

MEDICAL POLICY



MEDICAL POLICY DETAILS	
Medical Policy Title	CERVICAL CANCER SCREENING and HUMAN PAPILLOMA VIRUS (HPV) TESTING
Policy Number	2.02.04
Category	Technology Assessment
Effective Date	11/19/99
Revised Date	04/19/01, 07/19/01, 10/25/01, 01/23/03, 02/26/04, 02/24/05, 04/27/06, 04/26/07, 04/24/08, 11/20/08, 05/28/09, 05/27/10, 05/19/11, 05/24/12, 05/23/13, 05/22/14, 05/28/15, 05/25/16, 05/18/17, 03/15/18, 03/21/19
Product Disclaimer	<ul style="list-style-type: none"> • If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply. • If a commercial product (including an Essential Plan product) or a Medicaid product covers a specific service, medical policy criteria apply to the benefit. • If a Medicare product covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.

POLICY STATEMENT

- I. The Health Plan considers routine cervical cancer screening **and HPV testing** with FDA approved techniques (e.g., conventional Pap smear, liquid based cytology, cobas® HPV test) as **medically appropriate**.
- II. Based upon our criteria and review of the peer-reviewed literature, cervical cancer screening with the combined (cotesting) use of cervical cytology testing and an FDA approved test for high-risk subtypes of human papillomavirus (HPV) or an FDA approved test for high-risk subtypes of HPV alone is considered **medically appropriate** in women aged 30 to 65 years of age no more frequently than every 5 years.
- III. Based on our criteria and assessment of the peer-reviewed literature, including the United States Preventive Services Task Force (USPSTF) recommendations, cervical cancer screening should start at age 21 years. A PAP test no more frequently than every 3 years is considered **medically appropriate** in women who are average risk for cervical cancer.
- IV. Based on our criteria and assessment of the peer-reviewed literature, including the United States Preventive Services Task Force (USPSTF) recommendations, cervical cancer screening in women younger than 21 years is **not medically necessary**.
- V. Based on our criteria and assessment of the peer-reviewed literature, including the United States Preventive Services Task Force (USPSTF) recommendations, cervical cancer screening in women older than 65 years who have had adequate prior screening and are not otherwise at high risk for cervical cancer is **not medically necessary**.
- VI. Based on our criteria and assessment of the peer-reviewed literature, including the United States Preventive Services Task Force (USPSTF) recommendations, cervical cancer screening in women who have had a hysterectomy with removal of the cervix and who do not have a history of a high-grade precancerous lesion (ie, cervical intraepithelial neoplasia [CIN] grade 2 or 3) or cervical cancer is **not medically necessary**.
- VII. Based upon our criteria and review of the peer-reviewed literature, human papillomavirus (HPV) testing of high-risk sub-types has been medically proven to be effective and therefore, **medically appropriate** for use in the triage of patients with *atypical squamous cells of undetermined significance (ASCUS)* on cervical screening.
- VIII. Based upon our criteria and review of the peer-reviewed literature, HPV screening is **not medically appropriate** for women under age 30 years since these women frequently test positive for HPV and have an effective immune response that will clear the infection or reduce the viral load to undetectable levels within two years of the initial infection.

Medical Policy: CERVICAL CANCER SCREENING and HUMAN PAPILLOMA VIRUS (HPV) TESTING

Policy Number: 2.02.04

Page: 2 of 11

- IX. Based upon our criteria and review of the peer-reviewed literature, HPV testing has not been proven to be effective and is therefore, **not medically necessary** in the routine triage of women with *low-grade squamous intraepithelial lesions (LSIL)* found through screening examinations (e.g., cervical cytology).
- X. Based upon our criteria and review of the peer-reviewed literature, Papsure® as an adjunct to cervical cancer screening has not been medically proven to be more effective in improving net health outcomes than standard testing and is, therefore, considered **not medically necessary**.

POLICY GUIDELINES

- I. While our review of scientific evidence concludes that use of liquid based monolayer technology at least every three years is sufficient given the sensitivity, specificity, and cost-effectiveness of this technology; coverage will be provided at a frequency determined by the practitioner and member following informed discussions and shared decision-making.
- II. Since the utilization of the automated slide reading systems (e.g., FocalPoint™, ThinPrep® Imaging system, MonoPrep LBP processor) have not been proven to have a significantly greater sensitivity than the manual reading of specimens, the benefit for the use of these systems will generally be provided at the same level as that for manual reading of the specimen.

