# TABLE OF CONTENTS

Contributors to Guidelines ................................................................................................. v
Foreword by the Minister of Health .................................................................................. vii
Foreword by the Chief Medical Officer ............................................................................ ix
Abbreviation and Acronym List ......................................................................................... x

## PART 1 – ANTIRETROVIRAL THERAPY FOR ADOLESCENTS AND ADULTS

1. Objectives .................................................................................................................... 2
2. Principles of Antiretroviral Therapy ............................................................................. 3
3. WHO Staging for HIV Infection and Disease in Adolescents and Adults ............ 5
4. Antiretroviral Drugs ..................................................................................................... 6
5. Goals of Antiretroviral Therapy in Adolescents and Adults ........................................ 8
6. Eligibility Criteria – Indications for Antiretroviral Therapy ........................................ 9
7. Recommended First-Line and Alternate First-Line Antiretroviral Drug Regimens in Guyana ........................................................................................................... 11
8. Clinical and Laboratory Monitoring and Visit Schedules ........................................... 15
9. Managing Common Drug Adverse Events ................................................................. 19
10. Immune Reconstitution Syndrome ............................................................................ 23
11. Indications for Changing the First-Line Antiretroviral Drug Regimen in Guyana .... 24
12. Recommended Second-Line Antiretroviral Drug Regimen in Guyana ...................... 28
13. Principles and Monitoring of Adherence to Antiretroviral Drug Regimens ............ 30

Appendix 1-A. Guyana HIV testing algorithm: ELISA antibody test ............................... 33
Appendix 1-B. Guyana HIV testing algorithm: HIV rapid test ......................................... 34
Appendix 1-C. WHO staging system for HIV infection and disease in adolescents and adults ............................................................................................................. 35
Appendix 1-D. CDC AIDS surveillance case definitions for adolescents and adults ....... 37
Appendix 1-E. Guyana HIV management six-question assessment for adults ............... 38
Appendix 1-F. Drug-drug interactions ............................................................................. 39
Appendix 1-G. Laboratory monitoring schedule and follow-up visits for antiretroviral therapy ................................................................................................. 40
Appendix 1-H. Guiding principles for managing ARV drug toxicity .............................. 41
Appendix 1-I. Common toxicities of antiretroviral drugs by type .................................. 42
Appendix 1-J. Laboratory monitoring schedule for first-line antiretroviral regimen .... 43
Appendix 1-K. Recommended drug substitutions ............................................................. 44
<table>
<thead>
<tr>
<th>PART 4 – PROPHYLAXIS AND MANAGEMENT OF COMMON OPPORTUNISTIC INFECTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevention of opportunistic infections ........................................... 98</td>
</tr>
<tr>
<td>Syndromic Care of Common HIV-Related Illnesses ............................... 102</td>
</tr>
<tr>
<td>Chronic diarrhoea in adults .......................................................... 103</td>
</tr>
<tr>
<td>Respiratory problems .......................................................................... 112</td>
</tr>
<tr>
<td>Oral problems .................................................................................... 119</td>
</tr>
<tr>
<td>Neurologic problems ........................................................................... 120</td>
</tr>
<tr>
<td>Skin lesions ....................................................................................... 122</td>
</tr>
<tr>
<td>Paediatric Opportunistic Infection Prophylaxis .................................... 127</td>
</tr>
</tbody>
</table>

| PART 5 – FUTURE CONCERNS ................................................................. 128 |

| PART 6 – REFERENCES ................................................................. 129 |
Contributors to Guidelines

WORKING GROUP FOR 2005 GUIDELINES

1. Ministry of Health
   • Dr Rudy Cummings, Chief Medical Officer
   • Dr Navindra Persaud, Director, Disease Control Department
   • Dr Morris Edwards, Program Manager, National AIDS Program Secretariat
   • Dr Curtis Le Feur, Medical Officer, National AIDS Program Secretariat
   • Dr Michael Ali, Director (past), Genitourinary Medicine Clinic, Georgetown Public Hospital Corporation (GPHC)
   • Dr Shanti Singh, Director (current), Genitourinary Medicine Clinic, GPHC
   • Dr Shamdeo Persaud, Director, National Tuberculosis (TB) Control Program
   • Dr Jomo Osborne, Director, Maternal and Child Health Department

2. François-Xavier Bagnoud Center
   University of Medicine and Dentistry of New Jersey, USA
   • Dr Chuka Anude, Chief of Party and Country Program Director, Physician-Specialist (HIV Care, Treatment, and Support)
   • Dr Arry Dieudonne, Pediatric Infectious Disease Specialist
   • Dr Mary Boland, Executive Director
   • Dr Monica Reiss, Medical Writer
   • Gisele Pemberton, MPH, CHES, Program Manager
   • Nancy Lerner-Weiss, MSW, Global Programs and Technology Coordinator

3. Canadian Society for International Health
   • Dr John Farley, Infectious Disease Specialist (HIV-AIDS/Epidemiology)
   • Dr William Bowie, Infectious Disease Specialist (STIs)
   • Dr Gwen Stevens, Infectious Disease Specialist (HIV)
   • Dr Earl Hershfield, Infectious Disease Specialist (TB)
   • Ms Roumanya Benedict, Program Director

4. Centers for Disease Control and Prevention, Global Aids Program, Guyana
   • Dr Michele McConnell, Care and Treatment Specialist, CDC Atlanta
   • Mr Paul Moffat, Deputy Director, CDC GAP Guyana

Contact Information
The National AIDS Program Secretariat
   Program Manager, Tel. No: 226 5371 and 2278683
   Health Education Unit: Tel. No: 223-7139
   HIV/AIDS Hotline: Tel. No: 223-7138 and 2237139

The Genitourinary Medicine (GUM) Clinic
   Manager, Tel. No: 226-0664 and 2273744

The National Tuberculosis (Chest) Clinic
   Principal Tuberculosis Officer, Tel. No: 2257290

WRITING COMMITTEE
Chuka Anude with assistance from John Farley, Arry Dieudonne, Monica Reiss, Navindra Persaud, and Morris Edwards
AUGUST 2006 GUIDELINES REVISION COMMITTEE

WORKING GROUP

5. Ministry of Health
   • Dr Rudolf Cummings, Chief Medical Officer
   • Dr Shamdeo Persaud, Director, Disease Control
   • Dr Shanti Singh-Anthony, Program Manager, National AIDS Program Secretariat
   • Dr Jadunauth Raghunauth, Director, Genitourinary Medicine Clinic, Georgetown Public Hospital Corporation (GPHC)
   • Dr Jeetendra Mohanlall, Program manager National Tuberculosis Control Program
   • Dr Janice Woolford Director Maternal and Child Health
   • Ms Deborah Vitalis, Program Officer, PMTCT Program
   • Ms. Colette Gouviea, Chief Pharmacist, Ministry of Health

6. François-Xavier Bagnoud Center
   University of Medicine and Dentistry of New Jersey, USA
   • Dr Chuka Anude, Chief of Party and Country Program Director, Physician-Specialist (HIV Care, Treatment, and Support)
   • Dr Arry Dieudonne, Pediatric Infectious Disease Specialist
   • Dr Linda Podhurst, Executive Director
   • Dr Monica Reiss, Medical Writer
   • Gisele Pemberton Caribbean Program Manager
   • Nancy Lerner-Weiss, Global Programs and Technology Coordinator

7. François-Xavier Bagnoud Center-Guyana/
   University of Medicine and Dentistry of New Jersey, USA
   • Dr Chuka Anude, Chief of Party and Country Program Director, Physician-Specialist (HIV Care, Treatment, and Support)
   • Dr Moses Bateganya, Director Care and Treatment, Physician Specialist
   • Ms Mena Carto, Program Officer, Technical Services

8. Canadian Society for International Health
   • Dr Earl Hershfield, Infectious Disease Specialist (TB)
   • Ms Roumyna Benedict, Program Director
   • Dr Curtis Le Fleur, Technical Coordinator, Public Health Strengthening Project

9. Centers for Disease Control and Prevention, Global AIDS Program, Guyana
   • Dr Scott Filler, Care and Treatment Specialist, CDC Atlanta
   • Dr Douglas Lyon, Director, CDC GAP Guyana
   • Dr Amy Dubois, Deputy Director, CDC GAP Guyana

10. AIDS Relief Consortium
    • Dr Pamela Marks, PEPFAR Clinical Associate, IHV, University of Maryland
    • Dr Bruce Gilliam, Assistant Professor, University of Maryland
    • Dr Robert Redfield, Professor, University of Maryland

11. Dartmouth Medical School / Dartmouth-Hitchcock Medical Center
    • Dr Brian Marsh, Assistant Professor / FXB Guyana Consultant

12. Guyana HIV/AIDS Reduction and Prevention Program (GHARP)
    • Dr Jomo Osborne, Director, Technical Services
    • Dr Karen Gordon Boyle, Community and palliative care officer
FOREWORD

I welcome the second publication of the National Guidelines for Management of HIV Infected and HIV Exposed Adults and Children. This 2nd edition comes at a time when Guyana is poised to achieve universal access to treatment and care for PLWHAs.

Antiretroviral (ARV) therapy for the treatment of human immunodeficiency virus (HIV) is an important part of the overall response to HIV/AIDS in Guyana. Major advances in ARV therapy have been made since the advent of azidothymidine (AZT) in the early 1990s. There are now over twenty different ARV drugs in four different categories, which are available for treating persons living with HIV/AIDS (PLWHA). The availability of ARV drugs has made a dramatic difference in their longevity and quality of life. These drugs are crucial for lowering the viral load and interrupting transmission of HIV from one person to another.

The Guyana Government is committed to providing ARV treatment as part of a comprehensive management program for PLWHA. In 2002, the Guyana Government declared a universal treatment program for PLWHA. This was a bold move, but one fraught with financial difficulties. Yet financial constraints were not the only hurdles to overcome. Guyana was also faced with a severe lack of human resources and the technical expertise to fully roll out such an enormous undertaking. With generous assistance from the United States and Canadian governments and from the Joint United Nations Programme on HIV/AIDS (UNAIDS), United Nations International Children’s Emergency Fund (UNICEF) and the Pan American Health Organization (PAHO)/World Health Organization (WHO), the treatment program has grown by leaps and bounds. Guyana is proud of this evolving program, and we are gradually moving towards a model treatment program for PLWHA.

But treatment with ARV drugs is not the only concern medical practitioners have in the overall management of PLWHA. Another important aspect of the program is the differential treatment for children, adolescents, and adults. Unfortunately, many children are born infected through transmission of the virus from mother-to-child. The differences in dose and formulation (pills vs liquids) are important aspects of the treatment of children compared to the treatment of adolescents and adults.

There are other concerns, too. Another major concern is the co-infection of PLWHA with tuberculosis (TB). In these cases, persons must be managed for both HIV and TB. The TB drugs have serious interactions with some of the ARV drugs. Thus, different treatment regimens are necessary for PLWHA who are co-infected with TB.

The possibility of resistance to or diminished efficacy of ARV drugs in some PLWHA represents an additional concern for practitioners. It is important, therefore, that countries like Guyana establish treatment protocols for first-line and second-line drug regimens that minimise resistance and maximise efficacy. Guyana is in a fortunate position in that, in spite of cost constraint, Guyana is not limited in selecting drugs for care and treatment program.

PLWHA often present at clinic with one or more opportunistic infections and with concomitant sexually transmitted infections (STIs). Practitioners must be aware of these infections and must have clear treatment protocols with which to treat patients.
The Ministry of Health, in collaboration with the Government of the United States of America and the Canadian Government, has developed treatment protocols in response to the above circumstances. This document represents the first revision of these protocols to reflect evolving trends in the management of HIV-infected and HIV-exposed adults and children.

We are grateful to the United States Agency for International Development (USAID) and the US Centers for Disease Control and Prevention (CDC) and to the Canadian International Development Agency (CIDA) for their support in the development of these protocols. We are grateful also to the partners with whom these agencies contracted: François-Xavier Bagnoud Center (FXBC) of the University of Medicine and Dentistry of New Jersey (UMDNJ)), Family Health International (FHI) and the Canadian Society for International Health (CSIH). We are grateful to the staff of the Ministry of Health and the persons who have served on the National Committee for Treatment and Care of HIV/AIDS. The Ministry of Health has approved the treatment guidelines contained in this manual. We are hopeful that these guidelines will be adhered to by practitioners in the public health sector, and also by all medical practitioners, including those in the private sector and those who work in an NGO setting.

These revised guidelines answer central questions pertaining to many situations, including:

- Eligibility for the initiation of treatment in PLWHA who are asymptomatic
- The preferred first-line and second-line regimens
- Drugs or drug combinations that should be used or avoided
- Role of testing, including using CD4 lymphocyte counts, in managing PLWHA
- Preferred regimens for treating adults and children
- The preferred regimens for treating HIV infected pregnant women
- Preferred regimens for post exposure prophylaxis
- Preferred regimens for treating persons with HIV and TB co-infection
- Treating opportunistic infections

A major shift in these guidelines is the commencement of antiretroviral therapy among persons with CD4 counts of less than 350 instead of 200 and provision of expanded regimens for pregnant women instead of single dose nevirapine.

The guidelines are comprehensive and when used properly will enhance the ability of practitioners to provide quality service in the public and private sectors. As Minister of Health, I recommend the National Guidelines for Management of HIV-Infected and HIV-Exposed Adults and Children to all the professionals working with clients with HIV/AIDS. I urge all practitioners to become familiar with the guidelines.

Finally, these guidelines are not meant to be rigid. This a living document and will be subjected to periodic reviews by the National Committee for the Treatment and Care of HIV.

Dr. Leslie Ramsammy
Minister of Health
September, 1, 2006
FOREWORD

The completion of the current revision of the treatment protocol is in keeping with the principle of staying current with the latest thinking in care of patients with HIV and AIDS. The support from the US Global AIDS Program has been intangible and continues to support the increased access to care.

This effort continues to be comprehensive and we have again benefited from the in-country presence of technical expertise, which has taken on the preparation of the guidelines as a single task. Through the use of the technical expertise of the Francois-Xavier Bagnoud (FXB) Center of the University of Medicine and Dentistry of New Jersey, and the support of the US Centers for Disease Control and Prevention (CDC), we have been able to work in a very concentrated way, overcoming hurdles that would traditionally have burdened such an effort involving busy professionals. We were also fortunate to have technical comments from our Canadian partners as well, who gave unselfishly of their time to review the various drafts of this work. On this occasion we have also benefited from numerous other academic and technical interests.

When we began using antiretroviral preparations early in 2003 the need for a treatment protocol was recognized. Those attempts at preparing a protocol took into account the available medications and the laboratory support that we knew was accessible to us. This current edition takes into account the strategic approaches enhanced by many of the better endowed programmes.

Good use has again been made of both the regional and WHO guidelines while completing the current document. We have been fortunate to have had constant online support while refining the document from our American partners.

The publication of these guidelines will formally attempt to significantly increase the number of patients on treatment in Guyana. As this increase is pursued there will be increased laboratory capability to meet the new demands. Hopefully the increased microbiological expertise accompanied by that already installed will work to provide comfort to the clinicians and improve the patients’ health.

These guidelines provide the interesting challenge for training all involved in care and treatment – at their various levels – to understand the treatment needs of the patients. The challenges to introduce these guidelines may be less formidable as the programme is better endowed with staff and systems to improve patient outcomes.

As head of the treatment guidelines team, I wish to thank all who cooperated in the revision of the document. I am certain that this will be a standard process to ensure that the document continues to be relevant to its users and the eventual beneficiaries – the patients.

Dr. Rudolph O. Cummings, MD., MPH
Chief Medical Officer
Ministry of Health
Government of Guyana
## Abbreviation and Acronym List

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Word</th>
</tr>
</thead>
<tbody>
<tr>
<td>3TC</td>
<td>lamivudine</td>
</tr>
<tr>
<td>ABC</td>
<td>abacavir</td>
</tr>
<tr>
<td>AIDS</td>
<td>acquired immunodeficiency syndrome</td>
</tr>
<tr>
<td>ANC</td>
<td>antenatal care</td>
</tr>
<tr>
<td>APV</td>
<td>amprenavir</td>
</tr>
<tr>
<td>ART</td>
<td>antiretroviral therapy</td>
</tr>
<tr>
<td>ARV</td>
<td>antiretroviral</td>
</tr>
<tr>
<td>ATV</td>
<td>atazanavir</td>
</tr>
<tr>
<td>AZT or ZDV</td>
<td>azidothymidine (the chemical name) or zidovudine, the generic name for the same drug</td>
</tr>
<tr>
<td>CDC</td>
<td>United States Centers for Disease Control and Prevention</td>
</tr>
<tr>
<td>CMV</td>
<td>cytomegalovirus</td>
</tr>
<tr>
<td>d4T</td>
<td>stavudine</td>
</tr>
<tr>
<td>ddl</td>
<td>didanosine</td>
</tr>
<tr>
<td>DLV</td>
<td>delavirdine</td>
</tr>
<tr>
<td>DOT</td>
<td>direct observed therapy</td>
</tr>
<tr>
<td>DS</td>
<td>double strength</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>enzyme-linked immunosorbent assay</td>
</tr>
<tr>
<td>FTC</td>
<td>efavirenz</td>
</tr>
<tr>
<td>HAART</td>
<td>highly active antiretroviral therapy</td>
</tr>
<tr>
<td>HIV</td>
<td>human immunodeficiency virus</td>
</tr>
<tr>
<td>IDV</td>
<td>indinavir</td>
</tr>
<tr>
<td>INH</td>
<td>isoniazid</td>
</tr>
<tr>
<td>MAC</td>
<td><em>Mycobacterium avium complex</em></td>
</tr>
<tr>
<td>MCH</td>
<td>maternal and child health</td>
</tr>
<tr>
<td>MTCT</td>
<td>mother-to-child transmission of HIV</td>
</tr>
<tr>
<td>NFV</td>
<td>nelfinavir</td>
</tr>
<tr>
<td>NGO</td>
<td>nongovernmental organisation</td>
</tr>
<tr>
<td>NVP</td>
<td>nevirapine</td>
</tr>
<tr>
<td>OI</td>
<td>opportunistic infection</td>
</tr>
<tr>
<td>PCP</td>
<td><em>Pneumocystis pneumonia</em></td>
</tr>
<tr>
<td>PEP</td>
<td>post-exposure prophylaxis</td>
</tr>
<tr>
<td>PLWHA</td>
<td>people or person living with HIV/AIDS</td>
</tr>
<tr>
<td>PMTCT</td>
<td>prevention of mother-to-child transmission of HIV</td>
</tr>
<tr>
<td>RTV</td>
<td>ritonavir</td>
</tr>
<tr>
<td>SQV</td>
<td>saquinavir</td>
</tr>
<tr>
<td>T-20</td>
<td>enfuvirtide</td>
</tr>
<tr>
<td>TDF</td>
<td>tenofovir</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>

*National Guidelines for Management of HIV-Infected and HIV-Exposed Adults and Children*
The field of human immunodeficiency virus (HIV) infection management is rapidly evolving, with improved diagnostic methods, more effective treatment strategies, and stricter monitoring requirements. One of the goals of providing these guidelines is to ensure that antiretroviral (ARV) therapy in Guyana is based on scientific evidence and is “state-of-the art,” thereby providing standard protocols that support effective treatment and prevent the emergence of drug-resistant strains of HIV.

