Prior Authorization Review Panel
MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: Keystone First	**Submission Date**: 4/1/2024
Policy Number: ccp.1325	**Effective Date:** 9/2017 **Revision Date:** March 1, 2024
Policy Name: Vaginitis diagnostic testing	

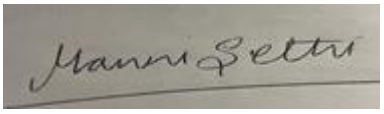
Type of Submission – Check all that apply:

- [ ] **New Policy**
- [x] **Revised Policy***
- [ ] **Annual Review – No Revisions**
- [ ] **Statewide PDL**

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any clarifying information for the policy below:

Requires Prior Authorization. See tracked changes below.

Name of Authorized Individual (Please type or print): Manni Sethi, MD, MBA, CHCQM	**Signature of Authorized Individual:** 

Vaginitis diagnostic testing

Clinical Policy ID: CCP.1325

Recent review date: 3/2024

Next review date: 7/2025

Policy contains: Bacterial vaginosis; vaginitis; vulvovaginal candidiasis; trichomoniasis.

Keystone First- CHIP has developed clinical policies to assist with making coverage determinations. Keystone First- CHIP's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by Keystone First- CHIP, on a case by case basis, when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Keystone First- CHIP's clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Keystone First- CHIP's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Keystone First- CHIP will update its clinical policies as necessary. Keystone First- CHIP's clinical policies are not guarantees of payment.

Coverage policy

The following diagnostic tests for vaginitis, when provided in accordance with guideline-directed care, are clinically proven and, therefore, may be medically necessary for members who present with symptoms of vaginitis based on clinical examination and history (American College of Obstetricians and Gynecologists, 2020; Workowski, 2015):

- Point-of-care testing (i.e., pH testing, potassium hydroxide "whiff test," or saline microscopy) or Gram stain with Nugent scoring for bacterial vaginosis.
- Microscopy and, if necessary, vaginal yeast culture for *Candida* species.
- Nucleic acid amplification testing for the diagnosis of *Trichomonas vaginalis* infection.
- U.S. Food and Drug Administration-approved nucleic acid-based microbial testing when any of the above tests are unavailable or inconclusive and the test results will impact care management (Workowski, 2015). See approved list: https://www.fda.gov/medical-devices/vitro-diagnostics/nucleic-acid-based-tests.

Repeat testing for *Trichomonas vaginalis* may be medically necessary within three months after treatment because of the high rates of infection recurrence (American College of Obstetricians and Gynecologists, 2020).

Limitations

The following tests are investigational/not clinically proven and, therefore, not medically necessary for diagnosis of vaginitis (American College of Obstetricians and Gynecologists, 2020; Workowski, 2015):

- Papanicolaou testing. However, for incidental findings of vulvovaginal candidiasis, bacterial vaginosis, or trichomoniasis on a Papanicolaou test, diagnostic confirmation may be medically necessary.
- Diagnostic testing that employs microarray or sequencing methods.
- Polymerase chain reaction testing for *Candida* species or bacterial vaginosis.

Routine screening for bacterial vaginosis in asymptomatic pregnant women for prevention of preterm delivery is investigational/not clinically proven and, therefore, not medically necessary (Owens, 2020).

Alternative covered services

In-network healthcare provider services for diagnosis and management of genital disorders.

Background

The most common causes of vaginitis include vulvovaginal candidiasis, bacterial vaginosis, and trichomoniasis. Less common etiologies include vulvar skin diseases, desquamative inflammatory vaginitis, and genitourinary syndrome of menopause. Bacterial vaginosis is associated with a high economic burden and marked racial disparities in prevalence (Peebles, 2019).

Vaginitis may have significant repercussions in terms of mental distress and physical discomfort, episodes of school or work absence, and sexual dysfunction (American College of Obstetricians and Gynecologists, 2020). Vaginitis is frequently seen in concert with sexually transmitted diseases, including human immunodeficiency virus. Distinguishing vaginal from vulvar symptoms is important to guide evaluation and treatment. Atrophic vaginitis is common with aging and the decreased ovarian production of estrogen. An accurate diagnosis of atrophic vaginitis among postmenopausal women is vitally important to choosing the appropriate treatment.

Diagnosis of vaginitis includes a clinical examination and history of perineal and vaginal discomfort, itching, or discharge, along with a choice of point-of-care testing, laboratory testing, and molecular (bacterial nucleic acid) diagnostic assays (Coleman, 2018). Point-of-care testing includes pH testing, a potassium hydroxide “whiff test” (amine odor test), and saline microscopy. The standard of care for determining the initial diagnosis relies on applying three of the four results from point-of-care testing to Amsel criteria:

- Homogeneous, thin, white discharge that smoothly coats the vaginal walls.
- Clue cells (e.g., vaginal epithelial cells studded with adherent coccobacilli) on microscopic examination.
- pH of vaginal fluid > 4.5.
- A fishy odor of vaginal discharge before or after addition of 10% potassium hydroxide.

