A Guide to Assessing Antiretroviral Therapy in HIV Hospitalized Patients

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Development Team

Michelle Foisy, BScPharm, PharmD, ACPR, FCSHP, AAHIVP (ongoing updates)
Northern Alberta Program, Royal Alexandra Hospital, Alberta Health Services, Edmonton, Alberta (all versions)
Contact: Michelle.Foisy@albertahealthservices.ca

Elliot Pittman, BScPharm, PharmD Candidate (2014 version only)
Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, Alberta

Reviewers

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Colleen Benson, Chantal Ho, Christine Hughes- HIV Pharmacists, Northern Alberta Program, Edmonton, AB
Jeff Kapler- HIV Pharmacist, Southern Alberta Program, Calgary, AB
Susan Fryters, Margaret Gray- Infectious Diseases Pharmacists, Pharmacy Services, Edmonton Zone
Deon Druteika, Margaret Gray, Mary Gunther- Clinical Practice Leaders, Pharmacy Services, Edmonton Zone
Emily Li- PharmD Candidate, University of Alberta, Edmonton, AB
Amy Semaka- Pharmacy Student, University of Alberta, Edmonton, AB (for assistance with ARV Assessment Form)

Abbreviation Legend

A AHC: Alberta Health Care; **AISH:** Assured Income for the Severely Handicapped; **ALP:** alkaline phosphatase; **ALT:** alanine aminotransferase; **ARF:** acute renal failure; **ARV:** antiretroviral; **AST:** aspartate aminotransferase; **B BCP:** birth control pill; **BID:** twice daily; **BMD:** bone mineral density; **BPMH:** best possible medication history; **C kcal:** calorie; **CAM:** complementary and alternative medicine; **Cap:** capsule; **CBC:** complete blood count; **CCB:** calcium channel blocker; **CI:** contraindicated; **CK:** creatinine kinase; **CNS:** central nervous system; **CrCl:** creatinine clearance; **CV:** cardiovascular; **CYP:** cytochrome P450; **D DOT:** daily observed therapy; **E EC:** enteric-coated; **ESLD:** end-stage liver disease; **F FDC:** fixed-dose combination; **G GI:** gastrointestinal; **H h:** hour(s); **H_2RA:** histamine (H2) receptor antagonist; **HAV:** hepatitis A virus; **HBV:** hepatitis B virus; **HCV:** hepatitis C virus; **HD:** hemodialysis; **HLA:** Human Leukocyte Antigen; **HSR:** hypersensitivity reaction; **I ICS:** inhaled corticosteroids; **ICU:** Intensive Care Unit; **ID:** Infectious Diseases; **INR:** international normalized ratio; **INSTI:** integrase strand transfer inhibitors; **IR:** immediate-release; **K kcal:** calorie(s); **KEC:** Kaye Edmonton Clinic; **M MI:** myocardial infarction; **Min:** minute(s); **N NIHB:** Non-Insured Health Benefits; **NNRTI:** non-nucleoside reverse-transcriptase inhibitor; **NPO:** nothing by mouth; **NR:** not recommended; **NRTI:** nucleoside/tide reverse-transcriptase inhibitor; **O OIs:** opportunistic infections; **P PD:** peritoneal dialysis; **PDE5:** phosphodiesterase type 5; **P-gp:** P-glycoprotein; **PI:** protease inhibitor; **PK:** pharmacokinetic; **PPI:** proton-pump inhibitor; **PRN:** as needed, q8h: every 8 hours; **Q qHS:** every night at bedtime; **R RAH:** Royal Alexandra Hospital; **ROS:** review of systems; **S SAC:** Southern Alberta Clinic; **SAP:** Special Access Program (Health Canada); **SC:** subcutaneous; **SCr:** serum creatinine; **S/E:** side-effect; Sol: solution; **STIs:** sexually transmitted infections; **T Tab:** tablet; **TID:** three times daily; **U UGT**: uridine glucuronosyl transferase; **V VL:** viral load; **X XR:** extended-release.

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How to Reference this Guide

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Where to Find this Guide

Bugs & Drugs Website (external site)
http://www.bugsanddrugs.ca/documents/HIVARVGuide.pdf (full guide)

AHS Pharmacy Sharepoint (internal site)
Sharepoint>Clinical Practice Tools>HIV>HIV ARV Assessment Guide (full guide)
https://share.ahsnet.ca/teams/PSPP/PCP/ClinicalPractice/ahsdocs/Antiretroviral%20Assessment%20Pocket%20Card%202017.pdf (pocket card)

Publication of the Original 2014 Guide

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Background

- HIV therapy is becoming increasingly complex as there are currently 26 available antiretroviral agents from 6 drug classes.
- In order for therapy to be effective, at least 3 active drugs are normally required from at least 2 different drug classes. Additionally, a very high level of adherence to therapy is required (>95%) in order to prevent break-through viremia and drug resistance.
- Published literature demonstrates high rates of medication errors in HIV inpatients, including patients receiving no medication when therapy is indicated, incorrect medications, incomplete/missing medications, incorrect dosing, incorrect adjustments in renal and hepatic dysfunction, drug-drug interactions, drug-food interactions, and drug scheduling issues.
- This guide was developed to assist clinicians in accurately and safely assessing antiretroviral therapy in the hospital setting. An emphasis is placed on seamless care and medication reconciliation on admission, during hospitalization and at the time of discharge in order to prevent medication errors.
- The guide outlines the steps in antiretroviral assessment in HIV-positive hospitalized patients throughout the course of hospitalization. Additional appendices to support the assessment process include sections on HIV laboratory tests, drug interactions, a comparison of antiretroviral agents, handy resources and clinic contact information.
- The patient assessment process is based on a framework previously outlined in the Patient Care Process Framework Document which was developed by the Faculty of Pharmacy & Pharmaceutical Sciences, University of Alberta and Pharmacy Services, Alberta Health Services, Edmonton Zone.

Step 1: Admission Assessment

A) Create a Patient Database (see ARV Assessment Form)

Component	Comments
Medical History	• **Confirm admission diagnosis/HIV status** • **Inform HIV outpatient clinic of admission** (Contact Information) • **Refer to Antiretroviral Assessment Form** (ARV Assessment Form) • Summary of previous and current medical conditions, including HBV, HCV, OIs, STIs, psychiatric, metabolic, etc. • Pregnancy or possibility of pregnancy • Vital signs, review of systems (ROS), height, weight
Social History	• Living arrangements • Income stability/job security • Social/family support • Alcohol/addictions/recreational drug use • Drug coverage plan (include ARV coverage, coverage for other medications) (ARV Dispensing/Coverage)

Laboratory Tests	• HIV-specific labs, including most recent CD4 count and HIV viral load (HIV Laboratory Tests)
	• HAV, HBV, HCV, toxoplasmosis serology, tuberculosis status if available
	• CBC, electrolytes
	• Organ function (assess overall stability)
	  ○ Renal (SCr, CrCl for renal drug dosing adjustments)
	  ○ Hepatic (ALT, AST, ALP, bilirubin, albumin, INR)

BPMH/ Medication Reconciliation	• Allergies/intolerances ○ Clarify the reaction, drug involved, date, and required treatment • Current ARV regimen (Step 1B: Assess ARV); study drugs • Other prescription and non-prescription drugs, including inhalers, patches, topical medications, recent intra-articular injections (e.g. corticosteroids) • CAM/Herbal medications *Note: For all medications, clarify indication, drug, dose, frequency, formulation, route of administration and adherence* **Hospital Admission ARV Seamless Care Tips:** • If patient was taking ARVs PTA, was the patient adherent? Check with patient, outpatient refill history, community pharmacy, HIV program. • Check for any reasons why ARVs should be held in the hospital (non-adherence in the community, patient instability, significant drug toxicity on admission, significant illness in hospital, NPO, etc). • In NPO/critical care/severe nausea patients it might be necessary to stop all ARVs for the short-term depending on feeds and drug malabsorption issues. • Avoid use of partial ARV regimens to minimize the development of resistance (continue all drugs or stop all drugs together). If uncertain consult with HIV program. • Check if the patient is receiving therapy for HBV or HCV co-infection as these therapies should generally be continued during hospitalization.