This is the first revision of the guidelines published in 2004-5 and the changes reflect progress in science, evidence base, harmonization with WHO guidance and adaptation to current health systems. Every healthcare worker is encouraged to consult the most recent version of this document when seeking information on the management of patients who are HIV-exposed or HIV-infected.
OBJECTIVES

The objectives of this document are to:

1. Provide guidelines to standardize the management of infants, children, adolescents, and adults in Guyana who are HIV-infected.

2. Ensure that ARV treatment protocols in Guyana reflect international standards of practice.

3. Present simplified algorithms for the counseling, assessment, diagnosis, treatment, clinical and laboratory monitoring, and follow-up of adults and children who are HIV-infected.

4. Facilitate the use of a public health approach to implementing highly active antiretroviral therapy (HAART).

5. Offer strategies for linking the PMTCT and tuberculosis programmes with the ARV programme.


7. Provide simplified guidelines for prophylaxis and management of opportunistic infections (OIs).

8. Strategise effective and known antiretroviral therapy models to the Guyana situation, considering the realities of challenges in human resources, health system infrastructure, socioeconomic status, and local availability of antiretrovirals.

The August 2006 revision is based on:

1. Simplifying the regimens and protocols and integrating HIV into primary Health care.

2. Aligning treatment in Guyana with recent evidence-based strategies / approaches based on current science and practice.

3. To employ a public health / health systems approach in care for HIV infected patients

4. Harmonization with CAREC / WHO recent guidelines

5. Proposing cost effective and sustainable interventions
PRINCIPLES OF ANTIRETROVIRAL THERAPY

The introduction of antiretroviral drugs has revolutionised the management of HIV-infected patients and reduced morbidity and mortality. The following principles guide the use of antiretroviral therapy:

- HIV is incurable using currently available antiretroviral drugs. Since HIV viral DNA is integrated into inactive memory T-cells and is basically unrecognisable by the immune system, it is estimated that the natural decay of these infected memory cells takes more than 70 years.

- CD4 lymphocyte count and viral load estimations should be used to monitor the progress of HIV infection and response to treatment.

- Absolute CD4 lymphocyte count should be used in children older than six (6) years and in adolescents and adults. Children less than six (6) years should be monitored immunologically using CD4 percentage (CD4%).

- Optimal suppression of viral replication should, in most cases, be achieved by Highly Active Antiretroviral Therapy (HAART), a “state-of-the-art” regimen that is a combination of three (3) or more ARV drugs given in appropriate combinations.

- The effectiveness of HAART is determined by
  - appropriate ARV drug combination
  - adherence to therapy
  - absence of severe immune suppression at initiation of therapy, and
  - management of drug toxicities and interactions.

- HAART is hardly ever an emergency and life-long ARV therapy should seldom be started without
  - assurance of adherence readiness and support
  - a strategic follow-up plan
  - regular counselling and psychosocial support

- Patient preparation and participation are critical to success. (See section on adherence strategies.)

- Delay or withhold the initiation of HAART if there are medical or laboratory contraindications.

- Monotherapy SHOULD NOT BE USED IN treatment of chronic HIV infection. Single dose Nevirapine can only be used in case of a pregnant woman without prior ART experience who is diagnosed HIV positive for the first time in the labour room and who is in established labor and to HIV exposed infants brought to hospital within 72 hours of birth if their mothers did not receive any ARVs during pregnancy. However the current revision suggest use of HAART after the first trimester in sites with access to HAART and CD4 testing.

- Bi-therapy should ideally not be used except in special circumstances, in PMTCT (where AZT and Single dose Nevirapine can be used.)

- Protease inhibitor-based regimens should not be used as first-line regimens in resource-constrained settings because of concerns about cost, preserving future treatment options, maintaining the “cold chain,” and pill burden.
Part 1 – Antiretroviral Therapy for Adolescents and Adults

- ARV drugs, particularly protease inhibitors have multiple interactions with other medications and should not be prescribed without a careful review of each patient’s current drug history, including herbal and traditional agents.
- The recommended first-line drugs in Guyana do not have stringent dietary rules, but patients taking some second-line medications will need to follow specific rules with regard to the timing of medicines and food.
- A single drug should not be added or substituted in a failing regimen except where HIV genotypic resistance testing is available.
- As often as possible, an active opportunistic infection should be excluded and managed before initiation of HAART to avoid paradoxical worsening of the patient’s clinical condition. To minimise likelihood of severe toxicities necessitating regimen switches, drugs that antagonise each other or worsen the toxicity profile should not be used together.
- If one of the drugs in a regimen is to be discontinued, it is recommended that the entire regimen be stopped. The only exception to this is when stopping nevirapine due to toxicity. In this case, continue the other drugs for one week for nevirapine washout. The long half-life of nevirapine could lead to effective monotherapy and possible development of resistance. Efavirenz, which is also an NNRTI, may also need a wash-out period.
- Stavudine use is discouraged due to issues with long-term toxicity.

**Diagnosis of HIV infection in adolescents and adults**

The gold standard for confirming HIV infection is the Western Blot method. Due to cost, low overall numbers of HIV-infected people, and quality assurance issues, Western Blot testing is not routinely available in Guyana. Instead, HIV infection in adolescents and adults is diagnosed with two antibody tests:

*Enzyme-linked immunosorbent assay (ELISA)*
This involves sequential testing using Murex™ and Vironostika™ test kits according to the validated algorithm (Appendix 1–A).

*Rapid testing*
Guyana uses the parallel HIV rapid testing algorithm with the Determine™ and Unigold™ test kits. Concordant results are reported. Discordant results are verified with Statpak™ as the tie-breaker test. The algorithm is in Appendix 1–B.
Classification systems

The World Health Organization (WHO) and Centers for Disease Control (CDC) classification systems provide a framework for treatment and follow-up care of HIV-infected patients. Both classification systems are based on clinical symptoms and immunologic tests and are included in Appendices 1–C and 1–D. *In Guyana, the WHO system is commonly used (Appendix 1–C).* The WHO staging system for children has been revised to include 4 stages instead of three.
ANTIRETROVIRAL DRUGS

There are four major classes of approved ARV drugs: nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), and entry inhibitors.

Nucleoside reverse transcriptase inhibitors (NRTIs)

These drugs inhibit the transcription of viral RNA into DNA, thereby interfering with viral replication (Table 1.1).

Table 1.1 NRTIs: dosages, dietary rules, selected adverse effects, and toxicities

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Dietary rules</th>
<th>Selected adverse effects, toxicities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zidovudine (AZT)</td>
<td>300 mg twice daily</td>
<td>None</td>
<td>Anaemia, neutropoenia</td>
</tr>
<tr>
<td>Stavudine (d4T)</td>
<td>&gt;60 kg, 40 mg &lt;60 kg, 30 mg twice daily</td>
<td>None</td>
<td>Peripheral neuropathy, pancreatitis</td>
</tr>
<tr>
<td>Lamivudine (3TC)</td>
<td>150 mg twice daily</td>
<td>None</td>
<td>Peripheral neuropathy, lactic acidosis (rare)</td>
</tr>
<tr>
<td>Didanosine (ddI)</td>
<td>&gt;60 kg, 400 mg once daily &lt;60 kg, 250 mg once daily</td>
<td>Take on empty stomach</td>
<td>Peripheral neuropathy, lactic acidosis, (rare)</td>
</tr>
<tr>
<td>Abacavir (ABC)</td>
<td>300 mg twice daily</td>
<td>None</td>
<td>Hypersensitivity reaction</td>
</tr>
<tr>
<td>Tenofovir (TDF)†§</td>
<td>300 mg once daily (See Table 1.2 below.)</td>
<td>None</td>
<td>Renal toxicity</td>
</tr>
<tr>
<td>Emtricitabine (FTC)</td>
<td>200 mg once daily</td>
<td>None</td>
<td>Skin discolouration</td>
</tr>
</tbody>
</table>

* The dose of tenofovir needs to be reduced to 250 mg once daily when given with didanosine.
† This dose applies to the extended-release formulation.
§ Concurrent use of TDF and DDI is discouraged Tenofovir also requires dose reduction in patients with compromised renal function. (See Table 1.2 below.)

Table 1.2 Dosing intervals for tenofovir in patients with compromised renal function

<table>
<thead>
<tr>
<th>Creatinine clearance (mL/min)*</th>
<th>Hemodialysis patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–49</td>
<td>Every 48 hr</td>
</tr>
<tr>
<td>10–29</td>
<td>Every 72–96 hr</td>
</tr>
<tr>
<td>&lt;10†</td>
<td>Every 7 days</td>
</tr>
</tbody>
</table>

* Calculated using ideal (lean) body weight.
† No pharmacokinetic (PK) data are available in patients with creatinine clearance (CLcr) <10 mL/min who are not maintained on HD; recommendation is based on extrapolation of the AUC and CLcr relationship in subjects with CLcr of 10–29 mL/min.
‡‡ Generally, once weekly dosing assuming three hemodialysis sessions per week of approximately 4 hours’ duration
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)

These drugs are chemically different from the NRTIs but also inhibit transcription of viral RNA into DNA in a competitive manner (Table 1.3).

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Dietary rules</th>
<th>Selected adverse effects, toxicities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nevirapine (NVP)</td>
<td>200 mg once daily for 14 days, then 200 mg twice daily</td>
<td>None</td>
<td>Rash, hepatotoxicity</td>
</tr>
<tr>
<td>Efavirenz (EFV)</td>
<td>600 mg once daily, preferably at night</td>
<td>Do not take with high-fat meals</td>
<td>Teratogenic, CNS effects, rash</td>
</tr>
</tbody>
</table>

Protease Inhibitors (PIs)

These drugs block protease, an enzyme that the HIV requires for replication. The protease enzyme is responsible for cutting long amino acid chains into smaller proteins (Table 1.4).

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Dietary rules</th>
<th>Selected adverse effects, toxicities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indinavir (IDV) OR Indinavir + ritonavir (IDV/r)</td>
<td>800 mg thrice daily OR 800 mg indinavir when boosted with 100 mg ritonavir twice daily</td>
<td>Drink plenty of water—at least 6 glasses every 24 hrs</td>
<td>Renal stones, metabolic changes</td>
</tr>
<tr>
<td>Nelfinavir (NFV)</td>
<td>1250 mg twice daily</td>
<td>Take with food</td>
<td>Metabolic change, diarrhoea</td>
</tr>
<tr>
<td>Lopinavir + ritonavir (LPV/r)</td>
<td>133.3 mg/33.3 mg [3 capsules] twice daily</td>
<td>None</td>
<td>Metabolic changes</td>
</tr>
<tr>
<td>Saquinavir (SQV) OR Saquinavir + ritonavir (SQV/r)</td>
<td>1200 mg thrice daily OR 1000 mg saquinavir when boosted with 100 mg ritonavir twice daily</td>
<td>None</td>
<td>Metabolic changes</td>
</tr>
<tr>
<td>Atazanavir (ATV)</td>
<td>400 mg once daily</td>
<td>Take with food</td>
<td>Hyperbilirubinaemia</td>
</tr>
</tbody>
</table>


Entry inhibitors

These drugs disrupt the interaction between the HIV virus and the cell surface, preventing the fusion of the HIV virus to the cell. They are a new class of drugs not available in Guyana. Enfuvirtide (T-20, Fuzeon®) is the only drug in this class currently approved for use in clinical practice.
The goals of antiretroviral therapy in adolescents and adults include:

- Maximising HIV suppression
- Preserving and restoring immune function
- Reducing HIV-related morbidity and mortality
- Decreasing risk of HIV transmission
- Improving quality of life

Meeting these goals is possible only when the following conditions are satisfied:

- Uninterrupted supply of drugs
- Laboratory support for clinical monitoring of treatment
- Support system for counselling, adherence, and follow-up
- Patient readiness and ability to adhere to therapy
- Management of drug side effects, toxicities, and interactions
- Prevention and, when necessary, management of concomitant opportunistic infections
ELIGIBILITY CRITERIA—INDICATIONS FOR ANTIRETROVIRAL THERAPY

NOTE: The criteria below have been adapted from the WHO (Appendix 1-C) and CDC guidelines (Appendix 1-D).

In view of the availability of CD4 testing in public hospitals in Guyana, adolescents and adults should begin receiving HAART when:

They have documented HIV infection
AND
- CD4 lymphocyte count <350 cells/mm$^3$ irrespective of WHO or CDC staging$^1$

OR
- WHO Stage 3 or 4 or CDC Stage B or C (symptomatic disease) irrespective of CD4 lymphocyte count

$^1$ Considering the occasional variability of the CD4 lymphocyte count, a CD4 test may be repeated in an asymptomatic (WHO Stage 1) patient before starting HAART, especially if there was a concomitant illness at the time of the previous CD4 test.

NOTE: In contrast to earlier strategies of initiating ART at CD4 lymphocyte count<200/mm$^3$, increased risk of disease progression, drug toxicity and poor response in patients with CD4 lymphocyte count <200/mm$^3$ has led to increasing the cut off for initiation to CD4 lymphocyte count of 350/mm$^3$. However, using nevirapine in women with CD4 count>250/mm$^3$ and men with CD4 lymphocyte count>400/mm$^3$ is not recommended to avoid the risk of fatal hepatotoxicity. Despite these recommendations, the clinician’s discretion should guide ART initiation in patients with a CD4 lymphocyte count closer to 350/mm$^3$. Patient readiness and commitment to start and continue therapy should help guide decision making.

Before initiating HAART in any patient, the physician should document HIV infection and assess the patient with the following six-questions (Appendix 1–E):

1. Does the patient who is HIV-infected have one or more of these medical indications for HAART?
   - CD4 lymphocyte count <350/mm$^3$ irrespective of symptoms
   - WHO Stage 3 or IV disease irrespective of CD4 lymphocyte count
   - Pregnant woman with CD4 lymphocyte count <350/mm$^3$

2. Is there a medical contraindication to or reason to defer the first-line regimen?
   - Renal insufficiency (creatinine >3x upper limit of normal [ULN])
   - Hepatic insufficiency (Liver function tests > 5x ULN)
   - Severe anaemia (Hb <6.9g/dl)*
   - Severe neutropenia (absolute neutrophil count <749 mm)*
   - Severe thrombocytopenia (platelets <49,999 mm)*
   - Current use of anti-TB medications†

3. Is there a current non-medical contraindication to the patient’s taking ARVs?
   - Denial of HIV status and ambivalence about starting lifelong therapy
   - Current use of herbal and traditional remedies that may react with ARVs
   - Ongoing serious substance abuse (alcohol, injection drugs, etc)
   - Psychiatric illness
   - Unstable social situation (eg, homeless, no social support, inability to travel to healthcare appointments)
   - Recent history of non-adherence
4. **Does the patient have an active opportunistic infection?**
   - Can TB be excluded? (symptoms, chest x-ray, sputum AFB culture, PPD)
   - Can CMV retinitis be excluded with an ophthalmologic exam?

5. **Is the patient pregnant?**
   - Administer pregnancy test. If positive, do not prescribe efavirenz (teratogenicity), ddI/d4T (risk of fatal lactic acidosis) or abacavir (safety in pregnancy unknown).

6. **Are adherence, clinical monitoring, and follow-up possible?**
   - Patient is motivated, understands the need for long-term medication.
   - Patient has attended 2–3 consecutive appointments.
   - Patient has discussed HIV disclosure with healthcare worker.
   - Patient is willing to have a drug adherence partner.
   - Patient lives within reasonable distance of an HIV treatment site

   * This is a relative contraindication and applies only when AZT is taken instead of d4T.
   † If nevirapine is used as the first-line drug, the risk of a drug interaction with rifampicin exists. Instead, use efavirenz.

**Guyana’s guiding principle for initiating ARV therapy**

*The guiding principle in Guyana is to begin therapy—according to WHO and CDC guidelines—when patients have AIDS-related illnesses or are at high risk of developing them due to a compromised immune system.*

**NOTE:** When pulmonary tuberculosis (WHO Stage 3) is diagnosed in a patient who is HIV-infected, the patient is eligible for ARV therapy. However, timing of initiation of HAART will depend on the current CD4 lymphocyte count. If the CD4 lymphocyte count is >350/mm³, tuberculosis treatment should be completed and patient reevaluated (See Part 3 about HIV-TB co-infection management.)
RECOMMENDED FIRST-LINE AND ALTERNATE FIRST-LINE ANTIRETROVIRAL REGIMENS IN GUYANA

The recommended first-line drug regimens consist of a combination of two (2) NRTIs and an NNRTI. There are also alternate first-line drugs for patients who for various reasons cannot receive the recommended first-line combination regimen.

Considerations when selecting HAART regimens in Guyana include:
- Potency
- Side effects profile
- Laboratory monitoring requirements
- Preservation of future treatment options
- Pill burden
- Likelihood of co-existing conditions
- Absence of known teratogenicity
- Potential drug interactions (Table 1.5) (Appendix 1-F)
- Cost*
- Refrigeration requirements

*Health care in Guyana is currently free in public facilities. HIV care is also free at both public and private HIV treatment sites.

First-line regimen

#Tenofovir (TDF) + emtricitabine (FTC) or lamivudine (3TC) + nevirapine (NVP)*

Taking nevirapine 200 mg once daily for 2 weeks (lead-in period)—and increasing the dose to 200 mg twice daily if no side effects are noted—is the standard of care in the Guyana National ARV Programme.

#TDF and FTC are available as Truvada.®

Nevirapine should not be taken by patients receiving any regimen containing rifampicin to treat TB, because rifampicin reduces serum levels of nevirapine. In these patients, efavirenz or a triple nucleoside regimen should be used. Nevirapine is not recommended for patients with a high CD4 lymphocyte count, especially for pregnant women with CD4 lymphocyte count >250/mm³. In these cases, an alternate first line regimen should be used.

Alternate first-line regimens

Recommended regimens in order of priority, depending on availability:
- TDF + FTC or 3TC + EFV
- TDF + FTC or 3TC +NVP
- *AZT + 3TC + NVP or EFV
- ABC + 3TC + NVP or EFV
- †d4T + 3TC + NVP or EFV
- AZT + 3TC + TDF

* Special care should be taken in patients with borderline hemoglobin who start on AZT-based regimens. There is the risk of anemia in such patients, especially if they have advanced immune suppression.
†Stavudine is not recommended due to severe long term toxicity (mitochondrial toxicity and lipodystrophy).

