Anthem

Clinical UM Guideline

Subject: Cervical Cancer Screening Using Cytology and Human Papillomavirus Testing
Guideline #: CG-MED-53
Status: Revised
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Description

This document addresses cervical cancer screening and testing for human papillomavirus (HPV) to assess cervical cancer risk. Cervical cancer screening is comprised of cervical cytology with Papanicolaou testing (also known as a 'Pap test') and testing for HPV DNA. Pap tests are used to identify pre-cancerous or cancerous tissues present on the cervix. Screening for HPV aids in identifying individuals at higher risk for developing cervical cancer.

Note: This document addresses the use of cervical cancer *screening* in the general population. It does not address the use of cervical cancer screening technologies or procedures for the *work-up* or *surveillance* of either individuals with known precancerous lesions or a known history of cervical cancer.

Note: For additional information on cervical cancer screening, please see:

- ADMIN.00002 Preventive Health Guidelines
- MED.00087 Optical Detection for Screening and Identification of Cervical Cancer

Clinical Indications

Medically Necessary:

Cervical cancer screening with cytology is considered **medically necessary** for individuals* who are 21 years of age or older.

Screening for the presence of HPV is considered **medically necessary** for individuals* who are 30 years of age or older.

Not Medically Necessary:

Cervical cancer screening with cytology is considered **not medically necessary** when the criteria above have not been met.

Screening for the presence of HPV is considered **not medically necessary** when the criteria above have not been met.

*The term "individual" in this document refers to any person with an intact cervix, regardless of gender identity.

Coding

The following codes for treatments and procedures applicable to this guideline are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services may be Medically Necessary when criteria are met:

CPT	
87623	Infectious agent detection by nucleic acid (DNA or RNA); Human Papillomavirus (HPV), low-risk types (eg, 6, 11, 42, 43, 44)
87624	Infectious agent detection by nucleic acid (DNA or RNA); Human Papillomavirus (HPV), high-risk types (eg, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68)
87625	Infectious agent detection by nucleic acid (DNA or RNA); Human Papillomavirus (HPV), types 16 and 18 only, includes type 45, if performed
88141	Cytopathology, cervical or vaginal (any reporting system), requiring interpretation by physician
88142	Cytopathology, cervical or vaginal (any reporting system), collected in preservative fluid, automated thin layer preparation; manual screening under physician supervision
88143	Cytopathology, cervical or vaginal (any reporting system), collected in preservative fluid, automated thin layer preparation; with manual screening and rescreening under physician supervision
88147	Cytopathology smears, cervical or vaginal; screening by automated system under physician supervision
88148	Cytopathology smears, cervical or vaginal; screening by automated system with manual rescreening under physician supervision
88150	Cytopathology, slides, cervical or vaginal; manual screening under physician supervision
88152	Cytopathology, slides, cervical or vaginal; with manual screening and computer-assisted rescreening under physician supervision
88153	Cytopathology, slides, cervical or vaginal; with manual screening and rescreening under physician supervision
88164	Cytopathology, slides, cervical or vaginal (the Bethesda System); manual screening under physician supervision
88165	Cytopathology, slides, cervical or vaginal (the Bethesda System); with manual screening and rescreening under physician supervision
88166	Cytopathology, slides, cervical or vaginal (the Bethesda System); with manual screening and computer-assisted rescreening under physician supervision
88167	Cytopathology, slides, cervical or vaginal (the Bethesda System); with manual screening and computer-assisted rescreening using cell selection and review under physician supervision
88174	Cytopathology, cervical or vaginal (any reporting system), collected in preservative fluid, automated thin layer preparation; screening by automated system, under physician supervision

88175	Cytopathology, cervical or vaginal (any reporting system), collected in preservative fluid, automated thin layer preparation; with screening by automated system and manual rescreening or review, under physician supervision
0500T	Infectious agent detection by nucleic acid (DNA or RNA), human papillomavirus (HPV) for five or more separately reported high-risk HPV types (eg, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68) (ie, genotyping)