Laboratory examination (e.g., Gram stain) might include a microscopic examination of the discharge or vaginal vault with culture for bacterial, fungal, and parasitic etiologies. Direct deoxyribonucleic acid probe and nucleic acid amplification assays are the primary commercial molecular assays available in the United States for diagnosing bacterial vaginitis. Microarray and sequencing technologies are emerging methods that are currently available for research purposes.

Findings

A systematic review (Nwankwo, 2017) of syndrome diagnosis in the evaluation of vaginitis followed the World Health Organization algorithm and reported high sensitivity (91.5% to 100%) but moderate to low specificity (0% to 27.5%) among women with vaginal symptoms. The authors noted the method’s substantial potential for overtreatment and physician error.

A systematic review (n = 4,155 women) examined the association between genital tract infection and preterm birth (before 37 weeks' gestation) and the impact of screening for infections during pregnancy on premature birth rate (Sangkomkamhang, 2015). The rate of preterm birth before 37 weeks' gestation was significantly lower in the intervention group (3% versus 5% in the control group) with a risk ratio of 0.55 (95% confidence interval 0.41 to 0.75; moderate-quality evidence). There is also evidence that routine screening of pregnant women before 20 weeks' gestation for vaginal infection is associated with cost savings when used for the prevention of preterm birth.

In 2020, we included updated guidance from the Centers for Disease Control and Prevention (Workowski, 2015), the American College of Obstetricians and Gynecologists (2020), and the U.S. Preventive Services Task Force (Owens, 2020), along with a systematic review and meta-analysis (Kahwati, 2020) that informed the Task Force recommendations. There is uniform consensus among guidelines for testing recommendations in patients presenting with symptomatic vaginitis.

There is less consensus for testing asymptomatic populations. The Centers for Disease Control and Prevention (Workowski, 2015) recommends routine *Trichomonas vaginalis* screening in women with human immunodeficiency virus infection because of the adverse events associated with asymptomatic trichomoniasis and human immunodeficiency virus infection. Screening can be considered in high prevalence settings (e.g., sexually transmitted disease clinics or correctional facilities) or for persons at high risk for infection (e.g., persons with multiple sex partners, exchanging sex for payment, illicit drug use, or a history of sexually transmitted disease). However, in such instances there are insufficient data supporting a correlation between screening and treatment for asymptomatic trichomoniasis and a reduction in health and health disparities or reduced community burden of infection. Decisions about screening might be informed by local epidemiology of infection rates.

We added a list of commercially available nucleic acid-based tests approved for diagnosing an infection with pathogens causing bacterial vaginitis (U.S. Food and Drug Administration, 2023). We modified the coverage and limitations sections to include information on types of medically necessary testing for symptomatic populations, based on new evidence-based guidance from the American College of Obstetricians and Gynecologists (2020), as follows:

- For the initial evaluation of patients with vaginitis symptoms, a complete medical history, physical examination of the vulva and vagina, and point-of-care testing of vaginal discharge (i.e., pH testing, a potassium hydroxide whiff test, and microscopy) are recommended (Level C = recommendation based primarily on consensus and expert opinion).
- For the diagnosis of bacterial vaginosis, Amsel criteria based on clinical testing or Gram stain with Nugent scoring is recommended (Level A = recommendations based on good and consistent scientific evidence).
- For the diagnosis of trichomoniasis, nucleic acid amplification testing is recommended (Level A).
- Patients should be retested within three months after treatment for *Trichomonas vaginalis* because of the high rates of infection recurrence (Level B = recommendations based on limited or inconsistent scientific evidence).
- For diagnosis of vulvovaginal candidiasis, one of the following two findings is required:
    - Visualization of spores, pseudohyphae, or hyphae on wet-mount microscopy.
    - Vaginal fungal culture or commercial diagnostic test results positive for *Candida* species.
- Papanicolaou tests are not reliable for the diagnosis of vaginitis (Level B).
- Diagnostic confirmation is recommended for incidental findings of vulvovaginal candidiasis, bacterial vaginosis, or trichomoniasis on a Papanicolaou test (Level B).

In 2022, we updated the references and made no policy changes.

In 2024, we added results of a cost effectiveness analysis (Bretelle, 2023) and a systematic review (Hoffmann, 2023) to the policy that provided conflicting results regarding the clinical value of routinely screening for bacterial vaginosis in low-risk pregnant women. No policy changes are warranted.

