

The Development of Antiretroviral Therapy Order Set for Admitted Adult HIV-Infected Patients

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Abstract

Purpose: The purpose of the project was to develop and implement an HIV order set to minimize medication prescribing errors. **Methods:** A consensus panel of 7 specialists participated in the order-set content and design for EPIC. The order set and policies were approved by the institutional pharmacy and therapeutics committee. A post-implementation consensus evaluated the HIV order set for ease of use, accuracy, and completeness. **Results:** An IT pharmacist developed the HIV order-set. To create the enhanced decision support tool and functionality in EPIC approximate builder time was 40 hours. Post-evaluation showed that an unavailable product such as ritonavir capsule is still orderable in the order-set. Many new products need to be added to the order-set due to the fast growing in the antiretroviral drug discovery area. **Conclusion:** In order to design the order-set aiming to prevent the chance of virological failure in the inpatient with HIV, it was important to strategically identify a team including both inpatient and outpatient representatives for the development and evaluation of the HIV order-set. It was critical to have an IT pharmacist specialist to support the design of building necessary and facilitate the update practice guidelines with the clinical team.

Keywords: HIV, medication errors, antiretroviral, order set, inpatient, infectious disease.

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Background

HIV management has been revolutionized over the past two decades due to increasing numbers of antiretroviral (ART) agents with improved tolerability. With advances in treatment options and increased understanding of the disease, HIV has become a chronic condition, revealing a new set of challenges for health care professionals¹. However, several studies have shown that medication errors in hospitalized HIV-infected patients continue to be problematic¹⁻⁷. It becomes more critical in this population to prevent virological failure and drug resistance. A 2014 review article evaluating 25 studies concerning medication errors in hospitalized HIV patients from 2000-2013, showed the overall incidence of medication errors ranged between 5.8% and 86% including both antiretroviral therapy(ART) and prophylaxis against opportunistic infections (OIs)¹.

The study that reported a relatively low error rate of 5.8% might be explained by the fact that staff pharmacists who have a lack of clinical expertise or training in patients with HIV we're not be able to identify potential problematic orders¹. The most common errors included antiretroviral dosing, scheduling, drug-drug interactions, and drug-food interactions¹. Similarly, in our institution found that missing doses (20%), under-dosing (13%), overdosing(13%), therapy omission(13%), and drug-drug interactions (12%) were the most prevalent ART errors at our teaching institution with 54% occurring on admission and 80% starting at prescribing of the medications⁴. This study also found that the service with a standardized admission order set did not experience any medication errors compared to the other services with no standardized order set. At Johns Hopkins Hospital in 2009, Yehia et al. found that errors occurred in 29% of admissions on the first 24 hours and in 7% on the second day (24 to 48 hours) of admissions³.

Although the hospital implemented Eclipsys® Sunrise Clinical Manager, a computerized provider order entry (CPOE) system, equipped with a number of clinical support tools which alert providers to potential drug-drug interactions and calculated creatinine clearance at the time of order entry, the system does not flag incomplete ART regimens, dosing, or scheduling errors³. The most common error was an incomplete regimen (58%), followed by incorrect doses (38%), incorrect scheduling (23%), and non-recommended drug-drug combinations (13%)³.

ACPOE or electronic medical record (EMR) system can lead to errors if a medication is non-formulary or does not appear when its name is entered into the electronic database^{3,4}. The researchers proposed that hospitals should recognize both advantages and disadvantages of CPOE, and should actively strive to fix features that facilitate medication errors such as educational and technological interventions during the first 24 hours³. Multiple factors could contribute to the high initial rate, including provider experience and adverse effect of CPOE³. Further emphasizing the importance of HIV order set design development and other strategies for customizing decision support software.

A retrospective review study at the University of Nebraska Medical Center in 2009 prior to the implementation of an EMR system found a 35% antiretroviral error rate, 31% of the errors were corrected within the first 24 hours, but 55% of errors never got corrected. The majority of the error type was drug omission⁷. The follow-up prospective study from the same group found that the incidence of errors in ART prescribing decreased significantly (RR 0.47, 95% CI: 0.34, 0.67) after implementation of an Epic EMR system (Epic Systems, Verona, WI, USA) and inclusion of an HIV pharmacist during the medication reconciliation process⁸.

All identified errors were corrected, 65% of the total errors within 24 hours and 81.4% within 48 hours with the combination of EPIC and a HIV specialist targeting patients admitted with HIV on ART. Medication errors were 9.4 times more likely to be corrected within 24 hours with HIV pharmacist intervention ($p < 0.001$). They also found that rate of omission errors was significantly lower (RR 0.36, 95% CI: 0.2, 0.64). HIV pharmacist intervention was a key to timely error correction⁸. Additionally, multiple studies have shown that clinical pharmacists and HIV specialized pharmacists are effective at decreasing ART medication errors⁹⁻¹².

