

Appendix B

Basic, Alternate and Expanded HIV Post Exposure Prophylaxis (PEP) Regimens (MMRW, 2001):

Basic PEP Regimen

- **Zidovudine (RETROVIR™; ZDV; AZT) + Lamivudine (EPIVIR™; 3TC); available as COMBIVIR™**
 - ZDV: 600 mg per day, in two or three divided doses, and
 - 3TC: 150 mg twice daily.

Advantages

- ZDV is associated with decreased risk of HIV transmission in the CDC case-control study of occupational HIV infection.
- ZDV has been used more than the other drugs for PEP in Health Care Provider (HCP).
- Serious toxicity is rare when used for PEP.
- Side effects are predictable and manageable with antimotility and antiemetic agents.
- Probably a safe regimen for pregnant HCP.
- Can be given as a single tablet (COMBIVIR™) twice daily.

Disadvantages

- Side effects are common and might result in low adherence.
- Source patient virus might have resistance to this regimen.
- Potential for delayed toxicity (oncogenic/teratogenic) is unknown.

Alternate Basic PEP Regimen

- **Lamivudine (3TC) + Stavudine (ZERIT™; d4T)**
 - 3TC: 150 mg twice daily, and
 - d4T: 40 mg (if body weight is <60 kg, 30 mg twice daily) twice daily.

Advantages

- well tolerated in patients with HIV infection, resulting in good adherence
- serious toxicity appears to be rare, and
- twice daily dosing might improve adherence

Disadvantages

- Source patient virus might be resistant to this regimen.
- Potential for delayed toxicity (oncogenic/teratogenic) is unknown.

- **Didanosine (VIDEX™, chewable/dispersible buffered tablet; VIDEX™ EC, delayed-release capsule; ddl) + Stavudine (d4T)**
 - ddl: 400 mg (if body weight is <60 kg, 125 mg twice daily) daily, on an empty stomach.
 - d4T: 40 mg (if body weight is <60 kg, 30 mg twice daily) twice daily.

Advantages

- Likely to be effective against HIV strains from source patients who are taking ZDV and 3TC.

Disadvantages

- ddl is difficult to administer and unpalatable.
- Chewable/dispersible buffered tablet formulation of ddl interferes with absorption of some drugs (e.g., quinolone antibiotics, and indinavir).
- Serious toxicity (e.g., neuropathy, pancreatitis, or hepatitis) can occur. Fatal and nonfatal pancreatitis has occurred in HIV-positive, treatment-naive patients. Patients taking ddl and d4T should be carefully assessed and closely monitored for pancreatitis, lactic acidosis, and hepatitis.
- Side effects are common; anticipate diarrhea and low adherence.
- Potential for delayed toxicity (oncogenic/teratogenic) is unknown.

Expanded PEP Regimen

Utilize basic PEP regimen plus one of the following:

- **Indinavir (CRIXIVAN™; IDV)**
 - 800 mg every 8 hours, on an empty stomach.

Advantages

- Potent HIV inhibitor.

Disadvantages

- Serious toxicity (e.g., nephrolithiasis) can occur; must take 8 glasses of fluid per day.
 - Hyperbilirubinemia common; must avoid this drug during late pregnancy.
 - Requires acid for absorption and cannot be taken simultaneously with ddl in chewable/dispersible buffered tablet formulation (doses must be separated by at least 1 hour).
 - Concomitant use of astemizole, terfenadine, dihydroergotamine, ergotamine, ergonovine, methylergonovine, rifampin, cisapride, St. John's Wort, lovastatin, simvastatin, pimozone, midazolam, or triazolam is not recommended.
 - Potential for delayed toxicity (oncogenic/teratogenic) is unknown.
- **Nelfinavir (VIRACEPT™; NFV)**
 - 750 mg three times daily, with meals or snack, or
 - 1250 mg twice daily, with meals or snack.

Advantages

- potent HIV inhibitor, and
- twice dosing per day might improve adherence.

