1579 patients and compared PCR results to samples realized by both the Nugent gram stain and a clinical evaluation using Amsel criteria. Next-generation sequencing was used to confirm differing results. After the resolution of discordant test results using next-generation sequencing, the BV-PCR assay reported a sensitivity of 98.7%, a specificity of 95.9%, a positive predictive value of 92.9% and a negative predictive value of 96.9% (Cartwright et al., 2018). These results show that this PCR-based assay can diagnose BV in symptomatic women efficiently.

Gaydos et al. (2017) conducted a cross-sectional, multi-site study into the clinical validation of this system (n=1740 symptomatic women) reported a sensitivity and specificity of 90.9% and 94.1%, respectively for the *Candida* group and 90.5% sensitivity and 85.8% specificity for BV. For *C. glabrata* specifically, the assay had only 75.9% sensitivity but 99.7% specificity. For trichomoniasis, the sensitivity and specificity were 93.1% and 99.3%, respectively (Gaydos et al., 2017). These researchers also compared the results of this test to clinician assessment. Again, to qualify for the study, the women must have at least one symptom of BV. Using Amsel's criteria, the investigational test sensitivity was 92.7% as compared to the 75.6% sensitivity of the clinician assessment. The authors conclude, "The investigational test showed significantly higher sensitivity for detecting vaginitis, involving more than one cause, than did clinician diagnosis. Taken together, these results suggest that a molecular investigational test can facilitate accurate detection of vaginitis (Schwebke et al., 2018)." It should be noted, however, that these studies only included symptomatic women, and, therefore, the possible clinical non-specificity (i.e., instances where an asymptomatic woman would test positive) is not addressed. Sherrard (2019) compared BV, candidiasis, and trichomoniasis diagnostic results from the BD MAX Vaginal Panel to a current test used in a UK specialist sexual health service center. The authors reported that the BD MAX Vaginal Panel had a sensitivity of 86.4% and specificity of 86.0% for *Candida* species, and a sensitivity of 94.4% and specificity of 79% for BV; the specificity for BV was lower in this study than what has been previously reported (Sherrard, 2019).

Sumeksri et al. (2005) conducted a study correlated to the *OSOM® BVBlue®* test. 173 pregnant women reported a sensitivity and specificity of 94% and 96% respectively, as compared to Gram stain score. These results were comparable to the previously reported values of 91.7% sensitivity and 97.8% specificity in an earlier, smaller study of non-menstruating women (n=57) (Myziuk et al., 2003). A larger study (n=288 women) reported a sensitivity of 88% and specificity of 91% as compared to the Amsel criteria. The authors of this report concluded that women who "are not in settings where the conventional diagnostic methods are either practical or possible… would greatly benefit from access to rapid and reliable point-of-care tests to improve the diagnosis and management of BV (Bradshaw et al., 2005)."

Clinical Utility and Validity

Anand et al. (2020) investigated the accuracy of Papanicolaou smear to diagnose bacterial vaginosis infection in women with women with clinically evident genital infection using the Nugent score on Gram-stained smear as the gold standard. In a prospective blinded cross-sectional study of 254 nonpregnant women between the ages of 30 and 50 conducted between August 2016 and August 2018, the researchers found that using the Nugent score for diagnosing BV as the gold standard, the Pap smears showed sensitivity and specificity of 70.9% (CI: 61.5%

- 79.2%) and 56.8% (CI: 48.2% - 65.2%), respectively. Moreover, they found that the positive percent value was 56.5% (CI: 47.8% - 64.9%), while the negative percent value was 71.2% (CI: 61.8% - 79.4%). These results indicated to the authors that though Pap smears are generally reserved for cervical cancer, the "Pap smear may serve as a means of diagnosing BV [bacterial vaginosis] infection in resource-constrained countries like India" (Anand et al., 2020).

