Republic of the Philippines
Department of Health
**OFFICE OF THE SECRETARY**

SEP 2 3 2014

**ADMINISTRATIVE ORDER**
No. 2014- 0031

**SUBJECT:** **Policies and Guidelines on the Use of Antiretroviral Therapy (ART) Among People Living with Human Immunodeficiency Virus (HIV) and HIV-exposed Infants**

## I. RATIONALE

The HIV epidemic in the country remains to be a threat to the health of Filipinos. Various strategies and activities still need to be implemented to control the HIV epidemic and achieve the Millennium Development Goal 6 of reversing HIV infection by 2015. Antiretroviral therapy (ART) protects people living with human immunodeficiency virus (PLHIV) from disease progression to AIDS and other non-AIDS complications and has been shown to be effective in improving overall survival of PLHIV similar to those non-infected. Because of optimal viral suppression, ART can be considered an effective strategy that contributes to prevention of HIV transmission, combined with other behavioral and bio-medical interventions. To maximize the effectiveness of ART at the population level, all PLHIV in need of treatment should receive affordable and effective treatment.

This guideline is developed to ensure safe and effective use of ART for PLHIV. It is a local adaption of the WHO Consolidated Guidelines on the use of antiretroviral drugs for treating and preventing HIV infection released in June 2013.

## II. OBJECTIVE

To provide guidelines for the use of Antiretroviral drugs (ARV) among PLHIV and infants exposed to HIV in the Philippines

## III. SCOPE AND LIMITATION

This guideline is intended for physicians from government and private health facilities managing PLHIV with established referral networks to Department of Health (DOH) - designated treatment hubs. It provides guidance on the ARV treatment for all PLHIV. It also includes ARV prophylaxis for infants born to HIV infected mothers.

## IV. DEFINITION OF TERMS

**A. Active TB disease** - refers to TB infection where the person has symptoms and clinical disease.

**B. Adherence counseling** - includes provision of information on HIV, manifestations of the disease, and benefits and side-effects of ARV; discussion on how the medications should be taken stressing on the importance of not missing any doses as well as risks associated to poor adherence, assessment of adherence to include identifying obstacles to adherence, and treatment planning to enhance adherence.

**C. Antiretroviral drug (ARV)** – drug used in the treatment and prevention of HIV infection. Different classes of antiretroviral drugs act at different stages of HIV life cycle thereby stopping or interfering with the production of the virus in the body.

**D. Antiretroviral therapy (ART)** – refers to the use of a combination of three or more ARV drugs to achieve viral suppression. This generally refers to lifelong treatment.

**E. HIV and AIDS Core Team (HACT)** – a multi-disciplinary team composed of doctors, nurses, pharmacists, social workers, and other health care providers that implements prevention, treatment and care services for HIV and AIDS in the hospital setting. Its specific functions are described in the Operating Guidelines for HIV and AIDS Core Team.

**F. HIV Counseling and Testing (HCT)** – a confidential process that enables individuals to examine their knowledge and behavior in relation to their personal risks of acquiring or transmitting HIV. Counseling helps an individual decide on whether or not to undergo HIV testing and provides support to an individual receiving his or her test result.

**G. Immune reconstitution inflammatory syndrome (IRIS)** – a spectrum of clinical signs and symptoms resulting from the restored ability of an individual's immune system to mount an inflammatory response and this is associated with immune recovery during ART. Also defined as paradoxical clinical worsening due to a subclinical and unrecognized opportunistic pathogen or previously known treated opportunistic pathogen in a setting of adequate response to ART.

**H. Opportunistic infections** – illnesses caused by various organisms, some of which usually do not cause disease in persons with healthy immune systems. Persons living with advanced HIV infection may suffer opportunistic infections of the lungs, brain, eyes and other organs.

**I. People Living with HIV (PLHIV)** – refers to persons infected with human immunodeficiency virus. With proper management and provision of ART, these individuals can continue to live well and be productive for many years.

**J. Treatment Hub** – a hospital facility with an established HIV/AIDS Core Team (HACT) providing prevention, treatment, care and support services to People Living with HIV (PLHIV) including but not limited to HIV Counseling and Testing, clinical management, patient monitoring and other care and support services. ARV can only be accessed through these facilities. Refer to Annex 1 for the complete list of treatment hubs in the country.

**K. Satellite Treatment Hub** – a hospital or clinic with health care providers trained by the Department of Health on primary HIV care. Services in the facility include HIV counseling and testing, adherence counseling, clinical assessment and management of newly-diagnosed patients with HIV, initiation and provision of ART, and monitoring of asymptomatic patients.

**L. Serodiscordant relationship** – refers to a sexual relationship between two persons in which one partner is living with HIV and the other is HIV-negative.

## V. TREATMENT GUIDELINES

### A. Determine if antiretroviral therapy is indicated

Early assessment of a patient's eligibility for ART and timely initiation of ART prevent other infections and comorbidities, improve overall survival of people living with HIV and prevents further transmission of HIV. The decision to start a patient on ARV shall be based on clinical assessment, comorbidities, CD4 level determination and patient's commitment to lifelong ART as shown in the table below.