NOTE: The NRTI backbone of tenofovir and emtricitabine is the first line regimen of choice because of its high potency, minimal toxicity, good resistance profile, ease of administration, dual effect on hepatitis B, and preservation of future treatment options.
### Table 1.5 Drug-drug interactions

<table>
<thead>
<tr>
<th>Drug category</th>
<th>Calcium channel blocker</th>
<th>Cardiac</th>
<th>Lipid lowering agents</th>
<th>Anti-mycobacterial</th>
<th>Anti-histamine</th>
<th>Gastro-intestinal drugs</th>
<th>Neuroleptic</th>
<th>Psychotropic</th>
<th>Ergot Alkaloids</th>
<th>Herbs</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indinavir (IDV)</td>
<td>amiodarone</td>
<td>simvastatin</td>
<td>rifampin</td>
<td>rifapentine</td>
<td>astemizole</td>
<td>terfenadine</td>
<td>cisapride</td>
<td>pimozide</td>
<td>midozolam triazolam</td>
<td>St John's Wort</td>
<td>atazanavir</td>
</tr>
<tr>
<td>Ritonavir (RTV)</td>
<td>bepridil</td>
<td>flecainide</td>
<td>propafenone</td>
<td>quinidine</td>
<td>simvastatin</td>
<td>rifapentine</td>
<td>astemizole</td>
<td>terfenadine</td>
<td>cisapride</td>
<td>pimozide</td>
<td>midozolam triazolam</td>
</tr>
<tr>
<td>Saquinavir (SQV)</td>
<td>None</td>
<td>simvastatin</td>
<td>rifampin</td>
<td>rifabutin</td>
<td>rifapentine</td>
<td>astemizole</td>
<td>terfenadine</td>
<td>cisapride</td>
<td>pimozide</td>
<td>midozolam triazolam</td>
<td>St John's Wort</td>
</tr>
<tr>
<td>Nelfinavir (NFV)</td>
<td>None</td>
<td>simvastatin</td>
<td>rifampin</td>
<td>rifapentine</td>
<td>astemizole</td>
<td>terfenadine</td>
<td>cisapride</td>
<td>pimozide</td>
<td>midozolam triazolam</td>
<td>St John's Wort</td>
<td></td>
</tr>
<tr>
<td>Lopinavir + ritonavir (LPV + RTV)</td>
<td>flecainide</td>
<td>propafenone</td>
<td>simvastatin</td>
<td>rifampin</td>
<td>rifapentine</td>
<td>astemizole</td>
<td>terfenadine</td>
<td>cisapride</td>
<td>pimozide</td>
<td>midozolam triazolam</td>
<td>St John's Wort</td>
</tr>
<tr>
<td>Atazanavir (ATV)</td>
<td>bepridil</td>
<td>simvastatin</td>
<td>rifampin</td>
<td>rifapentine</td>
<td>astemizole</td>
<td>terfenadine</td>
<td>cisapride</td>
<td>proton pump inhibitors</td>
<td>pimozide</td>
<td>midozolam triazolam</td>
<td>St John's Wort</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>None</td>
<td>none</td>
<td>none</td>
<td>rifapentine</td>
<td>astemizole</td>
<td>terfenadine</td>
<td>cisapride</td>
<td>none</td>
<td>midozolam triazolam</td>
<td>midozolam triazolam</td>
<td>Voriconazole</td>
</tr>
</tbody>
</table>
Cautions when using ARVs

NRTIs
- Zidovudine and stavudine should never be used together because of proven antagonism.
- Patients with severe peripheral neuropathy or a history of severe pancreatitis should receive zidovudine instead of stavudine.
- Zidovudine should not be used in patients with severe anaemia or neutropoenia.
- Combining stavudine and didanosine, in particular, should be avoided. Lactic acidosis and hepatotoxicity have been reported in pregnant women taking stavudine and didanosine. The risk of peripheral neuropathy with this combination is particularly high.
- Tenofovir and didanosine ideally should not be used together because of antagonism and a resultant decline in CD4 lymphocyte count.

NNRTIs
- *Efavirenz is contraindicated in pregnant women.* The drug should be used only when women of childbearing age are using effective contraceptive methods.
- Women who are HIV-infected and who become pregnant while taking efavirenz should be counselled about the risk of teratogenicity in their offspring. Their regimen should then be changed to a “pregnancy-friendly” regimen.
- Efavirenz is recommended for use in patients with TB co-infection who are receiving rifampicin.
- Nevirapine can be taken safely during pregnancy and is available in fixed-dose combinations. However it should be avoided in pregnant women with CD4 lymphocyte count >250/mm$^3$.
- *Nevirapine cannot be taken by patients receiving any regimen containing rifampicin to treat TB.*
- In Guyana, there is a practice of administering an extra dose of nevirapine to patients taking rifampicin and nevirapine to compensate for the 37% reduction in nevirapine levels. *This practice is not supported by any scientific evidence and should be discouraged until additional scientific evidence is obtained.*

PIs
- In resource-constrained settings, protease inhibitor-based regimens generally are not recommended as first-line, in spite of their potency. The following factors all play a role in this determination: high cost; high pill burden; food and water requirements; significant drug interactions with TB drugs, resulting metabolic abnormalities; the need for a “functioning cold chain” with ritonavir-boosted regimens, and the lack of co-formulations with NRTIs.
- A PI could be used as a first-line drug in these instances:
  - If the patient reacts severely to nevirapine (eg, grade 4 rash, Stevens-Johnson syndrome, toxic epidermal necrolysis), it is inadvisable to use efavirenz.
  - Viral types with known insensitivity to NNRTIs (HIV-2 and HIV-1 group O). Note that nelfinavir is not effective against HIV-2.
  - In a pregnant woman with CD4 lymphocyte count >250/mm3 in whom nevirapine cannot be used
  - In pregnant women who have had single dose Nevirapine in a previous PMTCT regimen in absence of resistance testing. This is more important if the woman needs HAART within 6 months of previous use of single dose Nevirapine.
Part 1 – Antiretroviral Therapy for Adolescents and Adults

Figure 1.1 Algorithm for HAART in adolescents and adults

Documented diagnosis of HIV infection

Baseline CD4 lymphocyte count determines frequency of testing (See section on CD4 testing schedule)

History, physical exam, and laboratory testing, including CD4 lymphocyte count

Eligibility criteria for HAART:
- WHO Stage 3 or IV or CDC Stage B or C
- CD4 lymphocyte count <350 mm$^3$

TB-HIV co-infected (active TB)
- Abnormal LFTs
- Normal creatinine
- No neuropathy

Active TB ruled out
- Normal LFTs & creatinine
- Neuropathy **
- Not anaemic

Active TB ruled out
- Normal LFTs & creatinine
- Anaemic (Hb<8g/dl)

TDF+3TC or FTC+ EFV

AZT or TDF + 3TC or FTC + NVP

TDF + 3TC or FTC NVP

- Regularly scheduled adherence counselling for those receiving therapy
- Clinical and laboratory monitoring and follow-up
- Referral to support group and services
- Nutritional counselling and support

KEY: LFT = liver function test, TB = tuberculosis, EFV = efavirenz, d4T = stavudine, 3TC = lamivudine, NVP= nevirapine, ZDV = zidovudine *HAART should be deferred if LFTS are >3ULN and the cause managed accordingly.
Regular monitoring is an essential component of effective ARV treatment, permitting early detection of adverse events, ongoing reinforcement of patient adherence, and periodic assessment of treatment efficacy.

Clinical monitoring

The first step in clinical monitoring is to establish a baseline, which should include:

- Detailed medical history
  - Essential demographic characteristics
  - Current and chronic illnesses
  - History of drug allergies
  - Hospitalisations
  - Date of confirmed diagnosis of HIV
  - Current medications, including traditional medications
  - History of ARV therapy (HAART, prophylaxis for PMTCT, etc)
  - Date of last menstrual period (for women of childbearing age), history of contraceptive use

- Detailed physical examination
  - Complete physical exam including nervous system and ophthalmologic exam, if possible
  - Exclude current active opportunistic infections

- Detailed nutrition assessment and counselling

- Detailed adherence assessment

- Detailed family history, which should includes filling the patient locator form, family members, next of kin, housing conditions, and treatment buddy

- Discuss ARV adverse events in detail (short-term and long-term)

NOTE: Clinical monitoring should be repeated at every follow-up visit.
Laboratory monitoring

Laboratory monitoring is a crucial component of administering effective and safe ARV therapy. Tests should be performed at baseline, before the initiation of HAART, and at follow-up visits as indicated below. (Table 1.6) (See Appendix 1–G.)

Table 1.6 Laboratory monitoring schedule and follow-up visits for ARV therapy

<table>
<thead>
<tr>
<th>Test</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV test</td>
<td>Baseline</td>
</tr>
<tr>
<td>CD4 lymphocyte count*</td>
<td>Baseline and every 3–6 months</td>
</tr>
<tr>
<td>CBC and differential*</td>
<td>Baseline, 1 month, and every 3 months</td>
</tr>
<tr>
<td>VDRL</td>
<td>Baseline and annually</td>
</tr>
<tr>
<td>HBsAg</td>
<td>Baseline</td>
</tr>
<tr>
<td>Pregnancy*</td>
<td>Baseline (as indicated)</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>Baseline (as indicated)</td>
</tr>
<tr>
<td>Liver function test*</td>
<td>Baseline, 2 weeks, 1 month, and every 3 months</td>
</tr>
<tr>
<td>Renal function test</td>
<td>Baseline and every 6 months</td>
</tr>
<tr>
<td>Visual Inspection with Acetic Acid (VIA)</td>
<td>Baseline and annually. Abnormal lesions should be referred for PAP smear</td>
</tr>
<tr>
<td>Pap smear (in those with abnormal VIA)</td>
<td>Baseline and annually if normal; every 6 months if abnormal</td>
</tr>
<tr>
<td>Urine dipstick</td>
<td>Baseline and every 6 months</td>
</tr>
<tr>
<td>PPD*</td>
<td>Baseline and annually</td>
</tr>
<tr>
<td>Toxoplasmosis immunoglobulin (IgG)</td>
<td>Baseline and repeat if CD4 lymphocyte count &lt;100 cells/mm³</td>
</tr>
<tr>
<td>Serum amylase, lipase</td>
<td>Baseline and if symptomatic</td>
</tr>
<tr>
<td>Serum glucose</td>
<td>Baseline and every 6–9 months for patients taking PIs</td>
</tr>
<tr>
<td>Serum lipids</td>
<td>Baseline and every 6–9 months for patients with abnormal baseline values</td>
</tr>
<tr>
<td>Optional tests</td>
<td></td>
</tr>
<tr>
<td>Serum lactate</td>
<td>When lactic acidosis is suspected</td>
</tr>
<tr>
<td>Viral load</td>
<td>Baseline and every 3 months, when test becomes available in Guyana</td>
</tr>
</tbody>
</table>

*Minimum required test

VDRL = Venereal Disease Research Lab test, HBsAg = hepatitis B surface antigen, ALT = alanine aminotransferase, AST = aspartate aminotransferase, bil = bilirubin, PPD = purified protein derivate, IgG = immunoglobulin G

Additional baseline tests are indicated for patients starting a PI or a second-line agent. These tests include serum glucose, serum amylase, serum lipid profile, etc. Other tests may be ordered based on other clinical symptoms or suspected drug toxicity.
Part 1 – Antiretroviral Therapy for Adolescents and Adults

Before initiating therapy

The baseline laboratory tests recommended before initiating HAART include:
- Documentation of a confirmed positive HIV antibody test result
- CD4 lymphocyte count (Absence of this result should not delay HAART in symptomatic but motivated patients.). Those in WHO clinical stage 3 or IV can start ART in absence of CD4 testing.
- Complete blood count (CBC)
- Liver function test (LFTs)
- Pregnancy test in women of childbearing age
- PPD
- Chest x-ray

CD4 lymphocyte counts
CD4 lymphocyte counts are useful for assessing immunologic function, determining need to initiate opportunistic infection prophylaxis, determining eligibility for HAART, assessing the effectiveness of HAART, and diagnosing immunologic failure. (See “Indications for Changing ARV Drug Regimen” below.)

An increase in the CD4 lymphocyte count is expected in an ARV-naïve patient who is adhering to the treatment regimen.

<table>
<thead>
<tr>
<th>CD4 testing schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 lymphocyte count &lt;350/mm³ = eligible for HAART</td>
</tr>
<tr>
<td>CD4 lymphocyte count &gt;350-400/mm³ = repeat test every 3 months</td>
</tr>
<tr>
<td>CD4 lymphocyte count 401–600/mm³ = repeat test every 6 months</td>
</tr>
<tr>
<td>CD4 lymphocyte count &gt;601/mm³ = repeat test every 9 months to 1 year</td>
</tr>
</tbody>
</table>

Plasma HIV-RNA levels (viral load testing)
Plasma viral load testing is not yet available in the public sector in Guyana but is a very useful tool for assessing response to HAART and detecting virologic failure.* In most resource-constrained settings, viral load testing is not available and is not required for initiating HAART.

Because viral load testing is not yet readily in the public sector in Guyana, immunologic and clinical parameters will be used to assess treatment response and failure.

Where such testing is available, HIV-RNA results should show that viral load has decreased by at least one log (10-fold) in 4 weeks and should be undetectable at 3 – 6 months in patients who are adhering to the ARV regimen >95% of the time. Before a diagnosis of virologic failure is made, which necessitates a change in therapy, the clinical and immunological profile should be reviewed by an experienced HIV clinician or discussed by a team of physicians.
Clinic visit schedule

- Pre-initiation: to assess support for and readiness to begin therapy, to provide for intensive education for patient and adherence* partner
- Initiation
- Two weeks post-initiation to assess short term toxicity
- One month post-initiation
- Monthly visits for drug refills and adherence counselling
- Physician visit every month for drug refills
- Subsequent visits should be scheduled based on treatment response, adherence assessment, signs and symptoms of disease, and adverse events. Longer intervals (2–3 months) can be given for patients who are stable and have a history of excellent adherence.

*An adherence partner is anyone selected by the index patient to assist him or her with drug adherence and social support. Ideally, it should be the partner or a member of the immediate family but could also be a friend, a coworker, etc. Whoever is chosen must be aware of the index patient’s diagnosis, and be willing to come for some clinic visits with the patient and to help support the patient with adherence to the medication.
Some side effects are mild and/or transient, while others may require supportive therapy, more frequent monitoring, or even drug withdrawal. When significant adverse events are present, a drug is considered toxic. Symptoms and laboratory investigations help determine when the effects of an ARV are toxic.

- Some of the side effects are common to all drugs in a class, while others may be specific to one drug.
- When toxicity appears to be caused by a specific ARV, a single-drug substitution is possible. In some cases, the entire regimen may need to be changed (Appendix 1-H).

Toxicities may be potentially fatal, disabling, or long-term (Table 1.7) (Appendix I).

Table 1.7 Antiretroviral drug toxicities

<table>
<thead>
<tr>
<th>Type</th>
<th>Drug</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potentially fatal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>ddI, d4T</td>
<td>Stop drug immediately. Change therapy.</td>
</tr>
<tr>
<td>Hypersensitivity reactions</td>
<td>ABC</td>
<td>Stop drug immediately. Do not re-challenge. Change therapy.</td>
</tr>
<tr>
<td>Toxic epidermal necrolysis</td>
<td>NVP</td>
<td>Stop drug immediately. Change therapy.</td>
</tr>
<tr>
<td>Stevens-Johnson syndrome</td>
<td>NVP</td>
<td>Stop drug immediately. Change therapy.</td>
</tr>
<tr>
<td>Lactic acidosis</td>
<td>All NRTIs</td>
<td>Stop drug immediately. Change therapy.</td>
</tr>
<tr>
<td>Psychosis, major depression</td>
<td>EFV*</td>
<td>Stop drug immediately. Change therapy.</td>
</tr>
<tr>
<td>Acute hepatotoxicity</td>
<td>NVP*</td>
<td>Manage according to criteria below.</td>
</tr>
<tr>
<td>Haematologic toxicity</td>
<td>AZT</td>
<td></td>
</tr>
<tr>
<td>Disabling</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>ddI, d4T</td>
<td>Stop drug immediately. Change therapy.</td>
</tr>
<tr>
<td>Hepatotoxicity</td>
<td>NNRTIs, PIs</td>
<td>Manage according to criteria below.</td>
</tr>
<tr>
<td>Long-term</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipoatrophy</td>
<td>NRTIs</td>
<td>Patient needs to be referred to an experienced HIV clinician.</td>
</tr>
<tr>
<td>Lipodystrophy</td>
<td>PIs, all NRTIs</td>
<td></td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>PIs, all NRTIs, EFV</td>
<td></td>
</tr>
<tr>
<td>Insulin resistance</td>
<td>d4T and PIs</td>
<td></td>
</tr>
<tr>
<td>Lactic acidosis</td>
<td>All NRTIs (d4T, ddI most commonly</td>
<td>Stop drug immediately and manage accordingly.</td>
</tr>
</tbody>
</table>

*Whenever NVP or EFV is stopped, the NRTI backbone should be continued for 5–7 days to allow it to wash out given the long half life and ease of development of resistance mutations.
Clinical assessment and management of common toxicities

Nevirapine

Rash
- The most common toxicity in patients receiving nevirapine is skin rash, which is more frequent in women than men, and in patients with CD4 lymphocyte count >350 mm$^3$.
- Within 2–8 weeks of initiating therapy, rash occurs in about 20% of patients taking nevirapine and skin manifestations may be mild, moderate, or severe.
- Antihistamines, analgesics, and mild topical steroids may be used to treat rash, but responses to these medications vary.
- During the lead-in period or at full dose, nevirapine should not be discontinued for rash events that are lower than grade 3. Rash grading is as follows:
  - Grade 1 = erythema, pruritus
  - Grade 2 = diffuse maculopapular rash or dry desquamation
  - Grade 3 = vesiculation or moist desquamation or ulceration
  - Grade 4 = any one of the following: mucous membrane involvement, toxic epidermal necrolysis (TEN) or suspected Stevens-Johnson syndrome, erythema multiforme, necrosis, or exfoliative dermatitis
- 5–7% of patients may develop a toxic epidermal necrolysis or Stevens-Johnson syndrome. In these patients, nevirapine should be discontinued.

Hepatotoxicity
- Hepatotoxicity occurs most commonly with nevirapine, which should not be given to patients with moderate to severe liver dysfunction.
- Hepatotoxicity occurs most commonly during the first weeks to months of treatment.
- Nevirapine should be permanently discontinued if hepatotoxicity is grade 3 or higher (transaminases >5 times the upper limit of normal). If hepatotoxicity is grade 2 or less, increasing the dose of nevirapine should be delayed. If the dose has already been increased, the patient should be monitored very closely. Other causes of hepatotoxicity must be ruled out.
- Acute hepatotoxicity may also occur without an increase in transaminases (LFTs).
- Baseline liver function tests must be performed for all patients who will receive nevirapine. Hepatitis B surface antigen should be performed as well.
- Females, particularly pregnant females, and patients with CD4 lymphocyte counts >250/mm$^3$ are at higher risk for hepatotoxicity with nevirapine.
- Efavirenz has been successfully substituted for nevirapine after hepatotoxicity but this has to be cautiously done with careful monitoring.
- Other drugs used for HIV or HIV-related illnesses can also cause hepatitis. These include isoniazid used for prophylaxis of latent TB and indinavir, which may cause unconjugated hyperbilirubinaemia resembling Gilbert’s syndrome.

Zidovudine

Haematologic toxicity
- Zidovudine is the ARV drug that most frequently causes haematologic toxicities, including anaemia, leucopenia, lymphopenia, and thrombocytopenia.
- It is mandatory for the patient to have a baseline complete blood count (CBC) before initiating HAART with AZT.
Part 1 – Antiretroviral Therapy for Adolescents and Adults

- Anaemia should be considered in patients who develop fatigue, shortness of breath, or weakness while taking zidovudine.
- Anaemia may occur in patients who are HIV-infected as a result of:
  - decreased production: infiltration tumor, like Kaposi sarcoma; infection, like TB; parvovirus B 19; drugs like zidovudine, amphotericin B, phenytoin, cotrimoxazole; and anaemia of chronic disease
  - increased destruction like hemolysis, drugs such as the sulphonamides and dapsone
- Patients taking zidovudine should be monitored as bone marrow suppression may occur at any time but is sometimes seen within 4–6 weeks or within 4–6 months.
- If the toxicity is grade 3 and above, the drug should be discontinued immediately.
  - Grade 3 anemia = <6.9g/dl
  - Grade 3 absolute neutrophil count = <749 mm$^3$
  - Grade 3 platelets = <49,999 mm$^3$
- In case of anaemia secondary to zidovudine, stavudine may be substituted for zidovudine.