Heelon et al. documented that review of ART orders by a clinical pharmacist significantly reduced the median length of time until an error was corrected from 84 hours to 15.5 hours ($p < 0.0001$)⁹. The success of medication error prevention relies on multiple system changes and ideally a multidisciplinary team of HIV specialized pharmacists and HIV providers, but this may not be feasible or to maintain at every health care center.

Optimizing the computerized software with an HIV order set could prevent the prescribing errors from occurring by standardizing and simplifying regimens at the electronic order entry. Guo et al. implemented customized order-entry sets (COES) to further prevent antiretroviral errors in addition to CPOE¹³. A total of 723 and 661 admissions were included in the pre-intervention and post-intervention periods, respectively. The antimicrobial stewardship team and HIV specialists developed customized order-entry sets (COES) to guide ARV prescribing and retrospectively reviewed their effect on error rates of initial ARV orders for inpatients before reconciliation. The COES developed by Guo et al. improved ARV prescribing habits, reduced the potential for prescribing incorrect regimens, and proved useful and cost-effective where HIV-specific medication reconciliation is unavailable.

Overall, the error rate decreased by 35% with COES (38.0% to 24.8%, $P < 0.01$)¹³. How they developed and implemented COES was not described. Many studies have suggested that implementation of standardized order sets, templates, or protocols can improve compliance with recommended process of care such as early administration of aspirin, prescription of angiotensin converting enzyme inhibitors, use of β -blockers for acute myocardial infarction¹⁴⁻²⁰, and improve patient outcomes¹⁵.

Although CPOE has been implemented in our institution with other system improvements, ART- related medication errors still occur due to lack of knowledge of providers^{4, 21-22} as well as the limited availability of HIV specialists. The development and implementation of an HIV order set in our teaching hospital, by translating research-based guidelines into daily practice, would be a potential tool to minimize medication prescribing errors, potential drug interaction, prevent unwanted adverse events, and prevent treatment failure in this patient population. The secondary goal is to increase awareness of HIV/AIDS management by all healthcare providers within our institution on the complexity of a treatment regimen, layers of dosing for renal drug interactions, and appropriate cocktails are written for the patient when admitted.

Methods

Setting Design

An 850-bed tertiary care teaching hospital located in North Central Florida provides services across northeast and north-central Florida. It is estimated that 340 adult HIV-infected patients are hospitalized per year, a doubling in census size compared to 10 years ago. The hospital implemented a CPOE (EPIC) for order entry and electronic patient charts.

Team Selection

The HIV order set team included each inpatient and outpatient services for two Infectious Disease physicians, two HIV/infectious disease pharmacists, and an informatics pharmacy specialist. In addition, two pharmacists specializing in internal medicine assisted in the review and identification of medication-related errors in regards to admission and discharge reconciliation.

Order set Design

The order set was designed based upon the April 2015 guidelines for the use of antiretroviral agents in HIV-1 infected adults and adolescents (aidsinfo.nih.gov)²³, the Florida/Caribbean AIDS Education and Training Center (AETC) pocket guides²⁴, medication package inserts, and drug monographs²⁵⁻²⁷.

A consensus panel of the above mentioned 7 specialists participated in the order set content and design for EPIC. The consensus building used the Delphi approach for the process of decision making to identify problems that were common and preventable in the hospital and community settings²⁸.

After a first draft of the order set was created, the team met every month for 3 months (3 meetings) to provide input and make revisions based on their expertise. A 7- page outline draft of the order set is in Appendix A and was used as a road map for the content and alert pathways for electronic development of the order set. The panel identified problems based on previous study insight from Snyder and colleagues and current issues with newer agents and treatment standards⁴.

The problems, how to best solve them, and what was feasible, clinically and financially, were discussed using the theory of constraints to prioritize problem resolution considering the best method for error prevention and not shifting errors due to technology. We identified and discussed our current constraints.

Order Set Development

A draft of the order set was developed for the IT pharmacist as seen in Appendix A. The goal of the group was to implement key clinical decision support (CDS) tools within the order set to guide providers on best practices when ordering ART medication. Examples of CDS included prompts to review and/or order HLA-B*5701 results prior to ordering abacavir, renal dose recommendations, and drug-drug and drug-food interaction information when applicable.

