

## HIV "PEP 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)

- HIV PEP is the use of antiretroviral drugs in an HIV-negative individual after a potential exposure to blood or bodily fluids that might contain HIV
- Many factors contribute to a significant exposure and a higher risk including a) the type of body fluid involved b) the type of injury or exposure that occurred c) the size of the inoculum d) and the attributes of the source patient
- Body fluids considered potentially infectious include: blood, serum, plasma, visibly bloody body fluids, semen and vaginal secretions, cerebrospinal fluid, synovial fluid, pleural fluid, peritoneal fluid, pericardial fluid and amniotic fluid
- Body fluids such as feces, nasal secretions, saliva, sputum, sweat, tears, urine and vomitus are NOT considered potentially infectious unless bloody
- Risk of HIV transmission:

Exposure route	Risk of HIV transmission per 10,000 exposures to an infected source
Blood transfusion	9,000 (90%)
Needle-sharing injection-drug use	70 - 80 (0.7 – 0.8%)
Receptive anal intercourse	50 – 338 (0.5 – 3.38%)
Percutaneous needle stick	30 (0.3%)
Receptive penile-vaginal intercourse	8 - 19 (0.08 – 0.19%)
Insertive anal intercourse	6 - 16 (0.06 – 0.16%)
Insertive penile-vaginal intercourse	5 - 10 (0.05 – 0.1%)
Receptive oral intercourse	1 (0.01%)
Insertive oral intercourse	0.5 (0.005%)

The risk of transmission to receptive partner increases with ejaculation and the presence of ulcers and sexually transmitted infections (STI) in the mucous membrane (oral, genital, rectal)

- Currently no antiretroviral has a Health Canada approved indication for prevention of HIV

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

- HIV PEP management usually involves 2- or 3-antiretroviral drugs (eg. Truvada<sup>®</sup> or Truvada<sup>®</sup> + raltegravir or dolutegravir or Kaletra<sup>®</sup> or boosted darunavir) at treatment doses started within 72 hours to complete 28 days
- use of zidovudine alone reduced the risk of HIV transmission by 81% in a retrospective case-control study in healthcare workers exposed to HIV
- No human prospective randomized trials to establish the optimal number of HIV medications for PEP and no data showing superiority of any regimen
- Recommendation for a 3-drug regimen is based on the proven potency in management of established HIV infection and to maximize effectiveness against potential drug resistance in source virus
- **Drug interactions compromising efficacy:**
- Strong inducers of glucuronidation or P450 enzyme system (especially isoenzyme 3A4) such as rifampin, carbamazepine, phenytoin, St. John's Wort may decrease levels of raltegravir, dolutegravir and protease inhibitors
- Polyvalent cations are known to chelate with integrase inhibitors (raltegravir, dolutegravir, elvitegravir) and require spaced administration times
- lopinavir/ritonavir and darunavir/ritonavir are known to decrease levels of other medications (eg. ethinyl estradiol and norethindrone and may compromise their effectiveness
- antiretrovirals such as rilpivirine, Stribild<sup>®</sup>, boosted-darunavir are recommended to be taken with food to maximize absorption

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

- nevirapine is NOT recommended for use in PEP (risk of hepatotoxicity)
- abacavir requires HLA-B\*5701 testing prior to use and is not practical prior to initiating for PEP
- Truvada<sup>®</sup> (emtricitabine/tenofovir) is primarily excreted renally and must be dose-adjusted in renal impairment:

Estimated Creatinine Clearance	≥ 50 mL/min	30 - 49 mL/min	<30 mL/min (including hemodialysis)
Recommended Truvada <sup>®</sup> dosing interval	every 24 hours	every 48 hours	Truvada <sup>®</sup> should not be administered

- No dosage adjustment is required for raltegravir, dolutegravir or boosted darunavir in renal impairment or in patients with mild or moderate hepatic impairment
- caution should be exercised when administering Truvada<sup>®</sup> to patients with known risk factors for renal disease and a history of renal dysfunction
- Acute exacerbations of hepatitis B have been reported in patients who are coinfectd with HIV and hepatitis B after the discontinuation of Truvada<sup>®</sup>
- Follow-up blood work is suggested at 2 weeks to monitor for toxicity (eg. ALT, SCr) and HIV testing at 6 weeks and 16 weeks
- **Drug interactions risking toxicity**
- Since emtricitabine and tenofovir are primarily eliminated by the kidneys, coadministration of Truvada<sup>®</sup> with drugs that reduce renal function or compete for active tubular secretion may increase serum concentrations tenofovir (eg. NSAIDS, acyclovir, valacyclovir, ganciclovir, valganciclovir, ritonavir)
- Protease inhibitors have the potential to increase the level of other medications, primarily through inhibition of P450 CYP3A4 system and cause toxicity

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

- primarily reasons for patients not adhering to PEP medications include intolerance, forgetting and financial barriers
- Strategies to support medication adherence include patient education, managing side effects, establishing routines, providing reminder systems/tools, reducing financial barriers to accessing medication, and addressing substance abuse and mental health needs
- Cost range from \$800 - \$1500 for a 28 day supply, depending on drug combinations used

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