**NOTE:** Macrocytosis is almost universal while taking AZT and is not an indication to switch agents or to conduct further diagnostic evaluation. In fact, progressive macrocytosis while taking AZT is an indication that the patient is adhering to the AZT dosing.

**Stavudine, didanosine and other NRTIs**

**Lactic acidosis**

- This is a metabolic syndrome associated with all NRTIs, but most common when stavudine or didanosine are used. The risk of developing lactic acidosis is higher when NRTIs are used in combination.
- Symptoms include nausea, vomiting, abdominal pain, fatigue, weight loss, lethargy, cold extremities, stupor, or coma (Table 1.8).
- Risk factors for lactic acidosis include female gender, obesity, pregnancy, and prolonged use of NRTIs.

### Table 1.8 Symptoms and laboratory findings in lactic acidosis

<table>
<thead>
<tr>
<th>Symptoms of lactic acidosis</th>
<th>Laboratory findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea, vomiting</td>
<td>Plasma lactate level &gt;5 mmol/L</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>pH &lt;7.25 (normal = 7.38–7.42)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>HCO$_3$ &lt;21mEq/L</td>
</tr>
<tr>
<td>Lethargy, fatigue</td>
<td>Increased Creatinine phosphokinase (CPK)</td>
</tr>
<tr>
<td>Hyperventilation, cyanosis</td>
<td>Increased Anion gap</td>
</tr>
<tr>
<td>Cold extremities, stupor, coma</td>
<td>Increased Lactate dehydrogenase (LDH)</td>
</tr>
</tbody>
</table>

- Lactic acidosis should be suspected in any patient taking an NRTI with unexplained acidosis (no evidence of diabetes, renal failure, dehydration, etc).
- The suspected NRTI therapy should be discontinued immediately and supportive therapy initiated, including maintaining airway potency and oxygen delivery, monitoring heart rhythm, and providing respiratory and haemodynamic support to improve perfusion.
Part 1 – Antiretroviral Therapy for Adolescents and Adults

- Bicarbonate replacement and re-starting NRTIs are controversial, although preliminary evidence shows that substitution with tenofovir or abacavir is possible. Consultation with an HIV expert is indicated.

- Lactic acidemia resolves within 3–6 months.

- This syndrome should be familiar to HIV care providers because of its severity and high case fatality rate.

Hyperlactataemia

- About 5% of patients taking NRTIs may have asymptomatic hyperlactataemia (plasma lactate levels 2–5 mmol/L) but symptomatic lactic acidosis is rare (<0.1% of cases).

Pancreatitis

- The combined use of didanosine and stavudine is the most common cause of pancreatitis, which is associated with mitochondrial toxicity.

- Other drugs likely to cause pancreatitis include isoniazid (INH), rifampicin and, in rare cases, lamivudine. Pancreatitis may be due to HIV or other viruses such as cytomegalovirus (CMV).

- Amylase should be monitored monthly in patients taking didanosine or stavudine; expert review is warranted if levels remain above normal, and the drug should definitely be discontinued if amylase levels are higher than 2.5 times the ULN.

- Didanosine and stavudine should not be used together in pregnant women because of increased risks of pancreatitis and lactic acidosis.

- Patients who experience didanosine- or stavudine-related pancreatitis should never be re-challenged with either drug.

Peripheral neuropathy

- For patients with baseline peripheral neuropathy, d4T and ddI should not be used. Such patients may need zidovudine or tenofovir instead of d4T.

Efavirenz

Psychosis, major depression

- Efavirenz should not be given to patients with a history of psychiatric illness.

- Efavirenz should not be given to pregnant women.

Tenofovir

- Nephrotoxicity-Fanconi syndrome. Renal failure ± Fanconi syndrome. Note: Increased creatinine occurs in these settings,

- Presents as hypophosphophatemia, glycosuria, hypokalemia, non-anion gap metabolic acidosis occurring primarily in patients who have inadequate dose adjustment of TDF with baseline renal dysfunction.

- Urinalysis and creatinine or BUN should be monitored at 3–6 month intervals. If possible, monitor serum K and PO4.

- Management is supportive. Discontinue TDF.

Other drugs

Other drugs used for HIV and HIV-related illnesses may cause hepatitis. These include isoniazid, which is given for prophylaxis in patients with latent TB, and indinavir, which may cause unconjugated bilirubinaemia resembling Gilbert’s syndrome.
Part 1 – Antiretroviral Therapy for Adolescents and Adults

IMMUNE RECONSTITUTION SYNDROME

Infrequently, when a patient who is HIV-infected begins HAART, a subclinical infection becomes reactivated. For example with many OIs, including TB, there may be a transient worsening of the infection 2–3 weeks after beginning ARV therapy. This is referred to as the immune reconstitution syndrome, and is a paradoxical deterioration in clinical status caused by the recovery of the immune system during HAART.

Depending on the infection involved, clinical presentation may include fever, lymphadenopathy, worsening pulmonary lesions, and expanding lesions of the central nervous system (CNS).

*If the immune reconstitution syndrome occurs, ARV therapy should not be interrupted. While this syndrome is self-limiting, a brief course of corticosteroids may be advisable to reduce central nervous system inflammation or severe respiratory symptoms.*

In addition to TB, the literature contains reports of other infections that have been reactivated, including *Mycobacterium avium complex* (MAC), cryptococcal meningitis, mild herpes zoster, and progressive multifocal leukoencephalopathy (PML). Progression of TB lesions with sparse organisms also has been observed. The biologic impact of immune reconstitution has been demonstrated by:

- Control of several chronic, untreatable OIs as a result of HAART
- Impressive decline in virtually all HIV-associated complications except lymphomas

If possible, all active OIs should be excluded or treated before initiating HAART, especially TB and CMV. OI prophylaxis should be considered in any HIV positive patient in the following instances:

- **TB prophylaxis should be given in any patient irrespective CD4 lymphocyte count level as long as there is a positive PPD (>5 mm) and active TB has been excluded.**
- **Pneumocystis pneumonia (PCP) prophylaxis:** Prophylaxis should be provided to all patients with a CD4 lymphocyte count <200/mm³. Do not start PCP prophylaxis with cotrimoxazole at the same time with nevirapine as both can cause a skin rash. At least a two-week period should separate the initiation of the two drugs.
- **Toxoplasmosis prophylaxis** should be provided to any patient whose CD4 lymphocyte count is <100/mm³
- **MAC prophylaxis:** Prophylaxis should be provided to any patient whose CD4 lymphocyte count is <50/mm³ and in whom active TB or MAC bacteremia can be excluded.
- **Primary and secondary prophylaxis** for virtually all OIs may be discontinued in a patient receiving HAART if the CD4 lymphocyte counts increase to well above the range within which the patient is at risk of acquiring the OIs in question by ≥6 months.
INDICATIONS FOR CHANGING THE FIRST-LINE ANTIRETROVIRAL DRUG REGIMEN IN GUYANA

There are four reasons for changing the first-line ARV drug regimen in Guyana:
- Toxicity
- Intolerance
- Treatment failure—immunologic, clinical and virologic
- New data showing superiority of different regimen

1. Toxicity

Deciding to substitute a different ARV depends on the ability to assign the toxicity to a specific ARV and on the severity of the toxicity symptoms (grade) (Appendix 1-H). When it can be determined that toxicity is related to a specific drug, a different drug that does not have the same side effect profile should be substituted; for example, substituting zidovudine for stavudine in patients who develop peripheral neuropathy. (Tables 1.9 and 1.10)

Given the limited options of ARV drugs available in Guyana, all efforts should be made to discourage premature switching to completely new alternative regimens and, when necessary, to pursue drug substitutions that will preserve future options.

Table 1.9 Clinical indications for stopping/changing first-line ARV drugs

<table>
<thead>
<tr>
<th>indication</th>
<th>Clinical indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>Severe discomfort or minimal intake for &gt;3 days</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Severe vomiting of all foods or fluids in 24 hours; orthostatic hypotension or IV therapy required</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>Orthostatic hypotension or IV therapy required. Also development of unexplained disabling chronic diarrhoea</td>
</tr>
<tr>
<td>Fever</td>
<td>Unexplained fever &gt;39.6°C (103°F) with abacavir hypersensitivity syndrome or Stevens-Johnson syndrome</td>
</tr>
<tr>
<td>Headache</td>
<td>Severe or requiring narcotic therapy</td>
</tr>
<tr>
<td>Rash</td>
<td>Moist desquamation, ulceration, or mucus membrane involvement, suspected Stevens-Johnson syndrome, erythema multiforme, exfoliative dermatitis, or necrosis requiring surgery</td>
</tr>
<tr>
<td>Allergic Reaction*</td>
<td>Generalised urticaria, angioedema or anaphylaxis</td>
</tr>
<tr>
<td>Peripheral Neuropathy</td>
<td>Severe discomfort, severe neuropathic pain, objective weakness, loss of 2–3 reflexes or absence of 2–3 sensory dermatomes</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Normal activity reduced by &gt;50%</td>
</tr>
</tbody>
</table>

*Patients with suspected hypersensitivity to abacavir should never be rechallenged as the reaction is potentially fatal.
Table 1.10 Laboratory indications for changing or stopping first-line drugs

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Toxicity grade 3 or higher</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Haematology</strong></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>&lt;6.9g/dl</td>
</tr>
<tr>
<td>Absolute neutrophil count</td>
<td>&lt;749/mm³</td>
</tr>
<tr>
<td>Platelets</td>
<td>&lt;49,999/mm³</td>
</tr>
<tr>
<td><strong>Chemistries</strong></td>
<td></td>
</tr>
<tr>
<td>Sodium</td>
<td>&lt;122 meq/L or &gt;159 meq/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>&lt;2.4 meq/L or &gt;6.6 meq/L</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>&gt;2.5 x upper limit of normal</td>
</tr>
<tr>
<td>Creatinine</td>
<td>&gt;3 x upper limit of normal</td>
</tr>
<tr>
<td>Glucose</td>
<td>&lt;39 mg/dL or &gt;251 mg/dL (fasting)</td>
</tr>
<tr>
<td><strong>Liver function tests</strong></td>
<td></td>
</tr>
<tr>
<td>AST (SGOT)</td>
<td>&gt;5 x upper limit of normal</td>
</tr>
<tr>
<td>ALT (SGPT)</td>
<td>&gt;5 x upper limit of normal</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>&gt;5 x upper limit of normal</td>
</tr>
<tr>
<td><strong>Pancreatic enzymes</strong></td>
<td></td>
</tr>
<tr>
<td>Amylase, lipase</td>
<td>&gt;2 x upper limit of normal</td>
</tr>
</tbody>
</table>

2. Intolerance

As much as possible, the quality of life of people living with HIV/AIDS (PLWA), who are receiving HAART, should be maintained. Therefore, if the patient is intolerant to any or all ARVs in the first-line regimen, the care provider may want to consider changing the drug(s) or changing the regimen (Appendix 1-K). As in all cases, this approach has to be carefully weighed as there are limited ARV alternatives in Guyana.

Table 1.11 Recommended drug substitutions

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Toxicity</th>
<th>Substitution</th>
</tr>
</thead>
<tbody>
<tr>
<td>d4T+3TC+NVP</td>
<td>- d4T related neuropathy or pancreatitis</td>
<td>- Switch d4T to AZT or TDF</td>
</tr>
<tr>
<td></td>
<td>- d4T-related lipoatrophy</td>
<td>- Switch d4T to TDF</td>
</tr>
<tr>
<td></td>
<td>- NVP-related severe hepatotoxicity</td>
<td>- Switch NVP to EFV</td>
</tr>
<tr>
<td></td>
<td>- NVP-related severe rash (not life threatening)</td>
<td>- Switch NVP to EFV</td>
</tr>
<tr>
<td></td>
<td>- NVP-related life-threatening rash (Stevens-Johnson Syndrome)</td>
<td>- Switch NVP to PI</td>
</tr>
<tr>
<td>AZT+3TC+NVP</td>
<td>- AZT related persistent GI intolerance, severe headache or severe hematological toxicity</td>
<td>- Switch AZT to TDF or ABC</td>
</tr>
<tr>
<td></td>
<td>- NVP related events</td>
<td>- As in above (Avoid switching to EFV in pregnancy. Instead, switch to PI.)</td>
</tr>
<tr>
<td>d4T+3TC+EFV</td>
<td>- d4T related neuropathy or pancreatitis</td>
<td>- Switch d4T to AZT</td>
</tr>
<tr>
<td></td>
<td>- d4T related lipoatrophy</td>
<td>- Switch d4T to TDF or ABC</td>
</tr>
<tr>
<td></td>
<td>- EFV related persistent CNS toxicity</td>
<td>- Switch EFV to NVP</td>
</tr>
<tr>
<td>AZT+3TC+NVP</td>
<td>- AZT related persistent GI intolerance or severe hematologic toxicity</td>
<td>- Switch AZT to TDF or ABC</td>
</tr>
<tr>
<td></td>
<td>- EFV related CNS toxicity</td>
<td>- Switch EFV to NVP</td>
</tr>
</tbody>
</table>
3. Treatment failure with first-line ARV drugs

The most frequent cause of treatment failure is nonadherence. When treatment failure occurs, the entire regimen or at least two (2) drugs in the regimen need to be changed. However, switching to second-line ARV drugs must not occur unless adherence counselling is done and adherence readiness is assured.

Treatment failure may be assessed virologically, immunologically, and/or clinically. A diagnosis of virologic failure cannot be made currently as viral load testing (PCR RNA) is not available in public hospitals in Guyana. However, virologic failure will be described in this section. Currently, a diagnosis of immunologic and clinical failure can be made in Guyana. Immunologic failure can be diagnosed by monitoring the CD4 lymphocyte count and clinical failure by the occurrence of new or previous opportunistic infections.

### Definition of virologic failure in adults

- Failure to achieve VL <400 c/mL by 24 wks
- Detectable viral load within 3–6 months of initiating HAART in an adherent patient
- Viral load becomes detectable (>0.5 log) after being undetectable. Isolated viral “blips” are defined as single VL measurements of 50-1000 c/mL. Persistent viral “blips” may indicate early virologic failure.

Before a diagnosis of virologic failure is made, an experienced HIV clinician should review the clinical picture. In Guyana, the case should be discussed in a clinical meeting before a decision to change therapy is done. Note virologic failure with viral load >1000 is an indication for resistance testing. This test is not currently available in Guyana.

### Definition of immunologic failure in adults

- Failure of CD4 lymphocyte count to improve by ~50 cells/mm$^3$ or worsening within 6 months of initiating HAART
- Return of CD4 lymphocyte count to pre-therapy baseline level or lower, without a concomitant infection to explain transient decrease in CD4 lymphocyte count
- >50% decrease in CD4 lymphocyte count from peak level, without a concomitant infection to explain transient decrease in CD4 lymphocyte count

NOTE: If patient is asymptomatic and treatment failure is being defined by CD4 criteria alone, a second CD4 lymphocyte count result must be obtained.

### Definition of clinical failure in adults

- Occurrence or recurrence of HIV-related opportunistic infection or malignancy 3 months after start of HAART
- This must be differentiated from immune reconstitution syndrome, which normally occurs in the first 3 months following HAART and is a reactivation of a previously latent infection.
- Recurrence of prior opportunistic infection
- Onset or recurrence of WHO stage 3 conditions

Consider treatment failure if a patient who has been on treatment for at least 3–6 months with good adherence develops one or more of the above.
Principles for managing therapeutic failure

- **Changing first-line ARV therapy and managing patients with suspected treatment failure should be done by an experienced HIV clinician.**
- Adherence problems remain the major cause of therapeutic failure and must be evaluated before the second-line therapy is initiated. If adherence cannot be assured, treatment should be suspended, patient counseled, and continued on cotrimoxazole until adherence can be assured.
- The second-line regimen must include drugs that retain activity against the patient’s virus strain. Ideally, all of the drugs should be new. If that is not possible, then at least one drug should be from a new class, in order to increase the likelihood of treatment success and minimise risks of cross-resistance.
- In the face of obvious therapeutic failure, do not continue the first-line regimen to avoid accumulation of resistant mutations.

4. **New data on superiority or inferiority of ARV drug regimens**

There are currently many ongoing studies and clinical trials to evaluate new drugs, drug combinations, novel ARV drug delivery models, and new treatment modalities. For example, the triple NRTI regimen, which was recommended initially by WHO, has been found to be somewhat inferior to the other regimens evaluated especially in patients with baseline viral loads >100,000.

*To keep pace with important scientific findings, which could affect the Guyana national ARV treatment protocol, the first- and second-line ARV drug regimens in this document will be reviewed regularly.*
Part 1 – Antiretroviral Therapy for Adolescents and Adults

RECOMMENDED SECOND-LINE ANTIRETROVIRAL DRUG REGIMENS IN GUYANA

Given the realities of ARV drug cross-class resistance and the absence of resistance testing in Guyana, the entire first line-drug regimen needs to be changed in the face of treatment failure.

Since the number of drug options is limited, and cost, availability of “cold chain,” pill burden, and drug-drug interactions are major concerns, the second-line drugs need to be carefully selected. Currently, for most people in Guyana, the second-line regimen is their last option for durable viral suppression.

The recommended second-line ARV drugs in Guyana and their doses are listed in Table 1.12.

Table 1.12  Second-line ARV drugs and dosages

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>*Tenofovir (TDF)</td>
<td>300 mg once daily</td>
<td>No food restrictions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Interacts with ddI</td>
</tr>
<tr>
<td>*Emtricitabine (FTC) or lamivudine (3TC)</td>
<td>200 mg once daily 150mg twice a day</td>
<td>Flare of hepatitis B (HbsAg) when antiretroviral is stopped.</td>
</tr>
<tr>
<td>Zidovudine (AZT)</td>
<td>300mg twice a day</td>
<td>Neutropoenia and anemia after weeks or months</td>
</tr>
<tr>
<td>Lopinavir/ritonavir (LPV/r)</td>
<td>133.3 mg/33.3 mg [3 capsules] twice daily</td>
<td>Take with food. Adjust dose with NVP, EFV, and hepatic dysfunction.</td>
</tr>
</tbody>
</table>

* Tenofovir and emtricitabine are available as a combination pill. Atazanavir 400 mg once daily or ATV 300 mg/RTV 100 mg qd. RTV boosting is required if ATV is combined with TDF or EFV and is often preferred.