B) Assess Antiretroviral (ARV) Therapy on Admission (see ARV Assessment Form)

Is Therapy Indicated?	
Is therapy indicated? Is there adequate ARV stock/drug coverage?	**Generally ARVs are indicated in all patients** • ARVs are indicated to reduce disease progression in all HIV-infected patients, and in particular when the CD4 count drops to the 350-500 cells/µL (0.350-0.500 cells x 10^9/L) range or lower. **Indication/Drug Supply Tips** ***Note: For patients with an indication for ARVs, but not currently on ARVs, the need for therapy and choices of therapy should be assessed by the ID physician/HIV team.*** • Unless there is a contraindication, a severe intolerance or other reason, it is important to continue ARVs that have been initiated in the outpatient setting while the patient is hospitalized. (Seamless Care Tips) • Secure inpatient ARV supply via hospital stock, patient stock or outpatient pharmacy that dispenses ARVs. • Early in the hospitalization consider whether the patient has ARV drug coverage for outpatient use to avoid gaps in therapy after discharge. (Discharge Assessment)
Is Therapy Correct?	
Is it the correct therapy?	**Verify current ARV regimen** • Potential sources: patient, Netcare, hospital Rexall sites (Edmonton), HIV outpatient program, community pharmacy. • For optimal efficacy, ARV combinations usually include 3 active drugs from at least 2 different drug classes. • In more complex cases, some patients are on 4-5 ARVs to overcome drug resistance. • There is ongoing research on 2 ARV drug combinations which are being used more commonly in stable/adherent patients. **ARV Tips** • Ritonavir and cobicistat are used as pharmacokinetic boosters and are not considered "active agents" against HIV. • In general, patients on these boosters should also be on at least 3 other active drugs. • There are many co-formulated products that contain 2 (fixed-dose combinations- FDCs) or 3 (single-tablet regimens-STRs) active drugs. • Pay special attention to generic, co-formulated products and trade names to avoid duplication of therapy. • Pay attention to drugs that have similar generic/trade names (e.g. ritonavir and Retrovir®) to avoid ordering the incorrect drug.
Are the doses correct?	**Verify normal ARV doses** (ARV Agents) • In some cases, drug dosing may differ from the product monograph. Verify with the outpatient/community pharmacy or Netcare if needed. • This may be due to drug interactions that require dosage adjustments of ARVs, off-label data supporting different dosing, dosage adjustments for organ dysfunction or dosage adjustments based on therapeutic drug monitoring.
Are doses adjusted for renal or hepatic impairment?	**Consider renal and hepatic dosage adjustments in patients with organ dysfunction** (ARV Agents; Handy Resources) ***Note: In complex cases that require ARV dosage adjustments, consultation with the ID physician/HIV team is recommended*** • When dose-adjusting ARVs, consider the stability of organ function and timeframe for anticipated recovery of function. • In cases of chronic renal or hepatic failure, decreased doses of ARVs may be indicated. • In cases of severe acute renal or hepatic failure, ARVs may need to be held until organ function normalizes. • In patients requiring dialysis, ARV dosing and scheduling may be altered. • Some FDCs should be avoided if the CrCL < 50 mL/min and need to be split up into single drug formulations. When uncertain, consult with the HIV program. • When holding or stopping ARVs, in general, it is important to stop/hold all drugs at once and to restart all drugs together to avoid the development of drug resistance. • For drugs that have a very long half-life (i.e. NNRTIs such as efavirenz) relative to other agents in a regimen (e.g. NRTIs), a staggered approach to stopping therapy may be indicated.
Is the drug formulation correct?	**Verify the drug formulation and route of administration** • Consider whether the patient is able to swallow the ARV formulation. • Consider drug absorption and alternate formulations that may be required while hospitalized (e.g. dysphagia, enteral tube feeding, surgical patients, ICU patients). (Handy Resources) **ARV Formulation Tips** • ARVs are most commonly are available in tablets or capsules which are quite large. • There are a number of pediatric formulations, including liquids and tablets with lower strengths. • There are currently very few parenteral formulations of ARVs (exceptions are zidovudine (IV) and enfuvirtide (SC)). • Specialized information on crushing tablets, opening capsules and liquid preparations should be consulted; consultation with the ID physician /HIV team is advised in complex cases. (Handy Resources)
Is Therapy Effective?	
Is therapy effective?	**Consider goals of therapy** • Reduce morbidity, mortality, and improve quality of life. • Restore and preserve immune function (measured by CD4 lymphocyte count). • Suppress plasma HIV viral load.

	• Prevent HIV transmission. **Review indications of efficacy** • Undetectable/not quantifiable or decreasing HIV viral load (e.g. < 40 copies/mL). • Normal or increasing CD4 count (>200 cells/µL, ideally in the normal range (360-1630 cells/µL)). Some patients are not able to achieve this degree of immune reconstitution. • Lack of opportunistic infections; overall well-being. **Clinical Tips:** • Monitoring efficacy: When starting therapy the HIV viral load is measured after 4-8 weeks to assess the initial response to therapy. In general, the CD4 count and viral load are monitored every 3- 6 months (and up to 12 mos in very stable patients), depending on the response to treatment and the stability of the patient. • If it has been > 3-4 months since the last HIV viral load and CD4 count, it may be recommended to repeat this blood work while hospitalized. Of note, in an acutely ill patient, the CD4 count may be lower than usual. Consult with the ID physician/HIV team prior to ordering laboratory tests as other specialized tests may be indicated (e.g. viral resistance testing (GART) or abacavir HLA testing). (HIV Laboratory Tests) • If the CD4 count is < 200 cell/µL, OI prophylaxis may be required to prevent certain infections like Pneumocystis pneumonia (PCP or PJP) (< 200), toxoplasmosis (CD4 < 100, if toxo Ab +) and Mycobacterium avium complex (MAC) (CD4 < 50). (Handy Resources- OI Guidelines)
Is Therapy Safe?	
Is the patient experiencing drug intolerance?	**Verify whether the patient is tolerating the current regimen** • Consider if the patient was admitted with a serious drug adverse event that may warrant holding ARVs (e.g. ARF, hepatitis, severe anemia, severe skin rash and pancreatitis). • Common problems include GI (nausea, anorexia, diarrhea) and metabolic toxicities (high lipids, diabetes). • Consider ancillary medication required to increase ARV tolerability (e.g. antiemetics for nausea; antidiarrheals in cases where infectious diarrhea is ruled-out). **Other Special considerations** • If a patient has HBV co-infection, it is important to avoid stopping ARVs that also treat HBV such as tenofovir, emtricitabine and lamivudine (can result in an HBV flare). • If a patient has HCV co-infection, caution is warranted as there are many drug interactions with ARVs and HCV treatment, and in certain circumstances ARVs may be deferred until HCV therapy is complete. • If a patient is pregnant, consultation with an HIV clinician is advised. (Handy Resources)
Is there a possibility for drug-drug interactions?	**Consider drug-drug interactions** • There are numerous drug interactions with ARVs; this necessitates checking for interactions with each medication. • Consider the effect of medications that inhibit or induce hepatic enzymes which may impact ARV concentrations (e.g. via CYP450 3A4/2D6 and P-gp inhibition and induction). • Consider the effect of potent enzyme inhibitors such as ritonavir and cobicistat on other drugs that are CYP 3A4 substrates. (ARV Agents; Drug Interactions; Handy Resources) • Consider important drug absorption interactions with ARVs and PPIs, H_2RAs, or multi-valent cations (chelation/complexation). (ARV Agents; Drug Interactions; Handy Resources)
Is there a possibility for drug-food interactions?	**Consider drug-food or nutritional supplement interactions** • With few exceptions, most ARVs are either better absorbed and/or better tolerated when given with food. (ARV Agents; Handy Resources) • Rilpivirine requires administration with at least 400 kcal of food for optimal absorption. • Consider drug interactions with liquid nutritional drinks (e.g. Ensure, Boost). For example, rilpivirine absorption is significantly compromised when given with a liquid nutritional drink (it should be given with solid food). (ARV Agents)
Are there any scheduling issues?	**Consider scheduling issues** • Most ARVs can be given in the morning and/or evening with food, however some patients might tolerate the medications better at a particular time of day. When possible, accommodate patient preferences. • Generally efavirenz is recommended at bedtime to avoid CNS side effects, however some patients can tolerate daytime dosing of this agent (verify with patient). • Schedule ARVs together on the same dosing schedule and avoid staggering dosing times (i.e. give once daily ARVs all together at the same time; give BID drugs together the same dosing times, etc); BID drugs should be given q 12h • Administer pharmacokinetic boosters (e.g. ritonavir, cobicistat) at the same time as the ARV they are boosting (e.g. darunavir + ritonavir should be taken together).
Can the Patient Adhere to Therapy?	
Can the patient adhere to ARVs?	**Verify whether the patient can adhere to ARVs while hospitalized** • Consider factors that may interfere with adherence (e.g. tolerability such as nausea and diarrhea, pill size/formulation, ability to swallow, ability to eat, patient is NPO, transitions between units/services, day passes or absences from ward at ARV dosing time).

