US Public Health Service Guidelines for the Management of Occupational Exposures to Human Immunodeficiency Virus and Recommendations for Postexposure Prophylaxis: Draft Update

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Agenda

- Background/Rationale for Update
- Summary of Key Draft Recommendations
- Questions

Background and Rationale for Update

Background

- Last guidelines update: 2013
- Recommendations included:
  - Raltegravir (Isentress) + tenofovir disoproxil fumarate/emtricitabine (Truvada) recommended as first-line post-exposure prophylaxis (PEP) regimen, and other 3-drug regimens as alternatives
  - Option to conclude exposed healthcare worker follow-up HIV testing at 4 months if using 4th generation HIV antigen/antibody test

What has changed since 2013?

1. Availability of new antiretroviral agents and regimens
   - Second-generation integrase strand transfer inhibitors (INSTIs) with higher genetic barriers to resistance: dolutegravir (approved 2013) and bictegravir (approved 2018)
2. Undetectable = Untransmittable (U=U): no documented sexual transmissions between serodifferent partnerships (2016)
3. No new documented occupational transmissions of HIV
4. First FDA-approved qualitative nucleic acid test (NAT) for HIV diagnosis (2020); shortest diagnostic window (10-33 days after exposure)

Rationale for 2023 Update

- Opportunity to:
  - Update recommendations for PEP regimens to include new ART agents
  - Review risk for transmission from patients with undetectable viral loads, diagnostic testing timeframe, interval from exposure after which there is no benefit, to determine if updates are needed
  - Align with forthcoming CDC non-occupational PEP recommendation updates

Timeline

- **February 2022-present:** Formulate working group; perform targeted systematic literature review; drafted recommendations; presented to expert panel
- **August 2023:** Present draft recommendations to HICPAC
- **September/October 2023:** Prepare draft of recommendations for posting in Federal Register
- **December 2023/January 2024:** Incorporate Federal Register comments
- **February 2024:** Publication

→ Concurrently: align recommendations with updates to non-occupational PEP guidelines (CDC Division of HIV Prevention)

Summary of Draft Recommendations

Draft Recommendations for the Management of HCP with an Occupational Exposure to HIV - 1

Bold = new draft recommendation

- HCP should report occupational exposures to blood and body fluids as soon as possible to occupational services
- For HCP who have an occupational exposure to HIV, PEP should be initiated as soon as possible up to 72 hours after the exposure, and taken for 28 days
- Initiating therapy after a longer interval might still be considered for exposures that represent a high risk of transmission
- Whenever possible, the HIV status of the source patient should be determined to guide appropriate use of HIV PEP

Draft Recommendations for the Management of HCP with an Occupational Exposure to HIV - 2

- Administration of HIV PEP should not be delayed while waiting for the source patient's test results
- If HIV PEP is initiated by exposed HCP and the source patient is later determined to be HIV negative, PEP should be discontinued, and no further HIV follow-up testing is indicated for exposed HCP
- Re-evaluation of exposed HCP is recommended within 72 hours after occupational exposure to assess for further counseling needs for exposed HCP and PEP tolerability
- Provide counseling to exposed HCP in accordance with CDC recommendations for HCP with occupational exposures, including the importance of adherence to HIV PEP

Draft Recommendations for the Management of Pregnant or Breastfeeding HCP with an Occupational Exposure to HIV

- The decision to offer HIV PEP to pregnant or exposed breastfeeding HCP should be based on the same considerations that apply to any HCP who sustains an occupational exposure to HIV.
- Additional counseling of exposed breastfeeding HCP should include risks and benefits of continued breastfeeding while taking PEP and while being monitored for HIV seroconversion, versus interrupting breastfeeding.

Draft Preferred HIV PEP Regimens – INSTI + 2 NRTIs

- **Biktarvy 1 PO once daily (bictegravir [BIC] 50 mg + tenofovir AF [TAF] 25 mg + emtricitabine [FTC] 200 mg)**

OR

- **Dolutegravir (Tivicay; DTG) 50 mg PO once daily + emtricitabine (FTC) 200 mg OR lamivudine† (3TC) 300 mg + tenofovir AF (TAF) 25 mg OR tenofovir DF† (TDF) 300 mg**

*Regimens within categories are listed in alphabetical order and not according to preference.