DESCRIPTION

The Papanicolaou (Pap) smear was introduced in the 1940's as a method of preventing invasive cervical cancer and has been credited with reducing the incidence of cervical carcinoma by 74% since its introduction. Certain cancers caused by infectious agents, such as human papillomavirus (HPV) could be prevented through treatment of the infection. Screening can help prevent cervical cancers by offering the opportunity to detect cancer early, when treatment is less extensive and more likely to be successful. HPV vaccines cannot protect against established infections, nor do they protect against all types of HPV, which is why vaccinated women should still be screened for cervical cancer.

Despite the dramatic impact of pap screening, concerns regarding Pap performance remain. Approximately 30 percent of cervical cancers result from errors in sampling and interpretation. The effort to reduce the number of undiagnosed cancers because of these errors has acted as a catalyst in the development of new screening technologies. FDA-approved developments in Pap screening technology have been aimed at reducing the rate of false-negative results. Some of the developments are liquid based monolayer slide preparation devices, such as ThinPrep (Cytoc Corporation), SurePath (TriPath Imaging), MonoPrep Pap Test (MonoGen, Inc.), and Liqui-PREP (LGM International).

Liquid based monolayer slide preparations are screening systems that utilize a different type of cell preparation than that used for conventional Pap smear slides. This technology involves dispersing the collected cervical cell sample in a liquid medium, then collecting the cells in a filter and depositing them in a thin layer on the slide. The liquid-based technique contrasts with the conventional method of preparation (that consists of directly swabbing the collected cells onto a glass slide) by removing much of the debris and red blood cells for a clearer slide and reduces artifacts in cellular morphology, thereby decreasing the rate of false negative smears and improving sensitivity.

The specimen obtained for the monolayer Pap test can be utilized to perform reflex testing (from the same liquid base) to test for other conditions, such as Human Papillomavirus (HPV), during the initial office examination of a patient undergoing a cervical examination and eliminates the need for an additional office examination to collect a specimen for HPV testing.

HPV is a common sexually transmitted disease that has an established causal link in the development of cervical cancer. The relationship between certain types of HPV and the development of cervical cancer is well established. There are more than 150 types of HPV, approximately 30 of which are prevalent in the cervix. Of these, some types (6, 11, 30, 34, 42, 43, 44, 49, 53, 54, 61, 64, and 69) make up the low- or no-oncogenic risk group because they are very unlikely to be associated with cervical cancer. Other types, referred to as high risk HPV sub-types, make up the intermediate and high-risk group (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, and 73) because they are associated with low-grade squamous intraepithelial lesions, high-grade intraepithelial lesions, and invasive cancers. Of the high-risk types, HPV 16 and 18 are the most carcinogenic and the most prevalent.

Medical Policy: CERVICAL CANCER SCREENING and HUMAN PAPILLOMA VIRUS (HPV) TESTING

Policy Number: 2.02.04

Page: 3 of 11

High-risk HPV subtypes have been identified in more than 90% of cervical cancers. All HPV types may regress without treatment (except cancer), but it is not possible to predict which will regress and when.

Three automated slide reading systems have been approved by the FDA:

- I. The ThinPrep Imaging System®, by Cytoc, is designed to be used with ThinPrep® monolayer slide preparations. The system, according to FDA labeling, is indicated for assisting in primary cervical cancer screening of ThinPrep® Pap test slides for the presence of cervical neoplasia, including its precursor lesions. The ThinPrep® Imaging System highlights areas for focused screening by cytotechnologists.
- II. FocalPoint™ (formerly called AutoPap), by TriPath Imaging, is approved by the FDA for primary screening and rescreening of Pap smears. The system reads each slide and identifies slides without abnormalities that do not require manual reading, slides that should be manually read, and slides that should have a second manual reading. The system is not intended to be used on slides from patients designated as high risk.
- III. The MonoPrep Pap Test (MPPT), by MonoGen, Inc., is used in conjunction with the MonoPrep LBP processor, to collect and prepare cervical-vaginal cytology specimens to screen for cervical cancer, its precursor lesions, and other cytological categories and conditions.

Papsure® is a method of cervical cancer screening in which a conventional Pap smear is combined with speculscopy, an endoscopic visualization of the cervix. Papsure® is utilized as an adjunct to the Pap smear and as a technique in selecting women with atypical Pap smears for further evaluation for colposcopy. It is thought that Papsure® will increase the sensitivity of cervical cancer screening by enhancing the visual inspection of the cervix. Following a cervical examination the cervix is washed with acetic acid (vinegar). A chemiluminescent disposable light, known as a Speculte®, is attached to the speculum. The cervix is visualized using a magnification loupe. Abnormal epithelial cells, those with increased keratinization and nuclear cytoplasmic ratios, show an increased reflection of light and appear white; while normal epithelial cells appear blue or purple. The white lesions may then be sampled for cytologic examination. Women with an abnormal Pap smear, even in the presence of a negative speculscopy examination, should be referred for additional evaluation.