When ordering abacavir, there is a prompt to inform the provider to review HLA-B result if available or order prior to initiating drug. Dose recommendations are provided for ART medications requiring renal dose adjustment (e.g., tenofovir, emtricitabine), as seen in Appendix A. The alert will notify a provider when they order the tenofovir- or lamivudine- containing combination products for a patient with a certain threshold of creatinine clearance (usually below 50 mL/min). Then, the order set would recommend using separate ARV agents with a renal dosing guidance. Drugs that require special instructions regarding food intake have customized administration instructions.

In terms of drug-drug interactions, for example at azanavir (ATV) and proton pump inhibitors (PPIs), there is alert text indicating that PPI is contraindicated. Details on how other acid lowering agents should be used with interacting ART medications are also provided.

For example, instructions to separate certain ART medications by at least 2 hour before or 10 hours after histamine-2 receptor antagonists (H₂RA). Medical providers are warned that concomitant use of simvastatin or lovastatin with ritonavir or cobicistat containing regimens is contraindicated. The order set provides details of alternative lipid lowering agents.

The safety benefits expected to be derived through use of this order set warranted methods to encourage its use throughout the organization. A proposal to require that all ART used for the management of HIV for inpatients must be ordered through the order set was presented to the Pharmacy and Therapeutics (P&T) Committee. This request was approved and an alert was put in place that requires providers to use the order set when attempting to order individual ART medications outside of the order set.

Post Evaluation

After the HIV order set went live, the pharmacists and the prescribers both entering orders and using the order set reviewed and provided a feedback for ease of use, accuracy, and completeness of the order set.

Results

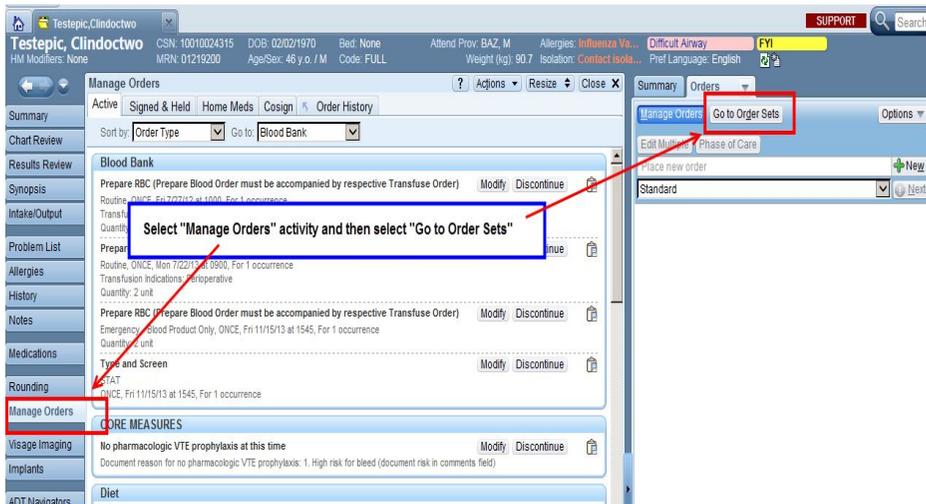
Order set Design

A detailed COES was created to improve ARV prescribing habits and computer-related errors. In addition, other system improvements have been made to prevent ARV-related medication errors (e.g., timing of liquid medication cart fill, NF inclusion, and medication reconciliation, automated pharmacist review upon verification, CPOE, and drug interaction drug software optimization).

In the academic hospital medication reconciliation for patients on ARV is completed by ID pharmacists who alert prescribing staff to the need for order correction. The COES was developed to facilitate the initial pharmacist verification process to prevent the errors from occurring and alerting to HIV pharmacist systematically.

Order Set Development

The following figures 1-6 are screens shots to illustrate how the order set appears for order entry. The HIV order set was developed by an IT pharmacist from an order set outline in appendix A. To create the level of decision support and functionality in EPIC approximate builder time was approximately 40 hours. This shows how the links are organized in EPIC. During a meeting prior to the "go live" for the order set the following were discussed, a consensus was reached to 1) add the name of the individual agents after the class of agents, 2) ensure that a minimum of 2 NNRTIs are selected, 3) a link for the AETC pocket prescribing guide, and 4) all new regimens require ID approval. From start to once the order set was implemented occurred over a year. This included 1) initial planning meetings, 2) creating the content as seen in Appendix A, 3) presenting to the PT&T committee, 4) 2 meetings to review and finalize the order set, and 5) and implementing the order set. A second PT&T approval was necessary for an additional policy change of all new ARV starts require ID consultation.