Step 2: Assessment During Course of Hospitalization

- For patients on ARVs, review medication profile daily or when medication changes are made.
- Monitor for common errors that may occur when transitioning from units including drug omissions, drug dosing issues, drug interactions with concurrent therapies prescribed over the course of hospitalization, scheduling of medications with food, auto-stops on antimicrobials (including ARVs and OI treatment/prophylaxis), etc.
- Monitor laboratory tests for toxicity and efficacy if these tests are ordered during hospitalization.
- Efficacy: CD4 count and HIV viral load (every 3-6 mos and up to every 12 mos in very stable patients).
- Toxicity: CBC/diff, renal/hepatic function, GI effects. Long-term effects drug-specific (e.g. ↑ lipids, ↑ glucose, ↓ bone mineral density (BMD))

Step 3: Discharge Assessment (see ARV Assessment Form)

Assess Discharge Prescriptions

- Discharge ARVs should be ordered by an authorized ARV prescriber (e.g. an ID physician) as this is a requirement for outpatient drug coverage.
- Ensure opportunistic infection prophylaxis medications are ordered if indicated. (Handy Resources)
- Verify that all other medications are ordered as appropriate including prescription, OTC and PRN drugs.
- If still indicated, re-start medications that were held on admission or during the course of hospitalization.

ARV Dispensing/Coverage

- Patients who have an active Alberta Health Care (AHC) number receive ARVs free of charge; prescriptions must be written by an authorized ARV prescriber (e.g. an ID physician) to be covered by the AHS Specialized High Cost Drug Program.
- ARVs covered in Alberta: http://insite.albertahealthservices.ca/PharmacyServices/tms-phm-SHCDP-list.pdf
- If a patient does not have active AHC, other forms of drug coverage may include:
    - Non-Insured Health Benefits (NIHB) for treaty status patients
    http://www.hc-sc.gc.ca/fniah-spnia/nihb-ssna/provide-fournir/pharma-prod/med-list/index-eng.php
    - Interim Federal Health (IFH) for refugee status patients
    http://www.cic.gc.ca/english/refugees/outside/arriving-healthcare/practitioners.asp
    - Private insurance, and compassionate access from the pharmaceutical industry.
- In the Edmonton Zone, adults may fill their ARV prescriptions at Rexall-Royal Alexandra Hospital or Rexall-Kaye Edmonton Clinic (KEC) sites, while paediatric patients may get their prescriptions filled at the Rexall-University of Alberta/Stollery Hospital or Rexall- KEC .
- In the Calgary Zone, adults may fill their ARV prescriptions at the dispensary located within the Southern Alberta Clinic, and paediatric patients may get their prescriptions filled at the Rexall-Alberta Children's Hospital.
- Consider coverage of medications other than ARVs.

ARV Adherence

- Address potential for non-adherence in outpatient setting.
- Reinforce important adherence and food requirements.
- Assess whether special adherence aids are required:
    - Medication schedule
    - Blister pack or daily observed therapy (DOT) at community pharmacy
    - Consider giving DOT ARVs with daily opioids/methadone to increase adherence
    - Beepers, reminders, supports
    - Delivery of medications

Outpatient Follow-up

- Arrange for follow-up with local HIV program to see treating ID Physician and/or HIV team.
- Arrange for follow-up with other health care providers such as the family physician.
- Communicate any changes in drug therapy to outpatient health care providers (e.g. physicians, HIV team, outpatient/community pharmacy).

Appendix 1. HIV Laboratory Tests

Lab Parameter	Description/Indication	Target/normal range	Monitoring Frequency/Comments
Absolute CD4 Lymphocyte Count (CD4 Abs or T-Cell Count) (cells x 10^9/L) *Note:* Multiply by 1000 to get cells/µL **Available on Netcare **(Hematology)***	- Major indication of immune function - Used to determine urgency of ARV therapy and OI prophylaxis - Indicator of disease progression and survival - Indicator of therapeutic response	> 200 cells/µL - Ideally within normal range of 360-1630 cells/µL (i.e. 0.360-1.630 x 10^9/L)	- When starting or modifying ARVs - Every 3-6months in most patients (depending on the response to treatment and the stability of the patient).
Plasma HIV RNA (Viral Load) (copies/mL) **Available on Netcare **(Microbiology)***	- Indicator of response to ARVs	- Optimal: < 40 or < 20 copies/mL depending on assay used (undetectable or not quantifiable)	- When starting or modifying ARV regimen - When starting therapy the HIV viral load is measured after 4-8 weeks to assess the initial response to therapy. - The HIV viral load is measured every 3-6 months in most patients (depending on the response to treatment and the stability of the patient).
HLA-B*5701 ** Available on Netcare **(Immunology)***	- Genetic marker of HLA allele - If positive, patient is predisposed to develop a HSR to abacavir	- Positive/Negative	- One-time genetic test - HLA-B*5701 positive patients should NOT be prescribed abacavir
Genotypic Antiretroviral Resistance Testing (GART) ** Not available on Netcare (Reports available only via HIV clinic directly)*	- Viral genotype to identify ARV-resistant mutations - Can be used to investigate failure of ARVs and to guide initiation or modification of therapy	- Wild-type generally indicates no resistance, however, reports should be interpreted by a clinician with expertise in HIV as a history of all past mutations from previous reports must be considered when selecting ARVs	- Generally obtained in initial assessment or when failing therapy - Requires a viral load of at least 250-500 copies/mL to perform resistance testing - To detect mutations, the patient should ideally be currently taking ARVs (or within 4 weeks)
Viral Tropism ** Not available on Netcare (Reports available only via HIV clinic directly)*	- The tropism test is performed to characterize the virus' coreceptor usage to enter the CD4 cell - For cell entry, some types of HIV attach to the CCR5 protein while others to the CXCR4 protein - When first infected with HIV, the CCR5 coreceptor pathway is most commonly seen; over time this can change to a CXCR4 pathway - Tropism testing is necessary when considering CCR5 antagonist therapy (maraviroc)	- Reported as CCR5, CXCR4, or dual tropic (CCR5 and CXCR4 together)	- A current/recent CCR5+ tropism test is required prior to starting maraviroc - Maraviroc will not work in CXCR4 or dual tropic viruses - Consult with HIV team for ordering and interpretation of results

*Note: In the Edmonton Zone, these labs are available on Netcare. In the Calgary Zone, these labs are available via Sunrise Clinical Manger (SCM), and can also be viewed on Netcare.