The Patient Protection and Affordable Care Act (PPACA) also requires coverage of cervical cancer screening in accordance with the recommendations of the U.S. Preventive Services Task Force (USPSTF). As of August 1, 2012, for all non-grandfathered policies, PPACA was expanded to include coverage for certain preventive services for women; including screening for cervical cancer in women age 21 to 65 with cytology (Pap smear) every 3 years or, for women age 30 to 65 years who want to lengthen the screening interval, screening with a combination of cytology and HPV testing every 5 years.

Cervical cancer screening is an important part of preventive health care and is supported by the Health Plan. Refer to our Preventive Health Guidelines for specific recommendations. Guidelines are located on our website at:

<https://www.excellusbcbcs.com/wps/portal/xl/prv/pc/cpg>.

RATIONALE

Several studies have been published that compare the efficacy of HPV based screening with cytology screening. Some study results favor HPV based screening although limitations need to be addressed and several questions remain that need to be answered (e.g., age to begin HPV based screening, length of screening intervals) before consideration can be given to recommending changes in screening protocols. No specialty societies have published statements recommending primary HPV based screening over cytology screening.

Cervical Cytology Screening

The recommendations of the U.S. Preventive Services Task Force (USPSTF) (revised February 2018) address cervical cancer screening in women who have a cervix, regardless of sexual history. The recommendations do not apply to women who have received a diagnosis of a high-grade precancerous cervical lesion or cervical cancer, women with in utero

Medical Policy: CERVICAL CANCER SCREENING and HUMAN PAPILLOMA VIRUS (HPV) TESTING

Policy Number: 2.02.04

Page: 4 of 11

exposure to diethylstilbestrol, or women who are immunocompromised (such as those who are HIV positive). The USPSTF recommends:

- I. Screening for cervical cancer in women age 21 to 65 years with cytology (Pap smear) every 3 years or, for women age 30 to 65 years who want to lengthen the screening interval, screening with a combination of cytology and human papillomavirus (HPV) testing every 5 years. (Recommendation: A)
- II. Against screening for cervical cancer in women younger than age 21 years (Recommendation: D).
- III. Against screening for cervical cancer in women older than age 65 years who have had adequate prior screening and are not otherwise at high risk for cervical cancer (Recommendation: D).
- IV. Against screening for cervical cancer in women who have had a hysterectomy with removal of the cervix and who do not have a history of a high-grade precancerous lesion (CIN grade 2 or 3) or cervical cancer (Recommendation: D).
- V. Against screening for cervical cancer with HPV testing, alone or in combination with cytology, in women younger than age 30 years (Recommendation: D).

Recommendation: A: The USPSTF recommends the service. There is high certainty that the net benefit is substantial. Offer or provide this service.

D: The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits. Discourage the use of this service.

The American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin (January 2016) addressing cervical cancer screening and prevention states:

- I. The following recommendations are based on good and consistent scientific evidence (Level A):
 - A. Cervical cancer screening should begin at age 21 years. With the exception of women who are infected with HIV, women younger than age 21 years should not be screened regardless of the age of sexual initiation or the presence of other behavior-related risk factors.
 - B. Women aged 21–29 years should be tested with cervical cytology alone, and screening should be performed every 3 years. Co-testing should not be performed in women younger than 30 years. Annual screening should not be performed.
 - C. For women aged 30–65 years, co-testing with cytology and HPV testing every 5 years is preferred.
 - D. In women aged 30–65 years, screening with cytology alone every 3 years is acceptable. Annual screening should not be performed.
 - E. Liquid-based and conventional methods of cervical cytology collection are acceptable for screening.
 - F. Screening by any modality should be discontinued after age 65 years in women with evidence of adequate negative prior screening results and no history of CIN 2 or higher. Adequate negative prior screening results are defined as three consecutive negative cytology results or two consecutive negative co-test results within the previous 10 years, with the most recent test performed within the past 5 years.
 - G. In women who have had a hysterectomy with removal of the cervix (total hysterectomy) and have never had CIN 2 or higher, routine cytology screening and HPV testing should be discontinued and not restarted for any reason.
 - H. Women with any of the following risk factors may require more frequent cervical cancer screening than recommended in the routine screening guidelines, which were intended for average-risk women: women who are infected with HIV, women who are immunocompromised, women who were exposed to diethylstilbestrol in utero, women previously treated for CIN 2, CIN 3, or cancer.
- II. The following recommendations are based on limited and inconsistent scientific evidence (Level B):
 - A. Women with a history of CIN 2, CIN 3, or adenocarcinoma in situ should continue screening for a total of 20 years after spontaneous regression or appropriate management of CIN 2, CIN 3, or adenocarcinoma in situ, even if it requires that screening continue past age 65 years.
 - B. Women should continue to be screened if they have had a total hysterectomy and have a history of CIN 2 or higher in the past 20 years or cervical cancer ~~ever~~ at any point. Screening with cytology alone every 3 years for 20 years after the initial post-treatment surveillance period seems to be reasonable for these women.
 - C. In women 25 years and older, the FDA-approved primary HPV screening test can be considered as an alternative to current cytology-based cervical cancer screening methods. Cytology alone and cotesting remain the options specifically recommended in current major society guidelines. If screening with primary HPV testing is used, it should be performed as per the ASCCP and SGO interim guidance.

