HIV Non-Occupational Post-Exposure Prophylaxis (nPEP) Clinical Guidance

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INTRODUCTION

This document presents a plan to enable health care practitioners to address HIV Non-Occupational Exposure Prophylaxis (nPEP) treatment using HIV medication to reduce the risk of HIV transmission after a potential exposure. Patients presenting for nPEP should be evaluated as soon as possible so treatment can be initiated within recommended 72- hour timeframe. Please note, exposure to HIV is considered a MEDICAL EMERGENCY.

Medical prevention and treatment updates are posted frequently to several websites, including: PEP New York Department of Health, HIV Info NIH, and the Centers for Disease Control and Prevention CDC. It is recommended that every practitioner be familiar with all relevant guidelines.

Specific Centers for Disease Control and Prevention (CDC) post-exposure guidelines, both occupational and non-occupational, are posted at CDC PEP.

If there are questions regarding the provision of nPEP, it is recommended that a practitioner contact the *Clinician Consultation Center PEPLINE* at *1-888-448-4911.*

INDICATIONS:

Two types of PEP treatment:

- **Non-occupational PEP (nPEP)** is treatment for an individual potentially exposed to HIV outside the workplace, for example, during episodes of unprotected sex, needle-sharing/injection drug use or exposure to blood or body fluids of a person with HIV (PWH). Non-occupational exposure is any direct mucosal, percutaneous or intravenous contact with potentially infectious body fluids (not including perinatal situations).

- **Occupational PEP (oPEP)** is treatment for an individual, who through workplace activity has been exposed to biohazardous products, potentially infectious body fluids or materials that may subject the individual to HIV.

Children and Adolescents:

This guideline does not specifically address the special needs of children and adolescents. There is a post-exposure prophylaxis regimen for patients 2–12 years old who weigh <40 kg that is provided through the New York State Department of Health AIDS Institute at Clinical Guidelines Program New York Department of Health.

CODING AND BILLING:

Coding for nPEP visits

- nPEP Initiation/nPEP RX 5705
- nPEP Follow-Up Visit 5706

For further coding information: HMS Service and Time Coding

Coding for nPEP labs

- County Health Departments (CHDs) without resources for funding lab on uninsured individuals may bill nPEP specific labs to the 02H program. Please be sure the patient is coded correctly to HMS 5705 initiation nPEP visit.

EVALUATION AND MANAGEMENT: Algorithm for Evaluation, Risk Assessment, and Management for a Non-Occupational Exposure:

STEP 1: Initial evaluation of exposure: Is patient presenting within 72 hours?	
CDC guidance is to consider for nPEP initiation if patient presents within 72 hours of exposure. *Go to step 2*	If presenting >72 hours post exposure, PEP is not recommended.

STEP 2: Risk Assessment: Is nPEP indicated?		
LOWER-RISK EXPOSURES: • Oral-vaginal contact (receptive and insertive) • Oral-anal contact (receptive and insertive) • Penile-oral contact (receptive or insertive) with or without ejaculation *Provide risk reduction strategies as appropriate and offer HIV testing.* ***Stop*** *– nPEP is not indicated unless factors below:* *Factors that increase transmission risk through sexual exposure include known source with incomplete viral suppression, presence of genital ulcer disease or other Sexually Transmitted Infection (STI), trauma at site, non-intact oral mucosa or blood exposure.*	**HIGHER-RISK EXPOSURES:** • Receptive and insertive vaginal or anal intercourse with PWH with incomplete viral suppression or unknown source • Needle sharing with PWH with incomplete viral suppression or unknown source • Injuries with mucosal trauma, exposure to blood or other potentially infected fluids from PWH with incomplete viral suppression or unknown source (including needle sticks with a hollow-bore needle, human bites, accidents) *nPEP is indicated, go to Step 3.*	**EXPOSURES THAT DO NOT WARRANT nPEP:** • Oral-to-oral contact without mucosal damage (kissing or mouth-to-mouth resuscitation) • Human bites not involving blood • Exposure to solid-bore needles or sharps not in recent contact with blood • Mutual masturbation without skin breakdown • Exposure to non-bloody saliva ***Stop*** *– nPEP not indicated. Provide risk reduction strategies as appropriate and offer HIV testing.*