Figures 1: Show how to pull up the order set in the computerized provider order electronic system - EPIC. First step: select "Manage orders" activity and then select "Go to Order Sets".

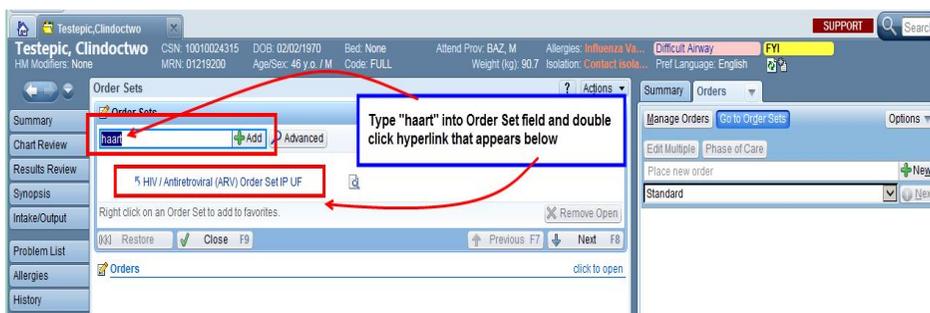


Figure 2: Show how to pull up the order set in the computerized provider order electronic system - EPIC. Second step: type "haart" into Order Set field and double click hyperlink that appears.

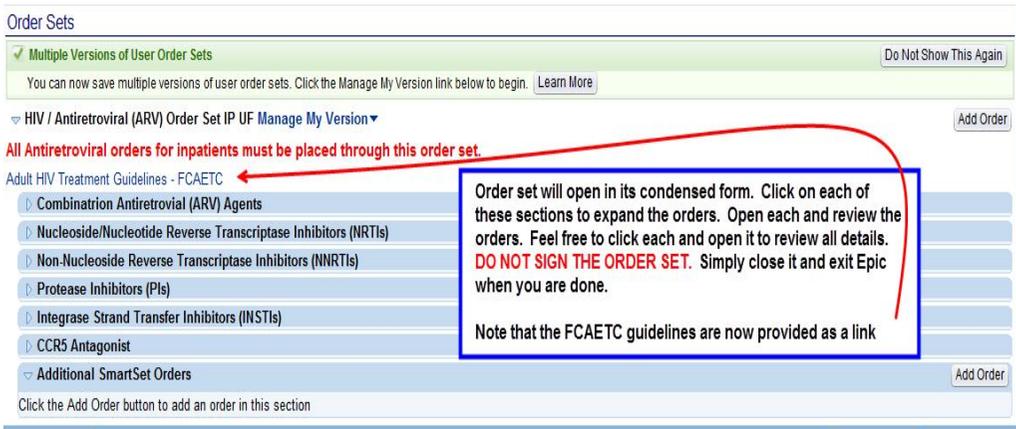


Figure 3: Order set will open in its condensed form. Click on each of the sections to expand the orders. A provider will be able to choose a combination pill or select by pharmacological classes. There will be alert texts hide under each antiretroviral when the provider select that medicine. There is also a link for the Florida/Caribbean AID Education and Training Center (FCAETC) if the provider would like to see a reference.

Implementation: Post Evaluation

The pharmacist reviewed the order set after go-live

After the order set went live in EPIC, an infectious disease (ID) specialized pharmacist reviewed the order set and provided a feedback that due to the rapid evolution in the world of HIV, there are many new ARV medications become available in the market. For instance, tenofovirafenamide, a renal-friendly tenofovir, got approved to use in two combination products e.g., Genvoya®, and Odefsey®. It is necessary to have those new ART drugs available for the patient who is admitted to the hospital.

Thus, the IT pharmacist and ID pharmacist need to continue working together in order to update the order set based on what are commonly being used in the outpatient setting as well as hospital formula availability.

The prescribers both entered orders using the HIV order set

An outpatient ID specialist provided the feedback that the order set as it was viewed from the outpatient clinic still has an orderable ritonavir capsule which is no longer used in HIV treatment. This might be due to EPIC assigns different workspace between inpatient and outpatient setting. The outpatient provider cannot access the inpatient EPIC view. However, the availability of the order set only in the inpatient setting may lead to a potential issue in a transition of care in the patient who is admitted to the hospital and discharged home. The provider also supports that the order set need to have new ART products that available to use in the outpatient setting.

Discussion

Order Set Design

Published literature suggests that errors in antiretroviral administration in the hospital setting predominately occur on admission with the majority of errors occurring at the prescribing node of the medication use process³⁻⁴. Having a clinical pathway and prioritizing specific alert messages, we hope to prevent medication errors related to dosing, selection, and timing of administration from occurring in addition to the other system improvements currently in place as shown with Guo and colleagues¹³.