Appendix 2. Drug Interactions

Red-Flag Interactions

- Significant drug interactions due to enzyme ***inhibition*** with PIs and pharmacokinetic boosters (ritonavir; cobicistat) leading to supratherapeutic concentrations and toxicity of substrate drugs include: **corticosteroids (oral, inhaled, injectable including intra-articular), inhaled fluticasone, salmeterol, statins, antipsychotics, antiarrhythmics, calcium channel blockers, ergot alkaloids, antifungals, narcotic analgesics, methadone, PDE5 inhibitors, midazolam and triazolam.**

- Significant drug interactions due to enzyme ***induction*** leading to subtherapeutic concentrations and resistance to ARVs include: **anticonvulsants (carbamazepine, phenytoin, phenobarbital), rifabutin, rifampin, St. John's Wort (*Hypericum perforatum*).**

- Significant interactions due to ***increased gastric pH*** and resulting ARV malabsorption include coadministration of **PPIs, H_2RAs, or antacids with atazanavir and rilpivirine.**

- Significant interactions due to ***cation chelation/complexation*** and resulting in ARV malabsorption include coadministration at the same time as **polyvalent cations (e.g. Ca, Al, Mg, Fe, Zn) with INSTIs (i.e. dolutegravir, elvitegravir, raltegravir). Spacing is required. (Individual ARVs for Spacing)**

General Principles (Handy Resources)

- **Ritonavir and cobicistat:** Are potent CYP3A and P-glycoprotein (P-gp) inhibitors/mild-moderate CYP2D6 inhibitors. They are used as pharmacokinetic boosting agents to increase concentrations of certain PIs and INSTIs. There are numerous drug interactions with these agents.

- **NNRTIs:** All NNRTIs are metabolized in the liver by various CYP isoenzymes. Several NNRTIs are also hepatic CYP inducers (e.g. 3A4, 2B6), which can decrease concentrations of substrate drugs. Concomitant administration of medications that induce/inhibit CYP enzymes can alter NNRTI drug concentrations.

- **PIs:** All PIs are metabolized in the liver primarily by CYP 3A4 isoenzymes and P-gp. Most PIs are also CYP 3A4 and P-gp inhibitors, which can increase concentrations of substrate drugs. Concomitant administration of medications that induce/inhibit CYP enzymes and P-gp can alter PI concentrations.

- **INSTIs:** Raltegravir and dolutegravir are eliminated by glucuronidation. Inducers of UGTA1 enzymes (e.g. rifampin, certain anticonvulsants) can reduce concentrations of these drugs. Elvitegravir is metabolized largely by CYP3A4 and is co-formulated with cobicistat to increase drug concentrations.

- **NRTIs:** In general, these drugs do not undergo hepatic transformation (exceptions are zidovudine and abacavir). Tenofovir alafendamie (TAF) is a P-gp substrate and inducers of P-gp (e.g. rifampin, certain anticonvulsants) are contraindicated due to a potential reduction in TAF concentrations; TAF should also be dose-adjusted with P-pg inhibitors (decreased dose).

- **CCR5 Antagonists:** Maraviroc is a CYP3A and P-gp substrate. Inducers and inhibitors of these pathways can affect drug concentrations.

- **Fusion Inhibitors:** No significant drug interactions with enfuvirtide.

Appendix 3. Antiretroviral Agents

Drug	Trade Name	Formulations and Strengths	Usual Adult Dose	Renal (R) and Hepatic (H) Adjustment	Food and Nutritional Considerations	Side-effects, Interactions, and Comments
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)						
abacavir (ABC)	Ziagen FDC: Trizivir, Kivexa/Epzicom (US), Triumeq	Tab: 300 mg Sol: 20 mg/mL	300 mg BID or 600 mg daily	R: No H: Yes	None	- GI intolerance - Headache - May increase risk of myocardial infarction (controversial) - Risk of hypersensitivity reaction (HSR) in individuals positive for the HLA-B5701 gene; HLA-B*5701 screen should be performed before initiation; if + test, avoid abacavir - Few drug interactions
didanosine (ddI)	Videx EC	EC Cap: 125,200,250,400 mg Sol: 10 mg/mL (SAP)	200 mg BID or 400 mg daily	R: Yes H: No	Take at least 90min before or 2h after meal (empty stomach)	- GI intolerance - Peripheral neuropathy - Mitochondrial toxicity[1] - Additive/synergistic toxicity with neurotoxins or pancreatoxins - Few drug interactions
emtricitabine (FTC)	Emtriva (US) FDC: Atripla, Complera, Stribild, Genvoya, Truvada	Cap: 200 mg (US) Sol: 10 mg/mL (US)	200 mg daily	R: Yes H: No	None (FDCs may have food requirements)	- Well-tolerated - Few drug interactions - Active against HBV - Only available in Canada in a FDC
lamivudine (3TC)	3TC/Epivir (US) (generics) FDC: Combivir, Kivexa/ Epzicom (US), Trizivir, Triumeq	Tab: 100,150,300 mg Sol: 10 mg/mL Note: 100 mg tabs also for HBV infection (Heptovir)	150 mg BID or 300 mg daily 100 mg tab for pediatrics and renal dosing	R: Yes H: No	None (FDCs may have food requirements)	- Well tolerated - Headache, insomnia - Few drug interactions - Active against HBV
stavudine (d4T)	Zerit (generics)	Cap: 15,20,30,40 mg Sol: 1 mg/mL (SAP)	≥ 60 kg: 40 mg BID < 60 kg : 30 mg BID	R: Yes H: No	None	- Peripheral neuropathy - Hyperlipidemia - Mitochondrial toxicity[1] - Additive/synergistic toxicity with neurotoxins or pancreatoxins - Few drug interactions
tenofovir disoproxil fumarate (TDF)	Viread FDC: Atripla, Complera, Stribild, Truvada	Tab: 150,200 (US); 300 mg Pwdr: 40 mg/g (US) Tab: 250mg (SAP)	300 mg daily	R: Yes H: No	None (FDCs may have food requirements)	- GI intolerance - Nephrotoxicity (ARF and proximal tubular toxicity) - Decrease in BMD - Few drug interactions - Active against HBV
tenofovir alafenamide (TAF)	Currently only available as FDC: Descovy, Genvoya, Odefsey HBV: Vemlidy (US)	See FDC	See FDC	See FDC	See FDC	- See separate FDC (Descovy, Genvoya, Odefsey) -TAF will largely replace TDF in most formulations - ↓ renal and bone toxicity with TAF vs. TDF - More drug interactions than TDF; avoid with potent P-gp inducers; dose adjust with P-gp inhibitors -TAF single tablet formulation for HBV indication (Vemlidy)
zidovudine (AZT, ZDV)	Retrovir (generics) FDC: Combivir, Trizivir	Cap: 100 mg Tab: 300 mg (US) IV: 10 mg/mL Syrup: 10 mg/mL	300 mg BID or 200 mg TID	R: Yes H: Yes	None (FDCs may have food requirements)	- GI intolerance - Headache, insomnia - Bone marrow suppression, macrocytic anemia, neutropenia - Mitochondrial toxicity[1] - Few drug interactions