Table 1. When to Start Antiretroviral Therapy (ART)

| Population | | Immunologic /Clinical Status | Recommendation |
|---|---|---|---|
| Adults and adolescents ≥ 10 years of age | HIV (+), asymptomatic | CD4 >350 and ≤500 cells/mm$^3$ | recommend ART |
| | | CD4 ≤350 cells/mm$^3$ | Start ART |
| | HIV (+), symptomatic | WHO clinical stage 3 or 4 irrespective of CD4 cell count (See Annex 2: WHO Clinical Staging of HIV Disease in adults, adolescents and children) | Start ART |
| | HIV (+) pregnant and/or breastfeeding woman | Regardless of CD4 count | Start ART |
| | HIV/TB co-infection | Presence of active TB disease, regardless of CD4 cell count | Start ART |
| | HIV/HBV co-infection | Individuals who require treatment for their HBV infection irrespective of CD4 cell count | Start ART |
| | HIV (+) in a serodiscordant relationship | Regardless of CD4 cell count or clinical staging | Start ART |
| Children 5 to <10 years of age | HIV (+), asymptomatic | CD4 >350 and ≤500 cells/mm$^3$ | recommend ART |
| | | CD4 ≤350 cells/mm$^3$ | Start ART |
| | HIV (+), symptomatic | WHO clinical stage 3 or 4 irrespective of CD4 cell count (See Annex 2: WHO Clinical Staging of HIV Disease in adults, adolescents and children) | Start ART |
| | HIV/TB co-infection | Presence of active TB disease, regardless of CD4 cell count | Start ART |
| Children < 5 years of age | | Regardless of CD4 cell count or clinical staging | Start ART |

**B. Perform adherence counseling**

The success of ARV therapy largely depends on patient's adherence to treatment. The benefits, toxicity, adherence issues and costs of treatment shall be a component of adherence counseling. A 95% adherence rate is required to prevent the development of drug resistance to ARV. Adherence counseling shall always be done prior to and while on treatment.

**C. Get laboratory tests prior to initiating ARV treatment**

1. Complete blood count (CBC)
2. TB screening: chest x-ray, sputum smear and/or gene expert
3. Pregnancy test for females of reproductive age
4. Hepatitis B screening (HBsAg)
5. CD4 cell count

**D. Choose initial ARV regimen** (See Annex 3: Antiretroviral Drugs and Doses, Instructions on Administration, and Major Types of Toxicities)

1. Recommended regimen for adults and adolescents (≥10 years of age)

   a. First-line regimen: 2 NRTI + 1 NNRTI

      i. Preferred first-line NRTI: Zidovudine (AZT) + Lamivudine (3TC)

      ii. Alternative first-line NRTI: Tenofovir (TDF) + Lamivudine (3TC)

      - recommended for patients with anemia (hemoglobin level ≤11 g/dL for adults and ≤10 g/dL for adolescents) or needing Hepatitis B treatment

      iii. First-line NNRTI: Nevirapine (NVP) or Efavirenz (EFV)

   In the Philippines, 70-75% PLHIV tolerate Nevirapine (NVP) thus patient with thorough understanding of the implications of both drugs in terms of immediate and long-term effects has option to choose whether he shall be initiated with either NVP or EFV as first-line NNRTI. History of allergy or atopy does not correlate to hypersensitivity to NVP. Efavirenz is the recommended NNRTI for patients who are taking Rifampicin or needing Hepatitis B treatment.

   b. Second-line regimen: 2NRTI + Lopinavir/ritonavir (LPV/r)
   - Tenofovir (TDF) + Lamivudine (3TC) + Lopinavir/ritonavir (LPV/r) if previously on Zidovudine (AZT) or Stavudine (d4T)
   - Zidovudine (AZT) + Lamivudine (3TC) + Lopinavir/ritonavir (LPV/r) if previously on Tenofovir (TDF)

2. Recommended regimen for children (3-10 years old)

   a. Preferred first-line regimen:

- Zidovudine (AZT) + Lamivudine (3TC) + (Efavirenz or Nevirapine)

b. Alternative first-line regimen:

- Tenofovir (TDF) + Lamivudine (3TC) + (Efavirenz or Nevirapine)
- Abacavir (ABC) + Lamivudine (3TC) + (Efavirenz or Nevirapine)

Tenofovir is preferred over Zidovudine for children with anemia (hemoglobin level ≤ 10 g/dL)

3. Recommended regimen for children (1-3 years old)

a. Preferred first-line regimen:

- Zidovudine (AZT) + Lamivudine (3TC) + (Nevirapine or Efavirenz)

b. Alternative first-line regimen:

- Abacavir (ABC) + Lamivudine (3TC) + (Nevirapine or Efavirenz)

4. Recommended regimen for HIV+ infants (<12 months)

a. No exposure to NNRTI or unknown exposure to maternal or infant ARV

i. Preferred first-line:

- Zidovudine (AZT) + Lamivudine (3TC) + Nevirapine (NVP)

ii. Alternative first-line:

- Abacavir (ABC) + Lamivudine (3TC) + Nevirapine (NVP)

b. History of any exposure to Nevirapine

i. Preferred first-line:

- Zidovudine (AZT) + Lamivudine (3TC) + Lopinavir/ritonavir (LPV/r)

ii. Alternative first-line:

- Abacavir (ABC) + Lamivudine (3TC) + Lopinavir/ritonavir (LPV/r)

Abacavir is preferred over Zidovudine for anemia in neonates (hematocrit level < 40%)

**E. Monitoring for ARV toxicity**

1. For AZT-containing regimen:
   CBC at 2, 4, 8, 12 and 24 weeks after starting ART and then every 6 months or as indicated
2. For TDF-containing regimen:
   Serum creatinine within 6 months of initiation then every 12 months or as indicated

3. For PI-containing regimen:
   Baseline lipid profile (triglyceride, total cholesterol and LDL) and FBS within 6 months then every 12 months or as indicated
4. For EFV-containing regimen:
   Baseline lipid profile (triglyceride, total cholesterol and LDL) within 6 months then every 12 months or as indicated

**F. Monitor response to treatment**

Although taking ART is a lifelong commitment, the first six months of therapy are especially important. A positive response to treatment is seen in a clinically stable patient, with no recurrence of opportunistic infections, improvement of weight and well-being, stability of immune status based on stable and increasing trend in CD4 count, maximal viral suppression and improved quality of life.