HCPCS

G0123	Screening cytopathology, cervical or vaginal (any reporting system), collected in preservative fluid, automated thin layer preparation, screening by cytotechnologist under physician supervision
G0124	Screening cytopathology, cervical or vaginal (any reporting system), collected in preservative fluid, automated thin layer preparation, requiring interpretation by physician
G0141	Screening cytopathology smears, cervical or vaginal, performed by automated system, with manual rescreening, requiring interpretation by physician
G0143	Screening cytopathology, cervical or vaginal (any reporting system), collected in preservative fluid, automated thin layer preparation, with manual screening and rescreening by cytotechnologist under physician supervision
G0144	Screening cytopathology, cervical or vaginal (any reporting system), collected in preservative fluid, automated thin layer preparation, with screening by automated system, under physician supervision
G0145	Screening cytopathology, cervical or vaginal (any reporting system), collected in preservative fluid, automated thin layer preparation, with screening by automated system and manual rescreening under physician supervision
G0147	Screening cytopathology smears, cervical or vaginal, performed by automated system under physician supervision
G0148	Screening cytopathology smears, cervical or vaginal, performed by automated system with manual rescreening
P3000	Screening papanicolaou smear, cervical or vaginal, up to 3 smears, by technician under physician supervision
P3001	Screening papanicolaou smear, cervical or vaginal, up to 3 smears, requiring interpretation by physician
Q0091	Screening papanicolaou smear; obtaining, preparing and conveyance of cervical or vaginal smear to laboratory

ICD-10 Diagnosis

	All diagnoses

When services are Not Medically Necessary:
For the procedure codes listed above when criteria are not met.

Discussion/General Information

According to the American Cancer Society (ACS) (2023a), about 14,000 new cases of invasive cervical cancer will be diagnosed in 2023 with approximately 4300 deaths occurring from the disease.

Cervical cancer screening is a highly effective method of identifying squamous cell cervical cancer. When identified early, cervical cancer can be treated and results in high survival rates. The 5-year relative survival rate for localized cervical cancer is 92% (ACS, 2023b).

Cervical cancer screening is comprised of cervical cytology with Papanicolaou testing (also known as a 'Pap smear' or "Pap test") and testing for human papillomavirus (HPV) DNA. Pap tests are used to identify pre-cancerous or cancerous cells present on the cervix. When such cells are found, excision treatments can be used to completely remove the cancerous tissue. The detection of HPV DNA is used as an indication of the cancerous potential of a lesion and the potential risk of developing cervical cancer in the future. According to the ACS, nearly all cases of cervical cancer test positive for HPV DNA. However, not all HPV types result in the development of cervical cancer. Two types of HPV, type 16 and type 18 have been found to be associated with 65% to 75% of all cervical cancers. Another 10 HPV types are associated with the remaining cases.

The United States Preventive Services Task Force (USPSTF, 2018) recommends regular cervical cancer screening for eligible individuals aged 21 to 65 years old (Grade A recommendation). Cervical cancer screening every 3 years with cervical cytology alone is recommended in individuals aged 21 to 29 years. For individuals aged 30 to 65 years, any of the following screening options are recommended:

- every 3 years with cervical cytology; or
- every 5 years with primary high-risk human papillomavirus (hrHPV) testing; or
- every 5 years with both hrHPV testing and with cytology (co-testing).

The evidence summary upon which the guideline was based (Melnikow, 2018) stated that there was consistent evidence from clinical trials that primary hrHPV screening increased detection of cervical abnormalities (i.e., high-grade dysplasia or more severe) in the initial round of screening by approximately 2 to 3 times compared with cytology alone.

The American College of Obstetricians and Gynecologists (ACOG) (2021) and the American Society for Colposcopy and Cervical Pathology (ASCCP) (2021) have endorsed the 2018 USPSTF guidelines. The 2021 ACOG Practice Advisory replaced the organization's 2016 Practice Bulletin.

The USPSTF (2018) guideline recommends (Grade A recommendation) cervical cancer screening for average risk individuals beginning at age 21. This age criterion is based on data that cervical cancer before age 21 is rare, disease progression is slow, and there is high likelihood that abnormal cervical cytology in individuals less than 21 would regress. As such, the task force consensus that screening individuals less than 21 years of age could result in more harm than benefit is based on the potential of overtreatment contributing to future adverse pregnancy outcomes.