FDC: Fixed Dose Combination

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)						
delaviridine (DLV)	Rescriptor	Tab: 100 mg,200 mg (US)	400 mg TID 600 mg BID	R: No H: Caution	Take with or without food	- Rash (usually self-limiting, unless high risk features[3]) - Headache, fatigue - Inhibitor of CYP 3A4, 2C9, 2C19
efavirenz (EFV)	Sustiva (generics) FDC: Atripla	Cap: 50,200 mg Tab: 600 mg Sol: 30 mg/L (SAP-discontinued Dec 2013)	600 mg daily	R: No H: Caution	Take qHS on empty stomach or with low-fat snack to minimize CNS S/E	- CNS effects such as vivid dreams, nightmares, insomnia, dizziness - Rash (usually self-limiting, unless high risk features[3]) - Hyperlipidemia - Inducer of CYP 3A4, 2B6 **- Avoid in pregnancy if possible**
etravirine (ETR)	Intelence	Tab: 25,100, 200 mg	200 mg BID 400 mg daily	R: No H: Caution	Take with food	- Nausea - Rash (usually self-limiting, unless high risk features[3]) - Inducer of CYP 3A4 (weak) - Inhibitor of CYP 2C, 2C19 (weak-moderate)
nevirapine (NVP)	Viramune/ Viramune XR (generics)	IR Tab: 200 mg XR Tab: 400 mg Syrup: 10 mg/mL (SAP)	IR: 200 mg daily x 14 days (lead-in) then 200 mg BID XR: 400 mg daily (after 14 day lead-in)	R: No H: Caution	Take with or without food	- Rash (may be more serious with hepatitis, check for high risk features[3]) - Avoid starting in men with CD4>400 and women with CD4>250 due to increased risk of hepatitis - Inducer of CYP 3A, 2B6
rilpivirine (RPV)	Edurant FDC: Complera; Odefsey (not covered in Alberta)	Tab: 25 mg	25 mg daily 50 mg daily with rifabutin	R: No H: Caution	Take with meal (400 kcal minimum) Do not take on an empty stomach or with a liquid nutritional drink	- Headache, dizziness, insomnia, vivid dreams, depression (mild-moderate) - Do not administer with PPIs (CI) - Spacing with H_2RAs and/or antacids (increased pH decreases RPV absorption) - Do not administer with a liquid nutritional drink (decreases RPV absorption) - Inducers/inhibitors of CYP 3A may affect RPV concentrations - Avoid initiation if viral load > 100,000 c/mL or CD4 < 200 cells/µL
Protease Inhibitors (PIs)						
atazanavir (ATV)	Reyataz FDC: Evotaz (not covered in Alberta)	Cap: 100 mg (US), 150, 200, 300 mg Pwdr: 50 mg/1.5 g dispersible oral powder packet (US)	400 mg daily (unboosted) or 300 mg daily with 100 mg RTV	R: No, unless on dialysis H: Yes	Take with food	- Rash (usually self-limiting, unless high risk features[3]) - Benign and reversible hyperbilirubinemia (UGT1A1) - Lower risk for metabolic S/E[2] than other PIs - Avoid/space from antacids, H_2RAs, and/or PPIs (decreased ATV absorption) - Inhibitor of CYP 3A and UGT1A1 - Ritonavir or cobicistat PK booster recommended; may use unboosted also in stable patients who cannot tolerate a PK booster
darunavir (DRV)	Prezista FDC: Prezcobix (Compassionate Access via Janssen)	Tab: 75, 150, 400, 600, 800 mg Susp: 100 mg/mL (not covered in Alberta)	DRV 600 mg + RTV 100 mg BID Or DRV 800 mg + RTV 100 mg daily (naïve subjects)	R: No H: Yes	Take with food	- GI intolerance - Headache - Rash (usually self-limiting, unless high risk features[3]) - Lower risk for metabolic S/E[2] than other PIs - Inhibitor of CYP 3A4 - Ritonavir PK booster required
fosamprenavir (fAPV)	Telzir/ Lexiva (US)	Tab: 700 mg Susp: 50 mg/mL	fAPV 1400 mg BID (unboosted) Or fAPV 700 mg + RTV 100 mg BID (bosted) Or	R: No H: Yes	Take with or without food Take suspension on an empty stomach (children can take with food)	- GI intolerance - Rash (usually self-limiting, unless high risk features[3]) - Metabolic S/E[2] - Inhibitor of CYP 3A4 - Ritonavir PK booster recommended

			fAPV 1400 mg + RTV 100-200 mg daily (boosted)			
indinavir (IDV)	Crixivan	Cap: 200,400mg 100 mg (US)	800 mg q8h (unboosted) Or IDV 800 mg + RTV 100-200 mg BID	R: No H: Yes	If given alone, take at least 1h before or 2h after a meal (empty stomach) If with ritonavir, take with or without food	- GI intolerance - Nephrolithiasis (drink 1.5 L fluid daily) - Benign and reversible indirect hyperbilirubinemia - Metabolic S/E[1] - Inhibitor of CYP 3A4 - Ritonavir PK booster recommended
lopinavir (LPV)	Kaletra (lopinavir/ ritonavir FDC)	FDC Tab: (LPV/RTV) 2 tabs (=400/100) BID or 4 tabs (=800/200) once daily Sol: 80/20 mg/mL	400/100 mg BID Or 800/200 mg daily (naïve subjects)	R: No H: Caution	Take tablets with or without food Take solution with food	- GI intolerance - Hepatitis - Metabolic S/E[2] - Inhibitor of CYP 3A4 - Ritonavir PK booster coformulation
nelfinavir (NFV)	Viracept	Tab: 250,625 mg Pwdr: 50 mg/g (US)	1250 mg BID Or 750 mg TID (unboosted)	R: No H: Caution	Take with food	- GI intolerance (secretory diarrhea responds well to fiber, calcium supplements) - Metabolic S/E[2], lipodystrophy - Inhibitor of CYP 3A4 - Only non-boostable PI - High variability in absorption
ritonavir (RTV)	See RTV in PK booster section below	See RTV in PK booster section below	See RTV in PK booster section below	See RTV in PK booster section below	See RTV in PK booster section below	See RTV in PK booster section below
saquinavir (SQV)	Invirase	Tab: 500 mg Cap: 200 mg	SQV 1000 mg + RTV 100 mg BID	R: No H: Yes	Take with or within 2 h after a meal	- GI intolerance - Metabolic S/E[2], lipoatrophy - Weak inhibitor of CYP 3A4 - Ritonavir PK booster required
tipranavir (TPV)	Aptivus	Cap: 250 mg Sol: 100 mg/mL (US)	TPV 500 mg + RTV 200 mg BID	R: No H: Yes	Take with food	- GI intolerance - Rash (usually self-limiting, unless high risk features[3]) - Metabolic S/E[2] - Liver enzyme elevation - Increased risk of intracranial hemorrhage - Inhibitor of CYP 2D6 - Inducer of CYP 3A4, 2C9 (overall inhibitor when boosted with ritonavir) - Ritonavir PK booster required
Integrase Strand Termination Inhibitors (INSTIs)						
dolutegravir (DTG)	Tivicay FDC: Triumeq	Tab: 50 mg Peds: 10, 25 mg tab and 5 mg dispersible tab (all under study)	50 mg daily (naïve subjects) Or 50 mg BID (experienced subjects or with certain CYP 450 enzyme inducers)	R: No H: Caution *See separate FDC for renal & hepatic adjustment*	Take with or without food Administer DTG **2h before or 6h** after taking medications containing polyvalent cations (eg. Al, Ca, Fe, Mg, Zn)- ↓ DTG absorption; however may be taken **with food** at the same time as Ca and Fe.	- Well tolerated - GI intolerance, headache, insomnia - CK and/or transaminase elevation - Non-pathogenic increase in SCr due to inhibition of renal tubular secretion (SCr: 10-15 µmol/L ↑) - Fewer drug interactions - Inducers/inhibitors of UGT1A1 may alter DTG concentrations
elvitegravir (EVG)	Vitekta (not covered in Alberta) FDC: Stribild (TDF/FTC/EVG/ cobi) FDC: Genvoya (TAF/FTC/EVG/ cobi)	Tab: 85,150 mg	85-150mg daily	R: No H: Caution *See separate FDC for renal & hepatic adjustment*	Take FDC with food Administer EVG **2h apart** from antacids or vitamin/mineral supplements containing polyvalent cations (eg. Al, Ca, Fe, Mg, Zn)- ↓ EVG absorption	- Well tolerated - GI intolerance, headache - CK and/or transaminase elevation - Non-pathogenic increase in SCr due to inhibition of renal tubular secretion by cobicistat (SCr: 10-15 µmol/L ↑) - Modest inducer of CYP 2C9 - Cobicistat PK booster required - Available in a FDC (Stribild, Genvoya)
raltegravir (RAL)	Isentress	Tab: 400 mg Chew Tab: 25,100	400 mg BID	R: No H: Caution	Take with or without food	- Well tolerated - GI intolerance, headache, pyrexia