Medical Policy: CERVICAL CANCER SCREENING and HUMAN PAPILLOMA VIRUS (HPV) TESTING

Policy Number: 2.02.04

Page: 5 of 11

- D. Women with ASC-US cytology and negative HPV test results, whether from reflex HPV testing or co-testing, have a low risk of CIN 3, but it is slightly higher than the risk in women with a negative cotest result, and it is recommended that they have co-testing in 3 years.
 - E. Cytology-negative, HPV-positive co-test results in women who are 30 years and older should be managed in one of two ways:
 - 1. Repeat co-testing in 12 months. If the repeat cervical cytology test result is ASC-US or higher or the HPV test result is still positive, the patient should be referred for colposcopy. Otherwise, the patient should have co-testing in 3 years.
 - 2. Immediate HPV genotype-specific testing for HPV-16 or HPV 18 can be performed. Women with positive test results for either HPV genotype should be referred directly for colposcopy. Women with negative results for both HPV genotypes should be retested in 12 months, with management of results as described in the 2012 ASCCP revised guidelines for the management of abnormal cervical cancer screening test results.
- III. The following recommendations are based primarily on consensus and expert opinion (Level C): Women who have received the HPV vaccine should be screened according to the same guidelines as women who have not been vaccinated

Published studies comparing the FocalPoint™ and ThinPrep® Imaging automated slide reading systems to traditional manual reading and rescreening identified the: 1) FocalPoint™ system to be between 4 to 7% more sensitive in determining a positive slide, depending on the cutoff, than traditional manual reading and approximately 1% more specific in identifying normal slides; and 2) the ThinPrep® Imaging system to be equivalent to manual review by a cytotechnologist.

Human Papillomavirus (HPV) Testing

Data from the Atypical Squamous Cells of Undetermined Significance/Low-Grade Squamous Intraepithelial Lesions Triage Study (ALTS) trial showed the triage of ASCUS smears using HPV testing for triage to immediate colposcopy was more sensitive and equally specific in identifying cervical intraepithelial neoplasia grade 3 (CIN 3) as repeat Pap smear using ASCUS as the threshold for colposcopy referral. Based primarily on the results of this trial, recent guidelines issued by the American Society for Colposcopy and Cervical Pathology recommend either repeat Pap smear, immediate colposcopy, or HPV testing for women who have ASCUS Pap smears.

In March 2003, the U.S. Food and Drug Administration (FDA) approved the Digene Hybrid Capture 2 (HC2) High-Risk HPV DNA test for screening women over 30 years of age for HPV infection when used along with a Pap test; in addition to the original approval for testing women with an abnormal Pap test to determine need for further evaluation. The approval was based upon several large clinical studies demonstrating HPV infection as a strong etiologic factor for cervical abnormalities, but often transient and nonspecific. The HC2 test can identify 13 strains of high-risk HPV DNA but cannot determine the specific HPV strain(s) in the specimen and reports only the presence or absence of high-risk HPV DNA.

On March 12, 2009, the FDA approved two DNA tests that identify HPV types:

- I. The Cervista™ HPV HR test, detects 14 high-risk HPV types in cervical cell samples; including the 13 types detected by the HC2 test plus one other (HPV 66).
- II. The Cervista™ HPV 16/18, detects the DNA sequences specific for HPV type 16 and HPV type 18 in cervical cells. In women age 30 and older or women with borderline cytology (e.g., ASCUS) the Cervista™ HPV 16/18 test can be used together with cytology and the Cervista™ HPV HR test to assess risk of cervical disease.

Both tests utilize an isothermal enzymatic DNA amplification process with a fluorescent read out and both are approved for use with ThinPrep® samples. The Cervista™ HPV tests (formerly known as Invader HPV) were developed by Third Wave Technologies which was acquired in 2008 by Hologic Inc., the manufacturer of the ThinPrep® Pap test.

