Appendix 1. Patient assessment process for antiretrovirals (part 1 of 3). Copyright © 2014 Michelle Foisy, PharmD, Northern Alberta Program, Royal Alexandra Hospital, Edmonton, Alberta. Reproduced by permission. This material will be updated by the copyright holder from time to time; the up-to-date version is available from: www.bugsanddrugs.ca/documents/HIVARVGuide.pdf

Step 1A: Create a Patient Database

Component	Comments
Medical History	• Reason for hospitalization • 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)
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)

Laboratory Tests	• HIV-specific labs, including most recent CD4 count and HIV viral load
	• HAV, HBV, HCV, toxoplasmosis serology, tuberculosis status if available
	• CBC, electrolytes
	• Organ function (assess overall stability)
	  • Renal (SCr, eGFR, 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 • Other prescription drugs, including inhalers, patches, topical medications, recent intra-articular injections • (e.g., corticosteroids) • OTC/CAM/Herbal medications *Note: For all medications, clarify indication, drug, dose, frequency, formulation, route of administration and adherence*

Step 1B: Assess Antiretroviral (ARV) Therapy on Admission

Is Therapy Indicated?	
Is therapy indicated?	**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 × 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. • Despite an indication for treatment, ARVs may be postponed or held in certain circumstances as directed by the ID physician/HIV team (e.g., unstable patient, current addictions, intolerances, not ready to start, needing a break from therapy). • In some cases the patient may not be actually taking ARVs, despite an active outpatient prescription, therefore it is important to verify adherence with the patient. • 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.
Is Therapy Correct?	
Is it the correct therapy?	**Verify current ARV regimen** • Potential sources: patient, ARV dispensing sites, 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; however this approach is still experimental. **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 or 3 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.

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Supplementary material for Pittman ES, Li EH, Foisy MM. Addressing medication errors involving HIV-positive inpatients: development of a clinician's guide to assessing antiretroviral therapy. *Can J Hosp Pharm*. 2015;68(6):470-3.

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Are the doses correct?	**Verify normal ARV doses** • In some cases, drug dosing may differ from the product monograph. • 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** ***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. • 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). **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.
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 (<40 copies/mL). • Normal or increasing CD4 count (>200 cells/μL, ideally in the normal range (360–1630 cells/μL)). • Lack of opportunistic infections; overall well-being. ***Note: If it has been > 3–4 months since the last HIV viral load and CD4 count, it is usually 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).***
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, anemia, pancreatitis). • 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.
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). • 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).

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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. • 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).
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. • Consider the effect of potent enzyme inhibitors such as ritonavir and cobicistat on other drugs that are CYP 3A4 substrates. • Consider important drug absorption interactions with ARVs and PPIs, H2RAs, or multi-valent cations.
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: Antiretroviral 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, etc.
- Monitor laboratory tests for toxicity and efficacy if these tests are ordered during hospitalization.

Step 3: Antiretroviral Discharge Assessment

Assess Discharge Prescriptions

- Discharge ARVs should be ordered by an authorized ARV prescriber.
- Ensure opportunistic infection prophylaxis medications are ordered if indicated.
- 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

- Ensure the patient has ARV drug coverage when discharged (check on provincial policy). If required by the province, ensure the prescription is written by an authorized ARV prescriber.
- If the patient does not have provincial drug coverage, other forms of drug coverage may include: Non-Insured Health Benefits (NIHB) for treaty status patients, Interim Federal Health (IFH) for refugee status patients, private insurance, and compassionate access from the pharmaceutical industry.
- Consider coverage of medications other than ARVs.
- Review with patient where to have outpatient ARV prescriptions filled (some provinces have designated pharmacies).
- Encourage that all discharge medications be filled at the same pharmacy when possible to promote seamless care.

ARV Adherence

- Address potential for non-adherence in outpatient setting.
- Assess whether special adherence aids are required:
    - Medication schedule
    - Blister pack or daily observed therapy (DOT)
    - Beepers, reminders, supports
    - Delivery of medications
    - Reinforcement of important adherence and food requirements

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 pharmacy).

Abbreviations: ALP: alkaline phosphatase; ALT: alanine aminotransferase; ARF: acute renal failure; ARV: antiretroviral; AST: aspartate aminotransferase; BID: twice daily; BPMH: best possible medication history; CAM: complementary and alternative medicine; CBC: complete blood count; CNS: central nervous system; CrCl: creatinine clearance; CYP: cytochrome P450; DOT: daily observed therapy; eGFR: estimated glomerular filtration rate; GART = genotypic antiretroviral resistance testing; H2RA: histamine (H2) receptor antagonist; HAV: hepatitis A virus; HBV: hepatitis B virus; HCV: hepatitis C virus; HLA: Human Leukocyte Antigen; ICU: Intensive Care Unit; ID: Infectious Diseases; INR: international normalized ratio; IV: intravenous; kcal: calorie(s); NNRTI: non-nucleoside reverse-transcriptase inhibitor; NPO: nothing by mouth; NRTI: nucleoside reverse-transcriptase inhibitor; OI: opportunistic infection; OTC: over-the-counter; PPI: proton-pump inhibitor; PRN: as needed; ROS: review of systems; SC: subcutaneous; SCr: serum creatinine; STI: sexually transmitted infection.

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Appendix 2. Antiretroviral assessment form. Copyright © 2014 Michelle Foisy, PharmD, Northern Alberta Program, Royal Alexandra Hospital, Edmonton, Alberta. Reproduced by permission. This material will be updated by the copyright holder from time to time; the up-to-date version is available from: www.bugsanddrugs.ca/documents/HIVARVGuide.pdf

ANTIRETROVIRAL ASSESSMENT FORM

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:

Addressograph
Patient
ULI
DOB
Physician

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

ADMISSION & DISCHARGE PLAN

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

For complete ARV guide and abbreviation key, see: http://www.bugsanddrugs.ca/documents/HIVARVGuide.pdf

Abbreviations: ALP: alkaline phosphatase; ALT: alanine aminotransferase; Anticoag: anticoagulant; ARV: antiretroviral; AST: aspartate aminotransferase; BCP: birth control pill; Benzo: benzodiazepine; caps: capsules; CCB: calcium channel blocker; COBI: cobicistat; CrCl: creatinine clearance; DOB: date of birth; eGFR: estimated glomerular filtration rate; EVG: elvitegravir; Hep A: hepatitis A virus; Hep B: hepatitis B virus; Hep C: hepatitis C virus; HLA: Human Leukocyte Antigen; ICS = inhaled corticosteroid; INSTI: integrase strand transfer inhibitor; N/A: not applicable; Narc: narcotic; NNRTI: non-nucleoside reverse-transcriptase inhibitor; NPO: nothing by mouth; NRTI: nucleoside reverse-transcriptase inhibitor; OI: opportunistic infection; PI: protease inhibitor; PPI: proton-pump inhibitor; RTV: ritonavir; SCr: serum creatinine; tabs: tablets; ULI = unique lifetime identifier; VL: viral load.

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