**1. Clinical response**

Frequency of clinical monitoring shall depend on patient's response to ART. Patients shall be followed-up on the minimum, at 2, 4, 8, and 12 weeks after starting ART and every six months once patient has been assessed to be stable. Reassessment of clinical stage, prevention and treatment of opportunistic infections, and assessment of symptoms of drug toxicities shall be made every visit. For patients with good compliance to ARV therapy, clinical response is recommended to be used together with CD4 count and viral load determination (whenever feasible) to detect treatment failure.

Clinical failure is defined as a new or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4) after 6 months of recommended treatment. This shall be differentiated from Immune Reconstitution Inflammatory Syndrome (IRIS) wherein exacerbation of previously subclinical coexisting infections (e.g. TB) may occur, resulting in an apparent worsening of disease after initiating ART. In IRIS, the switching of ART shall be inappropriate.

**2. Immunologic response**

Generally when ART is initiated, immune recovery starts and CD4 cell count rises occurring within the first year of treatment, plateaus, and then continues to rise further during the second year. Patients who initiated therapy with very low baseline CD4 T cell count may have less response to therapy. As a general rule, new and progressive severe immunodeficiency as demonstrated by declining CD4 cell counts shall alert the physicians to potential adherence problems or primary non-response to ART. However, any measurement that may indicate the need to consider switching shall be repeated and the low level confirmed before any change is implemented. Where resources are available, CD4 T cell count shall be done every six months for monitoring.

Reasonable working definitions of immunological failure are:

a. CD4 count falls to the baseline (or below) or
b. Persistent CD4 levels below 100 cells/$mm^3$
c. No concomitant or recent infection to cause a transient decline in the CD4 cell count

### 3. Virologic response

An individual must be taking ART for at least 6 months before it can be determined that a regimen has failed. If treatment failure is considered, viral assay shall be done before any change or shift on ART regimen. Virological failure is defined as plasma viral load above 1000 copies/ml after 4-8 weeks after providing adherence support. Where resources are available, viral load assay shall be done on the first 12-month of regimen and every 12 months thereafter.

## G. Change of treatment regimen

1. Drug toxicity and side effects (See Annex 3: Antiretroviral Drugs and Doses, Instructions on Administration, and Major Types of Toxicities)
   Antiretroviral drugs are substituted with drugs belonging to the same ARV class (eg. Tenofovir for Zidovudine where anemia occurs; Efavirenz for Nevirapine for hypersensitivity reactions). 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.
2. Treatment failure
   It is very important to regularly assess patients for treatment failure, determine the reasons for these and institute appropriate management immediately. If poor compliance is the cause of treatment failure, counseling for adherence shall be intensified and the current regimen continued. Viral load test shall be done 4-8 weeks after to reassess response to treatment.
3. Patients who are candidates for second-line ARV shall be managed in close coordination with the Research Institute for Tropical Medicine.
4. Drug interactions
   The physician shall be aware of all the drugs that the patient is taking when initiating ART and during treatment maintenance (See Annex 4: Key ARV Drug Interactions and Suggested Management).

## H. Lifelong ARV for HIV infected pregnant women

Once ARV therapy is initiated in HIV infected pregnant and/or breastfeeding women, it shall be maintained as lifelong treatment even after delivery and cessation of breastfeeding.

## I. ARV Prophylaxis for infants born to infected mothers (See Annex 5: Simplified Infant ARV Prophylaxis Dosing Recommendations)

All HIV-exposed infants shall be given once daily dosing of Nevirapine as ARV prophylactic regimen at birth or when HIV exposure is recognized postpartum. Table 2 summarizes the ranges of clinical scenarios and the duration of infant ARV prophylaxis.

Table 2. Infant ARV Prophylaxis for different Clinical Scenarios

| Scenario | Duration of infant ARV prophylaxis |
|---|---|
| **Mother diagnosed with HIV during pregnancy** | 6 weeks |
| **Mother diagnosed with HIV during labour or immediately postpartum and plans to breastfeed** | 6 weeks; consider extending this to 12 weeks |
| **Mother diagnosed with HIV during labour or immediately postpartum and plans replacement feeding** | 6 weeks |
| **Infant identified as HIV exposed after birth (through infant or maternal HIV antibody testing) and is breastfeeding** | Perform infant PCR; immediately initiate 6 weeks of NVP – strongly consider extending this to 12 weeks<br>(See Annex 6: Algorithm for Early Infant Diagnosis) |
| **Infant identified as HIV exposed after birth (through infant or maternal HIV antibody testing) and is not breastfeeding** | Perform infant PCR; initiate ARV therapy if the infant is infected<br>(See Annex 6: Algorithm for Early Infant Diagnosis) |
| **Infants of mothers who are receiving ART and are breastfeeding** | 6 weeks |
| **Infants of mothers who are receiving ART and are given replacement feeding** | 4-6 weeks |
| **Mother receiving ART but interrupts ART regimen while breastfeeding** | Until 6 weeks after maternal ART is restarted or until 1 week after breastfeeding ended, whichever comes first |

**J. Manage HIV and TB co-infection:**

All PLHIV shall be regularly screened for TB co-infection as per A.O. 2014-0005: Revised Policies and Guidelines in the Collaborative Approach of TB and HIV Prevention and Control. Diagnosis and treatment of TB follow the National Tuberculosis Program (NTP) Guidelines.

