AMERICAN CLINICAL LABORATORY ASSOCIATION

August 11, 2023

Dr. Joseph Chin
Deputy Director, Chief Medical Officer, Coverage and Analysis Group
Centers for Medicare & Medicaid Services
Mail Stop #S3-02-01
7500 Security Boulevard
Baltimore, Maryland 21244

RE: Proposed National Coverage Determination for Pre-Exposure Prophylaxis (PrEP) for Human Immunodeficiency Virus (HIV) Infection Prevention (Proposed Decision Memo CAG-00464N)

Dear Dr. Chin,

The American Clinical Laboratory Association (ACLA) is pleased to submit our written comments on the Proposed Decision Memo and Proposed National Coverage Determination (NCD) for Pre-Exposure Prophylaxis (PrEP) for Human Immunodeficiency Virus (HIV) Infection Prevention (CAG-00464N), hereafter referred to as the proposed NCD. ACLA is the national trade association representing leading laboratories that deliver essential diagnostic health information to patients and providers by advocating for policies that expand access to the highest quality clinical laboratory services, improve patient outcomes, and advance the next generation of personalized care.

ACLA applauds the Centers for Medicare & Medicaid Services (CMS) for recognizing the benefit of offering PrEP with effective antiretroviral therapy (ART) to Medicare beneficiaries at high risk of acquiring HIV. As noted by the Centers for Disease Control and Prevention (CDC) in its 2021 Clinical Practice Update for Preexposure Prophylaxis for the Prevention of HIV Infection in the United States, the overall estimated annual HIV incidence rate remained stable from 2014 through 2018.[1] However, according to 2018 data, higher percentages of newly diagnosed HIV infections were found for men having sexual activity with men and for Hispanic/Latino and African American heterosexuals. The CDC 2021 Update notes that "[e]quitable provision of PrEP to populations at highest risk of HIV acquisition is not occurring."

We agree with the CDC that improved access to HIV prevention methods, such as PrEP, are vital to help address these disparities. While we believe that this proposed NCD is poised to greatly increase access to PrEP for Medicare beneficiaries, there are many limitations included in the policy that will prevent Medicare beneficiaries from receiving the same standard-of-care treatment as individuals who are not Medicare beneficiaries.

[1] https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf at 21.

ACLA's concerns detailed below cover the disparities in care and financial burden between Medicare beneficiaries on PrEP and non-Medicare beneficiaries, the lack of clarity for Creatinine clearance-related maintenance testing for Medicare beneficiaries on certain types of PrEP, lack of coverage for CLIA-validated, non-FDA-approved or -cleared tests, and additional coding considerations.

A. Disparities in Care and Financial Burden between Medicare Beneficiaries on PrEP and Non-Medicare Beneficiaries on PrEP

The current CDC recommendations for PrEP use in men who have sex with men (MSM), heterosexual women and men, and persons who inject drugs include follow-up visits at least every 3 months to provide the following[2]: HIV testing, medication adherence counseling, behavioral risk reduction support, side effect assessment, STI (sexually transmitted infection) symptom assessment, and STI testing for high-risk groups.

Based on the current CDC recommendations, the standard of care provided for patients administered oral PrEP includes the following tests performed 4 times a year:

- HIV Antigen/Antibodies (Ag/Ab) test **and** HIV-1 RNA assay[3];
- STI screening for gonorrhea, chlamydia, and syphilis for MSM and transgender women who have sex with men including those who inject drugs;
- STI screening for gonorrhea and syphilis for heterosexual women and men including persons who inject drugs.

In addition, CDC recommendations include the performance of the following:

- Creatinine testing and calculated estimated creatinine clearance (eCrCl) or glomerular filtration rate (eGFR) for those on FTC/TDF (Truvada®) every 12 months for persons <50 years of age or with eCrCl≥90 ml/min at PrEP initiation and every six months for all other patients;
- Bacterial STI screening for all sexually-active patients every six months;
- Hepatitis B (HBV) at the initial visit and hepatitis C (HCV) screening tests at the initial visit and annually thereafter for high risk groups;
- Lipid profile screening for patients on oral doses of FTC/TAF (Descovy®) annually.

[2] The CDC guidelines on PrEP for the prevention of HIV infection are available at https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf; recommendations taken from Table 1a: Summary of Clinician Guidance for Daily Oral PrEP Use and Table 5: Timing of Oral PrEP-associated Laboratory Tests.