		mg Pwdr: 20 mg/mL oral banana flavoured granular powder (single-use packet of 100 mg raltegravir) (available in US; SAP in Canada) - 600 mg QD tab under study	1200 mg daily (2 x 600 mg QD tabs) –under study		Concurrent or staggered administration not recommended with Al and/or Mg. May be given with antacids containing $CaCO_3$. Space from Fe, Zn by several hours (↓ RAL absorption). Note: 600 mg tabs may have different cation spacing recommendations once marketed.	- CK and/or transaminase elevation - Fewer drug interactions - Inducers/inhibitors of UGT1A1 may alter RAL concentrations
Chemokine Receptor Antagonists (CCR5 Antagonists)						
maraviroc (MVC)	Celsentri / Selzentry (US)	Tab: 150,300 mg	150-600 mg BID, depending on regimen and drug interactions	R: Yes H: Caution	Take with or without food	- Well-tolerated - GI intolerance, headache, orthostatic hypotension - Hepatotoxicity - Fewer drug interactions - Inducers/inhibitors of CYP3A4/P-gp may affect MVC concentrations - Only effective if virus has R5 tropism (recent tropism screening test required; consult with HIV team regarding testing)
Fusion Inhibitors						
enfuvirtide (T20)	Fuzeon	108 mg/vial (pwdr for injection)	90 mg SC BID	R: No H: No	N/A	- Local injection site reactions, GI intolerance - Eosinophilia, increased rates of bacterial pneumonia - Only injectable (SC) ARV

Pharmacokinetic Boosters						
ritonavir (RTV)	Norvir FDC: Kaletra	Tab: 100 mg Cap: 100 mg Sol: 80 mg/mL	100-200 mg daily/BID as PK booster	R: No H: Caution	Take with food (better tolerated)	- GI intolerance - Hepatitis - Metabolic S/E[2] - Many drug interactions - Inhibitor of CYP 3A4, P-gp > 2D6 - Inducer of CYP 1A2, 2B6, 2C9, 2C19, UGT (clinically significant) - Not used for ARV properties; used exclusively as a PK booster
cobicistat (cobi)	Tybost (not covered in Alberta) FDC: Stribild, Genvoya, Prezcobix; Evotaz (not covered in Alberta)	Tab: 150 mg *See separate FDC for formulations/ strenghts*	150 mg daily as a PK booster; studied with elvitegravir 150 mg, ATV 300 mg and DRV 800 mg daily *See separate FDC for dosing*	R: Avoid starting if CrCl < 70 mL/min (if used with agents that require renal dosing) H: No *See separate FDC for renal & hepatic adjustment*	Take with food *See separate FDC for food considerations*	- Headache, insomnia, GI intolerance - Non-pathogenic increase in SCr due to inhibition of renal tubular secretion (SCr: 10-15 µmol/L ↑) - Many drug interactions - Inhibitor of CYP 3A4, P-gp > 2D6 - No ARV activity; used exclusively as a PK booster

Note: Drug names, strengths and formulations in red font available in the US (not in Canada).
1. Mitochondrial toxicity can lead to myopathy, lipoatrophy, peripheral neuropathy, pancreatitis, and lactic acidosis
2. Metabolic S/E include hyperglycemia/insulin resistance, and hyperlipidemia
3. High risk features of rash include desquamation or mucous membrane involvement (including eyes, mouth), fever, systemic symptoms, hepatic abnormalities

Appendix 4. Fixed-Dose Combination Antiretroviral Products

Brand Name	Composition	Usual Adult Dose	Renal (R) and Hepatic (H) Adjustments	Administration and Comments*
Quad Drug Combinations				
Stribild	Tenofovir disoproxil fumarate (TDF) 300 mg Emtricitabine 200 mg Elvitegravir (EVG) 150 mg Cobicistat 150 mg	1 tab daily	R: Avoid starting if CrCl < 70 mL/min Discontinue if CrCl < 50 mL/min H: CI in severe hepatic impairment	- Take with food (for optimal absorption) - Administer Stribild 2h apart from antacids or vitamin/mineral supplements containing polyvalent cations (eg. Al, Ca, Fe, Mg, Zn) (↓ EVG absorption) - Increased renal and bone toxicity with TDF vs. TAF
Genvoya (Compassionate Access by Gilead)	Tenofovir alafenamide (TAF) 10 mg Emtricitabine 200 mg Elvitegravir (EVG) 150 mg Cobicistat 150 mg	1 tab daily	R: Avoid if CrCL < 30 mL/min H: Not recommended in severe hepatic impairment	- Take with food (for optimal absorption) - Administer Genvoya 2h apart from antacids or vitamin/mineral supplements containing polyvalent cations (eg. Al, Ca, Fe, Mg, Zn) (↓ EVG absorption) - ↓ renal and bone toxicity with TAF vs. TDF
Triple Drug Combinations				
Atripla	Tenofovir disoproxil fumarate (TDF) 300 mg Emtricitabine 200 mg Efavirenz 600 mg	1 tab daily (hs)	R: Avoid if CrCl < 50 mL/min H: Avoid in mod-severe hepatic impairment	- Take qHS on empty stomach or with low-fat snack (to minimize CNS S/E of efavirenz) - See Truvada and efavirenz comments
Complera	Tenofovir disoproxil fumarate (TDF) 300 mg Emtricitabine 200 mg Rilpivirine (RPV) 25 mg	1 tab daily	R: Avoid if CrCl < 50 mL/min H: Avoid in severe hepatic impairment	- Take with meal (400 kcal minimum for optimal absorption) - Do not administer with PPIs (CI) - Avoid dosing with H_2RAs or antacids (decreased RPV absorption)-spacing required - Do not administer with a liquid nutritional drink (decreased RPV absorption) - Avoid initiation if viral load > 100,000 c/mL or CD4 < 200 cells/µL - Increased renal and bone toxicity with TDF vs. TAF - Active against HBV
Odefsey (Not covered in Alberta; Gilead compassionate program in future)	Tenofovir alafenamide (TAF) 25 mg Emtricitabine 200 mg Rilpivirine (RPV) 25 mg	1 tab daily	R: Avoid if CrCl < 30 mL/min H: Not studied in severe hepatic impairment	- Take with meal (400 kcal minimum for optimal absorption) - Do not administer with PPIs (CI) - Avoid dosing with H_2RAs or antacids (decreased RPV absorption)-spacing required - Do not administer with a liquid nutritional drink (decreased RPV absorption) - Avoid initiation if viral load > 100,000 c/mL or CD4 < 200 cells/µL - ↓ renal and bone toxicity with TAF vs. TDF - More drug interactions than TDF; avoid with potent P-gp inducers; dose adjust with P-gp inhibitors - Active against HBV
Trizivir	Zidovudine 300 mg Lamivudine 150 mg Abacavir 300 mg	1 tab BID	R: Avoid if CrCl < 50 mL/min H: CI in hepatic impairment	- Take with food (to minimize GI S/E) - Risk of hypersensitivity reaction (HSR) in individuals positive for the HLA-B5701 gene (ABC); HLA-B*5701 screen should be performed before initiation; if + test, avoid abacavir - May increase risk of myocardial infarction (controversial) (due to abacavir) - Should be combined with other ARVs; do not use alone to treat HIV (↑ failure rates)
Triumeq	Abacavir (ABC) 600 mg Lamivudine 300 mg Dolutegravir (DTG) 50 mg	1 tab daily Note: Additional 50 mg of dolutegravir should be given 12 hours after Triumeq if co-administered with certain CYP 450 enzyme inducers	R: Avoid if CrCl < 50 mL/min H: CI in moderate-severe hepatic impairment	- Take with or without food - May increase risk of myocardial infarction (controversial) (due to abacavir) - Risk of hypersensitivity reaction (HSR) in individuals positive for the HLA-B5701 gene (ABC); HLA-B*5701 screen should be performed before initiation; if + test, avoid abacavir - Administer DTG **2h before or 6h** after taking medications containing polyvalent cations (eg. Al, Ca, Fe, Mg, Zn)- ↓ DTG absorption; however may be taken **with food** at the same time as Ca and Fe.