Antituberculosis treatment shall be initiated first, followed by ART as soon as possible after the first two weeks of TB treatment. Patients shall be monitored closely for signs and symptoms of hepatotoxicity.

**K. Manage HIV and Hepatitis B and C co-infection:**

Hepatitis B and C treatment follows the existing international recommendations. However, the patients shall be followed up more closely because of the major risk of drug-related interactions of some ARV with anti-HCV drugs (See Annex 4: Key ARV Drug Interactions and Suggested Management).

**L. Recording and reporting of PLHIV on ART**

1. All HCT facilities, satellite treatment hubs and treatment hubs shall maintain patient records and reports that could generate data on HIV indicators:

a. Number of new clients seen in the facility
b. Number of newly-diagnosed PLHIV seen in the facility
c. Number and percentage of newly-diagnosed PLHIV who underwent baseline CD4 testing within 3 months after diagnosis
d. Number of PLHIV who are eligible for ART during the reporting period
e. Number of PLHIV who were eligible for ART and should have been started on ART within 4 weeks
f. Number and percentage of eligible PLHIV who newly initiated ART within 4 weeks
g. Number of HIV-infected pregnant women
h. Number and percentage of HIV-infected women who were already on ART prior to diagnosis of pregnancy
i. Number and percentage of HIV-infected pregnant women on ART
j. Number and percentage of PLHIV pregnant women who underwent baseline CD4 testing within 30 days after diagnosis
k. Number of live births to pregnant HIV-infected women in the past 12 months
l. Number and percentage of infants born to HIV-infected women (HIV-exposed infants) who underwent PCR testing for Early Infant Diagnosis six (6) weeks after birth
m. Number and percentage of infants born to HIV-infected women during the past 12 month who received ARV prophylaxis at birth or when HIV-exposure is recognized postpartum
n. Number of infants born to HIV-infected women who are breastfeeding during the past 12 months
o. Number and percentage of infants born to HIV-infected women who, during the past 12 months, are breastfeeding and provided antiretroviral intervention (i.e. maternal or infant ARV) to reduce mother-to-child transmission through breastfeeding
p. Number and Percentage of PLHIV on the same ART regimen after one, two, three, four and five years of initiation
q. Number and percentage of PLHIV who underwent viral load testing on the first 12 months of treatment
r. Number of PLHIV on continuous ART for at least 6 months
s. Number and percentage of PLHIV on continuous ART for at least 6 months who were hospitalized due to opportunistic infections

2. Existing flow and timelines of reports for both Epidemiology Bureau (EB) and National AIDS/STI Prevention and Control Program (NASPCP) shall be followed.
3. Confidentiality of records and reports shall be ensured by all health care workers.

## VI. ROLES AND RESPONSIBILITIES

### A. Disease Prevention and Control Bureau (DPCB) shall:

1. Convene the technical working group for HIV and regularly review this guidelines through wide consultation with clinicians, representatives from the treatment hubs and the PLHIV;
2. Disseminate this guidelines to the treatment hubs, satellite treatment hubs and professional medical societies;
3. Forecast centrally ARV needs of PLHIV and ensure timely procurement and distribution of ARV to treatment hubs;
4. Ensure compliance of the service providers to these guidelines through a monitoring team composed of NASPCP coordinators, treatment hub staffs and PLHIV groups;
5. Ensure provision of references and training on adherence counseling to participating physicians.

### B. Regional Offices (RO) shall:

1. Disseminate this guidelines and other related reference materials to DOH — retained hospitals and private DOH - accredited tertiary medical centers; local government units, and regional chapters of the professional medical societies;
2. Strengthen the system of referrals from various health facilities to DOH — designated treatment hubs;
3. Conduct the regular monitoring activities among treatment hubs and satellite treatment hubs;
4. Collate, analyse and submit reports to DPCB and EB.

### C. Treatment Hubs through its HIV AIDS Core Team (HACT) shall:

1. Conduct adherence counseling to PLHIV prior to and while on ART;
2. Provide treatment and clinical monitoring of patients under ART;
3. Provide technical assistance to other health facilities and community-based organizations in need of professional trainings on the clinical management of HIV infection;
4. Respond accordingly to referrals from various health facilities;
5. Submit monthly reports to DPCB and EB.

### D. Epidemiology Bureau (EB) shall:

1. Conduct systematic data collection and analysis with Infectious Disease for Prevention and Control Division (IDPCD), RO and partners
2. Provide technical assistance to programs to enhance and standardize its monitoring and evaluation system;
3. Analyse and disseminate reliable and timely information on NASPCP performance indicators.

**E. Research Institute of Tropical Medicine (RITM) shall:**

1. Conduct training programme on the clinical management of HIV infection in coordination with DPCB;
2. Work in coordination with other treatment hubs and satellite treatment hubs for patients who are candidates for second-line ART.

**F. Philippine Health Insurance Corporation (PHIC) shall:**

1. Implement the Outpatient HIV/AIDS treatment (OHAT) package based on this guidelines;
2. Review the OHAT package to ensure sustainable treatment for PLHIV.