Hilbert et al. (2016) performed a prospective longitudinal study on the use of molecular assays for the accurate detection and diagnosis of bacterial vaginosis using MDL *OneSwab*®. The authors quantified nine organisms associated with vaginal health or disease (*Gardnerella vaginalis, Atopobium vaginae, BV-associated bacteria 2 (BVAB2,* an uncultured member of the order *Clostridiales), Megasphaera phylotype 1 or 2, Lactobacillus iners, Lactobacillus crispatus, Lactobacillus gasseri,* and *Lactobacillus jensenii*) in a total of 149 women were enrolled in the study. DNA was extracted from clinical specimens using mechanical disruption and the QIAamp mini-kit from Qiagen; qPCR assay was used to quantify BV microbes and *Lactobacillus* species. Though the authors evaluated a broad variety of organisms with the potential to be diagnostic markers, results from the study indicated a sensitivity of 92% and specificity of 95% for three that were predictive of diagnosis of BV: *G. vaginalis*, *A. vaginae*, and *Megasphaera phylotypes 1 and 2;* outcomes were 94% PPV, and 94% NPV for BV. The authors summarized their findings by describing the molecular assay as a highly specific laboratory test to identify bacterial vaginosis (Hilbert et al., 2016).

The Aptima BV and Aptima Candida/Trichomonas vaginitis (CV/TV) NAAT molecular tests detect and qualitatively report results using a proprietary algorithmic analysis. Pathogens addressed by the test include: *Candida* species group (*C. albicans, C. tropicalis, C. parapsilosis, C. dubliniensis*), *Candida glabrata*, *Lactobacillu*s, *Gardnerella vaginalis*, *Atopobium vaginae*, and *Trichomonas vaginalis* (Hologic, 2024a). Hologic announced the FDA approval of the Aptima BV and Aptima CV/TV vaginitis tests in 2019 (Hologic, 2019). Schwebke et al. (2020) performed a multicenter, prospective clinical study to validate the performance of the Aptima BV and Aptima CV/TV test for bacterial vaginosis, vulvovaginal candidiasis, and trichomonas vaginitis. A total of 1,519 subjects were enrolled in the study. The authors reported sensitivity and specificity for the investigational tests when it came to provider-collected samples at 95.0% and 89.6% for BV. When it came to *Candida* species, sensitivity and specificity was 91.7% and 94.9% respectively; *C. glabrata* sensitivity and specificity was 84.7% and 99.1%; 96.5% and 94.1% for *T. vaginalis.* Patient-collected samples showed similar ranges of sensitivity and specificity. In conclusion, the authors wrote, "In a secondary analysis, clinicians' diagnoses, in-clinic assessments, and investigational-assay results were compared to gold standard reference methods. Overall, the investigational assays had higher sensitivity and specificity than clinicians' diagnoses and in-clinic assessments, indicating that the investigational assays were more predictive of infection than traditional diagnostic methods" (Schwebke et al., 2020).

There has been increasing literature and reviews regarding both NAAT and DNA hybridization probe proprietary-based diagnostic performance in the identification of bacterial vaginosis. A study by Richter et al. (2019) compared the performance of three molecular diagnostic assays. The assays included in the study were BD Affirm, Hologic ASR BV Assay, and the Aptima IVD BV Assay. A total of 111 women were enrolled in the study. Women had been given an Affirm test by their provider after describing symptoms that indicated a form of vaginitis. After the collection of additional specimens, samples were run on the different assays. As predicted by

clinicians, BV was the most common outcome of diagnosis for 45 of the patients (71%). The sensitivity and specificity for the Hologic ASR assay (diagnosing BV) was 75.6% and 81.8%. The Affirm assay had a sensitivity and specificity of 86.7% and 60.6% for BV, while the Aptima BV IVD assay showed sensitivities and specificities of 84.4% and 86.3%. According to the study, of the three molecular assays that were evaluated, "Aptima BV IVD demonstrated the highest specificity, which may reflect value for the *A. vaginae* target unique to that assay." The study also noted that "although assays that incorporate more bacterial targets are attractive since they reflect the bacterial diversity that has been reported in BV, it is uncertain whether they will provide better diagnostic accuracy to offset the higher cost usually charged for additional targets" (Richter et al., 2019).

