May 30, 2025

United States Preventive Services Task Force
5600 Fishers Lane
Mail Stop 06E53A
Rockville MD 20857

Dear Members of the Task Force:

We, the undersigned 39 organizations, write on behalf of people and communities affected by HIV, their care providers, public health practitioners, and community-based organizations.

We urge the U.S. Preventive Services Task Force (USPSTF) to expeditiously update its 2023 HIV Pre-Exposure Prophylaxis (PrEP) recommendation[1] to incorporate important new evidence, including clinical trial data on lenacapavir, a new twice-yearly PrEP formulation, and new findings on PrEP's effectiveness in women and other key populations.[2]

Since FDA approved the first daily oral PrEP medication in 2012, PrEP has been a critically important preventive intervention, first earning an "A" grade from the USPSTF in June 2019.[3] Additional options, including a second daily oral (October 2019) and a long-acting injectable (2021) have since been approved, and are included in the USPSTF current recommendation.

Despite PrEP's high efficacy, uptake remains low (just 4 in 10 eligible individuals are accessing it) and uneven across racial, ethnic, gender, age, and geographic lines. For example, only 8 percent of PrEP users in 2023 were women, even though women comprise 19 percent of new HIV diagnoses. Similarly, 14 percent of PrEP users are Black, even though Black people comprise 39 percent of all new HIV diagnoses.[4] Experts have underscored that maximizing the effectiveness of PrEP hinges on adherence and persistence, and that new PrEP products and interventions that increase adherence are key to maximizing PrEP's impact on individual and public health.[5]

Updating USPSTF recommendations to reflect the latest evidence and guidelines is also critical to ensure providers are informed about all available PrEP regimens and guideline-recommended clinical best practice.

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[1] https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/prevention-of-human-immunodeficiency-virus-hiv-infection-pre-exposure-prophylaxis

[2] In October 2021, HIV+Hepatitis Policy Institute joined 62 organizations in writing to USPSTF to request an early update of the 2019 PrEP recommendation to include the first long-acting injectable (https://hivhep.org/wp-content/uploads/2021/09/PrEP-Long-Acting-USPSTF-Final-Letter.pdf).

[3] https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/prevention-of-human-immunodeficiency-virus-hiv-infection-pre-exposure-prophylaxis-june-2019

[4] https://aidsvu.org/news-updates/aidsvu-releases-new-prep-data-and-launches-prepvu-org-a-new-prep-equity-platform/

[5] https://www.sciencedirect.com/science/article/abs/pii/S2352301823000796

Lenacapavir as PrEP

In October 2024, the FDA granted breakthrough designation to Gilead Sciences' twice-yearly injectable PrEP formulation, lenacapavir as PrEP, based on promising clinical trial data. In February 2025, the FDA accepted Gilead's New Drug Application under Priority Review, with a target approval date of June 19, 2025.[6]

The submission is based on the overwhelmingly successful results of two clinical trials: PURPOSE 1, which demonstrated zero HIV infections in cisgender women – the first Phase III PrEP trial to achieve this – and PURPOSE 2 evaluating efficacy in men and gender-diverse people. These studies included groups that had been largely overlooked in previous HIV prevention studies, such as women, adolescent girls, and pregnant/lactating people.[7] Results published in peer-reviewed journals showed significantly lower incidence with lenacapavir compared to background rates and FTC/TDF.[8] Both studies were stopped early by their Data Monitoring Committees once interim results proved lenacapavir was significantly more effective, making it unethical to continue withholding it from the control group. The study results were so groundbreaking that *Science* magazine named lenacapavir its 2024 "Breakthrough of the Year" – a distinction previously awarded to the momentous discovery of combination antiretroviral therapy in 1996.[9] Three additional trials (PURPOSE 3, 4, and 5) are in Phase II and will further broaden the evidence base for other key populations.[10]

With a dosing interval three times as long as any existing PrEP option, lenacapavir represents a major advance. Twice-yearly dosing could substantially improve PrEP adherence and persistence, offering broad appeal for patients and providers by providing a longer period of protection with one dose and fewer office visits. With a convenient alternative for PrEP users who have had difficulty adhering to a daily pill, including those who face barriers to accessing frequent in-person care, lenacapavir may provide an important new tool to improve both individual and public health outcomes.