The absence of HPV infection in conjunction with a normal Pap smear has a high negative predictive value and identifies a group of women at low risk for cervical abnormalities. HPV screening is not recommended for women under 30 years of age as HPV infections are most likely to be transient in this group.

Medical Policy: CERVICAL CANCER SCREENING and HUMAN PAPILLOMA VIRUS (HPV) TESTING

Policy Number: 2.02.04

Page: 6 of 11

Published clinical trials have provided evidence that HPV testing for high-risk sub-groups has utility in triaging patients with ASCUS results to avoid unnecessary invasive work-up but does not support the use of HPV testing in women with LSIL due to the high prevalence of HPV infection in women with this diagnosis.

The 2015 guidelines of the American Cancer Society for the early detection of cancer state:

- I. Cervical cancer screening should start at age 21,
- II. Women between the ages of 21 and 29 should have a Pap test every 3 years and HPV testing should not be used in this age group unless it's needed after an abnormal test result,
- III. Women between the ages of 30 and 65 should have a Pap test plus an HPV test every 5 years, however a Pap test may be performed alone every 3 years,
- IV. Women over age 65 who have had regular cervical cancer testing in the past 10 years with normal results should not be tested for cervical cancer. Once testing is stopped, it should not be started again. Women with a history of a serious cervical pre-cancer should continue to be tested for at least 20 years after that diagnosis, even if testing goes past age 65.
- V. A woman who has had her uterus and cervix removed (a total hysterectomy) for reasons not related to cervical cancer and who has no history of cervical cancer or serious pre-cancer should not be tested.
- VI. All women who have been vaccinated against HPV should still follow the screening recommendations for their age groups.

On April 24, 2014 the FDA approved the first HPV DNA test for women age 25 years and older that can be used alone to help a health care professional assess the need for a woman to undergo additional diagnostic testing for cervical cancer. Using a sample of cervical cells, the cobas® HPV Test detects DNA from 14 high-risk HPV types. The test specifically identifies HPV 16 and HPV 18, while concurrently detecting 12 other types of high-risk HPVs (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68). Based on results of the cobas® HPV test, women who test positive for HPV 16 or HPV 18 should have a colposcopy and women testing positive for one or more of the 12 other high-risk HPV types should have a Pap test to determine the need for a colposcopy. The FDA states health care professionals should use the cobas® HPV Test results together with other information, such as the patient screening history and risk factors, and current professional guidelines. The approval of the cobas® HPV DNA test did not change the recommendations of any current practice guidelines for cervical cancer screening.

According to the Centers for Disease Control and Prevention there are currently no guidelines for HPV testing in men nor is there a HPV test for men that has been approved by the FDA.

Speculoscopy (e.g., PapSure®) The Speculite® device was approved by the U.S. Food and Drug Administration (FDA) in December 2000 for vaginal illumination during the PapSure® procedure when used as an adjunct to conventional Pap smears. It is not intended to be used to grade lesions identified during the procedure.

Published, peer-reviewed literature has not demonstrated improvements in the net health outcome with the utilization of Papsure®. Society guidelines/statements issued by the US Preventive Services Taskforce, the American Cancer Society, and the American College of Obstetricians and Gynecologists, that focus upon techniques for cervical cancer screening, do not address Papsure® or speculoscopy.

Other techniques

Other methods of cervical cancer screening and/or HPV testing currently under investigation include testing of self-collected specimens, urine testing, and an ELISA based test of the biomarker p16(INK4A) for protein expression.

CODES

- *Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.*
- ***CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.***
- *Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.*

CPT Codes

Code	Description
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	with manual screening and rescreening under physician supervision
88147	Cytopathology smears, cervical or vaginal; screening by automated system under physician supervision
88148	screening by automated system with manual rescreening under physician supervision
88150	Cytopathology, slides, cervical or vaginal; manual screening under physician supervision
88152	with manual screening and computer-assisted rescreening under physician supervision
88153	with manual screening and rescreening under physician supervision
88164	Cytopathology, slides, cervical or vaginal (the Bethesda system); manual screening under physician supervision;
88165	with manual screening and rescreening under physician supervision
88166	with manual screening and computer-assisted rescreening under physician supervision
88167	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	with screening by automated system and manual rescreening or review, under physician supervision

Copyright © 2019 American Medical Association, Chicago, IL

HCPCS Codes

Code	Description
G0101	Cervical or vaginal cancer screening; pelvic and clinical breast examination
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