†Generic versions are available for tenofovir DF and lamivudine and may be used instead of the fixed-dose tablets Truvada (TDF+FTC) or Descovy (TAF+FTC).

Draft Alternative HIV PEP regimens – PI + 2 NRTIs

- **Prezcobix, 1 PO once daily (darunavir [DRV] 800 mg + cobicistat 150 mg) + emtricitabine (FTC) 200 mg OR lamivudine† (3TC) 300 mg + tenofovir AF (TAF) 25 mg OR tenofovir DF† (TDF) 300 mg**

•OR

- **Symtuza, 1 PO once daily (darunavir [DRV] 800 mg + cobicistat 150 mg + tenofovir alafenamide [TAF] 10 mg + emtricitabine [FTC] 200 mg)**

*Regimens within categories are listed in alphabetical order and not according to preference.

†Generic versions are available for tenofovir DF and lamivudine and may be used instead of the fixed-dose tablets Truvada (TDF+FTC) or Descovy (TAF+FTC).

Draft Alternative HIV PEP regimen – NNRTI + 2 NRTIs

- **Delstrigo, 1 PO once daily (doravirine [Pifeltro; DOR] 100 mg + tenofovir DF† [TDF] 300 mg + lamivudine† [3TC] 300 mg)**

OR

- **Doravirine (Pifeltro; DOR) 100 mg once daily + emtricitabine [FTC] 200 mg OR lamivudine† [3TC] 300 mg + tenofovir AF [TAF] 25 mg OR tenofovir DF† [TDF] 300 mg**

*Regimens within categories are listed in alphabetical order and not according to preference.

†Generic versions are available for tenofovir DF and lamivudine and may be used instead of the fixed-dose tablets Truvada (TDF+FTC) or Descovy (TAF+FTC).

Draft Alternative HIV PEP regimens* - INSTI + 2 NRTIs

- **Genvoya, 1 PO once daily (elvitegravir [EVG] 150 mg + cobicistat 150 mg + tenofovir AF 10 mg + emtricitabine [FTC] 200 mg)**

OR

- **Stribild, 1 PO once daily (elvitegravir [EVG] 150 mg + cobicistat 150 mg + tenofovir DF 300 mg + emtricitabine [FTC] 200 mg)**

OR

- **Raltegravir (Isentress; RAL) 400 mg PO twice daily + emtricitabine [FTC] 200 mg OR lamivudine† [3TC] 300 mg + tenofovir AF [TAF] 25 mg OR tenofovir DF† [TDF] 300 mg**

*Regimens within categories are listed in alphabetical order and not according to preference.

†Generic versions are available for tenofovir DF and lamivudine and may be used instead of the fixed-dose tablets Truvada (TDF+FTC) or Descovy (TAF+FTC).

Draft Preferred HIV PEP regimens for Recipients with Kidney Disease (CrCl>5 or on hemodialysis)

INSTI + 2 NRTIs:

- **Dolutegravir (Tivicay; DTG) 50 mg PO once daily + Dose-reduced* Emtricitabine (FTC) OR lamivudine (3TC) + Dose-reduced Tenofovir DF (TDF) or Tenofovir AF (AF)**

OR

- **Raltegravir (Isentress; RAL) 400 mg PO twice daily + Dose-reduced* Emtricitabine (FTC) OR lamivudine (3TC) + Dose-reduced Tenofovir DF (TDF) or Tenofovir AF (AF)**

PI + 2 NRTIs

- **Prezcobix 1 PO once daily (Darunavir [DRV] 800 mg + cobicistat 150 mg) + Dose-reduced* Emtricitabine (FTC) OR lamivudine (3TC) + Dose-reduced Tenofovir DF (TDF) or Tenofovir AF (AF)**

OR

NNRTI + 2 NRTIs

- **Doravirine (Pifeltro; DOR) 100 mg 1 PO once daily + Dose-reduced* Emtricitabine (FTC) OR lamivudine (3TC) + Dose-reduced Tenofovir DF (TDF) or Tenofovir AF (AF)**

*Regimens within categories are listed in alphabetical order and not according to preference.

†Generic versions are available for tenofovir DF and lamivudine and may be used instead of the fixed-dose tablets Truvada (TDF+FTC) or Descovy (TAF+FTC).