**G. Civil Society Organizations for Treatment, Care and Support shall:**

1. Work in coordination with the members of HACT in treatment hubs and satellite treatment hubs in providing care and support for PLHIV especially those on ART;
2. Encourage PLHIV to enroll and avail of the Philippine Health Insurance Corporation (PHIC) outpatient HIV/AIDS treatment package.

**VII. FINANCING**

A. The IDPCD shall allot funds for procurement of ARVs annually based on NASPCP forecasting.

B. The DPCB along with the Philippine National AIDS Council (PNAC) Secretariat and the PLHIV shall continuously mobilize resources for funding to ensure sustainability of HIV treatment.

**VIII. REPEALING CLAUSE**

Provisions from previous issuances that are inconsistent or contrary to the provisions of this order are hereby rescinded and modified accordingly. All other provisions of Administrative Order 2009-0006 dated January 13. 2009 and Administrative Order 2009-0016 dated May 20, 2009 stand in effect.

**IX. EFFECTIVITY**

This order shall take effect immediately upon approval.

**ENRIQUE T. ONA, MD**

Secretary of Health

## Annex 1. List of Treatment Hubs in the Philippines

| No. | Region | Treatment Hub | Address | Contact Number |
|---|---|---|---|---|
| 1 | CAR | Baguio General Hospital and Medical Center | Gov. Pack Rd., Baguio City | (074) 442-4216 loc 381 |
| 2 | I | Ilocos Training and Regional Medical Center | San Fernando City, La Union | (072) 6076418 loc 153 |
| 3 | II | Cagayan Valley Medical Center | Carig, Tuguegarao, Cagayan | (078) 304-1410 |
| 4 | III | Jose B. Lingad Memorial Regional Hospital | Brgy. San Dolores, San Fernando, Pampanga | (045) 961-3989 (Medicine Dept) |
| 5 | NCR | San Lazaro Hospital | Quiricada St., Sta. Cruz, Manila | (02) 732-3777 loc218 (H4OPD) loc212 (H4 ward) |
| 6 | NCR | Philippine General Hospital | Taft Ave., Manila | (02) 554-8400 loc 3249 |
| 7 | NCR | Research Institute for Tropical Medicine | Filinvest Corporate City, Alabang, Muntinlupa City | (02) 807-2628 loc 332 |
| 8 | NCR | Makati Medical Center | #2 Amorsolo St., Legaspi Village, Makati City | (02) 888-8999 loc 2336 loc 2134 (CTTM) |
| 9 | NCR | The Medical City | Ortigas Ave., Pasig City | (02) 988-1000 loc 6765 |
| 10 | V | Bicol Regional Training and Teaching Hospital | Rizal St., Legazpi City | (052) 4830016 Loc 4277 (PHU) |
| 11 | VI | Western Visayas Medical Center | Q. Abeto St., Mandurriao, Iloilo City | (033) 3212841/ (03) 321-0552 |
| 12 | VI | Corazon Locsin Montelibano Memorial Regional Hospital | Dept. of Internal Medicine, 3rd Flr. OPD Bldg., CLMMRH, Lacson St., Bacolod City | (034) 709-0244 |
| 13 | VII | Vicente Sotto Sr. Memorial Medical Center | B. Rodriguez, Sambag II, Cebu City | (032) 2539891 – 96 loc 102 |
| 14 | VII | Gov. Celestino Gallares Memorial Hospital | M. Parras St., Tagbilaran City | (038) 4114868 |
| 15 | VIII | Eastern Visayas Regional Medical Center | Magsaysay Boulevard, Tacloban City | (053) 3213121 (053) 3213363 |
| 16 | IX | Zamboanga City Medical Center | Dr. Evangelista St., Sta. Catalina, Zamboanga City | (062) 991-2934 |
| 17 | X | Northern Mindanao Medical Center | Provincial Capitol Compound Cagayan de Oro City | (08822)72-75-35; 72-37-35; 72-63-62 (088) 856-4147 |
| 18 | XI | Southern Philippines Medical Center | J. P. Laurel St., Bajada, Davao City | (082) 2272731 loc 4205 (082) 2869486 |

## Annex 2. WHO Clinical Staging of HIV Disease in Adults, Adolescents and Children

Source: Adapted from WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children. Geneva, World Health Organization, 2007 (www.who.int/hiv/pub/guidelines/HIVstaging150307.pdf)