In addition, the USPSTF (2018) guideline recommends beginning HPV testing at age 30. The USPSTF recommendations refer both to primary HPV testing and HPV co-testing. Several HPV test kits have been approved by the Food and Drug Administration (FDA) as primary HPV tests in individuals age 25 and older. These include the Cobas® HPV test (Roche Diagnostics), which was approved in 2014 as a primary screening test (previously approved as co-test along with cervical cytology) the Onclarity™ HPV assay (Beckton,

Dickenson and Company), which was FDA-approved in 2018. A number of other test kits have been approved for co-testing with cervical cytology (Fontham, 2020).

There is a Grade D recommendation (meaning, the USPSTF recommends against routinely providing to asymptomatic individuals and found at least fair evidence that testing is ineffective or that harms outweigh benefits) against cervical screening in the following populations:

- Individuals younger than 21 years of age;
- Women who have had a hysterectomy;
- Women older than 65 years of age.

In July 2020, the ACS published an updated cervical cancer screening guideline recommending cervical cancer screening beginning at age 25 (Fontham, 2020). For individuals aged 25 to 65, the ACS recommends a primary HPV test specifically approved as a primary screening test by the FDA every 5 years. If primary HPV testing is not available, they recommend either screening with an HPV test and Pap test every 5 years or cervical cytology every 3 years. As was the case in the development of other guidelines, the committee considered the balance of likely benefits and harms according to the age at screening initiation. The ACS recommendation used the same decision model as the USPSTF 2018 recommendation, which suggests that decreasing the age of HPV testing from 30 to 25 will result in additional colposcopies, but more life-years saved. The ACS recommendations reflect the impact of HPV vaccination, first introduced in 2007 and the entry of vaccinated cohorts, now in their 20s, into the screening-eligible age range. Cytology-based screening is much less efficient in vaccinated populations, as abnormal cytology disproportionately identifies minor abnormalities resulting from HPV types that are associated with lower cancer risk.

The 2021 ACOG Practice Advisory included the following statement regarding the 2020 ACS guidelines:

> Despite the demonstrated efficacy and efficiency of primary hrHPV testing, uptake of this screening method has been slow because of the limited availability of FDA-approved tests and the significant laboratory infrastructure changes required to switch to this screening platform. Limited access to primary hrHPV testing is of particular concern in rural and under-resourced communities and among communities of color, which have disproportionately high rates of cervical cancer incidence, morbidity, and mortality. Although cytology-based screening options are still included in the ACS guidelines in acknowledgement of these barriers to widespread access and implementation, ACS strongly advocates phasing out cytology-based screening options in the near future. Until primary hrHPV testing is widely available and accessible, cytology-based screening methods should remain options in cervical cancer screening guidelines. Although HPV self-sampling has the potential to greatly improve access to cervical cancer screening, and there is an increasing body of evidence to support its efficacy and utility, it is still investigational in the United States.

Special populations

HIV-infection
In 2021, the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), and the HIV Medicine Association of the Infectious Diseases Society of America, in their Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV, published an updated recommendation on cervical cancer screening for individuals who are HIV-positive. The document states, “new recommendation for cervical cancer screening to start at age 21 based on the HIV/AIDS Cancer Match Study with no reported cases of cervical cancer below the age of 25.” The guideline cited the HIV/AIDS Cancer Match Study which analyzed data from a population of 164,084 women with HIV and found no cases of invasive cervical cancer in women under 25 years-old over 69,900 person-years of follow-up (standardized incidence ratio [SIR], 0; 95% confidence interval [CI], 0 to 7.1). SIR is a ratio of the observed incidence of a disease to the expected incidence of a disease in the general population. The authors stated, “The rationale for beginning screening at age 21 is to provide a 3- to 5-year window prior to age 25, when the risk of ICC in WWH [women with HIV] exceeds that of the general population.” Match study data were published by Stier and colleagues in 2021.