STEP 3: Treatment – Initiate first dose of nPEP regimen—28 Day Regimen **PREFFERED REGIMEN**
For adults and adolescents aged ≥ 13 years

Tenofovir Disoproxil Fumarate 300 mg/Emtricitabine 200 mg (Truvada; TDF/FTC) PO daily **(or)** *TDF 300 mg/lamivudine 300 mg (Cimduo; TDF/3TC) once daily[a,d]

with

Raltegravir (Isentress; RAL) 400 mg twice daily[b,c]

or

*Raltegravir HD 1200 mg once daily[b,c]

or

Dolutegravir (Tivicay; DTG) 50 mg once daily[b,c,.e]

OR USE AN ALTERNATE REGIMEN ON THE NEXT PAGE

Treatment – Initiate first dose of nPEP regimen—28 Day Regimen **ALTERNATE REGIMEN** For adults and adolescents aged ≥ 13 years
TDF/FTC (Truvada) **(or)** *TDF/3TC (Cimduo) once daily[a,d] with Darunavir 800 mg (Prezista) ***plus*** ritonavir 100 mg (Norvir; RTV) once daily or *Atazanavir 300 mg (Reyataz) **(or)** *fosamprenavir 1400 mg (Lexiva) ***plus*** RTV 100 mg once daily or *Elvitegravir 150 mg/Cobicistat 150 mg/Emtricitabine 200 mg/Tenofovir Disoproxil Fumarate 300 mg (EVG/COBI/FTC/TDF) once per day (Stribild)[f]

[a] Lamivudine 300 mg PO daily may be substituted for emtricitabine.

[b] Raltegravir HD - Must be greater than 40 kg. Do not use if pregnant.

[c] DTG and RAL not to be taken concurrently with divalent cations (e.g., calcium and magnesium)

[d] Fixed drug combination of TDF/FTC and TDF/3TC dose adjust for CrCl < 50 mL/min

[e] Practitioners need to consider the risk of neural tube defect if choosing DTG in women of childbearing potential.

[f] Stribild - CrCl must be 70 mL/min or greater

[*] Unless otherwise noted, regimens are from CDC guidance. Regimens marked with asterisk (*) are from the New York State Department of Health AIDS Institute. Both websites are referenced on page three

PLEASE NOTE: Link to pediatric dosing chart is located on page 10

STEP 4: Baseline testing/labs

Exposed Person:

- HIV-1/2 antigen/antibody immunoassay GC/CT Nucleic-Acid Amplification Testing (NAAT) (based on site of exposure)
- Trichomoniasis NAAT*
- Rapid Plasma Reagin (RPR)
- Pregnancy test if appropriate
- HCV and HBV: Check history for hepatitis B vaccines; if unknown, draw hepatitis B surface antigen (HBsAg), and hepatitis B surface antibody (HBsAb).
- Complete Metabolic Profile

nPEP should not be continued in those who decline baseline HIV testing

Assess need for emergency contraception

Source Testing (*if source is available*):

- Obtain consent and test with a HIV-1/2 antigen/antibody immunoassay
- If the test results are not immediately available, continue exposed person's nPEP while awaiting results.
- If the source person's HIV screening test is negative, assess for the potential of at-risk exposures for HIV by history to assess need of continuing exposed person's PEP; consider HIV PCR RNA if appropriate. Continue exposed person's nPEP until results of the plasma HIV RNA assay are available.

WHEN THE SOURCE IS A KNOWN PWH

Past and current antiretroviral therapy (ART) experience, viral load data, and genotypic or phenotypic resistance data should be considered in selecting the nPEP regimen. Consult with a clinician experienced in managing HIV.

