

"PrEP Pearls" and Quick Resource for Assessment for Drug Therapy Problems

Assessment for Indication (eg. no valid indication or unnecessary drug, requires drug but not receiving)

- Pre-exposure prophylaxis (PrEP) is the daily use of antiretrovirals by an HIV-uninfected individual at risk for HIV to avert infection
- Recommended indications for PrEP use by men who have sex with men (MSM) include:
 - Adult man
 - Without acute or established HIV infection
 - Any male sex partner in past 6 months
 - Not in a monogamous partnership with a recently tested, HIV-negative man
 - AND at least one of the following:**
 - Any anal sex without condoms (receptive or insertive) in past 6 months
 - Any sexually transmitted infection diagnosed or reported in past 6 months
 - Is in an ongoing sexual relationship with an HIV-positive male partner
- Recommended indication for PrEP use by heterosexually active men and women:
 - Adult person
 - Without acute or established HIV infection
 - Any sex with opposite sex partner in past 6 months
 - Not in a monogamous partnership with a recently tested HIV-negative partner
 - AND at least one of the following:**
 - Is a man who has sex with both women and men
 - Infrequently uses condoms during sex with 1 or more partners of unknown HIV status who are known to be at substantial risk of HIV infection
 - Is in an ongoing sexual relationship with an HIV-positive partner
- Recommended indications for PrEP use by injection drug users:
 - Adult person
 - Without acute or established HIV infection
 - Any injection of drugs not prescribed by a clinician in past 6 months
 - AND at least one of the following:**
 - Any sharing of injection or drug preparation equipment in past 6 months
 - Risk of sexual acquisition
- Presently, the manufacturer of Truvada[®] (emtricitabine 200mg/tenofovir disoproxil fumarate 300mg) has not applied for regulatory approval of PrEP in Canada; Truvada has been approved for PrEP use by the US FDA since 2012

Assessment for Effectiveness (wrong drug or drug product, dose too low, drug-drug, drug-food interaction)

- Truvada[®] 1 tablet daily (as approved by US FDA)
- Tenofovir 300mg daily alone has been shown to be effective in clinical trials in injection drug users and heterosexually active adults (not MSM)
- Truvada[®] on demand (2 tablets taken 2-24 hours before sexual intercourse, 1 tablet 24 hours later and a fourth tablet 48 hours after the first drug intake) has shown to be effective in trials to reduce the risk of HIV sexual transmission among high-risk MSM by 86% (ANRS Ipergay Trial, CROI 2015)
- Pharmacokinetic studies suggest intracellular levels of tenofovir diphosphate correspond to an HIV risk reduction of 99% for 7 doses per week, 96% for 4 doses per week and 76% for 2 doses per week
- Maximum intracellular concentrations of tenofovir diphosphate are reached in blood after ~20 days of daily dosing, in rectal tissue at ~7 days and in cervicovaginal tissue at ~20 days

Safety (dose too high, adverse drug reaction, drug-drug interaction, drug-food interact)

- Truvada[®] (emtricitabine/tenofovir) should not be prescribed to any person for the indication of PrEP with an estimated creatinine clearance < 60 mL/min; thus renal function should be assessed at baseline and monitored at least every 6 months while taking Truvada[®]
- caution should be taken when administering Truvada[®] to patients with known risk factors for renal disease, a history of renal dysfunction or bone disease
- Severe acute exacerbations of hepatitis B have been reported in patients who are co-infected with HIV and hepatitis B after the discontinuation of Truvada[®]; thus hepatitis B testing should be done before PrEP is prescribed and vaccination offered if the patient is non-immune.
- Acute or chronic HIV infection needs to be excluded prior to initiating, reinitiating or continuing PrEP and assessment (ie. HIV testing) should be conducted every 3 months (before prescriptions are refilled or re-issued) while patients are taking PrEP; use of Truvada alone in HIV infection increases risk for development of resistance to either or both drugs
- Clinical signs and symptoms of acute HIV infection include:
fever, fatigue, myalgia, skin rash, headache, pharyngitis, cervical adenopathy, arthralgia, night sweats, diarrhea
- Small studies of periconception use of tenofovir in uninfected women in HIV-discordant couple was found to be safe in terms of pregnancy and infection
- Since emtricitabine and tenofovir are primarily eliminated by the kidneys, coadministration of Truvada[®] with drugs that reduce renal function or compete for active tubular secretion may increase serum concentrations of tenofovir (eg. NSAIDs, acyclovir, valacyclovir, ganciclovir, valganciclovir, ritonavir); short-term, occasional use likely safe.

Adherence (not taking as prescribed due to understanding, choice, forgetting, costs)

- PrEP's efficacy is critically dependent on medication adherence and PrEP adherence can decrease over time
- Strategies to support medication adherence include education, managing side effects (headache, nausea), establishing routines, providing reminder systems/tool, removing financial barriers to accessing medication, addressing substance abuse and mental health needs
- cost of Truvada is approximately \$800 per month

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