

NYS PEP Regimen Q & A

Why does NYS recommend zidovudine + lamivudine + tenofovir as a PEP regimen?

The Medical Care Criteria Committee chose this regimen because it is simple, effective, and well tolerated. Tenofovir was chosen as the third agent because it achieves high intracellular levels, has been effective in trials of PEP in primates, and has excellent tolerability.

Given the potential for resistance, should a more potent regimen than zidovudine + lamivudine + tenofovir be recommended for high-risk exposures?

Although the combination of 2 NRTIs plus tenofovir has had high failure rates in the treatment of established HIV infection, the situation of post-exposure prophylaxis is different for several reasons. The viral burden in the setting of a very recently exposed patient is likely to be lower than the viral burden of a patient with established infection. The use of a single agent proved to be efficacious in PEP in the healthcare setting and also in the prevention of vertical transmission.^{1,2} Furthermore, the efficacy of combination regimens of the more potent agents may be counterbalanced by the increased likelihood of poor adherence, resulting in diminished efficacy.

Using different medications for prophylaxis and treatment is not a new practice. For example, rifampin is used for prophylaxis of exposed persons against bacterial meningitis, but would not be considered an option for treatment of bacterial meningitis.

Why does NYS recommend tenofovir when simpler, more tolerable PIs have recently become available?

- 1) PIs have more drug-drug interactions and are more complicated than tenofovir to use in a PEP regimen.
- 2) The side effects associated with even new more tolerable PIs are more frequent and more severe than those associated with tenofovir.
- 3) Tenofovir acts before integration and PIs do not.

Should clinicians be concerned about renal toxicity associated with use of tenofovir?

Renal toxicity data are not definitive. Most of the initial cases of toxicity were in patients with advanced HIV disease and low CD4 cell counts and occurred after extended use of tenofovir, which is a different scenario than in patients using tenofovir for 1 month for PEP.

Is NYS recommending the zidovudine + lamivudine + tenofovir PEP regimen for adolescents as well as adults?

The committee for the Care of Children and Adolescents with HIV has recommended the use of this tenofovir-containing regimen in adolescents aged 13-18. Although the FDA-approved indication for the use of tenofovir in the treatment of HIV is only for adults, pediatric HIV specialists have used tenofovir extensively in children and adolescents and have observed a level of safety comparable to its use in adults. The committee believes that the benefits of this simpler, more tolerable regimen can safely be extended to adolescents.

Why does New York State recommend that PEP be initiated within 36 hours rather than 72 hours?

The sooner a PEP regimen is initiated, the greater the likelihood that it will be effective. Animal models of PEP have shown that effective ARV treatment is most likely to prevent infection when initiated within 24 hours of experimental exposure.³⁻⁷ It is unknown whether initiation of PEP beyond this point confers protection. Most ARV drugs require an intracellular activation step that delays the onset of antiviral activity. Thus, clinicians should begin PEP as soon as possible, ideally within 2 hours and generally not later than 36 hours, following exposures that carry the risk of HIV transmission. An absolute elapsed time after which PEP should not be administered, however, cannot be stated with certainty. Patients presenting after 36 hours should be considered for PEP on an individual basis.

Why does NYS recommend a #1 option for a PEP regimen when the CDC gives several options?

The committee believes that recommending one preferred regimen simplifies the process for frontline clinicians.

How can clinicians obtain guidance on use of the NYS regimen and guidelines?

Clinicians should call the Clinical Education Initiative's PEP Line.
HIV Antiretroviral Prophylaxis Provider Support/Educational Consult
Occupational Exposure; Sexual Assault; Clinical Management Issues



Adult (Over 18 years of age)

8:30 am – 4:00 pm Monday – Friday Call (315) 4646-5533 - Press “3” for an operator

All other hours Call (315) 363-5540- Ask for ID Physician on call

Pediatric (under 18 years of age)

8:30 am – 4:00 pm Monday – Friday Call (315) 464-6331

After Hours Call (315) 701-7190 – Ask for Pediatric ID Physician on call

References

1. Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatrics AIDS Clinical Trials Group Protocol 076 Study Group. *N Engl J Med* 1994;331:1173-1180.
2. Centers for Disease Control and Prevention. Case-control study of HIV seroconversion in health-care workers after percutaneous exposure to HIV-infected blood: France, United Kingdom, and United States, January 1988-August 1994. *MMWR Morb Mortal Wkly Rep* 1995;44:929-933.
3. Black RJ. Animal studies of prophylaxis. *Am J Med* 1997;102:39-44.
4. Otten RA, Smith DK, Adams DR, et al. Efficacy of postexposure prophylaxis after intravaginal exposure of pig-tailed macaques to a human-derived retrovirus (human immunodeficiency virus type 2). *J Virol* 2000;74:9771-9775.
5. Smith MS, Foresman L, Lopez GJ, et al. Lasting effects of transient postinoculation tenofovir [9-R-(2-Phosphonomethoxypropyl)adenine] treatment on SHIV (KU2) infection of rhesus macaques. *Virology* 2000;277:306-315.
6. Van Rompay KK, Berardi CJ, Aguirre NL, et al. Two doses of PMPA protect newborn macaques against oral simian immunodeficiency virus infection. *AIDS* 1998;12:F79-F83.
7. Van Rompay KK, Miller MD, Marthas ML, et al. Prophylactic and therapeutic benefits of short-term 9-[2-(R)-(phosphonomethoxy) propyl]adenine (PMPA) administration to newborn macaques following oral inoculation with simian immunodeficiency virus with reduced susceptibility to PMPA. *J Virol* 2000;74:1767-1774.