POST nPEP INITIATION MONITORING:

	Baseline	Week 1	Week 2	Week 4-6	Week 12	Week 24
Clinic Visit	√	At 48 hours √ or by phone	√ or by phone	√		
HIV Screening Test[a]	√			√	√	√[d]
Pregnancy Test	√			√		
Serum liver enzymes, BUN, creatinine, CBC	√			√		
STI Screening[a] ***Trichomoniasis NAAT GC/CT NAAT (based on site of exposure) RPR**	√		√ *(consider)*	√[e]		
Hepatitis B surface antigen (HBsAg) and surface antibody (anti-HBs) and core antibody (anti-HBc) [b, c]	√					√[c]
Hepatitis C virus (HCV) antibody[b,]	√					√[c]

[a] **Recommended even if nPEP is declined.**
[b] **For post-exposure management for hepatitis B** Management of Potential Exposure to Hepatitis B Virus **and hepatitis C,** Hepatitis Care
[c] **if exposed person susceptible at baseline**
[d] **If HCV acquired at baseline as delayed HIV seroconversion reported in persons who simultaneously acquire HIV and HCV**
[e] **If not presumptively treated at baseline**
***Labs marked with asterisk (*) are from the New York State Department of Health AIDS Institute, referenced on page three**

FREQUENTLY ASKED QUESTIONS:

Initial Evaluation:

Q: What is the timeframe for starting nPEP?

A: Ideally within two hours to no longer than 72-hours of exposure. After 72-hours of exposure, nPEP is not recommended. Please note that nPEP is not indicated for perceived exposures of negligible or no conceivable risk. Clinicians should be willing to decline requests for nPEP and provide supportive counseling and referrals in these situations.

Risk Assessment:

Q: How do we evaluate exposure?

A: Evaluate for the potential to transmit HIV based on (1) the type of body substance involved, (2) the route and manner of transmission and, (3) HIV status of the source patient. Treatment of the patient is the **PRIORITY** and should **NOT** be delayed while waiting for lab results.

Q: What elements should I consider when evaluating exposure?

A: There are four elements to consider (italicized):

- *Exposure Type*: type and amount of source fluid or material
- *Incident*: location of and manner of exposure to source fluid or material
- *Source Patient*: HIV, hepatitis B and hepatitis C status – If the source patient has HIV, determine the stage of disease, HIV viral load, current and previous ART and antiretroviral resistance in deciding if nPEP is needed and in selecting the regimen. Do not delay start of nPEP if indicated when the source information is not readily available.
- *Patient*: Hepatitis A and hepatitis B vaccination and vaccine-response status, other medical conditions, drug allergies, concomitant medications and pregnancy (and pregnancy potential) and breast-feeding status
- Decisions should be individualized, weighing the likelihood of transmission against the potential benefits and risks of treatment
- If source patient has an undetectable HIV viral load, nPEP for HIV is not indicated

Q: What do we do if the patient is too upset to discuss nPEP?

A: If the patient is too distraught to engage in a discussion about and/or commitment to the drug regimen at the initial assessment, the clinician should offer a first dose of the medication and arrange a follow up within 24 hours to further discuss the indications for nPEP. If possible, baseline STI and HIV-1/2 antigen/antibody immunoassay test should be obtained even if nPEP is refused.

Q: Should we always evaluate a patient seeking nPEP for previous exposure to HIV (separate from the event leading to the nPEP visit)?

A: The likelihood of pre-existing HIV should be determined for all individuals presenting for nPEP. Has the patient ever been tested, and if so, what was the date/result of their last HIV test? Note the number and types of unprotected exposures since the last HIV test. The likelihood of pre-existing HIV infection should be reviewed with the patient prior to nPEP prescription. If pre-existing HIV infection is likely, this information should be integrated into the risk-benefit assessment.

Q: What if the patient presenting with a high-risk exposure is on PrEP?

A: PrEP responsibly taken should be effective and PEP should not be needed if the source patient is not HIV positive and does not have resistance to the PrEP medication. This is an individualized decision that may warrant PEP initiation while gathering data on the source patient.

Q: If the source patient is available and consents to testing, what test(s) should be conducted?

A: If the source patient is available, has an unknown status and consents, HIV testing should be completed using an HIV-1/2 antigen/antibody immunoassay blood-based HIV test and maintain nPEP of the exposed patient until result known. Testing for other STIs, including hepatitis B and hepatitis C is recommended. Discontinue nPEP if the HIV testing is negative for the source patient.

Q: What information do you need if the source patient is a PWH?

A: If the source patient is a PWH, obtain history of antiretroviral medication, recent viral load, and history of drug resistance. Testing for other STIs, including hepatitis B and hepatitis C is recommended. Initiate treatment while gathering this information.

nPEP Treatment Considerations:

Q: How is nPEP started?

