Revised Policies and Guidelines on the Use of Antiretroviral Therapy (ART) among People living with Human immunodeficiency virus (HIV) and HIV-exposed infants

Sustainable Developmental Goals (SDGs)

- Expansion of access to treatment
- Ending the AIDS epidemic as a public health threat by 2030
- 90-90-90 targets
  - 90% of the people living with HIV know their status
  - 90% of the people who know their HIV status are receiving anti-retroviral therapy (ART)
  - 90% of the people receiving ART are virologically suppressed

Strategic Approaches to Control HIV

- TEST EARLY
- TREAT EARLY
- TREAT ALL

- Remove limitations on eligibility for ART among Filipinos living with HIV

ADMINISTRATIVE ORDER
No. 2017- _____

Revised Policies and Guidelines on the Use of

Antiretroviral Therapy (ART) among People living with Human

immunodeficiency virus (HIV) and HIV-exposed infants

- To ensure SAFE and EFFECTIVE USE of ART in a scale up program.
- It is a local adaption of the 2016 WHO recommendations on the use of antiretroviral drugs for treating and preventing HIV infection.

General Guidelines in Treatment

1. ART shall be initiated in all persons with confirmed positive HIV test result **regardless of clinical and immunologic status.**

General Guidelines in Treatment

2. The timing of ART initiation in the presence of certain opportunistic infections shall be delayed to prevent adverse effects of Immune reconstitution inflammatory syndrome (IRIS)

- Tuberculosis – ART to be started 2 weeks after starting TB meds
- Cryptococcal meningitis – ART to be started 5-6 weeks after starting anti-fungal medications
- CMV retinitis – ART to be started after at least 14-21 days of ganciclovir/valganciclovir

General Guidelines in Treatment

3. Early identification of TB among PLHIV shall be done through careful assessment of signs and symptoms (fever, cough, night sweats, weight loss) and diagnosis using Gene Xpert for MTB/RIF

- Prompt initiation of TB treatment is essential to improve survival of patients.
- TB diagnosis and management shall be based on the latest National TB Control Program Policies and Guidelines.