| Adults and adolescents [a] | Children |
|---|---|
| **Clinical Stage 1** | |
| Asymptomatic<br>Persistent generalized lymphadenopathy | Asymptomatic<br>Persistent generalized lymphadenopathy |
| **Clinical Stage 2** | |
| Moderate unexplained weight loss (<10% of presumed or measured body weight)<br>Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis)<br>Herpes zoster<br>Angular cheilitis<br>Recurrent oral ulceration<br>Papular pruritic eruption<br>Fungal nail infections<br>Seborrhoeic dermatitis | Unexplained persistent hepatosplenomegaly<br>Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis)<br>Herpes zoster<br>Lineal gingival erythema<br>Recurrent oral ulceration<br>Papular pruritic eruption<br>Fungal nail infections<br>Extensive wart virus infection<br>Extensive molluscum contagiosum<br>Unexplained persistent parotid enlargement |
| **Clinical Stage 3** | |
| Unexplained severe weight loss (>10% of presumed or measured body weight)<br>Unexplained chronic diarrhoea for longer than 1 month<br>Unexplained persistent fever (intermittent or constant for longer than 1 month)<br>Persistent oral candidiasis<br>Oral hairy leukoplakia<br>Pulmonary tuberculosis<br>Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia)<br>Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis<br>Unexplained anaemia (<8 g/dl), neutropaenia (<0.5 x $10^9$/l) and/or chronic thrombocytopaenia (<50 x $10^9$/l) | Unexplained moderate malnutrition not adequately responding to standard therapy<br>Unexplained persistent diarrhoea (14 days or more)<br>Unexplained persistent fever (above 37.5°C, intermittent or constant, for longer than one month)<br>Persistent oral candidiasis (after first 6 weeks of life)<br>Oral hairy leukoplakia<br>Lymph node tuberculosis<br>Pulmonary tuberculosis<br>Severe recurrent bacterial pneumonia<br>Acute necrotizing ulcerative gingivitis or periodontitis<br>Unexplained anaemia (<8 g/dl), neutropaenia (<50 x $10^9$/l) or chronic thrombocytopaenia (<0.5 x $10^9$/l)<br>Symptomatic lymphoid interstitial pneumonitis<br>Chronic HIV-associated lung disease, including bronchiectasis |

[a] In the development of this table, adolescents were defined as 15 years or older. For those aged less than 15 years, the clinical staging for children should be used.

| Adults and adolescents | Children |
|---|---|
| Clinical Stage 4 | |
| HIV wasting syndrome | Unexplained severe wasting, stunting or severe |
| Pneumocystis ( jirovecii) pneumonia | Malnutrition not responding to standard therapy |
| Recurrent severe bacterial pneumonia | Pneumocystis ( jirovecii) pneumonia |
| Chronic herpes simplex infection (orolabial, genital or anorectal of more than 1 month's duration or visceral at any site) | Recurrent severe bacterial infections (such as empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia) |
| Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs) | Chronic herpes simplex infection (orolabial or cutaneous of more than 1 month's duration or visceral at any site) |
| Extrapulmonary tuberculosis | Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs) |
| Kaposi sarcoma | Extrapulmonary tuberculosis |
| Cytomegalovirus infection (retinitis or infection of other organs) | Kaposi sarcoma |
| Central nervous system toxoplasmosis | Cytomegalovirus infection (retinitis or infection of other organs with onset at age more than 1 month) |
| HIV encephalopathy | Central nervous system toxoplasmosis (after the neonatal period) |
| Extrapulmonary cryptococcosis, including meningitis | HIV encephalopathy |
| Disseminated nontuberculous mycobacterial infection | Extrapulmonary cryptococcosis, including meningitis |
| Progressive multifocal leukoencephalopathy | Disseminated nontuberculous mycobacterial infection |
| Chronic cryptosporidiosis | Progressive multifocal leukoencephalopathy |
| Chronic isosporiasis | Chronic cryptosporidiosis (with diarrhoea) |
| Disseminated mycosis (extrapulmonary histoplasmosis, coccidioidomycosis) | Chronic isosporiasis |
| Lymphoma (cerebral or B-cell non-Hodgkin) | Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidioidomycosis, penicilliosis) |
| Symptomatic HIV-associated nephropathy or cardiomyopathy | Cerebral or B-cell non-Hodgkin lymphoma |
| Recurrent septicaemia (including nontyphoidal Salmonella) | HIV-associated nephropathy or cardiomyopathy |
| Invasive cervical carcinoma | |
| Atypical disseminated leishmaniasis | |