Double Drug Combinations				
Combivir (generics)	Zidovudine 300 mg Lamivudine 150 mg	1 tab BID	R: Avoid if CrCl < 50 mL/min H: Caution	- Take with food (to minimize GI S/E)
Descovy (Compassionate Access by Gilead)	Tenofovir alafenamide (TAF) 10 and 25 mg strengths Emtricitabine 200 mg	10/200 mg tab with ritonavir or cobicistat-boosted regimens 25/200 mg tab with other unboosted ARVs	R: Avoid if CrCl < 30 mL/min H: Caution; not recommended in severe hepatic impairment	- Take with or without food - ↓ renal and bone toxicity with TAF vs. TDF - More drug interactions than TDF; avoid with potent P-gp inducers; dose adjust with P-gp inhibitors - Active against HBV
Evotaz (not covered in Alberta; no compassionate access)	Atazanavir 300 mg Cobicistat 150 mg	1 tab daily	R: Avoid if CrCl < 70 mL/min and also on TDF; avoid ESRD/hemodialysis H: Avoid in hepatic impaired	- Take with food (for optimal absorption) - See atazanavir and cobicistat comments
Kaletra	Lopinavir/Ritonavir (RTV) 100/25mg (peds), 200/50mg (adult), 80/20mg/mL (peds)	2 tabs (=400/100) BID or 4 tabs (=800/200) once daily	R: No H: Caution in ESLD	- Take with food (to minimize GI S/E) - Solution must be taken with food (for optimal absorption) - GI intolerance, diarrhea - Higher risk of metabolic S/E than other PIs - Inhibitor of CYP 3A4 and P-gp - See ritonavir comments
Kivexa/ Epzicom (US)	Abacavir (ABC) 600 mg Lamivudine 300 mg	1 tab daily	R: Avoid if CrCl < 50 mL/min H: Reduce dose in mild, CI in moderate-severe hepatic impairment	- Take with or without food - May increase risk of myocardial infarction (controversial) (due to abacavir) - Risk of hypersensitivity reaction (HSR) in individuals positive for the HLA-B5701 gene (ABC); HLA-B*5701 screen should be performed before initiation; if + test, avoid abacavir
Truvada	Tenofovir disoproxil fumarate (TDF) 300 mg Emtricitabine 200 mg	1 tab daily	R: Adjustments required if CrCl ≤ 50 mL/min. Avoid if CrCl <30mL/min or dialysis H: No	- Take with or without food - See tenofovir (TDF) and emtricitabine comments
Prezcobix	Darunavir 800 mg Cobicistat 150 mg	1 tab daily	R: Avoid starting if CrCl < 70 mL/min and also on TDF (Truvada, Viread) H: CI in severe impairment	- Take with food (for optimal absorption) - See darunavir and cobicistat comments

Appendix 5. Handy Resources

General References and Guidelines	DHHS Guidelines (USA) http://aidsinfo.nih.gov/guidelines
HIV Drug Information HIV Patient Resources	AHS Knowledge Resource Service (KRS)- HIV Page http://krs.libguides.com/c.php?g=64378&p=414814 Toronto General Hospital Site http://hivclinic.ca HIV/HCV App (Toronto General Hospital Site)- HIV and HCV http://app.hivclinic.ca University of Montreal Site- French also www.hivmedicationguide.com CATIE HIV/HCV Information Canadian Site www.catie.ca University of Liverpool Site- HIV and HCV www.hiv-druginteractions.org and www.hep-druginteractions.org DHHS Guidelines (US): https://aidsinfo.nih.gov/guidelines AIDS Education and Training Center http://aidsetc.org/resources Johns Hopkins HIV Guide http://www.hopkinsguides.com/hopkins/ub/index/Johns_Hopkins_HIV_Guide/All_Topics/A HIV Insite (UCSF) http://hivinsite.ucsf.edu/InSite?page=Treatment
HIV Drug Interactions	Toronto General Hospital Site http://hivclinic.ca/drug-information/ HIV/HCV App (Toronto General Hospital Site)- HIV and HCV http://app.hivclinic.ca University of Montreal Site (App)- French also www.hivmedicationguide.com University of Liverpool Site (App)- HIV and HCV http://www.hiv-druginteractions.org/ and www.hep-druginteractions.org DHHS Guidelines (US) (see Drug Interactions) https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-treatment-guidelines/0/ HIV Insite (UCSF) http://hivinsite.ucsf.edu/insite?page=ar-00-02
HIV Drug-Food requirements:	Toronto General Hospital Site http://hivclinic.ca/main/drugs_extra_files/Food%20impact%20on%20ARV%20PK.pdf
HIV Drug Dosing in Renal or Hepatic impairment and Dialysis	Toronto General Hospital Site app.hivclinic.ca or http://hivclinic.ca/drug-information/ DHHS guidelines (US): https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/44/arv-dosing-for-renal-or-hepatic-insufficiency HIV Insite (UCSF) http://hivinsite.ucsf.edu/InSite?page=md-rr-18 AIDS Education and Training Centre (AETC) http://aidsetc.org/resource-type/pocket-guides https://aidsetc.org/resource/arv-therapy-adults-adolescents-%E2%80%93-september-2016 Dialysis Sites Gorriz JL et al. Nefrologia 2014;34:Suppl2:1-81 http://www.ncbi.nlm.nih.gov/pubmed/25467377 http://www.ayurvedavignan.in/freeEbooks/Renal-Drug-Handbook.pdf http://hivinsite.ucsf.edu/InSite?page=md-rr-18
Crushing HIV Medications ARV Liquid Formulations	Toronto General Hospital Site (see Crushing and Liquids) http://app.hivclinic.ca or http://hivclinic.ca/drug-information/additional-info/ Duggan JM et al. Am J Health-Syst Pharm 2015;72 :1555-65. http://www.ncbi.nlm.nih.gov/pubmed/26346211 Nyberg CR, et al. Topics Antiviral Med 2011;19(3):126-131. https://www.iasusa.org/sites/default/files/tam/19-3-126.pdf
Enteral ARV Administration	General Review of ARVs: Prohaska ES, et al. Am J Health Syst Pharm 2012;69(24):2140-6. http://www.ncbi.nlm.nih.gov/pubmed/?term=Prohaska+HIV Fulco PP. Am J Health Syst Pharm 2013;70(12):1016-7. http://www.ncbi.nlm.nih.gov/pubmed/23719876 Darunavir + Handy References: Kim CH, et al. CJHP 2014;67(1):39-42. http://www.ncbi.nlm.nih.gov/pubmed/24634526
Opportunistic Infection (OI) Guidelines	CDC Guidelines (USA) http://aidsinfo.nih.gov/guidelines
HIV and Pregnancy	Perinatal Protocol- Edmonton Zone http://www.bugsanddrugs.ca/documents/HIV_Protocol.pdf OR http://krs.libguides.com/content.php?pid=452758&sid=4589197 HIV-Maternity and Newborns Protocol- Calgary Zone http://krs.libguides.com/content.php?pid=452758&sid=4589197 DHHS Perinatal Guidelines http://aidsinfo.nih.gov/guidelines

