Healthy Blue

Clinical UM Guideline

Subject:	Cervical Cancer Screening Using Cytology and Human Papillomavirus Testing		
Guideline #:	CG-MED-53	**Publish Date:**	12/16/2020
Status:	Revised	**Last Review Date:**	11/05/2020

Description

This document addresses cervical cancer screening and testing for human papillomavirus (HPV) to assess cervical cancer risk. Currently cervical cancer screening comprises 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 Imaging Techniques for Screening and Identification of Cervical Cancer

Clinical Indications

Medically Necessary:

Cervical cancer screening with cytology is considered **medically necessary** for individuals* who meet either of the following criteria:

A. 21 years of age or older; **or**
B. Who are *chronically* immunosuppressed (for example, organ transplant recipients or seropositive for the human immunodeficiency virus [HIV]) regardless of age.

Screening for the presence of HPV is considered **medically necessary** for individuals* who meet either of the following criteria:

A. 30 years of age or older; **or**
B. Who are chronically immunosuppressed (for example, organ transplant recipients or seropositive for HIV) regardless of age.

Not Medically Necessary:

Cervical cancer screening with cytology is considered **not medically necessary** for all other indications including, but not limited to when the criteria above have not been met.

Screening for the presence of HPV is considered **not medically necessary** for all other indications including, but not limited, to 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) (2020a), about 13,800 new cases of invasive cervical cancer will be diagnosed in 2020, with approximately 4290 women dying 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, 2020b).

Cervical cancer screening comprises 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 cancer. The detection of HPV DNA is used as an indication of the cancerous potential of a lesion and the potential risk of the woman 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.

In its most recent guideline, the United States Preventive Services Task Force (USPSTF) (2018) recommends regular cervical cancer screening for eligible individuals aged 21 to 65 years old. 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 options are recommended: screening every 3 years with cervical cytology, every 5 years with primary high-risk human papillomavirus (hrHPV) testing, or every 5 years with both hrHPV testing and with cytology (cotesting). 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) (2016) recommends that individuals aged 21-29 years old should be screened every 3 years with cervical cytology alone. For individuals aged 30 to 65 years old, cotesting with cervical cytology and HPV testing every 5 years is recommended and cervical cytology alone every 3 years is also an acceptable option. ACOG (2016) recommends that cervical cancer screening should begin at 21 years of age, with the exception of women who are infected with HIV or who are otherwise immunocompromised. This is similar to the USPSTF guideline, with the exception of recommending co-testing for individuals age 30 to 65 every 5 years rather than every 3 years.

Most guidelines recommend cervical cancer screening for average risk individuals beginning at age 21, including the USPSTF (2018), ACOG (2016) and a combined guideline from the ACS, the American Society for Colposcopy and Cervical Pathology (ASCCP), and the American Society for Clinical Pathology (ASCP) (Saslow, 2012). As stated in the USPSTF guideline, the 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. Thus, the task force believed that, due to the potential of overtreatment leading to future adverse pregnancy outcomes, screening individuals less than 21 years of age could result in more harm than benefit.

In addition, the USPSTF (2018) and ACOG (2016) guidelines recommend beginning HPV testing at age 30. The USPSTF recommendations refer both to primary HPV testing and HPV cotesting and ACOG addresses only HPV cotesting. Two 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).

However, 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.

Special populations

As stated in the ACOG (2016) guideline, HIV infection and other immunocompromising conditions are an exception to the recommendation that cervical cancer screening begin at age 21. Recommendations from the Centers of Disease Control and Prevention (CDC), the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America state that, for women with HIV infection, a Pap test should be obtained twice during the first year after diagnosis of HIV infection, even if younger than 21 years, and if the results are normal, annually thereafter (Kaplan, 2009).

Data suggest that young women who have received solid organ transplantation are at higher risk of cervical cancer and screening women in this population who are under the age of 21 should be considered. The U.S. Transplant Center Match (TCM) Study was a large population based cohort study using data from the U.S. Scientific Registry

of Transplant Recipients (USSRTR) from 1987 to 2008 (Engels, 2011). A total of 175,732 subjects of any age with invasive cancers were included in the analysis. The authors reported that solid organ transplant recipients have an approximately 2-fold greater increase in risk of any type of cancer compared to the general public. While this study did not identify an increased risk of cervical cancer, the authors noted that this finding may be the result of a high rate of cervical cancer screening and rapid treatment of precancerous lesions. A follow-up investigation by Madeleine and others (2013) using USSRTR data reported on the incidence of HPV-related cancers in a cohort of 187,679 subjects with both invasive and *in situ* cancers and aged 18 years and older. In this study, 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 for *in situ* cervical cancer, and 1.0 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). As was commented on by Engels, the high rate of cervical cancer screening, rigorous surveillance of suspicious lesions, and rapid treatment of precancerous lesions may have had a significant impact on the rate of both *in situ* and invasive cervical cancers seen in the general population, as well as the study population.

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.

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. Engels EA, Pfeiffer RM, Fraumeni JF Jr, et al. Spectrum of cancer risk among US solid organ transplant recipients. JAMA. 2011; 306(17):1891-1901.
2. 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.
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.

Government Agency, Medical Society, and Other Authoritative Publications:

1. American Cancer Society (ACS). 2020a. Key statistics for cervical cancer. Available at: https://www.cancer.org/cancer/cervical-cancer/about/key-statistics.html. Accessed on September 28, 2020.
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3. American College of Obstetricians and Gynecologists. Practice Bulletin Number 168: Screening for Cervical Cancer. October, 2016.
4. 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. 2020 Jul 30. Epub ahead of print.
5. Kaplan JE, Benson C, Holmes, KK, et al. Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents. Recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. MMWR. 2009; 58(RR-4):1-207.
6. 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.
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8. 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.

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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	11/05/2020	Medical Policy & Technology Assessment Committee (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.