One population health population study initiated by Kong et al. (2021) noted that molecular testing is both a sensitive and specific approach to testing and also a welcome tool for providers using labor-intensive traditional practices. The authors address the issue of poor compliance by providers with established gold standard guidelines such as the Amsel criteria, as well as a varied and divergent approaches to office diagnostics. The widespread availability of molecular testing could help accomplish the diagnosis of vaginitis in a single visit. The authors conclude that "compared to CE, molecular tests offer high sensitivity and specificity that provide a precise treatment route. In addition to improved accuracy, recent evidence demonstrates that the combination of sensitive and specific laboratory testing as well as careful patient evaluation have the potential to reduce unnecessary follow-up visits and improve patient care" (Kong et al., 2021).

V. Guidelines and Recommendations

Centers for Disease Control and Prevention (CDC)

The CDC published updated guidelines for diseases characterized by vulvovaginal itching, burning, irritation, odor or discharge in their Sexually Transmitted Infections Treatment Guidelines, 2021 (CDC, 2021b). These guidelines state that "obtaining a medical history alone has been reported to be insufficient for accurate diagnosis of vaginitis and can lead to inappropriate administration of medication…. Therefore, a careful history, examination, and laboratory testing to determine the etiology of any vaginal symptoms are warranted. Information regarding sexual behaviors and practices, sex of sex partners, menses, vaginal hygiene practices (e.g., douching), and self-treatment with oral and intravaginal medications or other products should be elicited" (CDC, 2021b).

The CDC notes that "in the clinician's office, the cause of vaginal symptoms can often be determined by pH, a potassium hydroxide (KOH) test, and microscopic examination of a wet mount of fresh samples of vaginal discharge." However, the guidelines conclude that "in settings where pH paper, KOH, and microscopy are unavailable, a broad range of clinical laboratory tests … can be used" (CDC, 2021b).

For the evaluation of BV, the CDC recommends that "BV can be diagnosed by the use of clinical criteria (i.e., Amsel's Diagnostic Criteria) or by determining the Nugent score from a vaginal Gram stain"(CDC, 2021a). Additional tests are available: "The Osom BV Blue test (Diagnostics) detects vaginal sialidase activity. The Affirm VP III (Becton Dickinson) is an oligonucleotide probe test that detects high concentrations of G. vaginalis nucleic acids (>5 x 105 CFU of G.

vaginalis/mL of vaginal fluid) for diagnosing BV, *Candida* species, and *T. vaginalis*. This test has been reported to be most useful for symptomatic women in conjunction with vaginal pH measurement and presence of amine odor. . . Finally, the FemExam Test Card (Cooper Surgical) measures vaginal pH, presence of trimethylamine (a metabolic by-product of *G. vaginalis*), and proline aminopeptidase. . . This test has primarily been studied in resource-poor settings, and although it has been reported to be beneficial compared with syndromic management, it is not a preferred diagnostic method for BV diagnosis"(CDC, 2021a). The guidelines also state that due to insufficient evidence, "routine screening for BV among asymptomatic pregnant women at high or low risk for preterm delivery for preventing preterm birth is not recommended,"(CDC, 2021a), which is in compliance with the 2008 USPSTF recommendations and endorsed by the AAFP (USPSTF, 2008).

Regarding NAATs for BV, the CDC states that "BV NAATs 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. Despite the availability of BV NAATs, 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. Culture of *G. vaginalis* is not recommended as a diagnostic tool because it is not specific. Cervical Pap tests have no clinical utility for diagnosing BV because of their low sensitivity and specificity" (CDC, 2021a).