Medical Policy: CERVICAL CANCER SCREENING and HUMAN PAPILLOMA VIRUS (HPV) TESTING**Policy Number: 2.02.04****Page: 8 of 11**

Code	Description
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
G0476	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, 58, 68) for cervical cancer screening, must be performed in addition to pap test
P3000	Screening Papanicolaou smear, cervical or vaginal, up to three smears, by technician under physician supervision
P3001	Screening Papanicolaou smear, cervical or vaginal, up to three smears, requiring interpretation by physician
Q0091	Screening Papanicolaou smear; obtaining preparing and conveyance of cervical or vaginal smear to laboratory

ICD10 Codes

Code	Description
B97.7	Papillomavirus as the cause of diseases classified elsewhere
C53.0-C53.9	Malignant neoplasm of cervix uteri (code range)
C79.82	Secondary malignant neoplasm of genital organs
D06.0-D06.9	Carcinoma in situ of cervix (code range)
D39.0	Neoplasm of uncertain behavior of uterus
N87.0-N87.9	Dysplasia of cervix uteri (code range)
R87.610- R87.619	Abnormal cytological findings in specimens from cervix uteri (code range)
R87.620- R87.629	Abnormal cytological findings on specimens from vagina (code range)
R87.810- R87.811	High risk human papillomavirus [HPV] DNA test positive from female genital organs (code range)
R87.820- R87.821	Low risk human papillomavirus (HPV) DNA test positive from female genital organs (code range)

REFERENCES

American Cancer Society. Cancer Facts & Figures 2017. [<https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2017/cancer-facts-and-figures-2017.pdf>] accessed 2/11/19.

American Cancer Society. Guidelines for the early detection of cancer. Revised 2018 May 30 [http://www.cancer.org/docroot/PED/content/PED_2_3X_ACS_Cancer_Detection_Guidelines_36.asp] accessed 2/11/19.

American Cancer Society. Cervical cancer prevention and early detection. Revised 2014 Dec 11 [<http://www.cancer.org/acs/groups/cid/documents/webcontent/003167-pdf.pdf>] accessed 2/11/19.

American College of Obstetricians and Gynecologists Committee on Health Care for Underserved Women. ACOG Committee Opinion 624: Cervical cancer in low-resource settings. *Obstet Gynecol* 2015 Feb;125:526-8.

American College of Obstetricians and Gynecologists. ACOG practice bulletin #157: Cervical cancer screening and prevention. *Obstet Gynecol* 2016 Jan;127(1):e1-20.

Medical Policy: CERVICAL CANCER SCREENING and HUMAN PAPILLOMA VIRUS (HPV) TESTING

Policy Number: 2.02.04

Page: 9 of 11

*Anttila A, et al. Cervical cancer patterns with automation-assisted and conventional cytological screening: a randomized study. Int J Cancer 2011 Mar 1;128(5):1204-12.

*ASCUS-LSIL Triage Study (ALTS) Group. Results of a randomized trial on the management of cytology interpretations of atypical squamous cells of undetermined significance. Am J Obstet Gynecol 2003 Jun;188(6):1383-92.

*ASCUS-LSIL Triage Study (ALTS) Group. A randomized trial on the management of low-grade squamous intraepithelial lesion cytology interpretations. Am J Obstet Gynecol 2003 Jun;188(6):1393-400.

*ASCUS-LSIL Triage Study (ALTS) Group. Human Papillomavirus testing for triage of women with cytologic evidence of low-grade squamous intraepithelial lesions: baseline data from a randomized trial. J Natl Cancer Inst 2000;92:397-402.

*Belinson JL, et al. A population-based clinical trial comparing endocervical high-risk HPV testing using hybrid capture 2 and Cervista from the SHENCCAST II Study. Am J Clin Pathol 2011 May;135(5):790-5.

*Blatt AJ, et al, Comparison of cervical cancer screening results among 256,648 women in multiple clinical practices. Cancer Cytopathology 2015;123(5):282-288.

BlueCross BlueShield Association. Cervical cancer screening technologies with Pap and HPV - archived. Medical Policy Reference Manual Policy #2.04.09. 2011 Oct 4.

BlueCross BlueShield Association. Speculoscopy - archived. Medical Policy Reference Manual Policy #4.01.15. 2012 Sep 13.

Bouchard-Fortier G, et al. Co-testing for detection of high-grade cervical intraepithelial neoplasia and cancer compared with cytology alone: a meta-analysis of randomized controlled trials. J Public Health (Oxf) 2014 Mar;36(1):46-55.

*Castle PE, et al. Performance of carcinogenic human papillomavirus (HPV) testing and HPV16 or HPV18 genotyping for cervical cancer screening of women aged 25 years and older: a subanalysis of the ATHENA study. Lancet Oncol 2011 Sep;12(9):880-90.