[3] While HIV viral load quantitative RNA tests are typically used to assess the viral load of a patient with HIV, it is crucial to use as a screening tool for individuals on specific formulations of PrEP as the prophylaxis can prevent patients who have seroconverted from being detected using antigen/antibody screening tests. HIV RNA testing is recommended for visits following initiation of PrEP.

CDC recommendations for testing patients using cabotegravir injection PrEP[4] vary slightly from the above oral PrEP testing guidance:

- HIV Ag/Ab test and HIV-1 RNA assay one month following the first injection and then every two months beginning with the third injection;
- STI screening for gonorrhea, chlamydia, and syphilis for MSM and transgender women who have sex with men including those who inject drugs (every four months beginning with the third injection);
- STI screening for gonorrhea and syphilis for heterosexual women and men including persons who inject drugs (every four months beginning with the third injection);
- Bacterial STI screening for all heterosexually-active women and men (every six months beginning with the fifth injection);
- Chlamydia screening for heterosexually-active women and men (every twelve months);
- Quarterly HIV testing when discontinuing cabotegravir.

Under the proposed NCD, ordering providers may need to either cut back drastically on the recommended testing for Medicare patients on PrEP or proceed with ordering the recommended testing regimen while leaving the possibility that Medicare beneficiaries may need to pay for many CDC-recommended tests out of pocket. We are concerned that Medicare beneficiaries on PrEP will not have coverage for testing of HCV, HBV, gonorrhea, chlamydia, and syphilis. Additionally, it is unclear why recommended testing for HCV was not discussed in the proposed NCD, despite being included in clinical guidelines from the CDC regarding testing for patients on PrEP.

This lack of coverage for recommended maintenance tests goes against the goal of getting PrEP to every patient who could benefit and will have an outsized negative impact on patients who are unable to pay out-of-pocket for the standard of care testing regimens. **If patients cannot afford tests that are non-covered, they will often forego testing.** In addition, if PrEP is implemented, it needs to be safely monitored. A 2021 memo regarding the implementation of the Affordable Care Act (ACA) released by the Departments of Labor, Health and Human Services (HHS), and Treasury noted that private payers are required to cover the CDC-recommended testing regimen for PrEP with no cost-sharing to patients.[5] While we recognize these ACA requirements differ for private payers and Medicare, we strongly encourage CMS to ensure consistency of coverage across payer types and amend the NCD to ensure that Medicare beneficiaries receive the same standard-of-care treatment while taking PrEP without having to pay out-of-pocket for testing.

While CMS did not include any of the recommended additional screening tests for STIs as part of the proposed NCD, CMS does reference that STI screening tests might be included under the existing Screening for Sexually Transmitted Infections (STIs) and High-Intensity Behavioral

[4] The 2021 CDC guidelines note that cabotegravir injections may be indicated for patients with renal disease or patients who prefer injections every two months instead of an oral PrEP dosing schedule. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf at 47. For recommendations, see Table 1b: Summary of Clinician Guidance for Cabotegravir Injection PrEP Use and Table 7: Timing of CAB PrEP-associated Laboratory Tests.

[5] FAQS ABOUT AFFORDABLE CARE ACT IMPLEMENTATION PART 47 July 19, 2021, accessible here: https://www.dol.gov/sites/dolgov/files/EBSA/about-ebsa/our-activities/resource-center/faqs/aca-part-47.pdf.

Counseling (HIBC) to Prevent STIs NCD (NCD 210.10).[6] Unfortunately, even combining the coverage in the proposed NCD and NCD 210.10 will leave large gaps in coverage for Medicare beneficiaries on PrEP. Under the NCD 210.10, coverage for gonorrhea, chlamydia, and syphilis testing is provided only once per year for certain groups of beneficiaries. This schedule is greatly reduced compared to the recommended STI screening for individuals on PrEP. Additionally, under NCD 210.10, only women have access to testing for gonorrhea, chlamydia, and syphilis, with "high-risk" men gaining access only to syphilis testing.