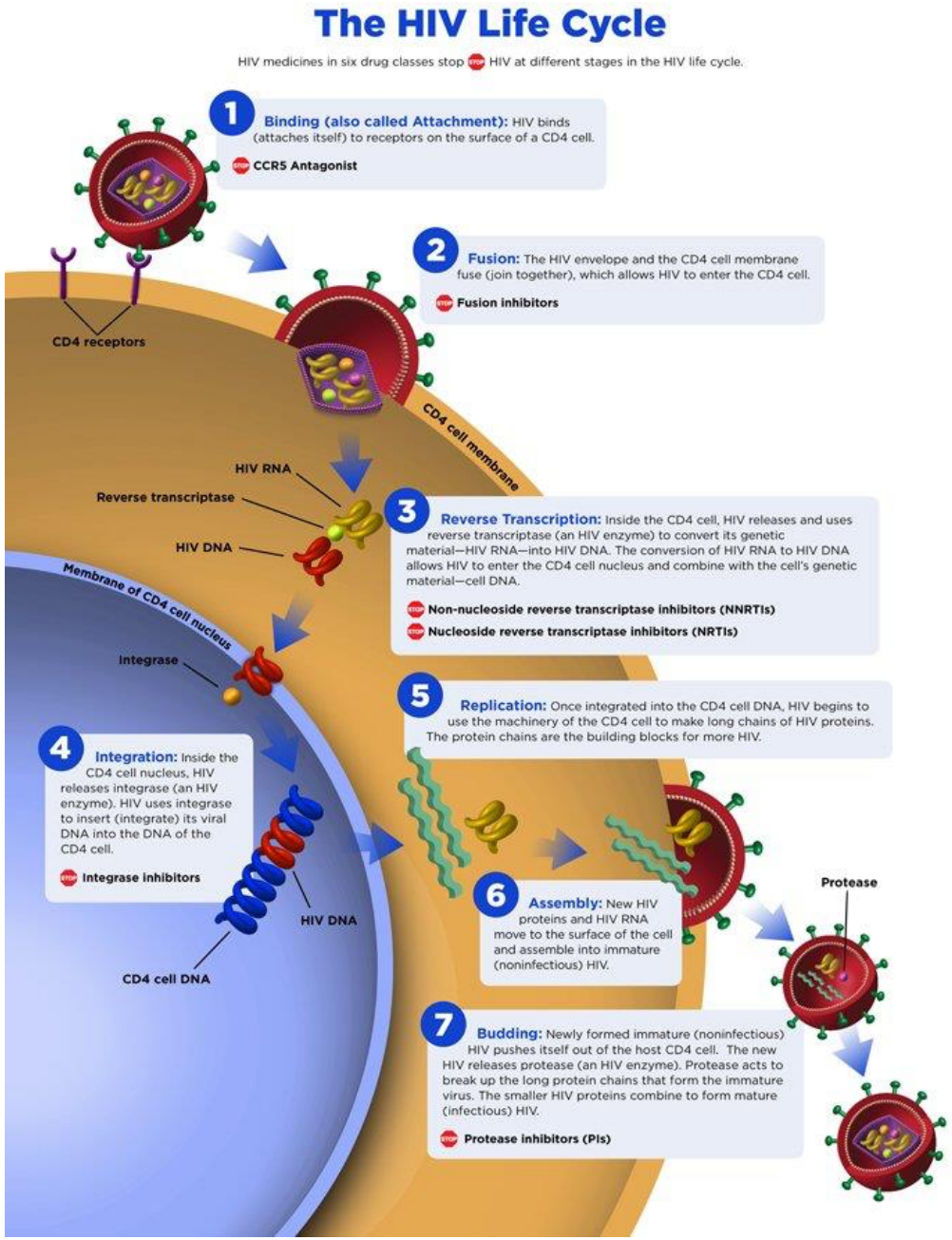
General Guidelines in Treatment

4. Adherence shall be assessed and reinforced every follow-up visit to prevent drug resistance and treatment failure.

5. Patients already stable on their current ART regimen shall be maintained on said regimen and monitored accordingly.

General Guidelines in Treatment

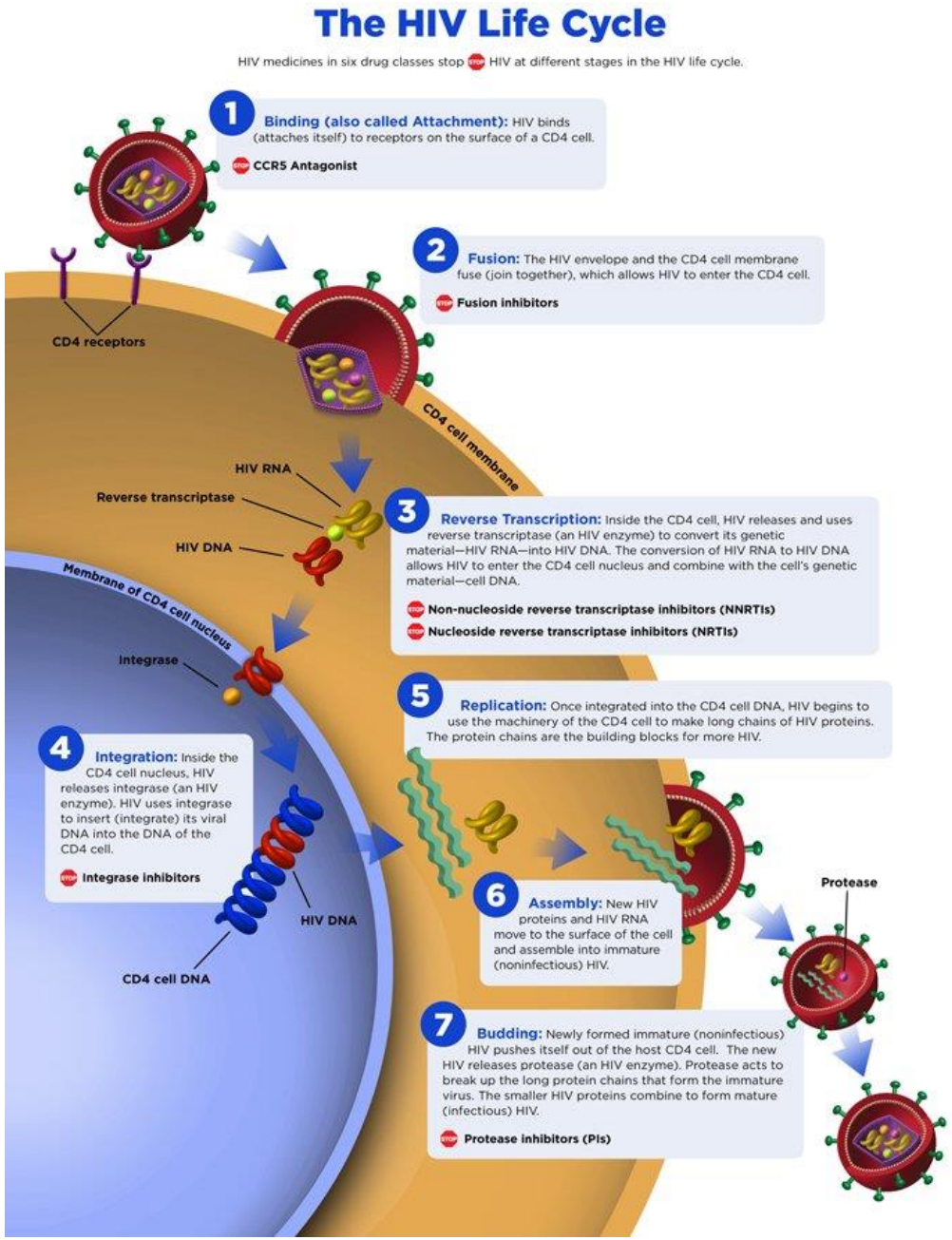
6. All HIV-exposed infants shall be given ARV prophylaxis at birth or when HIV exposure is recognized postpartum.