Centers for Disease Control and Prevention. Genital HPV infection – fact sheet. Updated 2017 Nov 16 [http://www.cdc.gov/std/HPV/STDFact-HPV.htm] accessed 2/11/19.

Centers for Disease Control and Prevention. HPV and men – CDC fact sheet. Updated 2016 Dec 28 [http://www.cdc.gov/std/hpv/STDFact-HPV-and-men.htm] accessed 2/11/19.

C Kitchener H, et al. The clinical effectiveness and cost-effectiveness of primary human papillomavirus cervical screening in England: extended follow-up of the ARTISTIC randomised trial cohort through three screening rounds. Health Technol Assess 2014 Apr;18(23):1-196.

Davey DD, et al. 2013 statement on human papillomavirus DNA test utilization. Am J Clin Pathol 2014 Apr;141(4):459-61.

Elfström KM, et al. Long-term HPV type-specific risks for ASCUS and LSIL: a 14-year follow-up of a randomized primary HPV screening trial. Int J Cancer 2015 Jan 15;136(2):350-9.

Felix JC, et al. The Clinical and Economic Benefits of Co-Testing Versus Primary HPV Testing for Cervical Cancer Screening: A Modeling Analysis J Womens Health (Larchmt). 2016 Jun;25(6):606-16. doi: 10.1089/jwh.2015.5708

*Gök M, et al. Experience with high-risk human papillomavirus testing on vaginal brush-based self-samples of non-attendees of the cervical screening program. Int J Cancer 2012 Mar 1;130(5):1128-35.

Huh WK, et al. Use of primary high-risk human papillomavirus testing for cervical cancer screening: interim clinical guidance. Gynecol Oncol 2015 Feb;136(2):178-82.

*Jesdapatarakul S, et al. Liqui-Prep® versus conventional Papanicolaou smear to detect cervical cells abnormality by split-sample technique: a randomized double-blind controlled trial. Diagn Cytopathol 2011 Jan;39(1):22-7.

*Kitchener HC, et al. Automation-assisted versus manual reading of cervical cytology (MAVARIC): a randomised controlled trial. Lancet Oncol 2011 Jan;12(1):56-64.

Medical Policy: CERVICAL CANCER SCREENING and HUMAN PAPILLOMA VIRUS (HPV) TESTING

Policy Number: 2.02.04

Page: 10 of 11

Klug SJ, et al. A randomized trial comparing conventional cytology to liquid-based cytology and computer assistance. Int J Cancer 2013 Jun 15;132(12):2849-57.

Malila N, et al. The HPV test has similar sensitivity but more overdiagnosis than the Pap test--a randomised health services study on cervical cancer screening in Finland. Int J Cancer 2013 May 1;132(9):2141-7.

*Massad LS, et al; 2012 ASCCP Consensus Guidelines Conference. 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. Obstet Gynecol 2013 Apr;121(4):829-46.

Massad LS, et al; 2012 ASCCP Consensus Guidelines Conference. 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. J Low Genit Tract Dis 2013 Apr;17(5 Suppl 1):S1-27.

Meinikow J, 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 Aug 21;320(7):687-705.

Monsonog J, et al. Prevalence of high-risk human papilloma virus genotypes and associated risk of cervical precancerous lesions in a large U.S. screening population: data from the ATHENA trial. Gynecol Oncol 2015 Apr;137(1):47-54.

*National Cancer Institute. Cervical cancer screening. Updated 2018 Jun 14.
[<http://www.cancer.gov/types/cervical/hp/cervical-screening-pdq>] accessed 2/11/19.

National Cancer Institute. HPV and cancer. 2015 Feb 9 [<http://www.cancer.gov/cancertopics/factsheet/Risk/HPV#r4>] accessed 2/11/19.

*New York State Consolidated Laws § 3216 (15) (A) and (B).

Pan QJ, et al. Liquid-based cytology and human papillomavirus testing: a pooled analysis using the data from 13 population-based cervical cancer screening studies from China. Gynecol Oncol 2014 May;133(2):172-9.

Partridge EE, et al; National Comprehensive Cancer Network. Cervical cancer screening. J Natl Compr Canc Netw 2014 Mar 1;12(3):333-41.

Patanwala IY, et al. A systematic review of randomized trials assessing human papillomavirus testing in cervical cancer screening. Am J Obstet Gynecol 2013 May;208(5):343-53.