Table 1.13  Second-line ARV drugs and dosages

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>*Tenofovir (TDF)</td>
<td>300 mg once daily</td>
<td>No food restrictions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Interacts with ddI</td>
</tr>
<tr>
<td>*Emtricitabine (FTC) or lamivudine (3TC)</td>
<td>200 mg once daily 150mg twice a day</td>
<td>Flare of hepatitis B (HbsAg) when FTC is stopped.</td>
</tr>
<tr>
<td>Lopinavir/ritonavir (LPV/r)</td>
<td>133.3 mg/33.3 mg [3 capsules] twice daily</td>
<td>Take with food. Adjust dose with NVP, EFV, and hepatic dysfunction.</td>
</tr>
</tbody>
</table>

Principles of using a second-line ARV regimen

NNRTIs
- No NNRTI can be used among the second-line drugs because the most common type of resistance—K103N resistant mutation—confers cross-class resistance to all NNRTIs.
**NRTIs**

- The combination of TDF + ddI cannot be used anymore because of concerns about persistent CD4 lymphocyte count decline and significant drug-drug interactions even though some studies have demonstrated sustained viral suppression. Using the combination would also entail dose reductions that are not easy with the current formulations.
- The decision to retain or use AZT with TDF is intended to delay the emergency of the K65 R mutation which rapidly develops when either TDF or ABC are used without a thymidine analog.
- LPV/r will be the backbone PI for second line therapy in Guyana. Potency, availability in adult and pediatric formulations, lack of need for cold chain with the new formulation make it an excellent choice for us in Guyana.
- 3TC which is one of the main backbone NRTIs in the first line in Guyana will be maintained in the second line. The commonest 3TC (FTC) mutation, M184V has been documented to be better than structured interruption in published research. The mutation makes the virus less fit and hyper susceptible to AZT and TDF.

**PIs**

- The PIs that may be suitable for patients in a resource-constrained setting include the Lopinavir/ritonavir combination, and atazanavir. Lopinavir/ritonavir must be stored in a refrigerator at the storage site before dispensing to the patient. After dispensing, the drugs are best kept refrigerated but may be kept at room temperature for about 30 days. A new formulation of Lopinavir/Ritonavir with lower pill burden is expected that will not need refrigeration.
- Indinavir, although a potent PI, is associated with substantial renal side effects and the patient needs to drink a large amount of water to prevent renal calculi. It is useful as an alternative when boosted with ritonavir. However, if unboosted, it has to be taken on an empty stomach. If not, there will be a 77% reduction in bioavailability leading to suboptimal dosing, selection of resistant mutant virus, and, possibly, cross-class resistance.

### Table 1.13 Recommended second line regimens

<table>
<thead>
<tr>
<th>First-line drugs</th>
<th>Recommended 2nd-line drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stavudine (d4T) or zidovudine (AZT)</td>
<td>Tenofovir (TDF)</td>
</tr>
<tr>
<td>+</td>
<td>+ Emtricitabine (FTC) or lamivudine (3TC)</td>
</tr>
<tr>
<td>+ Lamivudine (3TC)</td>
<td>+ Lopinavir/ritonavir (LPV/r)</td>
</tr>
<tr>
<td>+ Nevirapine (NVP) or efavirenz (EFV)</td>
<td></td>
</tr>
</tbody>
</table>

### Table 1.14 Recommended second line regimens

<table>
<thead>
<tr>
<th>First-line drugs</th>
<th>Recommended 2nd-line drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenofovir (FTC)</td>
<td>Tenofovir (TDF)</td>
</tr>
<tr>
<td>+ Emtricitabine (FTC) or lamivudine (3TC)</td>
<td>+ Zidovudine</td>
</tr>
<tr>
<td>+ Nevirapine (NVP) or efavirenz (EFV)</td>
<td>+ Emtricitabine (FTC) or lamivudine (3TC)</td>
</tr>
<tr>
<td></td>
<td>+ lopinavir/ritonavir (LPV/r)</td>
</tr>
</tbody>
</table>
Adherence is a fundamental component of effective ARV therapy. Adherence rates higher than 95% are necessary to achieve durable and sustained viral suppression. Lower levels of adherence correlate with virologic failure, evolution of drug resistance, and subsequent treatment failure.

Achieving high rates of adherence over a long period is a challenge and, in the absence of viral load testing, adherence counselling becomes crucial for preventing drug resistance.

The following principles should guide adherence counselling and facilitate adherence for patients receiving HAART:

- The patient should receive adherence counselling at baseline and at every visit.
- Adherence may be monitored by self-report, pill counting, pill identification, and adherence assessment evaluation.
- Having the patient involve an adherence “partner” or “buddy” is strongly encouraged. Whenever possible, as a matter of policy, every patient should be encouraged to disclose his/her status to a person of his/her choosing, who can act as an adherence partner and accompany the patient to important clinic visits.
- Patients who miss more than two (2) successive visit appointments without justifiable reason may be considered chronic defaulters and asked to withdraw from the treatment program.
- An adherence support system, including a community and/or peer support system, will be established to help with drug adherence.

Methods for achieving drug adherence

- **Patient-related**
  - Negotiate a regimen plan that is suitable to patient.
  - Plan adequate time for adherence counselling—more than two (2) visits at least 2–4 weeks apart—to ensure readiness before initiating HAART.
  - Involve partner to help with adherence.
  - Use memory aids whenever possible—timers/alarms clocks, pill boxes.
  - Plan ahead. Keep medications in key locations and obtain early refills.
  - Address active substance abuse and mental illness.

- **Provider-related**
  - Provide initial and on-going information on goals of therapy, drugs, food restrictions, and side effects.
  - Assessing adherence readiness before initiating HAART is compulsory, as is adherence monitoring at each visit.
  - Monitor and manage side effects.
  - Use a multidisciplinary approach.
Part 1 – Antiretroviral Therapy for Adolescents and Adults

- **Regimen-related**
  - Minimise adverse drug interactions.
  - Simplify regimen as much as possible.
  - Tell patients to anticipate some side effects and report them early.

- **Healthcare team-related**
  - Provide ongoing training on adherence for all team members.
  - Maintain an intense adherence monitoring and counselling strategy.
  - Educate volunteers, support groups, and community representatives.
Part 1 – Antiretroviral Therapy for Adolescents and Adults

APPENDICES
Appendix 1–A  Guyana HIV Testing Algorithm
ELISA Antibody Test
Appendix 1–B  Guyana HIV Testing Algorithm HIV Rapid Test

- Determine™
  - Concordant Positive
    - Report
  - Concordant Negative
    - Report
- UniGold™
  - Discordant
  - Stat-Pak™ Rapid Test as a tie-breaker
### Appendix 1–C Revised WHO clinical staging system of HIV infection and disease in adolescents and adults

#### Clinical Stage 1
- Asymptomatic
- Persistent generalized lymphadenopathy

#### Clinical Stage 2
- Unexplained persistent hepatosplenomegaly
- Papular pruritic eruptions
- Extensive wart virus infection
- Extensive molluscum contagiosum
- Recurrent oral ulcerations
- Unexplained persistent parotid enlargement
- Lineal gingival erythema
- Herpes zoster
- Recurrent or chronic URTI (otitis media, otorrhea, sinusitis, tonsillitis)
- Fungal nail infections

#### Clinical Stage 3
- Unexplained moderate malnutrition not adequately responding standard therapy
- Unexplained persistent diarrhea (≥14 days)
- Unexplained persistent fever (>37.5 intermittent or constant >1 month)
- Persistent oral Candida (outside of first 6-8 weeks of life)
- Oral hairy leukoplakia
- Acute necrotizing ulcerative gingivitis / periodontitis
- Symptomatic lymphoid interstitial pneumonitis
- Lymph node TB
- Pulmonary tuberculosis
- Severe recurrent presumed bacterial pneumonia
- Chronic HIV associated lung disease including bronchiectasis
- Unexplained anemia (<8g/dl), neutropenia (<500/mm3) or chronic thrombocytopenia (<50,000/mm3)
- HIV associated cardiomyopathy or HIV associated nephropathy

#### Clinical Stage 4
- Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy
- *Pneumocystis* pneumonia (PCP)
- Recurrent severe presumed bacterial infections (e.g. empyema, pyomyositis, bone or joint infection, meningitis but excluding pneumonias)
- Chronic herpes simplex infection >1 month
- Kaposi’s sarcoma
- Extrapulmonary tuberculosis
- Toxoplasmosis on the brain
- Oesophageal candidiasis
- CNS toxoplasmosis outside of neonatal period
- Cryptococcal meningitis
- HIV encephalopathy
- Cryptosporidiosis with diarrhea >1 month
- Isosporiasis with diarrhea >1 month
- Progressive multifocal encephalopathy
- Cytomegalovirus infection (retinitis)
- Acquired HIV associated fistula
- Cerebral or B cell non Hodgkin lymphoma
- Disseminated endemic mycosis
- Chronic cryptosporidiosis
- Chronic isosporiasis
Part 1 – Antiretroviral Therapy for Adolescents and Adults

- Disseminated non-tuberculous mycobacteria infection
- Cerebral or B cell non-Hodgkin lymphoma
- Progressive multifocal leukoencephalopathy
- Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy


a. Unexplained refers to when the condition is not explained by other causes.
# Appendix 1-D  CDC AIDS surveillance case definitions for adolescents and adults

<table>
<thead>
<tr>
<th>CD4 Cell Categories [mm³ (%)]</th>
<th>A: Asymptomatic, PGL or Acute HIV Infection</th>
<th>B: Symptomatic† (not A or C)</th>
<th>C*: AIDS Indicator Condition (1987)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1  &gt;500/mm³</td>
<td>A1</td>
<td>B1</td>
<td>C1</td>
</tr>
<tr>
<td>(≥29%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2  200–499/mm³</td>
<td>A2</td>
<td>B2</td>
<td>C2</td>
</tr>
<tr>
<td>(14–28%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3  &lt;200/mm³</td>
<td>A3*</td>
<td>B*</td>
<td>C3*</td>
</tr>
<tr>
<td>(&lt;14%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* All patients in categories A3, B3 and C1-3 are defined as having AIDS, based on the presence of an AIDS-indicator condition and/or a CD4 cell count of less than 200/mm³

† Symptomatic conditions not included in Category C that are: a) attributed to HIV infection or indicative of a defect in cell-mediated immunity or b) considered to have a clinical course or management that is complicated by HIV infection. Examples of B conditions include but are not limited to: bacillary angiomatosis; thrush; vulvovaginal candidiasis that is persistent, frequent or poorly responsive to therapy; cervical dysplasia (moderate or severe); cervical carcinoma in situ; constitutional symptoms such as fever (38.5°C) or diarrhoea lasting longer than 1 month; oral hairy leukoplakia; herpes zoster involving two episodes or more than 1 dermatome; idiopathic thrombocytopenic purpura (ITP); listeriosis; pelvic inflammatory disease (PID) (especially if complicated by a tubo-ovarian abscess); and peripheral neuropathy.

Appendix 1–E  Guyana HIV management six-question assessment for adults

The physician should assess the patient with the following six-questions:

1. **Does the patient who is HIV-infected have one or more of these medical indications for HAART?**
   - CD4 lymphocyte count <200/mm$^3$ irrespective of symptoms
   - WHO Stage 4 disease irrespective of CD4 lymphocyte count
   - WHO Stage 3 disease with CD4 lymphocyte count <350/mm$^3$
   - Pregnant woman with CD4 lymphocyte count <350/mm$^3$

2. **Is there a medical contraindication to or reason to defer the first-line regimen?**
   - Renal insufficiency [creatinine >3x upper limit of normal (ULN)]
   - Hepatic insufficiency (Liver function tests >5x ULN)
   - History of prior ARV use or intolerance (other than for PMTCT)
   - Severe anaemia (Hb <6.9g/dl)*
   - Severe neutropenia (absolute neutrophil count <749 mm)*
   - Severe thrombocytopenia (platelets <49,999 mm)*
   - Current use of anti-TB medications†

3. **Is there a current non-medical contraindication to the patient’s taking ARVs?**
   - Denial of HIV status and ambivalence about starting lifelong therapy
   - Current use of herbal and traditional remedies that react with ARVs
   - Ongoing serious substance abuse (alcohol, injection drugs, etc)
   - Psychiatric illness
   - Unstable social situation (eg, homeless, no social support, inability to travel to healthcare appointments)
   - Recent history of non-adherence

4. **Does the patient have an active opportunistic infection?**
   - Can TB be excluded? (symptoms, chest x-ray, sputum AFB culture, PPD)
   - Can CMV retinitis be excluded with an ophthalmologic exam?

5. **Is the patient pregnant?**
   - Administer pregnancy test. If positive, do not prescribe efavirenz (teratogenicity), ddI/d4T (risk of fatal lactic acidosis) or abacavir (hypersensitivity reaction).

6. **Are adherence, clinical monitoring, and follow-up likely to occur?**
   - Patient is motivated, understands the need for long-term medication.
   - Patient has attended 2–3 consecutive appointments.
   - Patient is willing to discuss diagnosis with one support person.

* This is a relative contraindication and applies only when AZT is used instead of d4T.
† If nevirapine is used as the first-line drug the risk of a drug interaction with rifampicin exists. Switching to efavirenz is indicated
### Appendix 1–F Drug-drug interactions

<table>
<thead>
<tr>
<th>Drug category</th>
<th>Calcium channel blocker</th>
<th>Cardiac</th>
<th>Lipid lowering agents</th>
<th>Anti-mycobacterial</th>
<th>Anti-histamine</th>
<th>Gastro-intestinal drugs</th>
<th>Neuroleptic</th>
<th>Psychotropic</th>
<th>Ergot Alkaloids</th>
<th>Herbs</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indinavir (IDV)</td>
<td>none</td>
<td>amiodarone</td>
<td>simvastatin</td>
<td>lovastatin</td>
<td>rifampin</td>
<td>rifapentine</td>
<td>astemizole</td>
<td>terfenadine</td>
<td>Cisapride</td>
<td>pimozide</td>
<td>midozolam</td>
</tr>
<tr>
<td>Ritonavir (RTV)</td>
<td>bepridil</td>
<td>amiodarone</td>
<td>flecaainide</td>
<td>propafenone</td>
<td>quinidine</td>
<td>simvastatin</td>
<td>lovastatin</td>
<td>rifapentine</td>
<td>astemizole</td>
<td>terfenadine</td>
<td>Cisapride</td>
</tr>
<tr>
<td>Saquinavir (SQV)</td>
<td>none</td>
<td>None</td>
<td>simvastatin</td>
<td>lovastatin</td>
<td>rifampin</td>
<td>rifabutin</td>
<td>rifapentine</td>
<td>astemizole</td>
<td>terfenadine</td>
<td>cisapride</td>
<td>pimozide</td>
</tr>
<tr>
<td>Nelfinavir (NFV)</td>
<td>none</td>
<td>None</td>
<td>simvastatin</td>
<td>lovastatin</td>
<td>rifampin</td>
<td>rifapentine</td>
<td>astemizole</td>
<td>terfenadine</td>
<td>cisapride</td>
<td>pimozide</td>
<td>midozolam</td>
</tr>
<tr>
<td>Lopinavir + Ritonavir (LPV + RTV)</td>
<td>none</td>
<td>flecaainide</td>
<td>propafenone</td>
<td>simvastatin</td>
<td>lovastatin</td>
<td>rifampin</td>
<td>rifapentine</td>
<td>astemizole</td>
<td>terfenadine</td>
<td>cisapride</td>
<td>pimozide</td>
</tr>
<tr>
<td>Atazanavir (ATV)</td>
<td>bepridil</td>
<td>None</td>
<td>simvastatin</td>
<td>lovastatin</td>
<td>rifampin</td>
<td>rifapentine</td>
<td>astemizole</td>
<td>terfenadine</td>
<td>cisapride</td>
<td>proton pump inhibitors</td>
<td>pimozide</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>none</td>
<td>None</td>
<td>none</td>
<td>rifapentine</td>
<td>astemizole</td>
<td>terfenadine</td>
<td>cisapride</td>
<td>none</td>
<td>midozolam</td>
<td>triazolam</td>
<td>dihydroergotamine (DHE 45) ergotamine (various forms) ergonovine methylergovonine</td>
</tr>
</tbody>
</table>
# Appendix 1–G Laboratory monitoring schedule and follow-up visits for antiretroviral therapy

<table>
<thead>
<tr>
<th>Test</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV test</td>
<td>Baseline</td>
</tr>
<tr>
<td>CD4 lymphocyte count*</td>
<td>Baseline and every 3–6 months</td>
</tr>
<tr>
<td>CBC and differential*</td>
<td>Baseline, 1 month, and every 3 months</td>
</tr>
<tr>
<td>VDRL</td>
<td>Baseline and annually</td>
</tr>
<tr>
<td>HBsAg</td>
<td>Baseline</td>
</tr>
<tr>
<td>Pregnancy*</td>
<td>Baseline (as indicated)</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>Baseline (as indicated)</td>
</tr>
<tr>
<td>Liver function test*</td>
<td>Baseline, 2 weeks, 1 month, and every 3 months</td>
</tr>
<tr>
<td>Renal function test</td>
<td>Baseline and every 6 months</td>
</tr>
<tr>
<td>Pap smear</td>
<td>Baseline and annually if normal; Every 6 months if abnormal</td>
</tr>
<tr>
<td>Urine dipstick</td>
<td>Baseline and every 6 months</td>
</tr>
<tr>
<td>PPD*</td>
<td>Baseline and annually</td>
</tr>
<tr>
<td>Toxoplasmosis immunoglobulin (IgG)</td>
<td>Baseline and repeat if CD4 lymphocyte count &lt;100 cells/mm³</td>
</tr>
<tr>
<td>Serum amylase, lipase</td>
<td>Baseline and if symptomatic</td>
</tr>
<tr>
<td>Serum glucose</td>
<td>Baseline and every 6–9 months for patients taking PIs</td>
</tr>
<tr>
<td>Serum lipids</td>
<td>Baseline and every 6–9 months for patients with abnormal baseline values or taking PIs, d4T, or efavirenz</td>
</tr>
</tbody>
</table>

**Optional tests**

| Serum lactate                                  | When lactic acidosis is suspected                 |
| Viral load                                     | Baseline and every 3-6 months, when test becomes available |

*Minimum required test

VDRL = Venereal Disease Research Lab test, HBsAg = hepatitis B surface antigen, ALT = alanine aminotransferase, AST = aspartate aminotransferase, bil = bilirubin, PPD = purified protein derivate, IgG = immunoglobulin G, ARV = antiretroviral
Appendix 1–H Guiding principles in the management of antiretroviral drug toxicity

1. Determine the seriousness of the toxicity.

2. Evaluate concurrent medications and establish whether the toxicity is attributable to an ARV drug or drugs or to a non-ARV medication taken at the same time.

3. Consider other disease processes (e.g. viral hepatitis in an individual on ARV drugs who develops jaundice) because not all problems that arise during treatment are caused by ARV drugs.