We applaud CMS for being forward-thinking and leaving the determination of which Medicare beneficiaries are at high-risk for contracting HIV to their physicians and health care practitioners based on the individual's clinical history. However, we anticipate there will be a large discrepancy between individuals considered for PrEP and individuals who are provided coverage for once-a-year STI screening tests under NCD 210.10. As CMS acknowledges in the proposed NCD, in 2019, MSM accounted for 65% of all new HIV infections.[7] This could leave the majority of Medicare beneficiaries on PrEP unable to access the STI screening tests under NCD 210.10.

Lack of Clarity for Creatinine Clearance Maintenance Testing for Patients on PrEP
While the policy discusses creatinine clearance and other tests to monitor negative side effects of PrEP, it does not include any specific recommendations or coverage indications. This is especially worrisome, as the Medicare population is more likely to experience these side-effects[8,9], as noted in the proposed NCD. We recommend that CMS include specific recommendations regarding coverage for creatinine testing and calculating eCrCl and eGFR for Medicare beneficiaries under this policy.

RECOMMENDATION: To ensure that Medicare beneficiaries on PrEP will receive the same standard of care as all other patients and for patient-safety to be assessed, we recommend the following red-line edits to Part B. Nationally Covered Indications of the NCD 210.15 draft text for the Medicare National Coverage Determinations Manual, found in Appendix B of the proposed NCD:

> *Additionally, for individuals being assessed for or who are taking PrEP using ART to prevent HIV infection, CMS proposes to cover HIV screening up to seven times annually, ~~and~~ a single screening for hepatitis B virus (HBV) and for hepatitis C virus (HCV), screening for gonorrhea and chlamydia (using multiple anatomic sites as necessary), and syphilis up to four times annually. For persons taking oral PrEP, estimated creatinine clearance (eCrCl) or estimated glomerular filtration rate (eGFR) must be measured and calculated at the beginning of treatment to assess if kidney function is in the range for safe prescribing of PrEP medication. eCrCl should be*

[6] Accessed here: https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?NCDId=352&ncdver=1&bc=AgAAgAAAAAAAAA%3D%3D.
[7] CDC, 2022a. HIV Statistics Overview. Accessed here: https://www.cdc.gov/hiv/statistics/overview/index.html
[8] Marcus JL, Hurley LB, Hare CB, et al. Preexposure prophylaxis for HIV prevention in a large integrated health care system: Adherence, renal safety, and discontinuation. J Acquir Immune Defic Syndr. Dec 15 2016;73(5):540-546. doi:10.1097/QAI.0000000000001129
[9] Gandhi RT, Bedimo R, Hoy JF, et al. Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults: 2022 Recommendations of the International Antiviral Society–USA Panel. JAMA. 2023;329(1):63–84. doi:10.1001/jama.2022.22246

assessed every 6 months for patients over age 50 or those who have an eCrCl <90 ml/min at initiation. For all other daily oral PrEP patients, eCrCl should be assessed at least every 12 months.

B. CMS Should Nationally Cover Screening Tests for PrEP, Regardless of Whether They are FDA-Cleared or -Approved Tests or Laboratory Developed Test (LDTs) Performed in CLIA-Certified Facilities

While we encourage CMS to expand the screening tests provided under this policy as outlined above, ACLA supports the move for national Medicare coverage of HIV screening and screening for HBV for patients considering or on PrEP. However, we adamantly oppose CMS's proposal to limit national coverage of these tests to those that are FDA-cleared or -approved. In the proposed NCD, CMS states: "*FDA approval or clearance of screening tests used consistent with FDA approved labeling provides a greater likelihood that a potential harm of screening testing, that is, taking action based on inaccurate screening test results, can be avoided. We further conclude that compliance by testing laboratories with CLIA regulatory requirements provides an additional, on-going safeguard for screening test quality. CMS considers these conditions essential to maximize patient safety*."

CMS did not include in the proposed NCD any evidence that FDA-approval or -clearance of screening tests used consistent with FDA-approved labeling provides a greater likelihood that a potential harm of screening testing can be avoided. There are multiple ways that CLIA-certified laboratories show evidence of an LDT's validity, other than submitting the test to the FDA for review. CLIA includes extensive requirements for laboratories to verify or establish a test's analytical performance characteristics before offering it and reporting patient results based on the test. CLIA regulations require that laboratories that use LDTs, that modify FDA-cleared or -approved tests, or that use a test system for which the manufacturer did not provide performance specifications, must establish the following performance characteristics before reporting patient test results: accuracy, precision, analytical sensitivity, analytical specificity to include interfering substances, reportable range of test results for the test system, reference intervals (normal values), and any other performance characteristic required for test performance.[10] CLIA regulations also require a laboratory director to ensure that test methodologies have the capability of providing the quality of results required for patient care, which is the case only when they are clinically relevant for the patient populations being tested (*i.e.*, are clinically valid).[11] Clinical validity also is ensured by accreditation by an approved third-party accreditation organization such as the College of American Pathologists, whose goals include ensuring that tests are analytically and clinically valid, that there is patient safety and patient access to testing, and that there is innovation and improvement of LDTs.[12]