Changes to clinical practice

PrEP delivery continues to evolve as providers integrate new tools and medications to better serve people who have a reason to use PrEP to prevent HIV. For example, a recent update to widely accepted IAS-USA HIV clinical guidelines has adopted the important recommendation that PrEP should be discussed with and offered to all sexually active individuals, all who ask for it, and all who engage in substance use.[11]

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[6] https://www.gilead.com/news/news-details/2025/us-fda-accepts-gileads-new-drug-applications-for-twice-yearly-lenacapavir-for-hiv-prevention-under-priority-review

[7] https://www.purposestudies.com/

[8] https://www.nejm.org/doi/full/10.1056/NEJMoa2411858 and https://www.nejm.org/doi/10.1056/NEJMoa2407001

[9] Science Magazine, Vol 386, Issue 6727. 2024 Breakthrough of the Year. Jon Cohen. The long shot, https://www.science.org/content/article/breakthrough-2024

[10] https://www.purposestudies.com/

[11] 2024 IAS-USA recommendations: https://jamanetwork.com/journals/jama/fullarticle/2827545

The introduction of lenacapavir will further reshape PrEP delivery and clinical practice. IAS-USA guidelines already recommend lenacapavir as PrEP pending FDA approval. While at this moment there are some unknowns, such as the recommended cadence of HIV and STI testing, lenacapavir's extended dosing interval suggests that less frequent clinic-based testing may be feasible. We urge USPSTF, in this update on PrEP, to include all the necessary medical visits, laboratory testing, and adherence counseling associated with the use of lenacapavir. Since the cadence of required in-person visits for testing could impact the convenience of twice-yearly PrEP, we also urge USPSTF to consider the role of home- and self-testing for HIV and STIs, which play an important role in telehealth PrEP programs.[12]

New evidence from the PURPOSE trials regarding the effectiveness of PrEP in women, including pregnant/lactating individuals, may expand the range of providers involved in PrEP delivery. For instance, OB/GYNs could become crucial prescribers, integrating PrEP into reproductive healthcare and potentially reaching women who have not yet been able to take advantage of PrEP.

New evidence and changes to clinical practice meet USPSTF criteria for early review

The evidence associated with lenacapavir as PrEP meets USPSTF criteria for early review,[13] including:

- *High public health burden of the condition.* HIV remains a critical public health concern, with 1.2 million people living with HIV in the United States, and over 39,000 new diagnoses in 2023. [14] The lifetime treatment cost per person averages $420,285.[15]

- *Large-scale study improves certainty of net benefit*. The PURPOSE 1 (N=5345) and PURPOSE 2 trials (N=3295) are large Phase III randomly controlled trials (RCTs). These two trials together represent the largest RCT program in HIV prevention for a single investigational agent, providing safety and efficacy evidence after 25,329 injections were administered. The PURPOSE program is the most globally, racially, ethnically, gender, and age-diverse Phase III HIV prevention clinical development program conducted to date.

- *New evidence conflicts with the current recommendation; study shows a change in magnitude of benefit; evidence has a potential to fill a gap in the chain of indirect evidence.* The PURPOSE program included populations who have often been underrepresented in HIV prevention trials, including women, adolescent girls, and gender-diverse people, providing evidence of benefit in populations for whom there are significant evidence gaps. For example, data from PURPOSE 1 has the potential to fill evidence gaps related to PrEP use in pregnant/lactating individuals, who were named in