Given the growing number of patients with HIV on ARV in our institution similarly to the study by Commers and colleagues, our team expects that the clinical pathway order set would be an initial tool for error prevention which could potentially happen before the consultation identifying if consultation is necessary and if necessary simplifying the process⁷. Ideally, this would in turn decrease the ID pharmacist time spent (typical: 1.5-2 hours per patient with HIV on ARV for the medication reconciliations on admission). This time is spent identifying what the patient should be taking to whether it is appropriate and the action necessary to resolve the potential or actual problem. In addition, having the right team of specialists is crucial for the order set development to look through the potential problems and improve the order set after implementation in the clinical setting.

Order Set Development

The HIV order set provides alerts to guide the focus and questions when resolving problems while conducting the medication reconciliation on admission. The incorporation of all of the complexities of ARV therapy into an electronic order set that enhances decision support is novel method to our institution when compared to the historical practice of ordering them one either from within the electronic health record or on paper. We work to improve admission medication reconciliation electronic accuracy to aid the discharge medication reconciliation. In addition, to pharmacist-led medication reconciliation and order entry via the HIV order set on admission, ongoing monitoring for medication errors by clinical pharmacists throughout the entire hospitalization is necessary. Brennan and colleagues found that, for the 14-patients prescribes incorrect regimens during hospitalization; 86% were discharged with the wrong drug regimen³¹. Incorrect antiretroviral regimens at the time of discharge may lead to ongoing errors in the community setting, thus increasing the likelihood of treatment failure.

Implementation: Post Evaluation

In our hospital as suggested in an earlier study by Snyder et al⁴, many strategies have been implemented including appropriate medication reconciliation, availability of ART medications on the hospital formulary, monitoring during transition of care points especially for discharge medication reconciliation, drug-drug and drug-drug interaction alters, and time when bulk liquids are prepared and sent to the floor. These system improvements require re-evaluation as care evolves based on the population being served. The individual conducting the medication reconciliations is in a position to report back on the nature of the errors as one method of keeping the order set up-to-date.

We proposed in addition to the HIV specialist reporting medication errors that are still occurring or as a result of order set–related confusion that after the annual AETC spring updates a meeting is held to list the necessary order set changes. Given the nature of HIV-related medication, this order set would require a minimum annual update. We experienced if appropriate prescriber order set awareness and education is not provided many will be unaware the order set is available as a resource tool. Strategically, contacting the chairs of departments to identify ideal times to provide prescriber awareness for use is recommended.

Limitation

A limitation of the order set at this time is that the order set mainly focus on ART agents which does not include OIs prophylaxis regimens. Adding OIs prophylaxis regimens into the HIV order set would be another potential quality improvement project in the future to guide differentiating from treatment and prophylaxis dosing.

Follow-up studies after the order set is live are warranted to assess the practicality in use and redesign the order set if necessary. Future studies are also needed to evaluate the impact of the order set for preventing medication errors.

Conclusion

In order to design the order set aiming to increase the chance of biological suppression in the inpatient with HIV, it was important to strategically identify a team including both inpatient and outpatient representatives for the development and implementation of the HIV order set. It was critical to have an IT pharmacist specialist to support the design of building necessary to aid in the ordering and verifying process. A Follow-up study after our interventions have been made is warranted.

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Appendix A: Antiretroviral Order Set for Adult HIV-infected Patients

Alert text for providers on the beginning of order set:

- Please verify when was the last time Pt has taken HIV medications [If off of meds, could be concerned for drug resistance]
- Verify with patients that “when was the last time you saw you HIV physician?”
- Verify with patients that “When was the last time you took you meds?”
- If poor historian, consider contacting an outpatient HIV provider.

Combo products

1. Combivir® (zidovudine 300mg/lamivudine 150mg) 1 tablet BID
 - *Should not use a combo product if pt has CrCl<50. Order separate ARV agents.*
2. Epzicom® (abacavir 600mg/ lamivudine 300mg) 1 tablet daily
 - *Must have a negative HLA*B 5701 test prior to use*

Epic layout for abacavir containing regimen

*HLA*B 5701 test done*

- Yes, (EPIC result shows up), use only if negative
- Yes, negative outside record reviewed

No

- Click to order HLA*B 5701 test, use abacavir only if negative
- Patient was already on abacavir prior to admission