The CDC provides information on multiple BV NAATs that are available and notes that "these tests are based on detection of specific bacterial nucleic acids and have high sensitivity and specificity for BV (i.e., *G. vaginalis, A. vaginae*, BVAB2, or *Megasphaera* type 1) and certain lactobacilli (i.e., *Lactobacillus crispatus, Lactobacillus jensenii*, and *Lactobacillus gasseri*). They can be performed on either clinician- or self-collected vaginal specimens with results available in <24 hours, depending on the availability of the molecular diagnostic platform. Five quantitative multiplex PCR assays are available: Max Vaginal Panel (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). Two of these assays are FDA cleared (BD Max Vaginal Panel and Aptima BV), and the other three are laboratory-developed tests. The Max Vaginal Panel provides results by an algorithmic analysis of molecular DNA detection of Lactobacillus species (*L. crispatus* and *L. jensenii*) in addition to *G. vaginalis, A. vaginae*, BVAB2, and *Megasphaera* type 1. This test has 90.5% sensitivity and 85.8% specificity for BV diagnosis, compared with Amsel criteria and Nugent score. It also provides results for Candida species and T. vaginalis. The Aptima BV detects *G. vaginalis, A. vaginae*, and certain *Lactobacillus* species including *L. crispatus, L. jensenii, and L. gasseri*, with sensitivity and specificity ranging from 95.0% to 97.3% and 85.8% to 89.6%, respectively (using either clinician- or patient-collected vaginal swabs). The three laboratory-developed tests (*NuSwab*® *VG, OneSwab*® BV Panel PCR with Lactobacillus Profiling by qPCR, and *SureSwab*® BV) have to be internally validated before use for patient care yet have good sensitivity and specificity, similar to FDA-cleared assays" (CDC, 2021a).

For the evaluation of vulvovaginal candidiasis, the CDC recommends: "Examination of a wet mount with KOH preparation should be performed for all women with symptoms or signs of VVC, and women with a positive result should be treated. For those with negative wet mounts but existing signs or symptoms, vaginal cultures for *Candida* should be considered" (CDC,

2021c). The most current guidelines for VVC diagnosis state that "vaginal culture or PCR should be obtained from women with complicated VVC to confirm clinical diagnosis and identify non–*albicans Candida*" (CDC, 2021c).

For the evaluation of trichomoniasis, the CDC recommends: "Diagnostic testing for *T. vaginalis* should be performed for women seeking care for vaginal discharge… Wet-mount microscopy traditionally has been used as the preferred diagnostic test for T. vaginalis among women because it is inexpensive and can be performed at the POC; however, it has low sensitivity (44%–68%) compared with culture. . . More highly sensitive and specific molecular diagnostic options are available, which should be used in conjunction with a negative wet mount when possible. NAATs are highly sensitive, detecting more *T. vaginalis* infections than wet-mount microscopy among women. . . The *OSOM*® trichomonas rapid test (Diagnostics) is an antigen-detection test that uses immunochromatographic capillary flow dipstick technology that can be performed at the POC by using clinician-obtained vaginal specimens. Results are available in approximately 10–15 minutes, with sensitivities of 82%–95% and specificity of 97%–100%, compared with wet mount, culture, and transcription-mediated amplification . . . The Solana trichomonas assay (Quidel) is another rapid test for the qualitative detection of *T. vaginalis* DNA and can yield results <40 minutes after specimen collection. . . The Amplivue trichomonas assay (Quidel) is another rapid test providing qualitative detection of *T. vaginalis* that has been FDA cleared for vaginal specimens from symptomatic and asymptomatic women"(CDC, 2022) and "the Affirm VP III (Becton Dickinson) is an oligonucleotide probe test that detects high concentrations of G. vaginalis nucleic acids (>5 x 105 CFU of G. vaginalis/mL of vaginal fluid) for diagnosing BV, *Candida* species, and *T. vaginalis*. This test has been reported to be most useful for symptomatic women in conjunction with vaginal pH measurement and presence of amine odor (sensitivity of 97%); specificity is 81% compared with Nugent" (CDC, 2021a).