A screening test is "validated" when it is performed in a CLIA-certified laboratory, whether the test is an LDT or whether it is an FDA-cleared or -approved test. CMS has provided no

[10] 42 C.F.R. § 493.1253(b)(2).
[11] 42 C.F.R. § 493.1445(e)(3)(1).
[12] Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS), "U.S. System of Oversight of Genetic Testing: A Response to the Charge of the Secretary of Health and Human Services (Apr. 2008).

evidence to the contrary. CMS should not finalize its proposal to limit national coverage of screening tests for patients considering or using PrEP to those that are FDA-cleared or - approved and it should nationally cover tests that are LDTs performed in CLIA-certified laboratories.

RECOMMENDATION: To ensure that Medicare beneficiaries on PrEP will receive the same standard of care as all other patients, we recommend the following red-line edits to Part B. Nationally Covered Indications of the NCD 210.15 draft text for the Medicare National Coverage Determinations Manual, found in Appendix B of the proposed NCD:

> *These screening tests are proposed to be covered with the appropriate FDA approved laboratory tests, laboratory developed tests performed in CLIA-certified laboratories, and point of care tests, used consistent with FDA approved labeling and in compliance with the Clinical Laboratory Improvement Act (CLIA) regulations.*

C. Additional Coding Considerations And Education Needed

ACLA appreciates that CMS designed the proposed NCD to be technology agnostic with the choice of appropriate test left up to the discretion of the ordering provider, as this will allow the policy to be forward-facing as new, novel test methodologies come to the market. As this policy is finalized and shared with stakeholders and Medicare Administrative Contractors (MACs), we recommend that additional care is taken to ensure that the appropriate procedure codes are included within the NCD manual and are inclusive of all the current screening tests that an ordering provider might select for the patient. We are concerned that additional education will be needed on the new ICD-10-CM codes for encounters related to HIV pre-exposure prophylaxis and PrEP and the Healthcare Common Procedure Coding System (HCPCS) codes related to HIV viral load quantitative RNA testing.

First, as of October 2023, the ICD-10 code Z29.81 will include both “encounter with health service for HIV pre-exposure prophylaxis” and “encounter with health service for HIV PrEP”. We ask CMS to confirm that this code can be used in support of obtaining the services in this policy (not only for an initial consultation).

Second, while the HIV viral load quantitative RNA tests typically are used to assess the viral load of a patient with a known HIV infection, it is also crucial to use as a screening tool for individuals on specific formulations of PrEP as the prophylaxis can prevent patients who have seroconverted from being detected using antigen/antibody screening tests. While PrEP treatment is progressively moving to be better understood by the public, we anticipate that there will be confusion by MACs and other stakeholders about why a HCPCS code typically used for patients to monitor a patient with a known HIV infection would be used on patients taking PrEP. We recommend that proactive education from CMS be provided to the MACs and other stakeholders who review claims to prevent inaccurate rejections for medically necessary tests that fall under this policy.

Thank you for your consideration of ACLA's comments and recommendations. We appreciate that CMS recognizes the benefits of offering PrEP with effective ART to Medicare beneficiaries at high risk of acquiring HIV. We welcome the opportunity to work collaboratively on this draft policy to ensure that Medicare beneficiaries will receive the full benefit of PrEP and current standard of care. The red-line edits included throughout this comment letter can be found consolidated in the attached Appendix.

Please contact Sarah Thibault-Sennett at sthibaultsennett@acla.com with any questions or to discuss further.