Immunosuppression without HIV-infection
In 2019, Moscicki and colleagues published an expert panel guideline on cervical cancer screening recommendations for immunocompromised women without HIV infection. The document noted that the relevant literature was reviewed and, given the small amount of data available, recommendations were “largely based on expert opinion”. For individuals who have had solid organ transplants or allogeneic hematopoietic stem cell transplants, cervical cytology is recommended for individuals under age 30. For individuals 30 years of age or older, co-testing with HPV is preferred, but cytology alone is acceptable. If cytology alone is used, annual testing is recommended unless the results of 3 consecutive tests are negative, in which case cytology can be performed every 3 years. If co-testing with HPV is performed, a baseline co-test with cytology and HPV is recommended and, if the cytology test is normal and HPV is negative, co-testing can be performed every 3 years. If transplants occur before the individual is 21 years old, the recommendation is to begin screening within 1 year of sexual debut.

The Moscicki publication cited an analysis of the U.S. Scientific Registry of Transplant Recipients (USSRTR) study (Madeleine, 2013). This analysis reported on the incidence of HPV-related cancers in a cohort of 187,679 solid organ transplant recipients. Risk data were presented in standardized incidence ratios (SIRs), which is a ratio of the observed incidence of a disease to the expected incidence of a disease in the general population. The reported SIR was 3.3 (95% CI, 2.6 to 4.2) for *in situ* cervical cancer, and 1.0 (95% CI, 0.8 to 1.3) for invasive cervical cancer. This indicated a greater than 3-fold increased risk of *in situ* cervical cancers and no increased risk for invasive cancers. Additionally, compared to subjects 50 years of age and older, subjects 18 to 34 years of age had a significantly greater risk of *in situ* cervical cancer (incidence rate ratio [IRR]=4.7). The median age at diagnosis was 38 years for *in situ* cervical cancer and 44.5 years for invasive cervical cancer and the median time from transplant to cervical diagnosis was 2.6 years for *in situ* cervical cancer and 3.8 years for invasive cervical cancer.

Diethylstilbestrol (DES)
The NIH (2021) recommends an annual medical examination that includes a pelvic examination and a Pap test that analyzes cells gathered from the cervix and the vagina for women who were exposed to DES *in utero*. DES use was discontinued in the United States in the 1970s and thus there are no longer any women who were exposed to DES *in utero* who are under 21 years old.

Definitions

High-risk human papillomavirus (HrHPV): Types of HPV that have been linked to an increased risk of cervical cancer. There are more than 100 types of HPV and at least 14 of these, including HPV 14 and 18, are known to cause cancer.

Screening: The testing of persons, in either the general population or those at high risk, for specific diseases or conditions in the absence of signs or symptoms of disease.

Surveillance: The ongoing systematic active observation or testing of a medical condition with the purpose of detecting changes that warrant new or additional interventions to prevent and control its worsening or spreading.

References

Peer Reviewed Publications:

1. Madeleine MM, Finch JL, Lynch CF, et al. HPV-related cancers after solid organ transplantation in the United States. Am J Transplant. 2013; 13(12):3202-3209.
2. Moscicki AB, Flowers L, Huchko MJ et al. Guidelines for cervical cancer screening in immunosuppressed women without HIV Infection. J Low Genit Tract Dis. 2019; 23(2):87-101.
3. Ogilvie GS, van Niekerk D, Krajden M, et al. Effect of screening with primary cervical HPV testing vs cytology testing on high-grade cervical intraepithelial neoplasia at 48 months: the HPV FOCAL randomized clinical trial. JAMA. 2018; 320(1):43-52.
4. Stier EA, Engels E, Horner MJ et al. Cervical cancer incidence stratified by age in women with HIV compared with the general population in the United States, 2002-2016. AIDS.2021; 35(11):1851-1856.

Government Agency, Medical Society, and Other Authoritative Publications:

1. American Cancer Society (ACS). 2023a. Key statistics for cervical cancer. Available at: https://www.cancer.org/cancer/cervical-cancer/about/key-statistics.html. Accessed on October 08, 2023.
2. American Cancer Society (ACS). 2023b. Survival rates for cervical cancer. Available at: https://www.cancer.org/cancer/types/cervical-cancer/detection-diagnosis-staging/survival.html. Accessed on October 08, 2023.
3. American College of Obstetricians and Gynecologists. Reaffirmed April 2023, Practice Advisory: Updated Cervical Cancer Screening Guidelines. Available at: https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2021/04/updated-cervical-cancer-screening-guidelines. Accessed on October 08, 2023.
4. Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), and the HIV Medicine Association of the Infectious Diseases Society of America. 2021. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. Available at: https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/human-0?view=full. Accessed on October 8, 2023.
5. Fontham ETH, Wolf AMD, Church TR et al. Cervical cancer screening for individuals at average risk: 2020 guideline update from the American Cancer Society. CA Cancer J Clin. 70(5):321-346.
6. Marcus JZ, Cason P, Downs LS Jr et al. The ASCCP Cervical Cancer Screening Task Force endorsement and opinion on the American Cancer Society updated cervical cancer screening guidelines. J Low Genit Tract Dis. 2021;25(3):187-191.
7. Melnikow J, Henderson JT, Burda BU, et al. Screening for cervical cancer with high-risk human papillomavirus testing: updated evidence report and systematic review for the US Preventive Services Task Force. JAMA. 2018; 320(7):687-705.
8. National Institutes of Health (NIH). 2021. Diethylstilbestrol (DES) and Cancer. Available at:https://www.cancer.gov/about-cancer/causes-prevention/risk/hormones/des-fact-sheet#q9. Accessed on October 8, 2023.
9. US Preventive Services Task Force, Curry SJ, Krist AH, Owens DK, Barry MJ, et al. Screening for cervical cancer: US Preventive Services Task Force recommendation statement. JAMA. 2018; 320(7):674-686.

Index

Cervical cancer

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

History

Status	Date	Action
Revised	11/09/2023	Medical Policy & Technology Assessment Committee (MPTAC) review. Reformatted Clinical Indications. Updated Description, Discussion/General Information and References sections.
Reviewed	11/10/2022	MPTAC review. Updated Discussion/General Information and References sections.
Revised	11/11/2021	MPTAC review. Removed bullet points in MN statements and removed criteria on chronically immunosuppressed individuals. Updated Discussion/General Information and References sections.
Revised	11/05/2020	MPTAC review. Updated Discussion/General Information and References sections. Corrected minor typographical error in first NMN statement. Reformatted Coding section
Reviewed	11/07/2019	MPTAC review.
Reviewed	01/24/2019	MPTAC review. Updated Discussion and References sections.
Revised	01/25/2018	MPTAC review.
Revised	01/17/2018	Hematology/Oncology Subcommittee review. Added “Using Cytology and” to title for clarification. Clarified MN and NMN statements regarding scope of document addressing only screening for HPV, not other types of HPV testing.
	01/01/2018	The document header wording updated from “Current Effective Date” to “Publish Date.” Updated Coding section with 01/01/2018 CPT changes; added 0500T, removed 88154 deleted 12/31/2017.
Revised	08/03/2017	MPTAC review.
Revised	07/10/2017	Hematology/Oncology Subcommittee review. Revised title. Added reference to ADMIN.00006 Preventive Health Guidelines to description section. Added MN and NMN statements regarding HPV testing. Changed the term ‘women’ to ‘individual’ in clinical indications section. Updated Coding, Rationale and References section.
Reviewed	11/03/2016	MPTAC review.
Reviewed	11/02/2016	Hematology/Oncology Subcommittee review. Updated References section.
New	11/05/2015	MPTAC review.
New	11/04/2015	Hematology/Oncology Subcommittee review. Initial document development.

Federal and State law, as well as contract language, and Medical Policy take precedence over Clinical UM Guidelines. We reserve the right to review and update Clinical UM Guidelines periodically. Clinical guidelines approved by the Medical Policy & Technology Assessment Committee are available for general adoption by plans or lines of business for consistent review of the medical necessity of services related to the clinical guideline when the plan performs utilization review for the subject. Due to variances in utilization patterns, each plan may choose whether to adopt a particular Clinical UM Guideline. To determine if review is required for this Clinical UM Guideline, please contact the customer service number on the member's card.

Alternatively, commercial or FEP plans or lines of business which determine there is not a need to adopt the guideline to review services generally across all providers delivering services to Plan’s or line of business’s members may instead use the clinical guideline for provider education and/or to review the medical necessity of services for any provider who has been notified that his/her/its claims will be reviewed for medical necessity due to billing practices or claims that are not consistent with other providers, in terms of frequency or in some other manner.