THE HIV LIFE CYCLE

1. Binding
2. Fusion
3. Reverse Transcription
4. Integration
5. Replication
6. Assembly
7. Budding

Source: aidsinfo.nih.gov



Six classes of HIV medicines stop HIV replication in the different HIV life cycle

1. NRTIs
2. NNRTIs
3. PIs
4. INSTIs
5. Fusion inhibitors
6. Coreceptor antagonists

Source: aidsinfo.nih.gov

Antiretroviral Drugs in the 2017 DOH ART Guidelines

1. NRTI
    a) Lamivudine (3TC)
    b) Zidovudine (AZT)
    c) Tenofovir (TDF)
    d) Abacavir (ABC)
2. NNRTI
    a) Efavirenz (EFV
    b) Nevirapine (NVP)
    c) Rilpivirine

3. Protease Inhibitor
    a) Lopinavir/ritonavir (LPV/r)
    b) Darunavir (DRV)
    c) Ritonavir (RTV)

Recommended ARV Regimen Per Age Group

1. Adults and Adolescents (≥10 years of age)
2. Children (3 – less than 10 years old)
3. Infants and children less than 3 years old

Recommended Regimen for Adults and Adolescents (≥10 years of age)

First line Regimen: 2 NRTI + 1 NNRTI

Preferred first line NRTI: **Tenofovir (TDF) + Lamivudine (3TC)**
Alternative first line NRTI: **Abacavir (ABC) + 3TC**

Patients with estimated Creatinine clearance of < 60 ml/min **ABC** is preferred over **TDF.**

First line NNRTI: Efavirenz (EFV)

For patients where EFV is contraindicated, **Rilpivirine** is an alternative NNRTI.

Alternative NNRTI

Patients to be started on **Rilpivirine** should be:

- Asymptomatic
- 12 years old and above
- CD4 cell count of greater than 350 cells/mm3
- Not pregnant
- Not on Rifampicin-containing regimen
- Not on antacids
- Not on Histamine 2 blockers
- Not on proton pump inhibitors

Recommended Regimen for Adults and Adolescents (≥10 years of age)

Second line Regimen: 2 NRTI + Boosted PIs

Preferred second line: 2 NRTI + Lopinavir/ritonavir (LPV/r)

- Zidovudine (AZT) + 3TC + LPV/r if previously on TDF or ABC
- TDF or ABC + 3TC + LPV/r if previously on AZT

Alternative second line: 2 NRTI + Darunavir (DRV) + Ritonavir (RTV)

- AZT + 3TC + DRV + RTV if previously on TDF or ABC
- TDF or ABC + 3TC + DRV + RTV if previously on AZT

Recommended Regimen for Children (3 years old to less than 10 years old)

First line regimen: 2 NRTI + 1 NNRTI

Preferred first line NRTI: ABC + 3TC
Alternative first line NRTI: AZT or TDF + 3TC

- TDF is preferred over AZT for children with anemia (hemoglobin levels ≤ 10g/dL)