Sincerely,

Sarah Thibault-Sennett, PhD
Senior Director, Reimbursement Policy, ACLA

APPENDIX:

Compiled red-line edits suggested to the Medicare National Coverage Determinations Manual provided in Appendix B of the Proposed National Coverage Determination for Pre-Exposure Prophylaxis (PrEP) for Human Immunodeficiency Virus (HIV) Infection Prevention (Draft NCD 210.15)

APPENDIX B

Medicare National Coverage Determinations Manual

Draft

We are seeking public comments on the proposed language that we would include in the Medicare National Coverage Determinations Manual. This proposed language does not reflect public comments that will be received on the proposed decision memorandum, and which may be revised in response to those comments.

Table of Contents
(Rev.)

A. General

Human immunodeficiency virus (HIV) continues to be a serious public health issue, with an estimated 1.2 million people aged 13 and older living with HIV in the United States. Due to continuing medical advances and earlier initiation and expanded access to medications, HIV is now considered a chronic condition rather than a terminal illness. Antiretroviral therapy (ART) is known to reduce HIV-related morbidity and mortality. Nearly half of the people in the United States diagnosed with HIV are aged 50 and older. Pre-exposure prophylaxis (PrEP) involves the use of ART on an ongoing basis (e.g., daily or bimonthly) or before and after HIV exposure events ("on-demand" or "event-driven" PrEP) to decrease the risk of acquiring HIV infection. When taken as prescribed, PrEP is highly effective for preventing HIV. PrEP can be an oral medication or an injection. Under §1861(ddd)(1) of the Social Security Act (the Act), the Centers for Medicare & Medicaid Services (CMS) has the authority to add coverage of "additional preventive services" through the Medicare national coverage determination (NCD) process if certain statutory requirements are met: (1) reasonable and necessary for the prevention or early detection of illness or disability, (2) recommended with a grade of A or B by the United States Preventive Services Task Force (USPSTF), and (3) appropriate for individuals entitled to benefits under Part A or enrolled under Part B.

B. Nationally Covered Indications

Effective for claims with dates of service on or after xx/xx/xx, CMS proposes that the evidence is adequate to conclude that the United States Preventive Services Task Force (USPSTF) recommends offering Pre-Exposure Prophylaxis (PrEP) with effective antiretroviral therapy (ART) to persons at high risk of Human Immunodeficiency Virus (HIV) acquisition with a grade of A recommendation, is reasonable and necessary for the prevention or early detection of illness or disability under §1861(ddd)(1) of the Social Security Act (the Act), and is appropriate for individuals entitled to benefits under Part A or enrolled under Part B.

CMS proposes to cover PrEP using antiretroviral drugs (whether oral or injectable) approved by the US Food and Drug Administration (FDA) to prevent HIV infection in individuals at high risk of HIV acquisition. The determination of whether an individual is at high risk for HIV infection is made by the physician or health care practitioner who assesses the individual's history. In addition, CMS proposes to also cover the administration of injectable PrEP using antiretroviral drugs to prevent HIV infection.

CMS also proposes to cover up to seven individual counseling visits, every 12 months, that include HIV risk assessment (initial or continued assessment of risk), HIV risk reduction and medication adherence. Counseling must be furnished by a physician or other health care practitioner and individuals must be competent and alert at the time that counseling is provided.

Additionally, for individuals being assessed for or who are taking PrEP using ART to prevent HIV infection, CMS proposes to cover HIV screening up to seven times annually*, ~~and~~* a single screening for hepatitis B virus (HBV) *and for hepatitis C virus (HCV), screening for gonorrhea and chlamydia (using multiple anatomic sites as necessary), and syphilis up to four times annually. For persons taking oral PrEP, estimated creatinine clearance (eCrCl) or estimated glomerular filtration rate (eGFR) must be measured and calculated at the beginning of treatment to assess if kidney function is in the range for safe prescribing of PrEP medication. eCrCl should be assessed every 6 months for patients over age 50 or those who have an eCrCl <90 ml/min at initiation. For all other daily oral PrEP patients, eCrCl should be assessed at least every 12 months.*

These screening tests are proposed to be covered with the appropriate FDA approved laboratory tests, laboratory developed tests performed in CLIA-certified laboratories, and point of care tests, used consistent with FDA approved labeling and in compliance with the Clinical Laboratory Improvement Act (CLIA) regulations.

C. Nationally Non-Covered Indications

Preventive services are non-covered by Medicare unless specifically covered in this NCD, any other NCD or in statute or regulations.

D. Other

Medicare Part B coinsurance and deductible are waived for this preventive service.