Disadvantages

- Concomitant use of astemizole, terfenadine, dihydroergotamine, ergotamine, ergonovine, methylergonovine, rifampin, cisapride, St. John's Wort, lovastatin, simvastatin, pimozone, midazolam, or triazolam is not recommended.
- Might accelerate the clearance of certain drugs, including oral contraceptives (requiring alternative or additional contraceptive measures for women taking these drugs).
- Potential for delayed toxicity (oncogenic/teratogenic) is unknown.

- **Efavirenz (SUSTIVA™; EFV)**
 - 600 mg daily, at bedtime.

Advantages

- Does not require phosphorylation before activation and might be active earlier than other antiretroviral agents (note: this might be only a theoretical advantage of no clinical benefit.)
- One dose daily might improve adherence.

Disadvantages

- Drug is associated with rash (early onset) that can be severe and might rarely progress to Stevens-Johnson syndrome.
- Differentiating between early drug-associated rash and acute seroconversion can be difficult and cause extraordinary concern for the exposed person.
- Nervous system side effects (e.g., dizziness, somnolence, insomnia, and/or abnormal dreaming) are common. Severe psychiatric symptoms are possible (dosing before bedtime might minimize these side effects).
- Should not be used during pregnancy because of concerns about teratogenicity.
- Concomitant use of astemizole, cisapride, midazolam, triazolam, ergot derivatives, or St. John's Wort is not recommended because inhibition of the metabolism of these drugs could create the potential for serious and/or life-threatening adverse events (e.g., cardiac arrhythmias, prolonged sedation, or respiratory depression).
- Potential for oncogenic toxicity is unknown.

- **Abacavir (ZIAGEN™; ABC); available as TRIZIVIR™, a combination of ZDV, 3TC, and ABC**
 - 300 mg twice daily.

Advantages

- potent HIV inhibitor, and
- well tolerated in patients with HIV infection.

Disadvantages

- Severe hypersensitivity reactions can occur, usually within the first 6 weeks of treatment.
- Potential for delayed toxicity (oncogenic/teratogenic) is unknown.

Antiretroviral Agents for Use as PEP Only With Expert Consultation

- **Ritonavir (NORVIR™; RTV)**

Disadvantages

- difficult to take (requires dose escalation),
- poor tolerability, and
- many drug interactions.

- **Saquinavir (FORTOVASE™, soft-gel formulation; SQV)**

Disadvantages

- Bioavailability is relatively poor, even with new formulation.

New York State Mandated Infection Control and Barrier Precautions

- **Amprenavir (AGENERASE™; AMP)**

Disadvantages

- Dosage consists of eight large pills taken twice daily.
- Many drug interactions.

- **Delavirdine (RESCRIPTOR™; DLV)**

Disadvantages

- Drug is associated with rash (early onset) that can be severe and progress to Stevens-Johnson syndrome.
- Many drug interactions.

- **Lopinavir/Ritonavir (KALETRA™)**

- 400/100 mg twice daily.

Advantages

- potent HIV inhibitor, and
- well tolerated in patients with HIV infection.

Disadvantages

- Concomitant use of flecainide, propafenone, astemizole, terfenadine, dihydroergotamine, ergotamine, ergonovine, methylergonovine, rifampin, cisapride, St. John's Wort, lovastatin, simvastatin, pimozone, midazolam, or triazolam is not recommended because inhibition of the metabolism of these drugs could create the potential for serious and/or life-threatening adverse events (e.g., cardiac arrhythmias, prolonged sedation, or respiratory depression).
- May accelerate the clearance of certain drugs, including oral contraceptives (requiring alternative or additional contraceptive measures for women taking these drugs).
- Potential for delayed toxicity (oncogenic/teratogenic) is unknown.

Antiretroviral Agents Generally Not Recommended For Use as PEP

- **Nevirapine (VIRAMUNE™; NVP)**

- 200 mg daily for 2 weeks, then 200 mg twice daily.

Disadvantages

- Associated with severe hepatotoxicity (including at least one case of liver failure requiring liver transplantation in an exposed person taking PEP)
- Associated with rash (early onset) that can be severe and progress to Stevens-Johnson syndrome
- Differentiating between early drug-associated rash and acute seroconversion can be difficult and cause extraordinary concern for the exposed person, and
- Concomitant use of St. John's Wort is not recommended because this might result in suboptimal antiretroviral drug concentrations.