Preferred first line NNRTI: EFV
Alternative first line NNRTI: Nevirapine(NVP)

Recommended Regimen for Infants and children less than 3 years old

Table 1. Sequencing of ARV formulations for newborns starting treatment

	0-2 weeks →	**2 weeks – 3 months →**	**3- 36 months**
Preferred	AZT+3TC+NVP	ABC or AZT + 3TC + LPV/r	ABC or AZT + 3TC + LPV/r
Alternative	AZT+3TC+NVP		ABC or AZT + 3TC + LPV/r

- Consider substituting LPV/r with EFV at 3 years of age after viral suppression is sustained
- ABC is preferred over AZT for anemia in neonates (hematocrit level <40%)

CD4 determination

- CD4 count is not required for initiation of ART
- CD4 determination, however, can be be done to determine need for prophylaxis and management of opportunistic infections

2016 PSMID Clinical Practice Guidelines for the Prevention, Diagnosis, and Treatment of Opportunistic Infections in HIV-infected Adults and Adolescents in the Philippines.

Adherence counseling

- Success of ARV therapy largely depends on patient's adherence to treatment
- 95% adherence rate prevents development of drug resistance
- Conduct adherence counseling before and during treatment
  - Benefits of treatment
  - Management of possible side effects
  - Adherence issues

Monitoring while on ART

- Lifelong therapy
- Requires continuous monitoring
- Close and more frequent monitoring during the first six months of initiation of ART
  - Identify immediate toxicities that could affect adherence
  - Identify early treatment failure for timely change of regimen

Monitoring while on ART

1. ARV toxicity
2. Clinical response
3. Virologic response

Frequency of monitoring

- Clinical monitoring will depend on patient's response to ART:
  - **2, 4, 8, and 12 weeks after starting ART then every six months once patient has been assessed to be stable.**
- ARV drug toxicity monitoring should be done at every visit.
- Clinical response monitoring with **viral load determination** should be done to detect treatment failure.

Monitoring ARV Toxicity

Minimum laboratory tests for patients on ART

REGIMEN CONTAINS	TESTS	TIMING
TDF	Serum Creatinine	within 6 months of initiation then every 12 months or as needed
EFV	Lipid profile (triglyceride, total cholesterol and LDL)	within 6 months of initiation then every 12 months or as needed
AZT	Complete blood count	2, 4, 8, 12 and 24 weeks after initiation then every 6 months or as needed
PI	Lipid profile (triglyceride, total cholesterol and LDL) and fasting blood sugar	within 6 months of initiation then every 12 months or as needed

Monitoring Response to Treatment

POSITIVE TREATMENT RESPONSE

- Clinically stable patient
- No recurrence of opportunistic infections
- Improvement of weight and well-being
- Stable immune status based on clinical assessment and evaluation
- Maximal viral suppression
- Improved quality of life

HIV Treatment failure

Adults and adolescents:

New or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4) after 6 months of effective treatment.

Children:

New or recurrent clinical event indicating advanced or severe immunodeficiency (WHO clinical stage 3 and 4 with the exception of TB) after 6 months of effective treatment.