Draft Preferred HIV PEP Regimens for Pregnant HCP

- **Same as for non-pregnant patients with exception of:**
  - **Biktarvy recommended as alternative due to incomplete data on pharmacokinetics in 2nd and 3rd trimesters**
  - **Regimens containing cobicistat (Genvoya, Stribild) not recommended due to reduced plasma drug exposure in pregnancy**

Draft Recommendations for PEP in the Setting of Exposures to Source Patients with HIV and Undetectable Serum Viral Load

- **For HCP who have an occupational exposure to HIV and the source patient is known or found to have an undetectable serum viral load:**
  a. **HIV PEP should be offered to exposed HCP.**
  b. **The decision to not take or discontinue PEP early should be made on a case-by-case basis with shared decision-making involving exposed HCP.**

Draft Recommendations for Laboratory Testing of the Exposed HCP

- Baseline laboratory tests of exposed HCP should be performed as soon as possible after exposure and should include:
  a. A rapid or lab-based fourth generation HIV Ag/Ab combination immunoassay
  b. Serum creatinine, aspartate transaminase (AST) and alanine transaminase (ALT)
- **Follow-up laboratory testing of the exposed HCP should include:**
  a. Interim test at weeks 4-6 post-exposure: Lab-based HIV Ag/Ab combination immunoassay and qualitative nucleic acid test (NAT) for all exposed HCP who had PEP initiated more than 24 hours after a single exposure, or who missed any PEP doses
  b. Final test at week 12 post exposure: Lab-based HIV Ag/Ab combination immunoassay and qualitative nucleic acid test (NAT) for all exposed HCP regardless of PEP administration or adherence
- **Routine follow-up testing of serum creatinine, AST and ALT is not necessary unless baseline tests are abnormal or there are clinical indications, such as signs or symptoms concerning for kidney or liver injury.**

Draft Recommendations for Expert Consultation for HIV PEP

1. Situations for which expert consultation is recommended for HIV PEP are described on the next slide
2. Obtaining expert consultation should not delay timely initiation of PEP.

Situations for which expert consultation for HIV PEP is recommended

Box 1: Situations for Which Expert Consultation for Human Immunodeficiency Virus (HIV) Postexposure Prophylaxis (PEP) Is Recommended

Delayed (ie, later than 72 hours) exposure report
- Interval after which benefits from PEP are undefined

Unknown source (eg, needle in sharps disposal container or laundry)
- Use of PEP to be decided on a case-by-case basis
- Consider severity of exposure and epidemiologic likelihood of HIV exposure
- Do not test needles or other sharp instruments for HIV

Known or suspected pregnancy in the exposed person
- Provision of PEP should not be delayed while awaiting expert consultation

Breastfeeding in the exposed person
- Provision of PEP should not be delayed while awaiting expert consultation

Known or suspected resistance of the source virus to antiretroviral agents
- If source person's virus is known or suspected to be resistant to 1 or more of the drugs considered for PEP, selection of drugs to which the source person's virus is -unlikely to be resistant is recommended
- Do not delay initiation of PEP while awaiting any results of resistance testing of the source person's virus

Toxicity of the initial PEP regimen
- Symptoms of most preferred and alternative regimens (eg, gastrointestinal symptoms and others) are often manageable without changing PEP regimen by prescribing antimotility or antiemetic agents
- Counseling and support for management of side effects is very important, as symptoms are often exacerbated by anxiety

Serious medical illness in the exposed person
- Significant underlying illness (eg, renal disease) or an exposed provider already taking multiple medications may increase the risk of drug toxicity and drug-drug interactions

Expert consultation can be made with local experts or through the following resources:

- Antiretroviral Pregnancy Registry at http://www.apregistry.com; telephone: 800-258-4263; fax: 800-800-1052; email: sm_apr@apregistry.com
- National Clinician Consultation Center (UCSF) Post-Exposure Prophylaxis Hotline at 888-448-4911.
- FDA (for reporting unusual or severe toxicity to antiretroviral agents): http://www.fda.gov/medwatch; telephone: 800-332-1088
- The CDC's Cases of Public Health Importance (COPHI) coordinator (for reporting HIV infections in HCP and failures of PEP) at telephone number 404-639-2050.
- HIV/AIDS Treatment Information Service at http:// aidsinfo.nih.gov/.

Questions?

Thank you!

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