Appendix 6. Contact Information

Edmonton Zone **Northern Alberta Program (NAP)**		
	Phone	**Fax**
NAP at the Royal Alexandra Hospital (RAH)	1-844-735-4811 (Toll-free) 780-735-4811 (Reception) 780-735-5340 (Nursing) 780-735-6760/5039 (Pharmacist)	780-735-4866
NAP at the Kaye Edmonton Clinic (KEC)	1-844-407-1852 (Toll-free) 780-407-1852 (General inquires) 780-407-8372 (Nursing) 780-407-8550/3643 (Pharmacist)	780-407-7827
STI Clinic	780-342-2324	780-425-2194
Rexall Outpatient Pharmacy (Royal Alexandra Hospital)	780-735-5296	780-735-5258
Rexall Outpatient Pharmacy (Kaye Edmonton Clinic)- Adult and Paediatric ARVs	780-407-4881	780-407-4886
Rexall Outpatient Pharmacy (University of Alberta/Stollery Hospital) – Paediatric ARVs	780-407-6990	780-407-1090
Hepatitis C Support Program (HSP)	780-407-1650	780-407-8659
Calgary Zone **Southern Alberta Clinic (SAC)**		
Southern Alberta Clinic (SAC) (also provides Hepatitis C support)	403-955-6399 (General inquires) 403-955-6388 (Pharmacy)	403-955-6355 403-955-6338
Rexall Outpatient Pharmacy (Alberta Children's Hospital) – Paediatric ARVs	403-955-7303	403-955-2499
General Information		
Health Canada Special Access Program	613-941-2108	613-941-3194

Appendix 7. Select References

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. July 14, 2016. Available from URL: https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-treatment-guidelines/0/

Aberg JA, Gallant JE, Ghanem KG et al. Primary care guidelines for the management of persons infected with HIV: 2013 update by the HIV Medicine Association of the Infectious Diseases Society of America. Clin Infect Dis 2014;58(1):1-10. Accessed at: http://cid.oxfordjournals.org/content/early/2013/11/12/cid.cit665.full

Tseng A, Foisy M, Hughes C et al. Role of the Pharmacist in Caring for Patients with HIV/AIDS: Clinical Practice Guidelines. CJHP 2012; 65(2):125-145. Accessed at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3329905/

Li E, Foisy MM. Antiretroviral and medication errors in hospitalized HIV-positive patients: a review of the literature. Ann Pharmacother 2014 May 8;48(8):998-1010. Abstract accessed at: http://www.ncbi.nlm.nih.gov/pubmed/24811394

Pittman ES, Li EH, Foisy MM. Addressing Medication Errors in HIV-Positive Inpatients: Development of a Clinician's Guide to Assessing Antiretroviral Therapy. Can J Hosp Pharm 2015;68(6):470-473. Appendix E15-E18. Accessed at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4690673/

Patient Care Process Framework. Faculty of Pharmacy, University of Alberta and AHS, Edmonton Zone, Aug 2013, version 1.3. Accessed at: https://www.ualberta.ca/pharmacy/preceptors/preceptors/training-and-resources/patient-care-process-module

ANTIRETROVIRAL ASSESSMENT FORM

Addressograph

Patient

ULI

DOB

Physician

HISTORY

Facility admitted to: Date of admission: (DD / MM / YY)

Reason for admission:

Medical conditions:

Social Hx: ☐ smoker ☐ substance use ☐ housing ☐ supports

Allergies/Intolerances:

Pregnant? ☐ yes ☐ no ☐ N/A Weight: Height:

LABS

CD4 Count: (DD / MM / YY) VL: (DD / MM / YY) SCr: (DD / MM / YY) CrCL: (DD / MM / YY)

ALT/AST/ALP: ☐ elevated ☐ within normal limits Bilirubin: (DD / MM / YY) HLA-B*5701: ☐ pos ☐ neg (DD / MM / YY)

Hep A: ☐ pos ☐ neg Hep B: ☐ pos ☐ neg Hep C: ☐ pos ☐ neg Other labs:

CURRENT ARV REGIMEN	GENERIC/ TRADE NAME	DOSE	SIG/ TIME TAKEN	Rx LAST FILLED
☐ 2 NRTIs + 1 PI*	1)			(DD / MM / YY) X days
*PI boosted w/RTV or COBI: ☐ yes ☐ no	2)			(DD / MM / YY) X days
☐ 2 NRTIs + 1 NNRTI	3)			(DD / MM / YY) X days
☐ 2 NRTIs + 1 INSTI*	4)			(DD / MM / YY) X days
*EVG boosted w/COBI: ☐ yes ☐ no	5)			(DD / MM / YY) X days
☐ Other				

MISSED DOSES: ____ in past week ____ in past month ARVs last taken ____ ☐ days ☐ months ☐ years ago

OTHER MEDS:

ARV PHARMACY: ☐ Rexall-KEC ☐ Rexall-RAH ☐ SAC

NON-ARV PHARMACY:

DRUG COVERAGE: ☐ AHC (for ARVs) ☐ Blue Cross ☐ AISH ☐ Income Support ☐ Health Benefits ☐ NIHB ☐ Private ☐ Other:

BLISTER-PACK/DOSETTE? ☐ yes ☐ no DAILY DISPENSE? ☐ yes ☐ no

RED-FLAG INTX: ☐ PPI ☐ H_2 blocker ☐ Anticonvulsant ☐ Benzo ☐ Antipsychotic ☐ Antiarrhythmic ☐ CCB ☐ Anticoag ☐ Methadone/Narc ☐ BCP ☐ Statin ☐ Corticosteroid/ICS ☐ Azole ☐ Macrolide ☐ PDE_5 inhibitor ☐ Cations ☐ Ergots ☐ Rifampin/Rifabutin ☐ St. John's Wort

HIV CLINIC ATTENDING: ☐ KEC ☐ RAH ☐ STI ☐ SAC LAST APPT ATTENDED: (DD / MM / YY)

HIV PHYSICIAN: FAMILY PHYSICIAN:

THERAPY ASSESSMENT

☐ **Contacted HIV team for guidance

Is therapy APPROPRIATE?	Is therapy EFFECTIVE?	Is therapy SAFE?
☐ indicated/correct drugs chosen	☐ suppressed viral load (<40 copies/mL)	☐ no adverse reactions
☐ at least 3 active drugs (most cases)	☐ normal CD4 (360-1630 cells/μL)	☐ no drug-drug interactions
☐ correct doses/intervals	☐ increasing CD4 (>200 cells/μL)	☐ no drug-food interactions
☐ adjusted for organ dysfunction	☐ lack of opportunistic infections	☐ no drug scheduling issues
☐ appropriate formulation (e.g. tabs, caps, liquid)		

Can the patient ADHERE to therapy? **ISSUES IDENTIFIED:**

Interfering factors:

- ☐ memory
- ☐ schedule
- ☐ tolerability
- ☐ dislike of meds
- ☐ anorexia
- ☐ absences from unit
- ☐ readiness to start
- ☐ pill size
- ☐ drug formulation
- ☐ NPO
- ☐ ability to swallow
- ☐ drug supply
- ☐ drug coverage
- ☐ substance abuse
- ☐ food insecurity
- ☐ unstable housing
- ☐ chaotic lifestyle
- ☐ other:

ADMISSION & DISCHARGE PLAN

- ☐ Re-ordered current ARV(s)
- ☐ Held current ARV(s)
- ☐ Changed current ARV(s)
- ☐ Ordered OI prophylactic med(s)
- ☐ Initiated other non-ARV med(s)
- ☐ Arranged for ARV prescription(s)
- ☐ Arranged for ARV drug coverage
- ☐ Addressed non-ARV drug coverage
- ☐ Arranged outpatient adherence aids: _____
- ☐ Arranged follow-up with patient's HIV team Date: _____ Time: _____
- ☐ Other:

FORM FAXED TO: ☐ HIV physician ☐ HIV team ☐ Family physician ☐ Outpatient ARV pharmacy: ☐ KEC ☐ RAH ☐ SAC

FORM COMPLETED BY: PHONE/PAGER: DATE: (DD / MM / YY)

Oct 15, 2014. Prepared by: Amy Semaka, Pharmacy Student (University of Alberta) & Michelle Foisy, PharmD, Northern Alberta Program (Edmonton, AB).
For complete ARV guide and abbreviation key, see guide at: http://www.bugsanddrugs.ca/documents/HIVARVGuide.pdf