4. Manage the adverse event according to severity. In general:
   - **Grade 4 (severe life-threatening reactions):** Immediately discontinue all ARV drugs, manage the medical event (i.e. symptomatic and supportive therapy) and reintroduce ARV drugs using a modified regimen (i.e. with an ARV substitution for the offending drug) when the patient is stabilized.\(^{a}\)
   - **Grade 3 (severe reactions):** Substitute the offending drug without stopping ART.\(^{a}\)
   - **Grade 2 (moderate reactions):** Consider continuation of ART as long as feasible. If the patient does not improve on symptomatic therapy, consider single-drug substitutions.\(^{a}\)
   - **Grade 1 (mild reactions) are bothersome but do not require changes in therapy.**

5. Stress the maintenance of adherence despite toxicity for mild and moderate reactions.

6. If there is a need to discontinue ART because of life-threatening toxicity, all ARV drugs should be stopped until the patient is stabilized.
# Appendix 1–I  Common toxicities of antiretroviral drugs by type

<table>
<thead>
<tr>
<th>Type</th>
<th>Drug</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Potentially fatal</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>ddl, d4T</td>
<td>Stop drug immediately. Change therapy.</td>
</tr>
<tr>
<td>Hypersensitivity reactions</td>
<td>ABC</td>
<td>Stop drug immediately. Do not re-challenge. Change therapy.</td>
</tr>
<tr>
<td>Toxic epidermal necrolysis Stevens-Johnson syndrome</td>
<td>NVP</td>
<td>Stop drug immediately. Change therapy.</td>
</tr>
<tr>
<td>Lactic acidosis</td>
<td>All NRTIs</td>
<td>Stop drug immediately. Change therapy.</td>
</tr>
<tr>
<td>Psychosis, major depression</td>
<td>EFV</td>
<td>Stop drug immediately. Change therapy.</td>
</tr>
<tr>
<td>Acute hepatotoxicity</td>
<td>NVP</td>
<td>Manage according to criteria below.</td>
</tr>
<tr>
<td>Haematologic toxicity</td>
<td>AZT</td>
<td></td>
</tr>
<tr>
<td><strong>Disabling</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>ddl, d4T</td>
<td>Stop drug immediately. Change therapy.</td>
</tr>
<tr>
<td>Hepatotoxicity</td>
<td>NNRTIs, PIs</td>
<td>Manage according to criteria below.</td>
</tr>
<tr>
<td><strong>Long-term</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipoatrophy</td>
<td>NRTIs</td>
<td></td>
</tr>
<tr>
<td>Lipodystrophy</td>
<td>PIs, all NRTIs</td>
<td>Patient needs to be referred to an experienced HIV clinician.</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>PIs, all NRTIs, EFV</td>
<td></td>
</tr>
<tr>
<td>Insulin resistance</td>
<td>d4T and PIs</td>
<td></td>
</tr>
<tr>
<td>Lactic acidosis</td>
<td>All NRTIs mainly d4T, ddl</td>
<td>Stop drug immediately and manage accordingly.</td>
</tr>
</tbody>
</table>

ddl = didanosine, d4T = stavudine, ABC = abacavir, NVP = nevirapine, NRTI = nucleoside reverse transcriptase inhibitor, EFV = efavirenz, AZT = zidovudine, NNRTI = non-nucleoside reverse transcriptase inhibitor, PI = protease inhibitor

Appendix 1–J  Laboratory monitoring schedule for first-line antiretroviral regimen

<table>
<thead>
<tr>
<th>Test</th>
<th>Baseline</th>
<th>0 Initiation</th>
<th>0.5</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>6</th>
<th>12</th>
<th>18</th>
<th>24</th>
<th>Every 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBC</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Liver function test (ALT, AST, bilirubin)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Renal function test</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>CD4 lymphocyte count</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Viral load</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Amylase</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NOTE: For second-line regimen, the above laboratory monitoring plan applies but additional tests for serum lipids and serum glucose are done 6 monthly.

## Appendix 1–K  Recommended drug substitutions

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Toxicity</th>
<th>Substitution</th>
</tr>
</thead>
<tbody>
<tr>
<td>D4T+3TC+NVP</td>
<td>- d4T related neuropathy or pancreatitis</td>
<td>Switch d4T to AZT</td>
</tr>
<tr>
<td></td>
<td>- d4T-related lipoatrophy</td>
<td>Switch d4T to TDF</td>
</tr>
<tr>
<td></td>
<td>- NVP-related severe hepatotoxicity</td>
<td>Switch NVP to EFV</td>
</tr>
<tr>
<td></td>
<td>- NVP-related severe rash (not life threatening)</td>
<td>Switch NVP to EFV</td>
</tr>
<tr>
<td></td>
<td>- NVP-related life-threatening rash (Stevens-Johnson Syndrome)</td>
<td>Switch NVP to PI</td>
</tr>
<tr>
<td>AZT+3TC+NVP</td>
<td>- AZT related persistent GI intolerance, severe headache or severe hematological toxicity</td>
<td>Switch AZT to TDF</td>
</tr>
<tr>
<td></td>
<td>- NVP related events</td>
<td>As in above (Avoid switching to EFV in pregnancy. Instead, switch to PI.)</td>
</tr>
<tr>
<td>D4T+3TC+EFV</td>
<td>- d4T related neuropathy or pancreatitis</td>
<td>Switch d4T to AZT or TDF</td>
</tr>
<tr>
<td></td>
<td>- d4T related lipoatrophy</td>
<td>Switch d4T to TDF</td>
</tr>
<tr>
<td></td>
<td>- EFV related persistent CNS toxicity</td>
<td>Switch EFV to NVP</td>
</tr>
<tr>
<td>AZT+3TC+NVP</td>
<td>- AZT related persistent GI intolerance or severe haematologic toxicity</td>
<td>Switch AZT to d4T/TDF</td>
</tr>
<tr>
<td></td>
<td>- EFV related CNS toxicity</td>
<td>Switch EFV to NVP</td>
</tr>
</tbody>
</table>

Treating infants, children, and adolescents younger than 13 years of age who are HIV-infected involves special considerations in the areas of the natural history of the disease—including differences in virologic and immunologic markers of disease—as well as diagnosis, ARV drug pharmacokinetics, and adherence to treatment.

**Natural history and diagnosis of HIV infection**

Paediatric HIV infection occurs primarily due to mother-to-child transmission (MTCT) during pregnancy, labour and delivery, or breastfeeding. In rare cases, it may also occur because of blood transfusion, rape, sexual abuse, or scarification.

Important considerations in the natural history and diagnosis of paediatric HIV infection include the following:

- Infants who are HIV-infected may be clinically normal at birth.
- The most common AIDS-defining illness in infants is *Pneumocystis* pneumonia.

Additional common signs of paediatric HIV infection include:
- failure to thrive (neurodevelopmental delay)
- oral candidiasis
- chronic diarrhoea
- recurrent bacterial infections
- hepatosplenomegaly
- generalised lymphadenopathy

- In general, children have a more rapid disease course than adults.
- HIV progression in children is bimodal, with 20%–30% of infected children being rapid progressors and about 70%–80%, slow progressors.
- If untreated, 30% progress to AIDS by one year of age and about 75% die by five years of age.
- CD4 lymphocyte counts are higher, variable, and age-dependent in young children and have a low predictive value for opportunistic infections, AIDS, or death.

**Markers of disease**

Infants and young children have higher CD4 lymphocyte counts than adults, declining slowly to adult levels by about 6 years of age. If the CD4 lymphocyte cell count is to guide treatment decisions, age-appropriate cell counts must be used.

- For children <6 years of age, CD4 cell percentage (%) is used to assess HIV disease progression, because it is a more accurate marker than CD4 lymphocyte count.
- For children >6 years of age, CD4 lymphocyte count is used.
- Plasma HIV RNA level is characteristically very high in HIV-infected newborns and children <2 years. Thus, complete virologic suppression is not always easily achievable.
Diagnosis of paediatric HIV infection

In resource-limited settings, the diagnosis of HIV infection in the paediatric population is challenging. Passively-transmitted maternal HIV antibodies persist for about 18 months after birth, rendering the results of the ELISA antibody and rapid tests unreliable. For this reason, HIV antibody testing is recommended at 18 months of age by which time maternal antibodies should have been cleared from the child’s system.

Antigen tests are needed for diagnosing children younger than 18 months of age. Virologic antigen tests such as HIV PCR DNA, HIV PCR RNA, p24 antigen assay, and HIV culture may be used for early diagnosis of paediatric HIV infection in various settings, keeping in mind their sensitivities and specificities differ.

Figure 2.1 Guyana HIV Testing Algorithm: ELISA Antibody Test

HIV PCR DNA or RNA testing

- HIV PCR DNA is the preferred method of diagnosis in infants younger than 18 months. If the child is 18 months or older, an HIV ELISA or rapid test may be conducted.
- HIV PCR RNA may also be used for diagnosis of paediatric HIV infection. Specific levels are diagnostic of HIV infection, especially when no prophylactic ARV therapy is being administered concurrently.
- Because of the difficulty of taking blood samples from infants, a heel sample will be used and 2 dry blood spots prepared according to the Guyana DBS protocol (See guidelines on infant testing.)
HIV PCR DNA or RNA test* will be conducted
- At 6-8 weeks of age in **exclusively formula-fed babies**
- Two months **after complete cessation of breastfeeding in breast fed babies**
  (Please refer to the latest protocol for PCR DNA testing in Guyana.)
- If the PCR DNA/RNA assay result is negative and the patient is clinically well, ELISA should still be done at 18 months to confirm the result.
- If the assay result is positive, the HIV PCR DNA or RNA test should be repeated on a new sample after 2 weeks or as soon as possible after two weeks to confirm the diagnosis.
  - **Two positive HIV PCR DNA results are diagnostic of paediatric HIV infection.**
  - **Two positive HIV PCR RNA results >10,000 are diagnostic of paediatric HIV infection.**
- Discordant results are considered indeterminate and the HIV PCR DNA/RNA test should be repeated.

**Figure 2.2 Guyana HIV Testing Algorithm: Rapid Test**

**HIV ELISA or rapid testing**

**Infants ≤18 months old:**
- HIV antibody test results are unreliable.
- An HIV ELISA or rapid test at 12 months can be considered in highly selected cases and can be recommended for symptomatic children who have AIDS-related illnesses in the absence of virologic testing capability.
- If the ELISA results are negative at 12 months and the child has not been breastfed for >3 months, the child is considered HIV-negative and other causes are sought to explain the child’s symptoms.
- If the ELISA results are positive at 12 months, the result may be due to the child’s or the mother’s antibodies and is inconclusive. HIV ELISA or rapid testing needs to be repeated at 18 months to confirm the child’s HIV status.
If mother’s HIV status is positive, a child is considered infected at 12 months when in:
- WHO Paediatric Clinical Stage 3
- OR
  - CDC Clinical Category C with CD4% less than 20%

The HIV ELISA will need to be repeated at 18 months to confirm HIV infection.

**Infant >18 months old:**
- The HIV ELISA or rapid test may be performed to confirm or rule out HIV infection.
  (Validated algorithms are in Appendices 2–A and 2–B.)
- In the unlikely event that the mother has continued to breastfeed, the ELISA test should be performed >2 months after cessation of breastfeeding.
Figure 2.3 Diagnosing HIV in infants >18 months who have been HIV-exposed

HIV-Exposed Infant

Non-breastfeeding infant*

HIV antibody test at 18 months†

Positive antibody test††

Child is HIV-infected

Refer for treatment and care

Negative antibody test††

Child is NOT HIV-infected

*Infants who are still breastfeeding beyond 18 months should be tested at least 2 months after cessation of breastfeeding.
† When resources allow antibody testing between 12 and 18 months, children who test negative during this time must have testing repeated at 18 months. Repeat test earlier if child develops symptoms compatible with HIV infection.
†† The antibody test used is HIV ELISA or HIV rapid test.
Classification systems

The World Health Organization (WHO) and US Centers for Disease Control (CDC) have developed classification systems to provide a framework for treatment and follow-up care of patients who are HIV-infected. The classification systems are based on clinical symptoms and immunological tests, and those for children are included in Appendices 2–C through 2–F. There is significant overlap between the WHO and CDC classification systems; the WHO criteria allow for easy classification in the clinical setting, while the CDC classification system allows for a greater degree of specificity in diagnosis.

**WHO staging system for HIV infection and disease**

The WHO staging system for children divides HIV progression into four clinically relevant stages—Stages I to 3. (See Appendix 2-C.)

This staging system was revised by WHO in consultation with paediatric experts in 2005. Using the WHO staging system provided here can help define parameters for initiating treatment in resource-constrained settings.

**CDC surveillance case definition**

The CDC AIDS surveillance case definitions include both immunologic and clinical categories. (See Appendices 2-D and 2-E.) This system uses a combination of symptoms and CD4 lymphocyte count levels to establish criteria for diagnosing AIDS.
GOALS OF ANTIRETROVIRAL THERAPY IN CHILDREN

The goals of antiretroviral therapy are
1. Promotion or restoration of normal growth and development
2. Prevention of complicating infections and HIV-related cancers
3. Improvement in quality of life
4. Prolongation of survival

The goal of viral load suppression to below detection levels is not always achievable in children, who may have very high plasma HIV RNA levels.

*It is universally recommended that treatment be initiated with triple drug combinations, since such combinations have been shown to slow disease progression, improve survival, produce a more sustained virologic response, and delay the emergence of viral resistance.*
Initiating ARV therapy in infants and children

The World Health Organization eligibility criteria for HAART in children with confirmed HIV infection—and the eligibility criteria adopted by Guyana—are as follows:

**Children younger than 12 months:**
- WHO stage 3 or IV irrespective of CD4%
- WHO Paediatric Stage 1 or 2 disease with CD4% <25%

**Children between 12 months and 5 years:**
- WHO Stage 3 or IV irrespective of CD4%
- WHO Stage 1 or 2 irrespective of CD4% <20%

**Children 5 years or older:**
- WHO Stage 3 or IV irrespective of CD4 lymphocyte count or CD4%
- CD4 lymphocyte count <350/mm³

**IMPORTANT:** When CD4 testing is available and virologic testing to confirm paediatric HIV infection is not, the WHO recommends that HAART be initiated in infants younger than 18 months, who are HIV-sero-positive and have WHO Stage 3 or IV disease with CD4% <25%. HIV antibody testing must be repeated at 18 months to confirm that the child is HIV infected. Only infants with confirmed HIV infection should continue to receive ARV therapy.

**Prioritising treatment: concomitant infections and conditions**

All children with a confirmed diagnosis of HIV should be treated according to the above eligibility criteria with priority given to the children with the conditions listed below:

1. Tuberculosis
2. Failure to thrive (See Appendix 2-C for definition of failure to thrive.)
3. Encephalopathy
4. Meningitis or septicaemia
5. Any other HIV-related illness
ANTIRETROVIRAL DRUGS FOR CHILDREN

The pharmacokinetics of drugs in children differs substantially from the pharmacokinetics of the same drugs in adults due to the following:

- Body composition
- Renal excretion
- Liver metabolism
- Gastrointestinal function

These differences are associated with potential variations in drug distribution, metabolism, and clearance, as well as potential differences in drug dosing requirements and adverse effects.

Research has shown that highly active antiretroviral therapy (HAART) in children results in improved morbidity and mortality rates that are similar in magnitude to the improvements observed in adults. Some of the ARVs taken by adults are also available in formulations designed for young children.

To avoid underdosing and the development of resistance, drug doses must be adjusted as a child grows.
The Working Group recommendations on regimens for use in initial therapy have been formulated based on:

- Drug availability
- Durability of viral suppression and clinical and immunologic response
- Data on the types and incidence of toxic effects
- Availability and drug formulations for children
- Dosing frequency
- Dosing adjustments necessary as the child grows
- Food or fluid requirements
- Potential drug-drug interactions
- Being able to take the same drugs on the same dosing schedule as the parent(s)

### First-line paediatric ARV regimen

Zidovudine (AZT) + lamivudine (3TC) + nevirapine (NVP) or *efavirenz (EFV)

*Efavirenz will be used in older children (> 3years or >10kg) due to lack of safety data and unavailability of appropriate pediatric formulations.

Zidovudine + lamivudine + nevirapine is a regimen that is well tolerated by children. All three drugs in the first-line regimen have paediatric liquid formulations stable at room temperature.

### Alternate paediatric first-line ARV regimens in order of priority

- Abacavir (ABC) + lamivudine (3TC) + nevirapine (NVP) or efavirenz (EFV)
- Stavudine (d4T) + lamivudine (3TC) + nevirapine (NVP) or efavirenz (EFV)
- Zidovudine (AZT)/ or abacavir (ABC)/ or stavudine (d4T) + lamivudine (3TC) + lopinavir/ritonavir(LPV/r)

### Adjunct treatments like nutritional support, anti-helminthic therapy, and vitamin A and/or multivitamins should also be given.
### Table 2.2 Antiretroviral drugs in children

#### Nucleoside reverse transcriptase inhibitors (NRTIs)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Formulation(s)</th>
<th>Dietary rules</th>
<th>Selected adverse events, toxicities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zidovudine (AZT)</td>
<td>240 mg/m²/dose twice daily*</td>
<td>10 mg/ml</td>
<td>None</td>
<td>Anaemia, neutropoenia, thrombocytopenia, headache</td>
</tr>
<tr>
<td>Lamivudine (3TC)</td>
<td>4 mg /kg/dose twice daily</td>
<td>10 mg/ml</td>
<td>None</td>
<td>Headache, nausea</td>
</tr>
<tr>
<td>Stavudine* (d4T)</td>
<td>≤30 kg=1 mg/kg/dose twice daily</td>
<td>1 mg/ml;†</td>
<td>None</td>
<td>Peripheral neuropathy, lactic acidosis</td>
</tr>
<tr>
<td></td>
<td>30 kg–60 kg=30 mg twice daily</td>
<td>20 mg, 30 mg, 40 mg capsules</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;60 kg=40 mg twice daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Didanosine* (ddI)</td>
<td>120 mg/m²/dose twice daily</td>
<td>10 mg/ml†</td>
<td>Administer on empty stomach, at least 30 min. before or 2 hrs after eating.</td>
<td>Peripheral neuropathy, pancreatitis, lactic acidosis</td>
</tr>
<tr>
<td>Abacavir (ABC)</td>
<td>8 mg/kg/dose twice daily</td>
<td>20 mg/ml solution††</td>
<td>None</td>
<td>Hypersensitivity reaction Do not re-challenge.</td>
</tr>
</tbody>
</table>

* Requires refrigeration.
†Refer to package insert for instructions on reconstituting powder into liquid form.
††Premixed

#### Non-nucleoside reverse transcriptase inhibitors (NNRTIs)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Formulation(s)</th>
<th>Dietary rules</th>
<th>Selected adverse events, toxicities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nevirapine (NVP)</td>
<td>2 months-8 years: 4 mg/kg daily for 14 days, then 7 mg/kg twice daily 8 years and older: 4 mg/kg daily for 14 days, then 4 mg/kg twice daily Max 200 mg twice daily</td>
<td>10 mg/ml syrup</td>
<td>None</td>
<td>Rash, hepatotoxicity</td>
</tr>
<tr>
<td>Efavirenz (EFV)</td>
<td>10 kg to &lt;15 kg=200 mg 15 kg to &lt;20 kg=250 mg 20 kg to &lt;25 kg=300 mg 25 kg to &lt;32.5 kg=350 mg 32.5 kg to &lt;40 kg=400 mg ≥40 kg=600 mg daily</td>
<td>50 mg, 100 mg, 200 mg, 600 mg tablets</td>
<td>None</td>
<td>CNS side effects: insomnia, dizziness, abnormal dreams</td>
</tr>
</tbody>
</table>
Table 2.2 Antiretroviral drugs in children (continued)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Formulation(s)</th>
<th>Dietary rules</th>
<th>Selected adverse events, toxicities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lopinavir/ritonavir (LPV/r)</td>
<td>7 kg to &lt;15 kg: 12/3 mg/kg twice daily</td>
<td>80 mg/ml lopinavir syrup and 20 mg/ml ritonavir syrup</td>
<td>Take with meal or light snack.</td>
<td>Metabolic changes, glucose intolerance, taste disturbances</td>
</tr>
<tr>
<td></td>
<td>15 kg to 40 kg: 10/2.5 mg/kg twice daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;40 kg: Maximum 400 mg/100 mg twice daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Make dose adjustments with nevirapine and efavirenz.*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Lopinavir/Ritonavir (LPV/r) Adjustment

<table>
<thead>
<tr>
<th>Weight</th>
<th>Dosage†</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 kg to &lt;15 kg</td>
<td>13 mg/kg twice daily</td>
</tr>
<tr>
<td>15 kg to 50 kg</td>
<td>11 mg/kg twice daily</td>
</tr>
<tr>
<td>&gt;50 kg</td>
<td>5 mL or 3 capsules (adult dose) twice daily</td>
</tr>
</tbody>
</table>

† Dosing based on the lopinavir component of lopinavir/ritonavir solution (80 mg/20 mg per mL).

