

[Sample Letter of Medical Necessity: Human Papillomavirus (HPV) Assay for Anal Cancer Screening]

<Date>

ATTN: <Medical Director/ Physician Name>, MD
<Institution/Insurance Company>
<Street Address>
<City>, <State> <Zip>

RE: <Patient Name>
DOB: <MM/DD/YYYY>
Member ID: <Insurance ID Number>
Group #: <Enter Group #>

Dear Doctor <Medical Director/ Physician Name>:

I am writing this letter on behalf of my patient, <Patient Name>, to request coverage for HPV testing to screen for infection of high-risk variants of HPV that have been associated with an increased risk of developing anal cancer.

I have determined that the <Test Name> test is medically necessary because of the following aspects of this patient's history:

<Patient Name> received anal cancer screening, including HPV screening, as part of their office visit. Screening was indicated due to <describe patient's clinical indication>.

1. <Indication #1 with ICD-10 code>
2. <Indication #2 with ICD-10 code>

<Add other personal history if relevant>

<Consider including the following if genotyping was performed:

The patient's HPV test result as part of screening was positive ("Detected") and thus HPV genotyping was included (<ICD-10 Code>) to understand if the HPV infection includes one or more of the HPV variants that are associated with a high risk of developing anal cancer. This information aids me as the clinician to determine next steps for patient treatment and is a critical part of managing this patient's health.>

Rationale for Testing

Anal cancer is the second most commonly diagnosed HPV-associated cancer in men and women,¹ and incidence and mortality rates have increased each year by an average of 2% (over 2008-2017) and 3% (over 2009-2018), respectively.² Sexual activity, smoking, HIV infection, immunosuppression, and a history of certain cancers (cervical, vaginal, and/or vulvar) are among the risk factors for anal cancer.³ The incidence of anal cancer is particularly high in HIV-infected men who have sex with men (MSM), with reported rates 30- to 100-fold higher than the general population.⁴⁻⁶ Women with HIV have the next highest risk, with reported incidences that are approximately 10-fold higher than the general population.^{5,7}

Anal cancer is strongly associated with high-risk variants of human papillomavirus (hrHPV). Of all HPV-attributable anal cancers, 85% are caused by the high-risk HPV 16 variant.⁸ Although hrHPV testing is a recommended practice for cervical cancer screening, there are limited recommendations for hrHPV testing for anal cancer screening due to a lack of evidence. Many

experts have advocated for the implementation of anal cancer screening programs because squamous cell carcinomas of the anal canal and cervix are clinically and histologically similar, and cervical cancer screening programs have been highly successful.⁸ Current guidelines for anal cancer screening recommend either digital anal rectal examination (DARE) and/or anal cytology (AC). In people at high risk, hrHPV testing alone is generally not recommended due to the high prevalence of HPV infection.⁸

Despite this, some organizations, including the American Society of Colon and Rectal Surgeons (ASCRS), Howard Brown Health system, and the New York State Department of Health, recommend the use of hrHPV testing as an adjunct to primary screening tests in people at high risk.⁹⁻¹¹ Studies support this approach. Screening algorithms involving hrHPV testing improve detection of high-grade squamous intraepithelial lesions (HSIL)/cancer compared with AC alone in patients at high risk (mostly MSM and/or HIV-positive individuals).¹²⁻¹⁴ hrHPV testing could also spare patients from undergoing an unnecessary high-resolution anoscopy (HRA). Anal cytologic screening guidelines recommend referral to HRA for those with squamous cells of undetermined significance (ASCUS)-positive cytology; however, in 1 study, the use of negative hrHPV testing results to forgo HRA in those with ASCUS would have spared 15.4% of patients from undergoing HRA.¹⁴

Adding HPV genotyping may improve diagnostic performance even further. In HIV-positive MSM, co-testing with AC and HPV genotyping provided the highest accuracy for detecting anal intraepithelial neoplasia grade 2 or higher (AIN2+).¹⁵ In patients undergoing anal dysplasia screening (mostly MSM), specificity to detect HSIL improved from 48% with hrHPV testing to 71% with HPV 16/18 testing.¹⁴

Another high-risk group for the development of anal dysplasia or cancer is women with a history of cancer of the cervix, vagina, and/or vulva.⁹ There is support for hrHPV testing to screen for anal cancer in women with cervical HPV infection, HSIL, or cancer. Studies have shown that the presence of cervical HPV is an independent risk factor for anal HPV detection, irrespective of reported anal intercourse.¹⁶ Women with cervical HPV infection also have a greater than 3-fold increase in the risk of anal HPV infection.¹⁶ Women specifically with cervical HPV 16 have an approximately 20-fold higher chance of also having anal HPV 16 compared to those without cervical HPV 16, as well as an increased risk of developing AIN2+.^{17,18} Approximately 80% of women with concomitant anal and cervical infections share at least 1 HPV type, indicating that these areas potentially serve as reservoirs of infection for each other.¹⁶ Lastly, women with a diagnosis of cervical HSIL or cancer have up to 23-fold higher prevalence of anal HSIL compared to those without cervical HSIL or cancer.¹⁸

Studies in HIV-positive women have shown that the ability of hrHPV to predict HSIL is similar to that of AC. Furthermore, the high negative predictive value of hrHPV testing may result in a decrease in the number of HRA procedures, which might have utility, particularly in women, since women report higher pain scores and have a greater reluctance to undergo HRA.^{7,12} Thus, there is support for the inclusion of hrHPV testing in anal cancer screening protocols for women.

In summary, the addition of hrHPV testing as an adjunct to anal cancer screening protocols increases the ability to detect anal dysplasia. Its use may be helpful in triaging patients with abnormal cytology for HRA and reduce the number of unnecessary HRAs that may occur with AC alone. Although anal cancer is rare enough to not warrant widespread screening guidelines, there are professional organizations that support the use of hrHPV testing for anal cancer screening. Therefore, I am requesting that <Patient Name> be approved for the <Test Name> offered by <Laboratory>.

I hope you will support the medical necessity of this test for <Patient Name>. Please feel free to contact me at <Physician Phone> if you have additional questions.

Sincerely,

<Physician Name>, MD
NPI #: <Physician NPI#>

Contact information:
< Address>
<City>, <State> <Zip>
Contact Phone: <phone number>

References

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