## Annex 3. Antiretroviral Drugs and Doses, Instructions on Administration, and Major Types of Toxicities

| Drug | Age, Dose, Frequency | Administration | Major types of toxicity | Risk factors | Suggested Management |
|---|---|---|---|---|---|
| Nucleoside Reverse Transcriptase Inhibitors (NRTI) | | | | | |
| **Lamivudine (3TC)**<br>Oral Sol'n:10mg/ml<br><br>Tablet available as fixed dose combination (FDC):<br>3TC 300 mg + TDF 300 mg;<br>3TC 150 mg + AZT 300 mg | Infant/Child:<br>Oral Sol'n:<br>3-5.9 kg: 3 ml twice daily<br>6-9.9 kg: 4 ml twice daily<br>10-13.9 kg: 6 ml twice daily<br><br>Adolescent/Adult:<br>3TC 150 mg PO every 12 hours or<br>3TC 300 mg once daily | - Take without regard to meals<br>- Tablet can be crushed and contents mixed with small amounts of water or food and taken immediately | | | |
| **Zidovudine (AZT)**<br><br>Syrup: 10 mg/ml<br>Tablet: 300 mg<br>Capsules: 100 mg, 200 mg<br><br>Tablet available as 3TC 150 mg + AZT 300 mg | Infant/Child:<br>Syrup:<br>3-5.9 kg: 6 ml twice daily<br>6-9.9 kg: 9ml twice daily<br>10-13.9 kg: 12ml twice daily<br><br>Adolescent/Adult:<br>AZT 300 mg PO every 12hours<br><br>600 mg/m$^2$/dose/day for HIV encephalopathy | - Take without regard to meals<br>- Tablet can be crushed and contents mixed with small amounts of water or food and taken immediately (solution is stable at room temperature) | Anemia, neutropenia, myopathy, lipoatrophy or lypodystrophy | Baseline anemia or neutropenia<br>CD4 count ≤ 200 cells/mm$^3$ | If substitute with TDF or ABC |
| | | | Lactic acidosis (rare) or severe hepatomegaly with steatosis | BMI > 25 (or BW>75kg)<br>Prolonged exposure to nucleoside analogues | |
| Abacavir (ABC)<br><br>Oral Soln: 20 mg/ml<br>(not available in Phil)<br><br>Tablet: 300 mg | Infant/Child:<br>Syrup:<br>3-5.9 kg: 3 ml twice daily<br>6-9.9 kg: 4 ml twice daily<br>10-13.9 kg: 6 ml twice daily<br>Adolescent/Adult:<br>300 mg PO twice daily or<br>600 mg PO once daily | - Take without regard to meals<br>- Tablet can be crushed and contents mixed with small amounts of water or food and ingested immediately | Hypersensitivity reaction (ABC should be stopped permanently) | Presence of HLA-B 5701 gene | |
| Nucleotide Reverse Transcriptase Inhibitors (NRTI) | | | | | |
| Tenofovir (TDF)<br><br>Available as fixed dose combination<br><br>3TC 300 mg + TDF 300 mg<br><br>3TC 300mg + TDF 300mg + EFV 600mg | Child:<br>25-29.9 kg: 200 mg PO once daily<br>30-34.9 kg: 300 mg PO once daily<br><br>Adolescent/Adult:<br>TDF 300 mg PO once daily | Take without regard to meals | Tubular renal dysfunction,<br>Fanconi syndrome | Underlying renal disease<br>Older age; BMI < 18 (or BW <50kg)<br>Untreated DM and untreated HPN<br>Concomitant use of nephrotoxic drugs or a boosted PI | If TDF is being used in first-line ART, substitute with AZT or ABC<br><br>If TDF is being used in second-line ART, substitute with ABC |
| | | | Decrease in bone mineral density | History of osteomalacia and pathological fracture<br>Risk factors for osteoporosis or bone loss | |
| | | | Lactic acidosis or severe hepatomegaly with steatosis | Prolonged exposure to nucleoside analogues<br>Obesity | |
| | | | Exacerbation of hepa B (hepatic flares) | Discontinuation of TDF due to toxicity | Use alternative drug for hepatitis B treatment |

| Drug | Dose | Administration | Major types of toxicity | Risk factors | Suggested Management |
|---|---|---|---|---|---|
| **Non-nucleoside Reverse Transcriptase Inhibitors** | | | | | |
| Efavirenz (EFV)<br><br>Capsule: 50 mg, 200 mg<br><br>Tablet 200 mg, 600 mg<br><br>Available as fixed dose combination<br><br>3TC 300mg + TDF 300mg + EFV 600mg | Child (> 3 years of age):<br>Capsule (liquid) dose:<br>10-15 kg: 200 mg (270 mg = 9 ml) once daily<br>15-<20kg: 250 mg (300 mg = 10ml) once daily<br>20-<25 kg: 300 mg (360 mg = 12 ml) once daily<br>25-<33 kg: 350 mg (450 = 15 ml) once daily<br>33-<40 kg: 400 mg (510 mg = 17 ml) once daily<br>Max dose for >40 kg: 600 mg once daily<br>Tablet (scored) 200mg:<br>10-13.9 kg: 1 tablet once daily<br>14.19.9 kg: 1.5 tablet once daily<br>20-24.9 kg: 1.5 tablet once daily<br>25-34.9 kg: 2 tablets once daily<br>Adolescent/Adult:<br>EFV 600 mg PO once daily | Take on an empty stomach and before bedtime as severe dizziness is possible upon initiation of therapy that resolves or becomes tolerable after a few days | Hypersensitivity reaction, Stevens-Johnson syndrome<br>Potential risk of neural tube birth defects (very low risk in humans)<br>Male gynecomastia | Risk factors unknown | Substitute with NVP.<br>If the person cannot tolerate either NNRTI, use boosted PIs |
| | | | Hepatotoxicity | Underlying hepatic disease – HBV and HCV co-infection;Concomitant use of hepatotoxic drugs | |
| | | | Convulsions | History of seizures | |
| | | | Persistent central nervous system toxicity (such as abnormal dreams, depression or mental confusion) | Depression or other mental disorder (previous or at baseline)<br>Daytime dosing | |
| Nevirapine (NVP)<br><br>Oral Soln: 10 mg/ml<br>Tablet: 200 mg | Infant/Child:<br>Liquid:<br>3-5.9 kg: 5ml once daily for 14 days, followed by 5 ml twice daily if no hypersensitivity reaction occurs<br>6-9.9 kg: 8 ml once daily for 14 days, followed by 5 ml twice daily if no hypersensitivity reaction occurs<br>10-13.9 kg: 10 ml once daily for 14 days, followed by 5 ml twice daily if no hypersensitivity reaction occurs<br><br>Dose for < 3 years: 200 mg/m$^2$ while taking Rifampicin for TB co-infection<br><br>Adolescent/Adult:<br>200 mg once daily for 14 days, followed by 200mg twice daily if no hypersensitivity reaction occurs | - Take without regard to meals<br>- Not recommended to be co-administered with rifampicin<br>- Tablets are scored and can be divided into two equal halves to give a 100 mg dose; can be crushed and combined with a small amount of water or food and immediately administered<br>- If mild/moderate rash develops, hold drugs; when rash clears, restart dosing from beginning of dose escalation; if severe rash, discontinue drug | STOP if any is observed:<br>Fever or feverish sensation<br>Flu-like symptoms such as muscle or body pains | | Substitute with EFV (for 3 years and older)<br>If the person cannot tolerate either NNRTI, use boosted PIs |
| | | | Hepatoxicity | Underlying hepatic disease<br>HBV and HCV co-infection<br>Concomitant use of hepatotoxic drugs (CD4 > 250 cells/mm3 in women; CD4>400 cells/mm3 for men)<br>First month of therapy (if lead-in dose is not used) | |
| | | | Severe skin rash and hypersensitivity reaction (Stevens-Johnsons Syndrome) | Risk factors unknown | |