Note: Use adult dosage recommendation for children >12 years of age.


Dosing

The paediatric dose of most ARVs approved for use in children is calculated based on the child’s weight, however, the zidovudine (AZT) and didanosine (ddI) doses are calculated using the child’s body surface area. Body surface area is calculated by height (in meters) squared divided by weight (in kilograms): m²/kg.

A Nomogram® may also be used to make this calculation easier (Appendix 2-F). The body surface area can be calculated by using the formula above or by using the Mosteller formula: [surface area (m²) = square root of height (cm) x weight (kg)/3,600]

Dosing for children will have to be recalculated at each visit, taking into account the weight and height of the child.

The information provided in Tables 2.2–2.4 will facilitate calculation of the appropriate dosing for commonly-used ARV medications. Intensive education and demonstration should occur at every clinic visit to ensure that the caregiver can implement the changes in the drug regimen as the child grows.

Initiating therapy

Pre-initiation and immediate post-initiation visits are crucial to establishing rapport with the family. This will foster communication about the treatment plan and provide nonjudgmental support. HAART initiation and follow-up must be a multidisciplinary and family effort with a strong psychosocial component.
Part 2 – Antiretroviral Therapy in Children

Before initiating HAART, the physician should assess every child with the five-question “test” below (Appendix 2-G).

1. **Does the child have a medical indication for HAART?**
   - Every HIV-infected child has to be assessed according to the national eligibility criteria as listed above.

2. **Is there a medical contraindication or reason to delay the planned first-line regimen?**
   - Renal insufficiency (creatinine >3x normal)
   - Hepatic insufficiency (liver function tests >5x normal)
   - Severe anaemia (Hb <6.9 g/dl)*
   - Severe neutropoenia (absolute neutrophil count <749 mm)*
   - Severe thrombocytopoenia (platelets <49,999 mm)*
   - Current use of anti-TB medications+

3. **Is there a current non-medical contraindication to ARV therapy?**
   - Current use of herbal and traditional remedies
   - Psychiatric illness
   - Severely unstable social situation
   - Recent history of serious medication non-adherence

4. **Is there a current active opportunistic infection?**
   - Can TB be excluded? (CXR, sputum AFB, symptoms, PPD)?
   - Can CMV retinitis be excluded (by ophthalmologic exam)?

5. **Are adherence follow-up and clinical monitoring follow-up possible?**
   - Is there any responsible caregiver to administer medications to the child?
   - Is there an adherence partner++ who knows and understands the child’s health problems in case the primary caregiver is ill or unavailable?

* These are relative and apply only when zidovudine (AZT) is taken instead of stavudine.
+ This applies when nevirapine (NVP) is in the first-line regimen. Dose adjustments or switching to efavirenz (EFV) is indicated.
++ If an infected mother is the primary caregiver, then an uninfected relative should act as an adherence partner. This is to assure continuation of HAART in the event of the mother’s death.
Part 2 – Antiretroviral Therapy in Children

Clinical and Laboratory Monitoring for Children

Clinical monitoring

Neurodevelopmental and growth assessments are a crucial adjunct for closely monitoring the efficacy of the treatment regimen. The first step in clinical monitoring is to establish a baseline, which should include:

- Detailed medical history
  - Essential demographic characteristics
  - Current and chronic illnesses
  - History of drug allergies
  - Hospitalisations
  - Date of confirmed diagnosis of HIV
  - Current medications including traditional medications
  - History of ARV therapy
  - Did mother take ARVs for PMTCT?
  - Are immunisations current?
  - Nutritional history
- Detailed physical examination
  - Measure vital signs, height, and body surface area. The growth chart must be used actively.
  - Complete targeted physical exam, including nervous system and ophthalmologic exam, if possible
  - Exclude current active opportunistic infections.
- Discuss ARV adverse events in detail (short- and long-term) with caregiver
- Detailed nutrition assessment with caregiver

Clinic visit schedule

It is recommended that HIV-infected children should at a minimum be seen at the following clinic times:

- Pre-initiation (to establish baseline)
- Initiation
- Two (2) weeks post-initiation
- One (1) month post-initiation
- Monthly visits for refill and adherence counselling
- Three (3) monthly physician visits
- Unscheduled ill visits

NOTE: Guidelines are written to serve as a “guide.” They are not intended to prevent practitioners from using sound clinical judgment or attending to patients in unscheduled visits. In certain instances, a patient may need to be referred to a physician with experience in caring for children with HIV infection.

Laboratory monitoring

Laboratory monitoring is a crucial component of effective and safe ARV therapy. The laboratory tests should be performed at baseline, before the initiation of HAART, and at follow-up visits as indicated. (Table 2.5)
Table 2.5 Laboratory monitoring schedule for children: baseline and follow-up visits

<table>
<thead>
<tr>
<th>Name of test</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV test (ELISA or PCR DNA)</td>
<td>Baseline</td>
</tr>
<tr>
<td>CD4% or lymphocyte count*</td>
<td>Baseline, then every 3-6 months</td>
</tr>
<tr>
<td>CBC and differential*</td>
<td>Baseline, one month, then every 3-6 months</td>
</tr>
<tr>
<td>HBsAg</td>
<td>Baseline</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>Baseline</td>
</tr>
<tr>
<td>PPD*</td>
<td>Baseline (regardless of BCG)</td>
</tr>
<tr>
<td>Liver function test*</td>
<td>Baseline, 2 weeks, one month, then every 3 months</td>
</tr>
<tr>
<td>Renal function test</td>
<td>Baseline and every 6 months</td>
</tr>
<tr>
<td>Urine dipstick</td>
<td>Baseline and every 6 months</td>
</tr>
<tr>
<td>Toxoplasmosis IgG</td>
<td>Baseline and annually if CD4 lymphocyte count &lt;100/mm³</td>
</tr>
<tr>
<td>Serum amylase</td>
<td>Baseline and when indicated</td>
</tr>
<tr>
<td>Serum glucose</td>
<td>When indicated</td>
</tr>
<tr>
<td>Serum lipids</td>
<td>When indicated</td>
</tr>
<tr>
<td>Optional tests</td>
<td></td>
</tr>
<tr>
<td>Serum lactate</td>
<td>When lactic acidosis is suspected</td>
</tr>
<tr>
<td>Viral load</td>
<td>Baseline and 3 months, then every 6 months when test becomes available</td>
</tr>
</tbody>
</table>

*Minimum required test
HBsAg = hepatitis B surface antigen, PPD = purified protein derivative

Minimum baseline tests

The minimum tests recommended before initiating HAART include:
- HIV antibody test (double ELISA test) or PCR DNA x 2 or PCR RNA >10,000 copies/mL x 2 when available
- CD4% or CD4 lymphocyte count
- Full blood count with differential (needed to compute CD4%)
- Liver function test
- Renal function test
- Pregnancy test (necessary for female children >10 years)

CD4% and lymphocyte cell counts

CD4% and lymphocyte counts are useful for assessing immunologic function, for diagnosing treatment failure, and for determining when to initiate opportunistic infection prophylaxis. (See section "When to Change ARVs.")

An increase in CD4% of 5%–10% or an increase in CD4 lymphocyte count of >100/mm³ in the first 6–12 months of therapy is typically seen in a patient who is ARV-naïve and adhering to the regimen.
CD4% and CD4 lymphocyte count testing schedules

For children <5 years old:
- If CD4% < 15–25% (depending on age), child is eligible for HAART
- If CD4% > 25–29% = repeat test every 3 months
- If CD4% ≥ 30% = repeat test every 6 months

For children ≥ 5 years old:
- CD4 lymphocyte count < 350/mm³ = eligible for HAART
- CD4 lymphocyte count 350–400/mm³ = repeat test every 3 months
- CD4 lymphocyte count 401–600/mm³ = repeat test every 6 months
- CD4 lymphocyte count > 601/mm³ = repeat test every 9 months

Table 2.6 Laboratory monitoring for children receiving first-line or alternate first-line regimen

<table>
<thead>
<tr>
<th>Test</th>
<th>Baseline</th>
<th>0 Initiation</th>
<th>0.5</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>6</th>
<th>12</th>
<th>18</th>
<th>24</th>
<th>Every 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBC differential</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Liver function test</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Renal function test (creatinine)</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4% or lymphocyte count</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Viral load</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Amylase (and when indicated)</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NOTE: For a second-line regimen, the above laboratory-monitoring plan applies and serum lipids and serum glucose levels are tested 6 monthly.

**Plasma HIV-RNA levels (viral load testing)**

Plasma viral load testing is a very useful tool for monitoring response to HAART. Normally, viral load testing is not required for initiating HAART in resource-constrained settings. Viral load should be lower by at least one log (10-fold) in 4–6 weeks and undetectable at 6 months in patients who are adhering strictly to therapy. In children, complete and sustained virologic suppression may be a more difficult goal to achieve.
INDICATIONS FOR CHANGING HAART IN CHILDREN

The first-line regimen may need to be changed due to:

- Intolerance of side effects
- Therapeutic failure
  - Virologic
  - Immunologic
  - Clinical
- Toxicities
  - Haematologic
  - Hepatic
  - Severe rash [Grade 3 or 4, toxic epidermal necrolysis syndrome (TENS), Stevens-Johnson syndrome]
  - Pancreatitis
  - Lactic acidosis
- New data showing therapeutic superiority or inferiority of different ARV regimens

Assessing treatment failure in children

Treatment failure cannot be determined until the child has had a reasonable trial on the ARV regimen—at least 24 weeks.

Definition of virologic failure in children

- <1.0 log fall in viral load after 12 weeks of treatment
- When the viral load is not suppressed to undetectable levels after 6 months of therapy
- A significant and reproducible increase in HIV RNA after substantial response of 5-fold (>0.7 log) in infants aged <2 years OR 3-fold (>0.5 log) in children >2 years


Definition of immunologic failure in children

- Disease progression—moving from CDC Immunologic Category 1 to 2 or Category 2 to 3
- For children in CDC Immunologic Category 3, a persistent decline in CD4% of 5% or more
- For all children, a rapid fall in CD4% of >30% in <6 months
- ≥50% fall from peak level on therapy of CD4 cell percentage (or for children >5 years of age, absolute CD4 lymphocyte count), in absence of other concurrent infection
- CD4% at or below pre-treatment baseline levels in absence of concurrent infection


### Definition of clinical failure in children

- Neurodevelopmental deterioration or development of encephalopathy
- Growth failure, i.e., a persistent and unexplained decline in weight-growth velocity despite adequate nutritional support
- Disease progression—moving from CDC Clinical Category A to B or B to C
- Recurrence of infection that is refractory to treatment
- Development of a WHO Stage 3 or 4 event (opportunistic infection or malignancy) in a child 24 weeks after starting ART

In the event of confirmed treatment failure, the following regimen is recommended:

**Abacavir + didanosine (ddI) + lopinavir/ritonavir (LPV/r)**

*There are yet no approved paediatric formulations for tenofovir.*

ADHERENCE ISSUES SPECIFIC TO CHILDREN

Non-adherence is the most common cause of therapeutic failure. Caregivers play a critical role in facilitating adherence.

Maximising adherence

- Adherence support and counselling for families with children receiving HAART must be a multidisciplinary effort.
- Consider a period of hospitalisation during management of therapeutic failure to assess adherence and reinforce that adherence to the regimen is fundamental to successful antiretroviral therapy.
- Education and empowerment of the family, including participating in a support group of families with HIV-infected children, may help families cope with life-long therapy and maximise medication adherence.
- If possible, before initiating therapy a home visit should be made to assess whether there is sufficient readiness and support to maximise adherence.
- All children with unresolved issues about adherence should have ARV therapy delayed until adherence readiness is assured.
- The reluctance of families to disclose the child’s HIV diagnosis may interfere with adherence during day care and school hours.

Role of caregivers

- A primary caregiver must be identified and adherence readiness and support ascertained before initiating HAART.
- A child’s developmental level influences his or her ability and willingness to take medications. Therefore, the child is dependent on the caregiver for medication administration, and commitment and vigilance are necessary on the part of the caregiver.
- If an infected mother or a different infected relative is the primary caregiver, then an uninfected relative should know the child’s condition, be able to facilitate administering medication, and act as an adherence partner. This is to prevent discontinuation of HAART in the event of the primary caregiver’s illness or inability to care for the child.
- Since a substantial proportion of the children may be orphans, who are being cared for by grandparents or elderly guardians, attention should be paid to the health and well-being of the guardian, with particular attention to his or her eyesight.
- Many medications are not palatable and some children may vomit medications. Encouraging the caregiver to be patient and understanding is important, but if persistent vomiting continues, consult with an experienced HIV clinician.
APPENDICES
Appendix 2–A  Guyana HIV Testing Algorithm
ELISA Antibody Test

1. ELISA Murex
   - Non-Reactive: Report Negative
   - Reactive: Repeat ELISA Vironostika in duplicate
     - Negative in duplicate: Report Negative
     - Negative and Positive: Report Indeterminate (Repeat with fresh specimen)
     - Positive in duplicate: Confirm by HIV - Determine
       - Negative: Report Indeterminate (Repeat with fresh specimen)
       - Positive: Report Positive
Appendix 2–B  Guyana HIV Testing Algorithm
Rapid Test

- Determine™
  - Concordant Positive
    - Report
  - Concordant Negative
    - Report

- UniGold™
  - Concordant Positive
    - Report
  - Concordant Negative
    - Report

Stat-Pak™ Rapid Test as a tie-breaker
### Appendix 2-C  WHO clinical staging of HIV and AIDS for infants and children with established HIV infection

<table>
<thead>
<tr>
<th>Clinical Stage 1&lt;sup&gt;a&lt;/sup&gt;</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>▪  Asymptomatic</td>
<td></td>
</tr>
<tr>
<td>▪  Persistent generalized lymphadenopathy</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Stage 2&lt;sup&gt;a&lt;/sup&gt;</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>▪  Unexplained persistent hepatosplenomegaly</td>
<td></td>
</tr>
<tr>
<td>▪  Papular pruritic eruptions</td>
<td></td>
</tr>
<tr>
<td>▪  Extensive wart virus infection</td>
<td></td>
</tr>
<tr>
<td>▪  Extensive molluscum contagiosum</td>
<td></td>
</tr>
<tr>
<td>▪  Recurrent oral ulcerations</td>
<td></td>
</tr>
<tr>
<td>▪  Unexplained persistent parotid enlargement</td>
<td></td>
</tr>
<tr>
<td>▪  Lineal gingival erythema</td>
<td></td>
</tr>
<tr>
<td>▪  Herpes zoster</td>
<td></td>
</tr>
<tr>
<td>▪  Recurrent or chronic URTI (otitis media, otorrhea, sinusitis, tonsillitis)</td>
<td></td>
</tr>
<tr>
<td>▪  Fungal nail infections</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Stage 3&lt;sup&gt;a&lt;/sup&gt;</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>▪  Unexplained moderate malnutrition not adequately responding standard therapy</td>
<td></td>
</tr>
<tr>
<td>▪  Unexplained persistent diarrhea (≥14 days)</td>
<td></td>
</tr>
<tr>
<td>▪  Unexplained persistent fever (&gt;37.5 intermittent or constant &gt;1 month)</td>
<td></td>
</tr>
<tr>
<td>▪  Persistent oral Candida (outside of first 6-8 weeks of life)</td>
<td></td>
</tr>
<tr>
<td>▪  Oral hairy leukoplakia</td>
<td></td>
</tr>
<tr>
<td>▪  Acute necrotizing ulcerative gingivitis / periodontitis</td>
<td></td>
</tr>
<tr>
<td>▪  Symptomatic lymphoid interstitial pneumonitis</td>
<td></td>
</tr>
<tr>
<td>▪  Lymph node TB</td>
<td></td>
</tr>
<tr>
<td>▪  Pulmonary tuberculosis</td>
<td></td>
</tr>
<tr>
<td>▪  Severe recurrent presumed bacterial pneumonia</td>
<td></td>
</tr>
<tr>
<td>▪  Chronic HIV associated lung disease including bronchiectasis</td>
<td></td>
</tr>
<tr>
<td>▪  Unexplained anemia (&lt;8g/dl), neutropenia (&lt;500/mm&lt;sup&gt;3&lt;/sup&gt;) or chronic thrombocytopenia (&lt;50,000/mm&lt;sup&gt;3&lt;/sup&gt;)</td>
<td></td>
</tr>
<tr>
<td>▪  HIV associated cardiomyopathy or HIV associated nephropathy</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Stage 4&lt;sup&gt;a&lt;/sup&gt;,</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>▪  Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy</td>
<td></td>
</tr>
<tr>
<td>▪  <em>Pneumocystis</em> pneumonia (PCP)</td>
<td></td>
</tr>
<tr>
<td>▪  Recurrent severe presumed bacterial infections (e.g. empyema, pyomyositis, bone or joint infection, meningitis but excluding pneumonias</td>
<td></td>
</tr>
<tr>
<td>▪  Chronic herpes simplex infection &gt;1 month</td>
<td></td>
</tr>
<tr>
<td>▪  Kaposi’s sarcoma</td>
<td></td>
</tr>
<tr>
<td>▪  Extrapulmonary tuberculosis</td>
<td></td>
</tr>
<tr>
<td>▪  Toxoplasmosis on the brain</td>
<td></td>
</tr>
<tr>
<td>▪  Oesophageal candidiasis</td>
<td></td>
</tr>
<tr>
<td>▪  CNS toxoplasmosis outside of neonatal period</td>
<td></td>
</tr>
<tr>
<td>▪  Cryptococcal meningitis</td>
<td></td>
</tr>
<tr>
<td>▪  HIV encephalopathy</td>
<td></td>
</tr>
<tr>
<td>▪  Cryptosporidiosis with diarrhea &gt;1 month</td>
<td></td>
</tr>
<tr>
<td>▪  Isosporiasis with diarrhea &gt;1 month</td>
<td></td>
</tr>
<tr>
<td>▪  Progressive multifocal encephalopathy</td>
<td></td>
</tr>
<tr>
<td>▪  Cytomegalovirus infection (retinitis)</td>
<td></td>
</tr>
<tr>
<td>▪  Acquired HIV associated fistula</td>
<td></td>
</tr>
</tbody>
</table>
Part 2 – Antiretroviral Therapy in Children

- Cerebral or B cell non-Hodgkin lymphoma
- Disseminated endemic mycosis
- Chronic cryptosporidiosis
- Chronic isosporiasis
  - Disseminated non-tuberculous mycobacteria infection
- Cerebral or B cell non-Hodgkin lymphoma
  - Progressive multifocal leukoencephalopathy
  - Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy


a. Unexplained refers to when the condition is not explained by other causes.
Appendix 2-D  CDC immunologic categories based on age-specific CD4 lymphocyte counts and percent of total lymphocytes

<table>
<thead>
<tr>
<th>Immunologic category</th>
<th>&lt;12 months mm(^3) (%)</th>
<th>1–5 yrs mm(^3) (%)</th>
<th>6–12 yrs mm(^3) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category 1: No evidence of suppression</td>
<td>≥1,500 (&gt;25%)</td>
<td>≥1,000 (&gt;25%)</td>
<td>≥500 (&gt;25%)</td>
</tr>
<tr>
<td>Category 2: Evidence of moderate suppression</td>
<td>750–1,499 (15–24%)</td>
<td>500–999 (15–24%)</td>
<td>200–499 (15–24%)</td>
</tr>
<tr>
<td>Category 3: Severe suppression</td>
<td>&lt;750 (&lt;15%)</td>
<td>&lt;500 (&lt;15%)</td>
<td>&lt;200 (&lt;15%)</td>
</tr>
</tbody>
</table>

Source: Adapted from: US Centers for Disease Control and Prevention. 1994. Revised classification system for human immunodeficiency virus infection in children less than 13 years of age. MMWR (RR–22).