In the updated Sexually Transmitted Infections Treatment Guidelines, the CDC also mentions the FDA-cleared Aptima *T. vaginalis* assay that may be used for detection of *T. vaginalis* from symptomatic or asymptomatic women (CDC, 2022).

American Academy of Family Physicians (AAFP)

The AAFP published an article (Hainer & Gibson, 2011) on the diagnosis of vaginitis which states that: "Physicians traditionally diagnose vaginitis using the combination of symptoms, physical examination, pH of vaginal fluid, microscopy, and the whiff test. When combined, these tests have a sensitivity and specificity of 81 and 70 percent, respectively, for BV; 84 and 85 percent for vulvovaginal candidiasis; and 85 and 100 percent for trichomoniasis when compared with the DNA probe standard…A cost-effectiveness analysis of diagnostic strategies for vaginitis undiagnosed by pelvic examination, wet-mount preparation, and related office tests showed that the least expensive strategy was to perform yeast culture, gonorrhea and chlamydia probes at the initial visit, and Gram stain and *Trichomonas* culture only when the vaginal pH exceeded 4.9. Other strategies cost more and increased duration of symptoms by up to 1.3 days" (Hainer & Gibson, 2011).

In 2018, the AAFP published the following guidelines:

- "Symptoms alone cannot differentiate between the causes of vaginitis. Office-based or laboratory testing should be used with the history and physical examination findings to make the diagnosis. (C evidence rating)
- Do not obtain culture for the diagnosis of bacterial vaginosis because it represents a polymicrobial infection. (C evidence rating)
- Nucleic acid amplification testing is recommended for the diagnosis of trichomoniasis in symptomatic or high-risk women. (C evidence rating)" (Paladine & Desai, 2018).

U.S. Preventive Services Task Force Recommendations (USPSTF)

In 2020, the USPSTF published recommendations discouraging the use of screening for BV in pregnancy: "The USPSTF recommends against screening for bacterial vaginosis in pregnant persons not at increased risk for preterm delivery". On a similar note, the USPSTF maintains its 2008 recommendation stating "that the current evidence is insufficient to assess the balance of benefits and harms of screening for bacterial vaginosis in pregnant persons at increased risk for preterm delivery" (Owens et al., 2020).

American College of Obstetrics and Gynecology (ACOG)

The ACOG published in 2020 Practice Bulletin Number 215 on vaginitis in nonpregnant patients. These guidelines were reaffirmed in 2022. In these guidelines, the ACOG made these recommendations for diagnostic testing based on good and consistent scientific evidence (Level A):

- "The use of Amsel clinical criteria or Gram stain with Nugent scoring is recommended for the diagnosis of bacterial vaginosis."
- "Nucleic acid amplification testing is recommended for the diagnosis of trichomoniasis."
- "In a symptomatic patient, diagnosis of vulvovaginal candidiasis requires one of the following two findings: 1) visualization of spores, pseudohyphae, or hyphae on wet-mount microscopy or 2) vaginal fungal culture or commercial diagnostic test results positive for *Candida* species."

The ACOG also published recommendations based on limited or inconsistent scientific evidence (Level B), along with a series of recommendations based on consensus and expert opinion (Level C). Those relating to diagnostic testing are reported below:

- "Patients should be retested within 3 months after treatment for *T vaginalis* because of the high rates of infection recurrence" (Level B).
- "Pap tests are not reliable for the diagnosis of vaginitis. Diagnostic confirmation is recommended for incidental findings of vulvovaginal candidiasis, bacterial vaginosis, or trichomoniasis on a Pap test" (Level B).
- "A complete medical history, physical examination of the vulva and vagina, and clinical testing of vaginal discharge (i.e. pH testing, a potassium hydroxide [KOH] "whiff test", and microscopy) are recommended for the initial evaluation of patients with vaginitis symptoms" (Level C).