- *Should not use a combo product if pt has CrCl<50. Order separate ARV agents.*

3. Trizivir® (abacavir 300mg/ zidovudine 300mg/ lamivudine 150mg)1 tablet BID

- *Must have a negative HLA *B 5701 test prior to use*

Epic layout for abacavir containing regimen (similar to layout #2)

- *Should not use a combo product if pt has CrCl<50. Order separate ARV agents.*

4. Truvada® (tenofovir 300mg/emtricitabine 200 mg) 1 tablet daily

- CrCl 30-49: 1 tablet every 48 hours
- CrCl<30: combo product should not be used. Use separate agents
- Alert text: Consider as possible cause renal dysfunction, needs renal dose adjustment if renal dysfunction present
- Alert text: Avoid concomitant nephrotoxic agents

5. Atripla® (tenofovir 300mg/efavirenz 600mg/emtricitabine 200mg) 1 tablet qHs

- *Should not be used combo product if pt has CrCl<50. Order separate ARV agents.*
- *Take on empty stomach.*

6. Complera® (tenofovir 300mg/rilpivirine 25mg/emtricitabine 200mg) 1 tablet daily with food

- *Should not be used combo product if pt has CrCl<50. Order separate ARV agents.*
- *Take with food.*
- **Contraindicated w/ PPI** (put a hard stop)
- *H2 blockers - separate at least 12 hrs before or 4 hrs after RPV*
- *Antacid – should be taken at least 2 hrs before or 4 hrs after RPV.*

- *Caution in Pt w/ QT prolongation.*
 - *Not recommended to use if HIV RNA >100,000 copies/mL or CD4 <200 cells/mm³*
7. Triumeq® (abacavir 600mg/dolutegravir 50mg/ lamivudine 300mg) 1 tablet daily
- *Must have a negative HLA *B 5701 test prior to use*

Epic layout for abacavir containing regimen(similar to layout #2)

- *Should not use a combo product if pt has CrCl<50. Order separate ARV agents.*
8. Stribild® (tenofovir 300mg/elvitegravir 150 mg/cobicistat 150mg/emtricitabine 200mg) 1 tablet daily
- *Take with food.*
 - *Contraindicated with lovastatin and simvastatin (put a hard stop). Choose atorvastatin, pravastatin, or rosuvastatin.*
 - *Do not initiate if CrCl<70. Stop if CrCl<50.*
 - *Should not use a combo product if pt has CrCl<50. Order separate ARV agents.*
 - *Multiple drug interactions with Cobicistat via CYP3A4, 2D6(Alert text)*

Separate ARV agents

1. NRTI backbone regimen

- Tenofovir, TDF (Viread®)
 - Alert text: Consider as possible cause renal dysfunction, need to be renally dose adjusted.
 - Alert text: Avoid concomitant nephrotoxic agents
 - CrCl ≥ 50 300 mg po daily
 - CrCl 30-49 300 mg q48h
 - CrCl 10-29 300 mg twice weekly (q72-96h)
 - Hemodialysis 300 mg q7d
 - CrCl<10 but not on HD *Not recommended*
- Emtricitabine, FTC (Emtriva®)

- CrCl ≥ 50 200 mg capsule po daily or 240 mg oral sol po daily
- CrCl 30-49 200mg capsule q48h or 120 mg oral sol q24h
- CrCl 15-29 200mg capsule q72h or 80 mg oral sol q24h
- CrCl <15 or HD 200mg q96h p HD or 60 mg q24h
- Abacavir, ABC (Ziagen®)
- *Must have a negative HLA*B 5701 test prior to use*

Epic layout for abacavir containing regimen(similar to layout #2)

- 600 mg po daily or 300 mg po bid
- Child-Pugh score 5-6 (Class A) 200 mg po BID (use oral sol)
- Child-Pugh score >6 (Class B, C) *Contraindicated*
- Lamivudine, 3TC (Epivir®)
 - CrCl ≥ 50 300 mg po daily or 150 mg po BID
 - CrCl 30-49 150 mg daily
 - CrCl 15-29 150 mg x1, then 100 mg q24h
 - CrCl 5-14 150mg x1, then 50 mg q24h
 - CrCl <5 or HD 50mg x1, then 25 mg q24 p HD
- Zidovudine, AZT (Retrovir®)
 - CrCl ≥ 15 300 mg po BID or 200 mg po TID
 - CrCl <15 or HD 100mg TID or 300 mg daily p HD
- Stavudine, d4T (Zerit®)
 - CrCl ≥ 50 40 mg po BID (≥ 60 kg), 30 mg po BID (<60 kg)
 - CrCl 26-50 20 mg q12h (≥ 60 kg), 15 mg q12h (<60 kg)
 - CrCl ≤ 25 , or HD 20 mg q24h (≥ 60 kg), 15 mg q24h (<60 kg) q daily (dose after HD on dialysis days)
- Didanosine, ddl
 - Take on empty stomach (30 mins before or 2 hours after a meal)
 - Videx® (10 mg/mL oral solution)
 - ≥ 60 kg: CrCl ≥ 60 200 mg po BID or 400 mg po daily
 - CrCl 30-59 200 mg po daily
 - CrCl 10-29 150 mg po daily
 - CrCl <10, or HD 100 mg po daily
 - <60 kg CrCl ≥ 60 125 mg po BID or 250 mg po daily