A: A starter pack of the preferred regimen should be provided at the time of initial evaluation. A starter pack usually consists of a three to five-day supply. NOTE: Medications can be changed at follow up if appropriate based on source patient resistance (if available), efficacy data, toxicity, pill burden/ease of dosing, potential drug interactions, cost and pregnancy risk. Prophylactic antiemetic and antidiarrheal agents can be used for control of side effects.

Q: How long is nPEP treatment given and under what circumstances would treatment be discontinued?

A:The total nPEP treatment is 28 days and should **NOT** be administered for less than 28 days unless:

- The source is determined to be uninfected via confirmatory HIV test
- There are intolerable side effects and no alternative medications are available
- The exposed individual changes her/his mind about nPEP after re-examining the risks and benefits

STI and Hepatitis Treatment/Vaccination:

Q: Do you always test for STIs when considering nPEP treatment?

A: Based upon the 2015 CDC Treatment Guidelines, assessment for STIs may be deferred per the option of the treatment practitioner and patient. Many specialists recommend preventative therapy at initial examination because follow-up with patients can be difficult.

Q: What if the patient is exposed to a known hepatitis B carrier?

A: Post-exposure hepatitis B vaccination, without HBIG, should adequately protect against HBV infection. Hepatitis B vaccination should be administered to patients at the time of the initial examination if they have not been previously vaccinated. Follow-up doses of vaccine should be administered following recommendations by the Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP). Hepatitis C testing is recommended.

Pregnancy Testing and Emergency Contraception:

Q: Is pregnancy testing recommended?

A: All women of child-bearing potential should be tested for pregnancy. If the presenting exposure is vaginal, patient should return for repeat testing if her menstrual cycle is delayed. Pregnant women can receive nPEP. Emergency Contraception (EC) should be offered if an exposure could result in pregnancy.

Post nPEP Monitoring:

Q: When do you conduct patient follow up after starting nPEP?

A: All patients receiving nPEP should be re-evaluated within three days of the exposure to review the exposure and available source person data, evaluate adherence and monitor for side effects or toxicities associated with the nPEP regimen. The exposed person should be evaluated as per guidance above (on page six) while receiving nPEP to assess treatment adherence, side effects of treatment, interval physical complaints and emotional status.

Q: When would additional testing be required related to nPEP?

A: During the treatment period, other blood tests may be indicated to monitor for side effects of treatment. The timing and specific testing indicated varies based on the nPEP regimen used. See the table above on page six for general guidelines. Clinicians should be aware of the resources available within the community that offer medical and supportive counseling/adherence services following non-occupational exposure. Patients with signs or symptoms of acute HIV infection should be referred for further assessment when nPEP is provided outside of an expert clinical context.

HIV Serological Screening Tests

Q: What is the advantage of the HIV-1/2 antigen/antibody immunoassay in nPEP baseline testing?

A: A HIV-1/2 antigen/antibody immunoassay is the recommended serologic screening test. This test is an antibody/antigen combination immunoassay test which can simultaneously detect both HIV-1/HIV-2 antibodies and HIV-1 p24 antigens and will generally be positive within 14–15 days of infection. HIV screening should be confirmed with an FDA-approved HIV-1/HIV-2 antibody-differentiation assay.

HIV Seroconversion

Q: At what point could HIV seroconversion take place?

A: If HIV infection develops after an exposure, it will generally occur within two to four weeks of exposure. HIV testing at baseline, four weeks, and 12 weeks is recommended after significant exposures, regardless of whether the individual accepts or declines PEP treatment. Delayed seroconversion to HIV positive status has been reported in persons who acquire acute HCV infection at the same time as HIV; HIV testing at 24 weeks in this scenario is recommended. Point-of-care HIV tests (rapid tests) are less sensitive than laboratory-based HIV tests; therefore, exposed persons should be tested with laboratory-based HIV tests whenever possible.

Q: What are the symptoms of acute HIV infection?

