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A PEP Talk on PrEP-ing for HIV Prevention

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The human immunodeficiency virus (HIV) is the virus that causes acquired immunodeficiency syndrome (AIDS) if not managed with antiretroviral (ARV) therapy.[1] HIV is predominantly transmitted through sexual intercourse, sharing needles for injectable drugs, and other routes of bloodborne exposure.[1] In 2019, roughly 1.2 million people within the United States (U.S.) were living with a diagnosis of HIV, including 7,731people in Oregon.[2,3] Although the rate of new HIV infections in the US has been declining, there were approximately 36,801 new HIV diagnoses nationwide in 2019.[2] In the U.S. certain communities have been disproportionally affected by HIV, including men who have sex with men and transgender individuals. However, globally women have consistently accounted for approximately half of those who are living with HIV.[1,2] In addition to comprehensive harm reduction strategies, including treatment as prevention initiatives, preventive therapy should include preexposure prophylaxis (PrEP) and postexposure prophylaxis (PEP) with ARV therapy when indicated (**Table 1**). This newsletter will review the pharmacological therapies and management considerations that comprise PEP/PrEP therapy for the prevention of HIV infection.

Table 1: Indications for PEP and PrEP[4,5,6,7]

Postexposure Prophylaxis	Preexposure prophylaxis
To be started as soon as possible and no more than 72 hours after possible exposure to HIV, via: ➢ Sex ➢ Shared needles or other items used to inject drugs ➢ Sexual assault ➢ Occupational exposure	People without HIV who: ➢ Injects non-prescribed drugs ➢ Has condomless sex ➢ Has sex with a partner living with HIV with a detectable or unknown HIV viral load, or who is not on ARV treatment, or whose ARV treatment status is not known ➢ Those with a HIV positive sexual partner ➢ Has had a recent STI ➢ Expresses interest PrEP

Abbreviations: ARV – antiretroviral therapy; HIV – human immunodeficiency virus ; IV – intravenous; STI – sexually transmitted infection

Screening and Testing for HIV

Screening for PEP treatment includes identification of possible HIV exposures, which can be categorized as occupational and non-occupational exposures. Types of exposures that warrant initiation of PEP include the following: 1) exposure to potentially infectious bodily fluids (e.g., blood, breast milk, genital secretions, or blood stained saliva), 2) exposure to mucous membranes (e.g., sexual exposure, splashes to eyes, nose or oral cavity), or 3) exposure to HIV via parenteral routes (e.g., shared needles or syringes for injection drug use or accidental needlesticks).[6] The initiation of PEP should be started as soon as possible and no more than 72 hours after exposure. The exposed individual should be offered PEP as soon as possible even if the HIV tests results are not yet available.[6] While all generations of HIV testing methods are acceptable, the utilization of a 4th generation HIV testing method allows for earlier detection of HIV infection.[6]

Screening for PrEP includes an assessment of potential exposures and risks of HIV acquisition. All adult and adolescent patients should be offered PrEP if they are interested or feel that they would benefit from PrEP. HIV screening should be discussed and completed. Patients with a negative HIV screening test should be considered for PrEP. Patients who have had a potential high risk exposure event and/or have had symptoms of acute retroviral syndrome in the previous 4 weeks should be considered for an HIV viral load RNA test as well before starting PrEP.[7] Patients should also be screened for other sexually transmitted infections (STIs), hepatitis, and pregnancy status. Patients with a positive HIV test at any time should be referred to an HIV specialist for starting a complete ARV treatment regimen as soon as possible.

Pharmacological Therapies

There are no randomized controlled trials evaluating ARV for PEP. Rather, the efficacy for PEP therapy has been established based upon extrapolated data from animal models, perinatal clinical trials, and observational studies.[6] Selection of an appropriate regimen is based on additional patient factors, such as age, renal function, and any known or suspected ARV resistance in the source person, if that information is available.Recommendations from the Center for Disease Control (CDC) specify that treatment for PEP should consist of a 3-drug antiretroviral regimen with a duration of 28 days (**Table 2**).[6]

Table 2. FDA Approved PEP Regimens[8,10,11]

Agents	Dosing	Dosing Considerations
Tenofovir disoproxil fumarate + emtricitabine (TRUVADA)	300mg/200 mg daily	➢ Avoid with CrCl < 60 ml/min ➢ Insufficient data to recommend tenofovir alafenamide-containing products (Descovy) for PEP
PLUS EITHER		
Raltegrevir (ISENTRESS)	400 mg twice daily	
OR		
Dolutegravir (TIVICAY)	50mg daily	➢ Avoid or separate from antacids and laxatives containing cations

Abbreviations: CrCl= creatinine clearance; INSTI= integrase strand transfer inhibitor

Randomized, placebo controlled trials have demonstrated that daily administration of PrEP reduces the incidence of HIV among men who have sex with men by 42% to 86%.[12] The efficacy of PrEP in heterosexual men and women and persons who inject drugs has also been demonstrated.[7] FDA approved agents for PrEP consist of 2-drug ARV regimens, that are available in combination products (**Table 3**). Selection of the appropriate agent is based on renal function, cost and HIV exposure risk (e.g. Tenofovir alafenamide + emtricitabine has not been studied in individuals who inject drugs or in cis-gender females). PrEP should be taken continuously as long as continued HIV prevention is warranted.[7] There is limited data on the safety of the developing fetus when PrEP is used in pregnant patients,however, data available from the Antiretoviral Pregnancy Registry on pregnancy outcomes provide no evidence of adverse effects among fetuses exposed to PrEP therapies.[7] With the increased risk of HIV acquisition with exposure being present during pregnancy, pregnant people who are at risk for HIV exposure or ask to be on PrEP should be started on PrEP.[7]