Clinical failure vs. IRIS

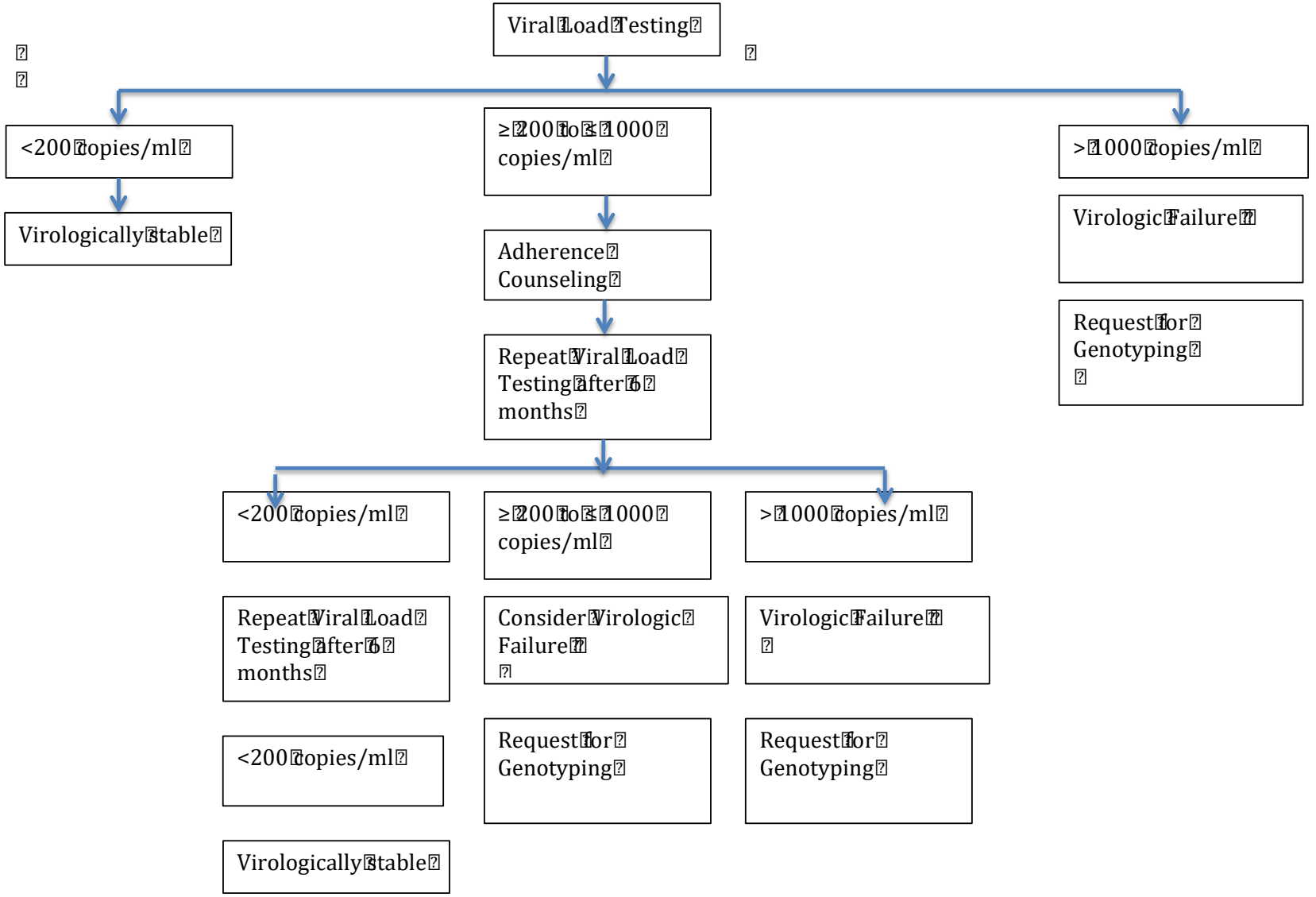
Immune Reconstitution Inflammatory Syndrome (IRIS)

- Exacerbation of previously coexisting subclinical infections (e.g. TB) may occur, resulting in an apparent worsening of disease after initiating ART
- Switching of ART is inappropriate in patients with IRIS

Monitoring Virologic Response

- HIV Viral load determination shall be done 6 months after initiating ART to detect early virologic failure
- For stable patients, repeat HIV viral load determination at 6 months and every 12 months thereafter

Interpretation of Viral Load Test Results



Virologic Failure

- Plasma viral load above 1000 copies/mL at any time beyond 6 months

Monitoring Treatment Failure

- Regularly assess patients for treatment failure
- Determine reasons for treatment failure
- Institute appropriate management immediately

- Ex. If poor compliance is the cause of treatment failure:
  - Intensify counseling for adherence
  - Continue current regimen
  - Viral load test must be done 4-8 weeks after to reassess response to treatment

Management of suspected Treatment Failure

- Patient must be on ART continuously for 4-8 weeks before doing viral load assay
- Viral load assay must be done before any change or shift on ART regimen
- Blood specimen from the patient must be sent for drug resistance testing before shifting to 2nd line regimen
- Patients with virologic failure shall be managed in close coordination with an Infectious disease specialist

Conditions Requiring Change of ART Regimen

1. Drug toxicity and side effects
2. Drug Interactions
3. Treatment failure

Drug toxicity and side effects

- Delaying substitutions or switches in drugs when there are signs of adverse drug effects may cause harm and may affect adherence leading to drug resistance and treatment failure.