- CrCl 30-59 150 mg po daily
 CrCl 10-29 100 mg po daily
 CrCl <10, or HD 75 mg po daily
- Videx^{EC}® (*capsule formulation*)
- ≥60 kg: CrCl ≥60 400 mg po daily
 CrCl 30-59 200 mg po daily
 CrCl 10-29 125 mg po daily
 CrCl <10, or HD 125 mg po daily
 - <60 kg CrCl ≥60 250 mg po daily
 CrCl 30-59 125 mg po daily
 CrCl 10-29 125 mg po daily
 CrCl <10, or HD 75 mg po daily (use ddl oral sol)

2. NNRTI based

- Efavirenz, EFV (Sustiva®)
 - 600 mg po daily at or before bedtime (*take on empty stomach, otherwise, avoid high fat meal*) to avoid CNS side effects.
 - *Take on empty stomach*
- Etravirine, ETR (Intelence®)
 - 200 mg po BID or 400 mg daily
 - Child-Pugh Class C: no dosage recommendation
 - Take with food
- Rilpivirine, RPV (Edurant®)
 - 25 mg po daily
 - Child-Pugh Class C: no dosage recommendation
 - Take with food
 - **Contraindicated w/ PPI** (*put a hard stop*)
 - *H2 blockers - separate at least 12 hrs before or 4 hrs after RPV*
 - *Antacid – should be taken at least 2 hrs before or 4 hrs after RPV.*
 - *Not recommended to use if HIV RNA >100,000 copies/mL or CD4 <200 cells/mm³*
- Nevirapine, NVP (Viramune®)
 - 200 mg po daily for first 14 days, then 200 mg po BID or 400 mg po daily (Viramune® XR formulation)
 - Need separate order for nevirapine and nevirapine XR

- Child-Pugh Class B or C: contraindicated
- Contraindicated in females with CD4 >250, and males CD4 >400
- Delavirdine, DLV (Rescriptor®) *Rarely used*
- 400 mg po TID
- Take with food

3. PI based – Contraindicated with lovastatin and simvastatin (*put a hard stop*); choose pravastatin (preferred agent), atorvastatin, rosuvastatin; use lowest dose necessary

- Lopinavir/ritonavir, LPV/RTV (Kaletra®)
 - 400mg/100mg PO BID or 800mg/200mg PO daily
 - Must give 400mg/100mg PO BID in pregnancy, dose increase to 600mg/150mg BID in 2nd and 3rd trimesters
- Atazanavir, ATV (Reyataz®)
 - 400 mg PO Daily (naïve pt)with food
 - 400 mg + Norvir® 100 mg daily (in 2nd& 3rd trimester pregnancy) with food
 - 300mg + Norvir® 100 mg daily (boosted in naïve and experienced pt or w/**tenofovir**) with food
 - *Take with food*
 - **Contraindicated w/ PPI**
 - If patient is on PPI drip, contact an outpatient HIV provider for an alternative agent.
 - At least 2 hours before or 10 hours after H2RA
 - At least 2 hours before or 1 hour after Antacid
- Darunavir, DRV (Prezista®) ***Unboosted DRV is NOT recommended***
 - DRV 800 mg + RTV 100 mg once daily with food if patients do not have DRV mutations [V11I, V32I, L33F, I47V, I50V, I54L, I54M, T74P, L76V, I84V, L89V]
 - DRV 600 mg + RTV 100 mg BID with food
 - Severe hepatic impairment: not recommended
 - Take with food
 - *Caution with sulfa allergy*
- Saquinavir, SQV (Invirase®) ***Unboosted SQV is NOT recommended***
 - 1000mg + **Norvir®** 100mg PO BID within 2 hours of a meal
 - Child-Pugh Class C: contraindicated with coadministration with RTV
 - Take with food
- Fosamprenavir, FPV (Lexiva®)