Table 3. FDA Approved PrEP Regimens[8,9]

Agents	Dosing	Dosing Considerations
Tenofovir disoproxil fumarate + emtricitabine (FTC/TDF; TRUVADA)	300mg/200 mg daily	➢ Avoid with CrCl < 60 ml/min ➢ Avoid if decreased bone mineral density ➢ Avoid with daily or high-dose NSAIDs
Tenofovir alafenamide + emtricitabine* (FTC/TAF; DESCOVY)	25mg/200 mg daily	➢ Avoid with CrCl < 30 ml/min ➢ Prefered if decreased bone mineral density

Abbreviations: CrCL = creatinine clearance
*= Approval does not include those at risk from IV drug use or sexual acquisition from receptive vaginal sex.

Medication adherence is necessary to ensure successful therapy with both PEP and PrEP. Clinical trials have shown a clear association between observed efficacy and adherence to therapy, with little to no efficacy seen in participants with the lowest adherence rates.[12,13] Thus, identifying potential adherence barriers, providing education regarding common medication side effects, and reviewing patient's current medications are critical components of treatment. Recently, cabotegravir,the first injectable treatment was FDA approved for PrEP.[14] It is a long acting injectable given every 2 months after an initial oral lead-in period. It was studied in men, transgender women and cisgender women at risk of acquiring HIV.[14]

PEP and PrEP regimens are both generally well tolerated. Side effects associated with both PEP and PrEP therapy are typically mild, but may include nausea, fatigue, malaise, diarrhea, headache, and rash.[6,7] Contrainidications to PEP and PrEP therapies can be found in **Table 4**. Concurrent medications should be screened to identify potential drug interactions that may affect the efficacy, safety, or monitoring requirements of PEP and PrEP treatment.

Table 4: Contraindications to PEP and PrEP Regimens[6,7,8,9,10,11]

Contraindications and Precautions
• Hypersensitivity to any single PEP or PrEP agent • Severe renal dysfunction (CrCl < 30ml/min) • Individuals with unknown (do not start PrEP) or positive HIV-1 status (Do not start PrEP or PEP) • Coadministration with dofetilide (dolutegravir only) • Certain medications (carbamazepine, phenobarbital, phenytoin, rifampin)

Follow Up and Monitoring

For patients requiring either PEP or PrEP, ensuring that the patient has an established healthcare provider is imperative to ensure proper follow up and increase the likeliness of successful and sustainable HIV prevention. After the initiation of PEP, providers should monitor the patient's renal function, liver function tests, and complete blood count to assess for any developing toxicities starting at 2 weeks.[6] Patients should undergo repeat testing for HIV at 4 weeks and 3 months after therapy initiation. Repeat testing for hepatitis C and sexually transmitted infections (STIs) should also occur.[6] For patients on PrEP, monitoring includes HIV and pregnancy (for those who can become pregnant) screening every 3 months, STI screening at least every 6 months (or every 3 months if indicated), and renal function.[7]

Any person who is at continued risk for HIV exposure should continue to take PrEP. Harm reduction and sexual health and safety topics may be reviewed and/or the person may be offered referral to additional services for assistance. Patients on PrEP should also be evaluated for adherence and drug interactions at each visit.

Policy Needs and Impacts

An individual's lack of awareness of risk for HIV transmission is a major barrier to appropriate prevention strategies.[15,16] Even with current government public health programs focused on increasing the awareness of risk and testing, those unaware of their HIV status account for 45% of new HIV transmissions.[17] The major barriers to awareness include: social stigma, cost of HIV testing, unawareness of risk factors and where to receive care for HIV.[16] There is a need for increased testing efforts and access to HIV treatment.

To enhance community education and access to resources, Oregon has empowered pharmacists to play a more active role in the screening and prevention of HIV. On June 23rd, 2021, the Oregon state legislature passed HB 2958, which

clarified that Oregon licensed pharmacists have the legal authority prescribe and dispense PEP or PrEP to patients after completion of a patient assessment.[18] This bill also requires insurers to reimburse pharmacists for consultation with patients, while also prohibiting the requirement of a prior authorization for PEP or PrEP therapies for the first 60 days of treatment. With Oregon pharmacists already having the legal authority to prescribe PEP and PrEP before the passing of this bill, HB 2958 provides additional incentives to pharmacists while also removing barriers to providing access to these HIV preventative therapies.

Resources

- University of Liverpool online HIV drug interaction checker
- Oregon Board of Pharmacy PrEP and PEP protocols
- HIV Alliance
- Cascade AIDS Project
- Oregon PrEP Provider List
- The Oregon AIDS Education & Training Center

Conclusion

HIV prevention is an important public health issue that impacts the Oregon community at large. With the multitude of preexisting barriers to HIV testing, prevention opportunities, and treatment, it is imperative that healthcare providers discuss PrEP with all adult and adolescent patients and identify those who may more specifically benefit from PrEP. Likewise, knowledge of available resources can help address additional health and social issues and minimize gaps in adequate HIV care and prevention. Knoweldge of appropriate screening and testing for HIV in combination with a foundational knowledge of the available pharmacological agents for HIV prevention are two of the three essential initiatives of the End HIV Oregon campaign to prevent new HIV transmissions.

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