The ACOG mentions in Bulletin Number 215 that an advanced single-swab panel test that combines multiplex PCR and DNA probe technology could be a promising alternative to microscopy for BV, trichomoniasis, and candidiasis (ACOG, 2020).

Infectious Diseases Society of America (IDSA) Clinical Practice Guidelines

The IDSA has published an updated clinical guideline (Pappas et al., 2016) for the management of candidiasis in which recommendations include diagnosing vulvovaginal candidiasis before proceeding with empiric antifungal therapy. The usual diagnosis is clinical based on signs and symptoms of vaginitis such as pruritus, irritation, vaginal soreness, vulvar edema, erythema and many others. Clinical signs and symptoms are nonspecific and could be attributed to causes other than vulvovaginal candidiasis. Therefore, authors recommend confirming clinical diagnosis by a wet -mount preparation with saline and 10% KOH to demonstrate the presence of yeast and a normal pH. In cases where signs and symptoms are suggestive of vulvovaginal candidiasis, but microscopic findings and pH are negative, culture testing confirms the diagnosis according to published guidelines. The IDSA also discusses the possible use of PCR in diagnosing invasive candidiasis, even though the guidelines later state that "Cultures of blood or other samples collected under sterile conditions have long been considered diagnostic gold standards for invasive candidiasis…The role of PCR in testing samples other than blood is not established" (Pappas et al., 2016).

In the 2018 IDSA *A Guide to Utilization of the Microbiology Laboratory for Diagnosis of Infectious Diseases*, the IDSA states, "For vaginosis (altered vaginal flora) a Gram stain and recently available microbiome-based assays are more specific than culture and probe testing for *Gardnerella vaginalis* alone… A number of point-of-care tests can be performed from a vaginal discharge specimen while the patient is in the healthcare setting. Although point-of-care tests are popular, the sensitivity and specificity for making a specific diagnosis vary widely and these assays, while rapid, are often diagnostically poor (Miller et al., 2018)." The IDSA notes that the FDA has approved the use of the Max Vaginal Panel by Becton Dickinson in symptomatic females. "Preliminary data show greater specificity of this approach compared to methods that identify only *G. vaginalis*, as well as consistency in both reproducible as well as standardized results" (Miller et al., 2018).

Society of Obstetricians and Gynecologists of Canada (SOGC)

The SOGC published guidelines for the screening and management of BV in pregnancy. These guidelines state that the following:

- "In symptomatic pregnant women, testing for and treatment of bacterial vaginosis is recommended for symptom resolution. Diagnostic criteria are the same for pregnant and non-pregnant women (I-A).
- Asymptomatic women and women without identified risk factors for preterm birth should not undergo routine screening for or treatment of bacterial vaginosis (I-B).
- Women at increased risk for preterm birth may benefit from routine screening for and treatment of bacterial vaginosis (I-B).
- Testing should be repeated one month after treatment to ensure that cure was achieved (III-L)" (Yudin & Money, 2017).

The SOGC also published guidelines regarding the screening and management of trichomoniasis, VVC, and BV. These guidelines state that "Bacterial vaginosis should be diagnosed using either clinical (Amsel's) or laboratory (Gram stain with objective scoring system) criteria (II-2A)" (van Schalkwyk & Yudin, 2015).

VI. Applicable State and Federal Regulations

DISCLAIMER: If there is a conflict between this Policy and any relevant, applicable government policy for a particular member [e.g., Local Coverage Determinations (LCDs) or National Coverage Determinations (NCDs) for Medicare and/or state coverage for Medicaid], then the government policy will be used to make the determination. For the most up-to-date Medicare policies and coverage, please visit the Medicare search website https://www.cms.gov/medicare-coverage-database/search.aspx . For the most up-to-date Medicaid policies and coverage, please visit the applicable state Medicaid website.