A: Patients acutely infected with HIV will often experience at least some symptoms of the acute retroviral syndrome. Fever and flu-like symptoms are common in acute HIV infection but are nonspecific. Rash, mucocutaneous ulcers, oropharyngeal candidiasis and meningismus are more specific. Symptoms may also include fatigue or malaise, joint pain, headache, loss of appetite, night sweats, myalgias, lymphadenopathy, oral and/or genital ulcers, nausea, diarrhea or pharyngitis. Acute HIV infection is often not recognized in the primary care setting because of the similarity of the symptom complex with that of the flu or other common illnesses. If the exposed person presents with signs or symptoms of acute HIV seroconversion, an HIV serologic screening test should be used in conjunction with a plasma HIV RNA assay to diagnose acute HIV infection. (see the *CDC Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens* at Laboratory testing for the diagnosis of HIV infection : updated recommendations (cdc.gov)).

Pharmacy Considerations

Q: What role does the pharmacist play in nPEP treatment?

A: Pharmacists play a role in dispensing nPEP regimens. In order to ensure more timely access of nPEP medications to patients, practitioners should be aware that the use of “phone-in” oral prescriptions may result in faster dispensing and avoid situations where drug access might be limited. When nPEP is prescribed to a patient receiving other prescription and non-prescription medications, a complete drug profile review should take place to assess for any drug-drug interactions. No medications should be dispensed as part of an nPEP regimen if all medications are unavailable at the same time.

Q: Where can I locate nPEP medications when needed?

A: It is beneficial to coordinate with local pharmacies in determining which ones have nPEP medications in stock or can order them quickly. Practitioners can discuss the treatment with local pharmacies and the need for an urgent response when prescribing nPEP medications. Pharmacists with specific questions regarding nPEP therapy are welcome to contact the PEP Hotline at (888) 448-4911, available seven days a week from 9:00 a.m.–2:00 a.m. EST. Sample medication regimens for HIV treatment can be obtained by practitioners working within CHDs.

nPEP Follow Up

Q: What are the options for post nPEP follow up?

A: There are three options for follow up:

Option 1: Each facility or clinic practitioner performing an examination, including sexual assault exams, should solicit a relationship with a qualified medical practitioner who is knowledgeable about HIV treatment and nPEP and can receive patients within three to five days of the initial exam and referral.

Option 2: The initial facility's health care practitioner may have the patient return to their facility for follow-up treatment if no other option is available.

Option 3: If there is not an established relationship and/or no physician available, then sexual assault victims who have been assessed by a Practitioner and have met the criteria for nPEP can be referred to another primary care Practitioner or a local infectious Disease Physician.

REFERRALS AND RESOURCES

Mental health/substance abuse may contribute significantly to the risk of subsequent exposures. nPEP should be provided with services that address ongoing needs of patient risk behaviors. Practitioners should be aware of local resources for mental health/substance abuse treatment. Additional resources are listed below:

Resources for rape crisis:

- For information about rape crisis services, see *HIV Prophylaxis for Victims of Sexual Assault*: Exposure Risk Evaluation - AIDS Institute Clinical Guidelines (hivguidelines.org)
- National Sexual Assault Telephone Hotline: Rape Crisis Center services to mitigate sexual assault trauma (1-800-656-HOPE).
- In Florida, call the Rape Crisis Hotline 1-888-956-7273.
- For local service information in Florida, see the Florida Council Against Sexual Violence (FCASV) fcasv.org/information/find-your-local-center or their home website, Florida Council Against Sexual Violence (fcasv.org)

HIV and other STIs support:

- HIV Hotline for patients in need of HIV-specific support (1-800-CDC-INFO).
- For STI treatment guidelines: CDC - STD Treatment

Pregnancy and nPEP

- Pregnancy nPEP options: If PEP is started for a pregnant exposed person, the recommendation is to call the Clinician Consultation Center at (888) 448-8765 (24 hours, seven days a week) to speak with consultant on Perinatal HIV/AIDS for the most updated options related to pregnancy and breastfeeding.

nPEP

- For in depth information on nPEP regimens: PEP to Prevent HIV Infection - AIDS Institute Clinical Guidelines (hivguidelines.org)
- Patient assistance information, websites, and co-pay information: PEP Patient Assistance

Pediatric Regimen Guidelines

- New York State Department of Health AIDS Institute at PEP to Prevent HIV Infection - AIDS Institute Clinical Guidelines (hivguidelines.org)