- Antiretroviral drugs are substituted with drugs belonging to the same ARV class

Examples of drug toxicity requiring shift in ART regimen

1. **Increase in serum creatinine while on TDF**
   - **SHIFT TDF to ABC** when estimated Creatinine clearance is less than 60 mL/min.
2. **Psychosis or other severe adverse event while on ART**
   - **Early adverse event** (< 3 months after initiating ART) - REFER to Infectious Disease specialist for further management
   - **Late adverse event** (> 3 months after initiating ART) – consider shifting to Rilpivirine if patient fulfills the following:
     - Undetectable viral load within the past 4 weeks
     - Not on Rifampicin-containing regimen
     - Non- pregnant
     - Not taking antacids, histamine 2 blockers or proton pump inhibitors

Drug Interactions

- Be aware of **all the drugs** that the patient is taking when initiating ART and during treatment maintenance including:
  - alternative medicines
  - herbal remedies
  - dietary supplements
- Annex 4: Key drug interactions and suggested management

Drug Interactions

- Patients on both ART and TB treatment with adverse reactions to EFV should be referred to the Infectious Disease specialist for further management.

Treatment Failure

- Patients with virologic failure shall be managed in close coordination with an Infectious Disease specialist.
- Blood specimen must be sent for drug resistance testing before shifting to 2nd line regimen.

ARV Prophylaxis for infants born to infected mothers

- Infants born to HIV-infected mothers shall be given ARV prophylaxis at birth or when HIV exposure is recognized postpartum.

Table 2. Infant ARV Prophylaxis for different Clinical Scenarios

Scenario	Infant ARV prophylaxis	Duration
Infants of mothers who are receiving ART for at least 4 weeks and are breastfeeding	daily NVP	6 weeks
Infants of mothers who are receiving ART for at least 4 weeks and are on replacement feeding		
Infants born to mothers with HIV who are at HIGH RISK* of acquiring HIV (breastfed or formula fed)	Start treatment at birth (see Table 1)	6 weeks
Infants who are at HIGH RISK* of acquiring HIV including those first identified as exposed to HIV during the postpartum period (breastfeeding/replacement feeding)	Start treatment at birth (see Table 1)	12 weeks

ARV Prophylaxis for infants born to infected mothers

High Risk Infants

- Born to women with established HIV infection who have received less than four week of ART at the time of delivery OR
- Born to women with established HIV infection with viral load > 1000 copies/ml in the four weeks before delivery, if viral load measurement is available OR
- Born to women with incident HIV infection during pregnancy or breastfeeding OR
- Identified for the first time during postpartum period, with or without a negative HIV test prenatally

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ARV Prophylaxis for infants born to infected mothers

- The presence of HIV infection in infants and children less than 18 months old shall be established following the existing early infant diagnosis algorithm.
- Specific policies and guidelines shall be developed in 2017 on the integrated Prevention of Mother to child transmission (PMTCT) which shall serve as reference guide to all health care service delivery facility settings.

Managing HIV and TB co-infection in patients who are not yet on ART

- Anti-TB treatment shall be initiated first, followed by ART as soon as possible after the first two weeks of TB treatment.
- Monitor closely for side effects.

Managing HIV and TB co-infection in patients who are already on ART

When to shift ART regimen:

- Shifting of regimen shall be considered for patients already on ART who are diagnosed with TB because of possible drug interaction with TB medication (i.e. Rifampicin).
- If there is another physician managing TB of the patient, the HACT physician should closely coordinate with the TB-treating physician to ensure safety and effectiveness of the HIV / TB management.

Managing HIV and TB co-infection in patients who are already on ART

When to shift ART regimen:

For infants and children less than 3 years old on ART regimen containing NVP or LPV/r:

- Recommended regimen is ABC + 3TC + AZT
- Once TB therapy has been completed, this regimen shall be stopped and the initial regimen should be restarted.

Managing HIV and Hepatitis B and C co-infection

- All people infected with HIV shall be tested for Hepatitis B surface antigen (HBsAg) and antiHBsAg.
- Vaccinate if non-immune (antiHBSAg non reactive)
- Treatment of Hepatitis B and C shall be based on the latest available local treatment guidelines.

Monitoring and Evaluation

- All Primary HIV care clinic and treatment hubs shall maintain and update patient records and reports from which the following HIV indicators can be generated:

a) Linkage to care

b) ART indicators

c) Indicators for Co-morbidities

d) Prevention of mother to child (PMTCT) indicators

END