Food and Drug Administration (FDA)

On October 28, 2016, the FDA approved an automatic class III designation for the BD MAX™ Vaginal Panel (FDA, 2016). Following the initial approval, an additional 510(k) Substantial Equivalence Determination Decision Summary was released on October 21, 2019, with the following note: "Routine post market surveillance activities informed BD of an unanticipated high rate of nonreportable result rate for the BD MAX Vaginal Panel. Through investigations, BD identified four design modifications intended to improve the tolerance of the BD MAX Vaginal Panel without significantly impacting the validated clinical and analytical performance. . . One of the four design modifications was determined to be significant with the potential to affect the safety or effectiveness of the device and is the focus of this submission. The cumulative changes require minor modifications to the labeling" (FDA, 2019b).

On May 23, 2019, the FDA approved the use of the Aptima® BV Assay for the detection and identification of bacterial vaginosis. According to the FDA, "the Aptima BV assay is an in vitro nucleic acid amplification test that utilizes real time transcription-mediated amplification (Schwebke et al., 2020) for detection and quantitation of ribosomal RNA from bacteria associated with bacterial vaginosis (BV), including Lactobacillus (*L. gasseri, L. crispatus*, and L. *jensenii*), *Gardnerella vaginalis*, and *Atopobium vaginae*. The assay reports a qualitative result for BV and does not report results for individual organisms. The assay is intended to aid in the diagnosis of BV on the automated Panther system using clinician-collected and patient-collected vaginal swab specimens from females with a clinical presentation consistent with vaginitis and/or vaginosis" (FDA, 2019a).

Many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). LDTs are not approved or cleared by the U. S. Food and Drug Administration; however, FDA clearance or approval is not currently required for clinical use.

VII. Applicable CPT/HCPCS Procedure Codes

Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all inclusive and is subject to updates. In addition, codes listed are not a guarantee of payment.

CPT	Code Description
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 Proprietary test: Aptima® BV Assay Lab/Manufacturer: Hologic, Inc
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 (Do not report 81514 in conjunction with 87480, 87481, 87482, 87510, 87511, 87512, 87660, 87661) Proprietary test: BD MAX™ Vaginal Panel Lab/Manufacturer: Becton Dickson and Company
82120	Amines, vaginal fluid, qualitative
83986	pH; body fluid, not otherwise specified
87070	Culture, bacterial; any other source except urine, blood or stool, aerobic, with isolation and presumptive identification of isolates
87149	Culture, typing; identification by nucleic acid (DNA or RNA) probe, direct probe technique, per culture or isolate, each organism probed
87150	Culture, typing; identification by nucleic acid (DNA or RNA) probe, amplified probe technique, per culture or isolate, each organism probed
87210	Smear, primary source with interpretation; wet mount for infectious agents (eg, saline, India ink, KOH preps)
87480	Infectious agent detection by nucleic acid (DNA or RNA); Candida species, direct probe technique
87481	Infectious agent detection by nucleic acid (DNA or RNA); Candida species, amplified probe technique
87482	Infectious agent detection by nucleic acid (DNA or RNA); Candida species, quantification
87510	Infectious agent detection by nucleic acid (DNA or RNA); Gardnerella vaginalis, direct probe technique
87511	Infectious agent detection by nucleic acid (DNA or RNA); Gardnerella vaginalis, amplified probe technique
87512	Infectious agent detection by nucleic acid (DNA or RNA); Gardnerella vaginalis, quantification