The AuTop randomized controlled trial compared the clinical and economic outcomes of point-of-care quantitative real time polymerase chain reaction (molecular) screening and treatment of bacterial vaginosis versus usual care with no molecular screening (ClinicalTrials.gov identifier: NCT02288832; n = 6,671). Participants were low-risk pregnant women before 20 weeks' gestation without previous preterm births or late miscarriages, recruited from 19 French perinatal centers. The screening test quantified the deoxyribonucleic acid levels of *Atopobium vaginae and Gardnerella vaginalis*. Addition of molecular screening in low-risk pregnant women did not significantly reduce preterm birth rates (3.8% versus 4.6% in controls) or associated costs. A subgroup analysis showed the screen and treat strategy was significantly more effective than usual care (at a nonsignificantly lower total cost) in nulliparous women but not significantly different in multiparous women (Bretelle, 2023).

A systematic review and meta-analysis of 13 trials (n = 143,534) compared screening with Gram stain, pH screening, pH self-screening, or pH screening plus Gram stain to no screening in low-risk pregnant women. Regular screening of vaginal flora compared to no screening significantly reduced the odds of preterm birth before 37 weeks, extreme preterm birth before 32 weeks, low birthweight under 2500 g, and very low birthweight under 1000 g. However, the quality of evidence was considered very low for most results, the overall risk of bias was concerning, and testing and treatment protocols were highly variable (Hoffmann, 2023).

References

On January 29, 2024, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were "vaginitis," "vaginal discharge," and "vaginal infection." We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

American College of Obstetricians and Gynecologists. Committee on Practice Bulletins—Gynecology. Vaginitis in nonpregnant patients: ACOG Practice Bulletin, Number 215. *Obstet Gynecol*, 2020;135(1):e1-e17. Doi:10.1097/AOG.0000000000003604.

Bretelle F, Loubière S, Desbriere R, et al. Effectiveness and costs of molecular screening and treatment for bacterial vaginosis to prevent preterm birth: The AuTop randomized clinical trial. *JAMA Pediatr*. 2023;177(9):894-902. Doi: 10.1001/jamapediatrics.2023.2250.

ClinicalTrials.gov. Medico-economic impact of screening Atopobium vaginae and Gardnerella vaginalis in molecular biology by "point-of-care" during pregnancy (AuTop). ClinicalTrials.gov identifier: NCT02288832. https://clinicaltrials.gov/study/NCT02288832. Last updated posted April 13, 2023.

Coleman JS, Gaydos CA. Molecular diagnosis of bacterial vaginosis: An update. *J Clin Microbiol,* 2018. 2018;56(9):e00342-18. Doi: 10.1128/JCM.00342-18.

Hoffmann E, Váncsa S, Váradi A, et al. Routine screening of abnormal vaginal flora during pregnancy reduces the odds of preterm birth: A systematic review and meta-analysis. *Sci Rep*. 2023;13(1):13897. Doi: 10.1038/s41598-023-40993-x.

Kahwati LC, Clark R, Berkman N, et al. Screening for bacterial vaginosis in pregnant adolescents and women to prevent preterm delivery: Updated evidence report and systematic review for the U.S. Preventive Services Task Force. *JAMA.* 2020;323(13):1293-1309. Doi: 10.1001/jama.2020.0233.

Nwankwo TO, Aniebue UU, Umeh UA. Syndromic diagnosis in evaluation of women with symptoms of vaginitis. *Curr Infect Dis Rep*. 2017;19(1):3. Doi: 10.1007/s11908-017-0558-9.

Owens DK, Davidson KW, Krist AH, et al. Screening for bacterial vaginosis in pregnant persons to prevent preterm delivery: U.S Preventive Services Task Force recommendation statement. *JAMA.* 2020;323(13):1286-1292. Doi: 10.1001/jama.2020.2684.

Peebles K, Velloza J, Balkus JE, McClelland RS, Barnabas RV. High global burden and costs of bacterial vaginosis: A systematic review and meta-analysis. *Sex Transm Dis*. 2019;46(5):304-311. Doi: 10.1097/olq.0000000000000972.

Sangkomkamhang US, Lumbiganon P, Prasertcharoensuk W, Laopaiboon M. Antenatal lower genital tract infection screening and treatment programs for preventing preterm delivery. *Cochrane Database Syst Rev*. 2015;(2):CD006178. Doi: 10.1002/14651858.CD006178.pub3.

U.S. Food and Drug Administration. Nucleic acid-based tests. https://www.fda.gov/medical-devices/vitro-diagnostics/nucleic-acid-based-tests. Current as of May 26, 2023.

Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines. *MMWR Recomm Rep.* 2015;64(Rr-03):1-137. https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6403a1.htm.

Policy updates

7/2017: initial review date and clinical policy effective date: 9/2017

7/2018: Policy references updated. Policy ID changed.

8/2019: Policy references updated.

10/2020. Policy references updated. Coverage modified.

10/2021: Policy references updated.

11/2022: Policy references updated.

3/2024: Policy references updated.