Pileggi C, et al. Is HPV DNA testing specificity comparable to that of cytological testing in primary cervical cancer screening? Results of a meta-analysis of randomized controlled trials. Int J Cancer 2014 Jul 1;135(1):166-77.

Rijkaart DC, et al. Human papillomavirus testing for the detection of high-grade cervical intraepithelial neoplasia and cancer: final results of the POBASCAM randomized controlled trial. Lancet Oncol 2012 Jan;13(1):78-88.

Roelens J, et al. p16INK4a immunocytochemistry versus human papillomavirus testing for triage of women with minor cytologic abnormalities: a systematic review and meta-analysis. Cancer Cytopathol 2012 Oct 25;120(5):294-307.

Rustagi AS, et al. Cervical screening and cervical cancer death among older women: a population-based, case-control study. Am J Epidemiol 2014 May 1;179(9):1107-14.

Saslow D, ACS-ASCCP-ASCP Cervical Cancer Guideline Committee. American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology screening guidelines for the prevention and early detection of cervical cancer. CA Cancer J Clin 2012 May-Jun;62(3):147-72.

Sawaya GF, et al; Clinical Guidelines Committee of American College of Physicians. Cervical cancer screening in average-risk women: best practice advice from the Clinical Guidelines Committee of the American College of Physicians. Ann Intern Med 2015 Jun 16;162(12):851-9.

*Sherman ME, et al. Effects of age and human papilloma viral load on colposcopy triage: data from the randomized Atypical Squamous Cells of Undetermined Significance/Low-Grade Squamous Intraepithelial Lesion Triage Study (ALTS). J Natl Cancer Inst 2002 Jan 16;94(2):102-7.

Smelov V, et al. Long-term HPV type-specific risks of high-grade cervical intraepithelial lesions: a 14-year follow-up of a randomized primary HPV screening trial. Int J Cancer 2015 Mar 1;136(5):1171-80.

Medical Policy: CERVICAL CANCER SCREENING and HUMAN PAPILLOMA VIRUS (HPV) TESTING

Policy Number: 2.02.04

Page: 11 of 11

Taylor S, et al. A comparison of human papillomavirus testing of clinician-collected and self-collected samples during follow-up after screen-and-treat. *Int J Cancer* 2011 Aug 15;129(4):879-86.

United States Preventive Services Task Force. Cervical cancer screening. *U.S. Preventive Services Task Force Recommendation Statement*. AHRQ Publication No. 11-05156-EF-2, 2012 Mar

[<https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/cervical-cancer-screening2>] accessed 2/8/18.

*Wright TC Jr. HPV DNA testing for cervical cancer screening. FIGO 6th Annual Report on the results of treatment in gynecological cancer. *Int J Gynaecol Obstet* 2006 Nov;95 Suppl 1:S239-46.

*Wright TC, et al. 2006 consensus guidelines for the management of women with abnormal cervical cancer screening tests. *Am J Obstet Gynecol* 2007 Oct;197(4):346-55.

*Wright TC Jr; et al. Evaluation of HPV-16 and HPV-18 genotyping for the triage of women with high-risk HPV+ cytology-negative results. *Am J Clin Pathol* 2011 Oct;136(4):578-86.

Zhou H, et al. Clinical performance of the Food and Drug Administration-Approved high-risk HPV test for the detection of high-grade cervicovaginal lesions. *Cancer Cytopathol*. 2016 May;124(5):317-23. doi: 10.1002/cncy.21687.

Yin D, et al. The diagnostic value of serum hybrid capture 2 (HC2) HPV DNA in cervical cancer: a systematic review and meta-analysis. *Tumour Biol* 2014 Sep;35(9):9247-53.

*Key Article

KEY WORDS

Cervista™, cobas® HPV test, DNA with PAP, HPV, HPV DNA testing, Human Papillomavirus, HC 2, Hybrid Capture 2, Liqui-PREP®, Pap/ Papanicolaou smear: Direct visualization, Monolayer, Optical; FocalPoint™, MonoPrep Pap Test (MPPT), PapSure®, Speculite®, Speculoscopy, SurePath, ThinPrep®

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

There is currently a National Coverage Determination (NCD) for Screening Pap Smears and Pelvic Examinations for Early Detection of Cervical or Vaginal Cancer. Please refer to the following websites for Medicare Members:

<http://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=185&ncdver=3&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=New+York+-+Upstate&KeyWord=cervical+cancer+screening&KeyWordLookUp=Title&KeyWordSearchType=And&bc=gAAAACA AAAA&>

There is currently a National Coverage Determination (NCD) for Cervical Cancer with Human Papillomavirus (HPV).

Please refer to the following website: <https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=365&ncdver=1&bc=AAAAGAAAAAA&>