87660	Infectious agent detection by nucleic acid (DNA or RNA); Trichomonas vaginalis, direct probe technique
87661	Infectious agent detection by nucleic acid (DNA or RNA); Trichomonas vaginalis, amplified probe technique
87797	Infectious agent detection by nucleic acid (DNA or RNA), not otherwise specified; direct probe technique, each organism
87798	Infectious agent detection by nucleic acid (DNA or RNA), not otherwise specified; amplified probe technique, each organism
87799	Infectious agent detection by nucleic acid (DNA or RNA), not otherwise specified; quantification, each organism
87800	Infectious agent detection by nucleic acid (DNA or RNA), multiple organisms; direct probe(s) technique
87801	Infectious agent detection by nucleic acid (DNA or RNA), multiple organisms; amplified probe(s) technique
87808	Infectious agent antigen detection by immunoassay with direct optical (ie, visual) observation; Trichomonas vaginalis
87905	Infectious agent enzymatic activity other than virus (eg, sialidase activity in vaginal fluid)
0330U	Infectious agent detection by nucleic acid (DNA or RNA), vaginal pathogen panel, identification of 27 organisms, amplified probe technique, vaginal swab Proprietary test: Bridge Women's Health Infectious Disease Detection Test Lab/Manufacturer: Bridge Diagnostics/ThermoFisher and Hologic Test Kit on Panther Instrument
0352U	Infectious disease (bacterial vaginosis and vaginitis), multiplex amplified probe technique, for detection of bacterial vaginosis–associated bacteria (BVAB-2, Atopobium vaginae, and Megasphera type 1), algorithm reported as detected or not detected and separate detection of Candida species (C. albicans, C. tropicalis, C. parapsilosis, C. dubliniensis), Candida glabrata/Candida krusei, and trichomonas vaginalis, vaginal-fluid specimen, each result reported as detected or not detected Protietary test: Xpert® Xpress MVP Lab/Manufacturer: Cepheid®
Q0111	Wet mounts, including preparations of vaginal, cervical or skin specimens

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IX. Revision History

Revision Date	Summary of Changes
12/01/2021	Initial Effective Date
08/18/2022	Updated background, guidelines and recommendations, and evidence based scientific references. Literature review did not necessitate modification to coverage criteria. Revisions to CC7 & CC8. Added CC 12. Added code 87801 Revised code disclaimer statement
09/15/2023	Updated background, guidelines and recommendations, and evidence based scientific references. Literature review necessitated the following changes in coverage criteria: CC8, removed "when limited to known pathogenic species" and provided clarifying language. CC8 now reads: "For individuals with symptoms of bacterial vaginosis (BV), NAAT specific to the diagnosis of BV (e.g., Aptima® BV; OneSwab® BV Panel PCR with Lactobacillus Profiling by qPCR; SureSwab® Advanced BV, TMA) and single or multitarget PCR testing for the diagnosis of BV MEETS COVERAGE CRITERIA. **Addition of new CC9: "9) NAAT panel testing designed to detect more than one type of vaginitis (VVC, BV, and/or trichomoniasis; e.g., BD MAX™ Vaginal Panel, NuSwab® VG, Xpert® Xpress MVP) DOES NOT MEET COVERAGE CRITERIA. **Added PLA code 0352U Note: Updated description for code 81514 to include (Do not report 81514 in conjunction with 87480, 87481, 87482, 87510, 87511, 87512, 87660, 87661).

	Revisions to CC7 & CC8. Added CC 12. Added code 87801 Revised code disclaimer statement Committee approved: 08/15/2023 DCH approved: 09/15/2023
09/15/2023	Off cycle coding modification Added PLA code 0330U. Committee Approved: 08/15/2023 DCH approved: 09/15/2023
04/16/2024	Off-cycle Review, no updates outside of the coverage criteria: Following discussion with our clinical advisory board (CAB) and experts in the field, the decision was made to change CC9 from DNMCC to MCC. Now reads: "9) NAAT panel testing designed to detect more than one type of vaginitis (VVC, BV, and/or trichomoniasis; e.g., BD MAX™ Vaginal Panel, NuSwab® VG, Xpert® Xpress MVP) MEETS COVERAGE CRITERIA." Title changed from "Diagnosis of Vaginitis including Multi-target PCR Testing" to "Diagnosis of Vaginitis" Committee approved: 02/12/2024 DCH approved: 04/16/2024
06/05/2024	Reviewed and Updated: Updated the background, guidelines and recommendations, and evidence-based scientific references. Literature review did not necessitate any modifications to coverage criteria. Committee approved: 05/14/2024 DCH approved: 06/05/2024