[12] https://jamanetwork.com/journals/jama/fullarticle/2827545
[13] https://www.uspreventiveservicestaskforce.org/uspstf/sites/default/files/2023-11/procedure-manual-2023.pdf (page 22)
[14] https://www.cdc.gov/hiv-data/nhss/hiv-diagnoses-deaths-and-prevalence-2025.html
[15] https://journals.lww.com/stdjournal/abstract/2021/04000/estimated_lifetime_hiv_related_medical_costs_in.15.aspx

the 2023 recommendation as a research need. Published evidence from PURPOSE 1 supports the efficacy of lenacapavir in pregnant women, with no cases of HIV acquisition among pregnant participants.[16]

- *High level of existing controversy.* There has been persistent debate among clinical providers related to certain aspects of the safety and effectiveness of PrEP in women, including time to protection, concentrations of the drug in vaginal mucosa as compared to rectal mucosa, "forgiveness" for missed PrEP doses,[17] and concerns for pregnant or breastfeeding people. Data from the PURPOSE studies may help resolve these open questions.

- *Study was identified by a reliable source* and *published in a peer-reviewed journal*. Lenacapavir as PrEP was named *Science* magazine's 2024 "Breakthrough of the Year." [18] *Science* is published by the American Academy for the Advancement of Science, the world's largest scientific society. The PURPOSE 1[19] and 2[20] Phase III results were reported in the *New England Journal of Medicine*.

USPSTF Should Expedite Timely Review of Future PrEP Formulations and Guidelines

We urge USPSTF to take account of the transformative evidence and changes in clinical practice described above and initiate an expeditious early review of the HIV PrEP recommendation.

The PrEP drug development pipeline is active, with new oral and injectable long-acting formulations under investigation that may further revolutionize HIV prevention. USPSTF's recommendation for the prescription of PrEP "using effective antiretroviral therapy to persons who are at increased risk of HIV acquisition" has never been drug-specific but instead subsumes all FDA-approved PrEP formulations. As new PrEP formulations are approved, we call on USPSTF to rapidly assess emerging HIV prevention evidence for inclusion into its recommendations on an ongoing basis, ensuring clinicians and patients benefit from the latest scientific advances without a multi-year delay.

If you have any questions or comments, please contact Carl Schmid, Executive Director, HIV+Hepatitis Policy Institute at cschmid@hivhep.org or (202) 462-3042, or Kevin Herwig, Health Policy Manager, HIV+Hepatitis Policy Institute at kherwig@hivhep.org or (617) 666-6634.

Act Now: End AIDS (ANEA) Coalition
ADAP Advocacy Association

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[16] Bekker et al. 2024
[17] Marrazzo J, Tao L, Becker M, et al. HIV Preexposure Prophylaxis with Emtricitabine and Tenofovir Disoproxil Fumarate among Cisgender Women. JAMA. 2024;331(11):930–937. doi:10.1001/jama.2024.0464
[18] Science Magazine, Vol 386, Issue 6727. 2024 Breakthrough of the Year. Jon Cohen. The long shot, https://www.science.org/content/article/breakthrough-2024
[19] https://www.nejm.org/doi/10.1056/NEJMoa2407001
[20] https://www.nejm.org/doi/full/10.1056/NEJMoa2411858

AIDS Action Baltimore
AIDS Alabama
AIDS Foundation Chicago
AIDS United
APLA Health
Association of Nurses in AIDS Care
AVAC
California STD/HIV Controller's Association
Callen-Lorde Community Health Center
Center for Health Law and Policy Innovation
Colorado Health Network
Colorado Organizations and Individuals Responding to HIV/AIDS (CORA)
Community Access National Network
Community Resource Initiative (CRI)
CrescentCare
DAP Health
Equality California
Equitas Health
Fast-Track Cities Institute
Five Horizons Health Services
Georgia AIDS Coalition
HealthHIV
HIV+Hepatitis Policy Institute
International Association of Providers of AIDS Care
Lambda Legal Defense and Education Fund
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Sage
Silver State Equality
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