| Drug | Dose | Administration | Major types of toxicity | Risk factors | Suggested Management |
|---|---|---|---|---|---|
| **Protease Inhibitors (PIs)** | | | | | |
| Indinavir (IDV)<br>400 mg capsules | 800 mg PO every 12 hours to be given with ritonavir 100 mg PO | For RTV-boosted IDV - take with or without food<br>Take with plenty of water to avoid nephrolithiasis<br><br>Not recommended to be co-administered with rifampicin | Nephrolithiasis | | |
| Lopinavir/ritonavir (LPV/r)<br><br>Syrup: 80/20 mg/ml<br><br>Tablet: Lopinavir 200mg/ Ritonavir 50 mg | <u>Child:</u><br>3-5.9kg: 1ml every 12 hours<br>6-9.9 kg: 1.5 ml every 12 hours<br>10-13.9 kg: 2ml every 12 hours<br>14-19.9 kg: 2.5 ml every 12 hours<br>20-24.9 kg: 3 ml every 12 hours<br><br><u>Adult:</u><br>2 tablets PO every 12 hours | Take without regard to meals<br><br>Not recommended to be co-administered with rifampicin | GI intolerance<br>Lipodystrophy | Risk factors unknown | |
| | | | Hepatotoxicity | Underlying hepatic disease<br>HBV and HCV co-infection<br>Concomitant use of hepatotoxic drugs | |
| | | | Pancreatitis | Advanced HIV disease | |
| | | | QT interval prolongation | Congenital long QT syndrome<br>Hypokalemia<br>Concomitant use of drugs that may prolong the QT interval | |
| | | | Electrocardiographic abnormalities (PR and QT interval prolongation, torsades de pointes) | People with pre-existing conduction system disease<br><br>Concomitant use of other drugs that may prolong the PR interval | |

Computation of Body Surface Area:

$$BSA\ (m^2) = \sqrt{\frac{Ht\ (Cm) \times Wt\ (kg)}{3600}}$$

## Annex 4. Key ARV Drug Interactions and Suggested Management

(Source: www.hiv-druginteractions.org)

| ARV drug | Key interactions | Suggested Management |
|---|---|---|
| AZT | Ribavirin and peg-interferon | substitute AZT with TDF<br>Avoid AZT and ribavirin combination if possible; causes anemia |
| Boosted PI (LPV/r) | Rifampicin | substitute with EFV (for ≥ 3years of age) substitute with NVP at 200 mg/m$^2$ (for < 3 years of age) |
| | Lovastatin and simvastatin | Use an alternative dyslipidemia agent (e.g. pravastatin) |
| | Estrogen-based hormonal contraception | Use alternative or additional contraceptive methods |
| | Methadone and buprenorphine | Adjust methadone and bruprenorphine doses as appropriate |
| | Astemizole and terfenadine | Use alternative antihistamine agent (loratadine and cetirizine) |
| | TDF | Monitor renal function |
| EFV | Amodiaquine | Use an alternative antimalarial agent |
| | Methadone | Adjust the methadone dose as appropriate |
| | Estrogen-based hormonal contraception | Use alternative or additional contraceptive methods |
| | Astemizole and terfenadine | Use an alternative anti-histamine agent |
| | Interferon | Needs close monitoring since drug interaction may cause severe depression |
| NVP | Rifampicin | Substitute with EFV (for ≥3 years of age); ensure NVP dose at 200 mg/m$^2$ (< 3 years old) |
| | Itraconazole and ketoconazole | Use an alternative antifungal agent (e.g. fluconazole) |

## Annex 5. Simplified Infant ARV Prophylaxis Dosing Recommendations

Source: Adapted from Antiretroviral drugs for treating pregnant women and preventing HIV infections in infants: recommendations for a public health approach. Geneva WHO, 2010)

| Infant age | NVP Daily dosing | AZT[a] Daily Dosing |
|---|---|---|
| Birth[b] to 6 weeks[c] | | |
| • Birthweight 2000-2499 g | 10 mg once daily | 10 mg twice daily |
| • Birthweight ≥ 2500g | 15 mg once daily | 15 mg twice daily |
| >6 weeks to 6 months [d] | 20 mg once daily | |
| >6 months to 9 months | 30 mg once daily | |
| >9 months until breastfeeding ends | 40 mg once daily | |

[a] If the mother is using replacement feeding, infant AZT can be substituted for infant NVP

[b]Infants weighing < 2000 g should receive mg/kg dosing; the suggested starting dose is 2 mg/kg once daily.

[c]Recommended for 6 weeks, but 4 weeks may be considered in the settings with replacement feeding

[d]Dosing beyond 6 weeks of age in special situations in which prolonged dosing of up to 12 weeks should be considered (such cases as the mother having limited ART and not likely to be virally suppressed; the infant is identified as HIV exposed after birth and is breastfeeding)

## Annex 6. Algorithm for Early Infant Diagnosis