- ARV-naïve
 - FPV 1400 mg BID or
 - FPV 1400 mg + RTV 100-200 mg once daily
 - FPV 700 mg + RTV 100 mg BID
- PI-experienced pt (*Once-daily dosing **NOT** recommended*)
 - FPV 700 mg + RTV 100 mg BID
- With Efavirenz (EFV)
 - FPV 700 mg + RTV 100 mg BID
 - FPV 1400 mg + RTV 300 mg once daily
- Childs Pugh Score-**Naïve pt ONLY**
 - 5-9700 mg BID
 - 10-15350 mg BID
- Childs Pugh Score-**Naïve or experienced pt**
 - 5-6700 mg BID + RTV 100mg daily
 - 7-9450mg BID + RTV 100mg daily
 - 10-15300mg BID + RTV 100mg daily
- Nelfinavir, NFV (Viracept®)
 - 1250 mg BID or 750 mg TID
 - Take w/ food
 - *Do not use in mod-severe hepatic impairment*
- Indinavir, IDV (Crixivan®) *Rarely used*
 - 800 mg q8h (*take 1 hour before or 2 hours after meals; may take w/ skim milk or low-fat milk*)>>
Please make this regimen orderable
 - IDV 800 mg + RTV 100-200 mg BID (*take w/o regard to meals*)
- Tipranavir, TPV (Aptivus®) **Unboosted TPV is NOT recommended**
 - TPV 500 mg + RTV 200 mg BID
 - With RTV tablet; take with meals. With RTV capsule or solution; take without regard to meals
 - Child-Pugh Class B or C: Contraindicated
 - Contraindicated with simvastatin, lovastatin, and atorvastatin. Choose rosuvastatin

4. INSTI based

- Dolutegravir, DTG (Tivicay®)
 - 50 mg once daily
 - 50 mg BID (when coadministered w/ EFV, FPV/r, TPV/r, or rifampin; certain INSTI mutations; clinically suspected INSTI resistance)
 - Polyvalent cations (Mg, Al, Ca) may decrease levels separate by 2 hours
 - Child-Pugh Class C: Contraindicated

- Raltegravir, RAL (Isentress®)
 - 400 mg BID
 - Severe hepatic impairment: Not recommended
- Elvitegravir, EVG (Vitekta®)

Dosage of VITEKTA	Dosage of Concomitant Protease Inhibitor	Dosage of Concomitant Ritonavir
85 mg orally once daily	atazanavir 300 mg orally once daily	100 mg orally once daily
	lopinavir 400 mg orally twice daily	100 mg orally twice daily
150 mg orally once daily	darunavir 600 mg orally twice daily	100 mg orally twice daily
	fosamprenavir 700 mg orally twice daily	100 mg orally twice daily
	tipranavir 500 mg orally twice daily	200 mg orally twice daily

5. Fusion inhibitor

- Enfuvirtide, T-20 (Fuzeon®)
 - 90 mg sc BID

6. CCR5 Antagonist

- Maraviroc, MVC (Selzentry®)
 - 150 mg BID when given w/ strong CYP3A inhibitors (with or without CYP3A inducers) including PIs (except TPV/r)
 - 300 mg BID when given with NRTIs, T20, TPV/r, NVP, RAL, and weak CYP3A inhibitors or inducers
 - 600 mg BID when given with CYP3A inducers including EFV, ERT, etc. (w/o a CYP3A inhibitor)
 - *Not a first-line drug. If the patient is not already on Maraviroc prior to admission, consider consulting an ID specialist or outpatient HIV provider.*
 - *Perform tropism assay prior to use (phenotypic tropism assay is preferred over genotypic)*
 - *Do not use in pt with dual/mixed tropic or CXCR4-tropic virus*

Epic layout for maraviroc containing regimen

Tropism assay

- Yes (test result show up), only use if CXCR5 positive.
- Yes, outside record reviewed, virus CCR5 tropic

Do not use in pt with dual/mixed tropic or CXCR4-tropic virus

- No
- Click to order Tropism assay
- Patient was already on maraviroc prior to admission

7. Pharmacokinetic enhancers

- a. Cobicistat (Tybost®)
 - i. Cobicistat 150 mg daily + atazanavir 300 mg daily
 - ii. Cobicistat 150 mg daily + darunavir 800 mg daily
 - iii. Multiple drug interactions via CYP3A4, 2D6 (*Alert text*)
 - iv. Should be taken with food
- b. Ritonavir (Norvir®)
 - i. Only used as a booster for other PIs
 - ii. 100-200 mg/day with a protease inhibitor. Use only at low dose with other PIs
 - iii. Multiple potential drug-drug interactions via CYP3A4.