Appendix 2-D2: Proposed WHO classification of human immunodeficiency virus associated immunodeficiency in infants and children

<table>
<thead>
<tr>
<th>Classification of HIV-associated immunodeficiency</th>
<th>&lt;11 months (%)</th>
<th>Age-related CD4 values</th>
<th>≥5 years (cell/mm(^3))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not significant</td>
<td>&gt;35</td>
<td>&gt;30</td>
<td>&gt;25</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt;25</td>
<td>&lt;20</td>
<td>&lt;15</td>
</tr>
</tbody>
</table>

Source: Based on WHO global and regional consultations (Adapted from WHO. Needs date?)
Appendix 2-E CDC Clinical categories for children with HIV

**CATEGORY N: NOT SYMPTOMATIC**
Children who have no signs or symptoms considered to be the result of HIV infection or who have only one of the conditions listed in Category A.

**CATEGORY A: MILDLY SYMPTOMATIC**
Children with two or more of the conditions listed below but none of the conditions listed in Categories B and C.
- Lymphadenopathy (≥0.5 cm at more than two sites; bilateral = one site)
- Hepatomegaly
- Splenomegaly
- Dermatitis
- Parotitis
Recurrent or persistent upper respiratory infection, sinusitis, or otitis media

**CATEGORY B: MODERATELY SYMPTOMATIC**
Children who have symptomatic conditions other than those listed for Category A or C that are attributed to HIV infection.
Examples of conditions in clinical Category B include but are not limited to:
- Anemia (<8 gm/dL), neutropenia (<1,000/mm^3), or thrombocytopenia (<100,000/mm^3) persisting ≥30 days
- Bacterial meningitis, pneumonia, or sepsis (single episode)
- Candidiasis, oropharyngeal (thrush), persisting (>2 months) in children >6 months of age
- Cardiomyopathy
- Cytomegalovirus infection, with onset before 1 month of age
- Diarrhea, recurrent or chronic
- Hepatitis
- Herpes simplex virus (HSV) stomatitis, recurrent (more than two episodes within 1 year)
- HSV bronchitis, pneumonitis, or esophagitis with onset before 1 month of age
- Herpes zoster (shingles) involving at least two distinct episodes or more than one dermatome
- Leiomyosarcoma
- Lymphoid interstitial pneumonia (LIP) or pulmonary lymphoid hyperplasia complex
- Nephropathy
- Nocardiosis
- Persistent fever (lasting >1 month)
- Toxoplasmosis, onset before 1 month of age
- Varicella, disseminated (complicated chickenpox)

**CATEGORY C: SEVERELY SYMPTOMATIC**
- Serious bacterial infections, multiple or recurrent (i.e., any combination of at least two culture-confirmed infections within a 2-year period), of the following types: septicemia, pneumonia, meningitis, bone or joint infection, or abscess of an internal organ or body cavity (excluding otitis media, superficial skin or mucosal abscesses, and indwelling catheter-related infections)
- Candidiasis, esophageal or pulmonary (bronchi, trachea, lungs)
Appendix 2-E  CDC Clinical categories for children with HIV
(continued)

CATEGORY C: SEVERELY SYMPTOMATIC (continued)
- Coccidioidomycosis, disseminated (at site other than or in addition to lungs or cervical or hilar lymph nodes)
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis or isosporiasis with diarrhea persisting >1 month
- Cytomegalovirus disease with onset of symptoms at age >1 month (at a site other than liver, spleen, or lymph nodes)
- Encephalopathy (at least one of the following progressive findings present for at least 2 months in the absence of a concurrent illness other than HIV infection that could explain the findings): a) failure to attain or loss of developmental milestones or loss of intellectual ability, verified by standard developmental scale or neuropsychological tests; b) impaired brain growth or acquired microcephaly demonstrated by head circumference measurements or brain atrophy demonstrated by computerized tomography or magnetic resonance imaging (serial imaging is required for children <2 years of age); c) acquired symmetric motor deficit manifested by two or more of the following: paresis, pathologic reflexes, ataxia, or gait disturbance
- Herpes simplex virus infection causing a mucocutaneous ulcer that persists for >1 month; or bronchitis, pneumonitis, or esophagitis for any duration affecting a child >1 month of age
- Histoplasmosis, disseminated (at a site other than or in addition to lungs or cervical or hilar lymph nodes)
- Kaposi’s sarcoma
- Lymphoma, primary, in brain
- Lymphoma, small, noncleaved cell (Burkett’s), or immunoblastic or large cell lymphoma of B-cell or unknown immunologic phenotype
- Mycobacterium tuberculosis, disseminated or extrapulmonary
- Mycobacterium, other species or unidentified species, disseminated (at a site other than or in addition to lungs, skin, or cervical or hilar lymph nodes)
- Mycobacterium avium complex or Mycobacterium kansasii, disseminated (at site other than or in addition to lungs, skin, or cervical or hilar lymph nodes)
- Pneumocystis pneumonia
- Progressive multifocal leuкоencephalopathy
- Salmonella (nontyphoid) septicemia, recurrent
- Toxoplasmosis of the brain with onset at >1 month of age
- Wasting syndrome in the absence of a concurrent illness other than HIV infection that could explain the following findings: a) persistent weight loss >10% of baseline OR b) downward crossing of at least two of the following percentile lines on the weight-for-age chart (e.g., 95th, 75th, 50th, 25th, 5th) in a child ≥ 1 year of age OR c) <5th percentile on weight-for-height chart on two consecutive measurements, ≥=30 days apart PLUS a) chronic diarrhea (i.e., at least two loose stools per day for >30 days) OR b) documented fever (for U> 30 days, intermittent or constant)
### Appendix 2-E  CDC Clinical categories for children with HIV

(continued)

<table>
<thead>
<tr>
<th>Immunologic category</th>
<th>Clinical category N</th>
<th>Clinical category A</th>
<th>Clinical category B</th>
<th>Clinical category C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>N1</td>
<td>A1</td>
<td>B1</td>
<td>C1</td>
</tr>
<tr>
<td>No suppression (≥29%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate suppression (14–28%)</td>
<td>N2</td>
<td>A2</td>
<td>B2</td>
<td>C2</td>
</tr>
<tr>
<td>Severe suppression (&lt;14%)</td>
<td>N3</td>
<td>A3</td>
<td>B3</td>
<td>C3</td>
</tr>
</tbody>
</table>

Appendix 2–F  Nomogram®

Appendix 2–G The Guyana paediatric HIV management five-question test

1. **Does the child have a medical indication for HAART?**
   - Every HIV-infected child has to be assessed according to the national eligibility criteria as listed above.

2. **Is there a medical contraindication or reason to delay the planned first-line regimen?**
   - Renal insufficiency (creatinine >3x normal)
   - Hepatic insufficiency (liver function tests >5x normal)
   - Severe anaemia (Hb <6.9 g/dl)*
   - Severe neutropoenia (absolute neutrophil count <749 mm)*
   - Severe thrombocytopoenia (platelets <49,999 mm)*
   - Current use of anti-TB medications+

3. **Is there a current nonmedical contraindication to ARV therapy?**
   - Current use of herbal and traditional remedies
   - Psychiatric illness
   - Severely unstable social situation
   - Recent history of serious medication non-adherence

4. **Is there a current active opportunistic infection?**
   - Can TB be excluded? (CXR, sputum AFB, symptoms, PPD)?
   - Can CMV retinitis be excluded (by ophthalmologic exam)?

5. **Are adherence follow-up and clinical monitoring follow-up possible?**
   - Is there any responsible caregiver to administer medications to the child?
   - Is there an adherence partner+++ who knows and understands the child’s health problems in case the primary caregiver dies?

---

* These are relative and apply only when zidovudine (AZT) is taken instead of stavudine.
+ This applies when nevirapine (NVP) is in the first-line regimen. Dose adjustments or switching to efavirenz (EFV) is indicated.
+++ If an infected mother is the primary caregiver, then an uninfected relative should act as an adherence partner. This is to prevent discontinuation of HAART in the event of the mother’s death.
# Appendix 2–H  Laboratory monitoring schedule for children: baseline and follow-up visits

<table>
<thead>
<tr>
<th>Name of test</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV test (ELISA or PCR DNA)</td>
<td>Baseline</td>
</tr>
<tr>
<td>CD4% or lymphocyte count*</td>
<td>Baseline, then every 3 months</td>
</tr>
<tr>
<td>CBC and differential*</td>
<td>Baseline, one month, then every 3 months</td>
</tr>
<tr>
<td>HBsAg</td>
<td>Baseline</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>Baseline</td>
</tr>
<tr>
<td>PPD*</td>
<td>Baseline (regardless of BCG)</td>
</tr>
<tr>
<td>Liver function test*</td>
<td>Baseline, 2 weeks, one month, then every 3 months</td>
</tr>
<tr>
<td>Renal function test</td>
<td>Baseline and every 6 months</td>
</tr>
<tr>
<td>Urine dipstick</td>
<td>Baseline and every 6 months</td>
</tr>
<tr>
<td>Toxoplasmosis IgG</td>
<td>Baseline and annually if CD4 lymphocyte count &lt;100 mm$^3$</td>
</tr>
<tr>
<td>Serum amylase</td>
<td>Baseline and every 3 months for patients taking ddl, d4T</td>
</tr>
<tr>
<td>Serum glucose</td>
<td>Baseline and every 3 months</td>
</tr>
<tr>
<td>Serum lipids</td>
<td>Baseline and every 3 months</td>
</tr>
<tr>
<td><strong>Optional tests</strong></td>
<td></td>
</tr>
<tr>
<td>Serum lactate</td>
<td>When lactic acidosis is suspected.</td>
</tr>
<tr>
<td>Viral load</td>
<td>Baseline and 3 months, then every 6 months when test becomes available</td>
</tr>
</tbody>
</table>

*Minimum required test

HBsAg = hepatitis B surface antigen, PPD = purified protein derivative
This section will highlight major issues concerning ARV therapy in women, patients with co-infections, injection drug users, and those who require post-exposure prophylaxis (PEP).
A high viral load is the most important risk factor for mother-to-child transmission (MTCT) of HIV. Highly active antiretroviral therapy (HAART) is the best ARV regimen for prevention of MTCT (PMTCT) because it adequately suppresses viral load while protecting the health of the mother. See Table 3.1 for information on determining eligibility for HAART. (For full details of prevention of mother-to-child transmission (PMTCT) in HIV-infected pregnant women, please consult the Manual of the National Protocol for PMTCT.)

**Recommendations**

- All pregnant women who are HIV-infected—especially those living in regions close to an HIV treatment site—should receive top priority for CD4 lymphocyte testing to determine eligibility for HAART. At the post-test counselling visit, a blood draw for CD4 testing should be arranged and the results reviewed as soon as possible.
- For management of pregnant women following CD4 testing, see Table 3.1 below.
- For recommendations concerning prescribing ARVs for pregnant women in specific clinical situations, see Appendix 3–A.

**Table 3.1 Eligibility criteria for HAART pregnant HIV-infected women**

<table>
<thead>
<tr>
<th>CD4 lymphocyte count</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤350 cells/mm³</td>
<td>Eligible for HAART after 1st trimester Refer to nearest HIV treatment site.</td>
</tr>
<tr>
<td>&gt;350 cells/mm³</td>
<td>See recommendations in Table 2.</td>
</tr>
<tr>
<td>Unknown CD4 lymphocyte count and asymptomatic</td>
<td>See recommendations in Table 2.</td>
</tr>
<tr>
<td>Unknown CD4 lymphocyte count and symptomatic (WHO Stage 3 or IV, CDC Immune Category 3 or Clinical Category C)</td>
<td>Eligible for HAART Refer to nearest HIV treatment site.</td>
</tr>
</tbody>
</table>

- It is preferable to start HAART after the first trimester.
- Women already receiving HAART should continue the regimen if they become pregnant. However, their regimens should be changed to a pregnancy friendly regimen.

**HAART regimens for pregnant women: general principles for drug selection**

**Efavirenz**

_Efavirenz is contraindicated in pregnant women who are HIV-infected because of concerns about teratogenicity—especially in the first trimester._ If a pregnant woman is taking efavirenz, switch her immediately to nevirapine. Efavirenz is generally discouraged in women with child bearing potential except if adequate contraception is assured.
Part 3 – Antiretroviral Therapy in Special Circumstances

**Didanosine and stavudine**
The didanosine and stavudine combination should be avoided in pregnant women because of the increased risk of lactic acidosis. If a pregnant woman is taking didanosine and stavudine, switch her immediately to a regimen that will not increase the risk of lactic acidosis such as zidovudine and lamivudine.

**Nevirapine**
- Pregnant women who are HIV-infected with a CD4 lymphocyte count of >250 cells/mm³ should not receive a nevirapine-based HAART regimen because of a 12-fold risk of severe hepatotoxicity. Such toxicity has not been documented in cases where it is used as a single dose for PMTCT.
- Nevirapine and PIs reduce the efficacy of oral contraceptive pills. All women on the nevirapine-based HAART regimen who are taking contraceptive pills should always use condoms or should change their contraceptive method.
- In approximately 20%–75% of women, single-dose nevirapine for PMTCT usually results in drug-resistant HIV mutations. When these women receive HAART, they are at a potential risk for virologic and therapeutic failure, especially if they need HAART within 6 months of receiving single dose Nevirapine. When they become eligible for HAART, Kaletra should be preferably considered as part of their first line regimen.

**Zidovudine**
- Haemoglobin should be carefully monitored regularly when a pregnant woman is taking zidovudine. (Refer to the protocol for Detection, Prevention and Treatment of Iron Deficiency Anemia for general management of anemia in pregnancy.).
The roll-out of the new PMTCT treatment guidelines will commence at the HIV Care & Treatment sites across the country. All pregnant women who test positive will be referred for care at sites that have ARVs as appropriate. The different regimens to be used in other PMTCT sites will be influenced by several factors including:
- Availability of HAART or close proximity to a treatment site
- Availability of CD4 testing
- Ease of laboratory monitoring (hemoglobin estimation)
- Availability of drug prescribers for ART program (physicians/medex)

For an infant whose mother is HIV-infected but did not receive nevirapine for prophylaxis, the timing of nevirapine dosing selected for the infant will depend on whether the newborn is brought to a PMTCT site within 72 hours of birth.

**Table 3.2 Clinical situations and recommendations for the use of antiretroviral drugs in pregnant women**

<table>
<thead>
<tr>
<th>Clinical Situation</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mother</strong></td>
<td><strong>Baby</strong></td>
</tr>
<tr>
<td><strong>SCENARIO 1:</strong> ARV naïve HIV positive pregnant woman.</td>
<td>If patient lacks access to CD4 lymphocyte count testing or HAART</td>
</tr>
<tr>
<td></td>
<td>AZT 300mg BD from 28 weeks, oral AZT 300mg 3hourly in labor and single dose NVP 200mg in labor. Mother to receive oral AZT 300mg bd +Lamivudine (3TC) for 1 week postpartum.</td>
</tr>
<tr>
<td></td>
<td>Single dose nevirapine 200mg will be given in areas where AZT cannot be prescribed either due to lack AZT or where prescribers are not available</td>
</tr>
<tr>
<td></td>
<td>If patient has access to CD4 lymphocyte count testing or HAART</td>
</tr>
<tr>
<td></td>
<td>And/or is symptomatic (WHO Stage 3 or 4) or has CD4 lymphocyte count &lt;250</td>
</tr>
<tr>
<td></td>
<td>Treat with HAART (AZT + 3TC + NVP) preferably after first trimester.</td>
</tr>
<tr>
<td></td>
<td>If CD4 &gt;250 ≤350 and has access to HAART</td>
</tr>
<tr>
<td></td>
<td>Treat with AZT/3TC/LPV/r preferably after 1st trimester and continue HAART after delivery*</td>
</tr>
<tr>
<td></td>
<td>If CD4 &gt;350 and has access to HAART</td>
</tr>
<tr>
<td></td>
<td>Treat with AZT/3TC/ LPV/r. HAART to be stopped after delivery and patient re evaluated for eligibility to HAART</td>
</tr>
<tr>
<td></td>
<td>Baby to receive single dose NVP 2mg/kg at birth and oral AZT 4mg/kg bd for 1 week postpartum.</td>
</tr>
</tbody>
</table>
### Part 3 – Antiretroviral Therapy in Special Circumstances

<table>
<thead>
<tr>
<th>Clinical Situation</th>
<th>Recommendation</th>
<th>Baby</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Scenario 2.</strong> Previous ARV experienced HIV positive pregnant woman</td>
<td>If patient has had single dose NVP in previous pregnancy, consider LPV/r instead of NVP as part of HAART. If patient has failed 1st line ARVs, consider initiating second line therapy if eligible, and guided by the drug regimen used in first line treatment and pregnancy safety category of the new regimen</td>
<td></td>
</tr>
</tbody>
</table>

**SCENARIO 3:** HIV positive woman currently on ART who becomes pregnant

- Continue HAART. Discontinue ddi/d4T combination, EFV, or TDF and switch to more pregnancy friendly regimen.
- Mother to continue HAART postpartum.
- Baby to receive single dose NVP 2mg/kg and AZT 4mg/kg bd for one week.

**SCENARIO 4:** ARV naïve HIV positive pregnant woman in labor

- Give single dose NVP 200mg immediately.
- Give oral AZT and Lamivudine (3TC) for 4 weeks.
- Single dose NVP 2mg/kg at birth
- Oral AZT 4mg/kg bd for 4 weeks

**SCENARIO 5:** Child born to an ARV naïve HIV positive mother

- Mother to be evaluated for ART eligibility.
- Single dose NVP immediately or within 72 hours of birth.
- AZT immediately after birth and continued for 4 weeks

**SCENARIO 6:** Child born to HIV positive mother taking ARV prophylaxis for > 4 weeks

- Mother to continue with HAART or be evaluated for ART eligibility.
- Single dose NVP immediately and AZT for 1 week

*The regimen can be simplified after delivery to an efavirenz or triple nucleoside based regimen.

- AZT will only be prescribed **IF** the hemoglobin level is ≥9g/dl. For those women whose hemoglobin falls below 7 grams, discontinue treatment with AZT.
- In areas where there is no AZT, the minimum PMTCT package is single dose nevirapine at the onset of labor and single nevirapine syrup for the baby.
- Laboratory monitoring will need to be more intensive for patients starting regimens containing AZT (ie, HAART or AZT from 28 weeks). The monitoring schedule will be as follows:
  - Baseline tests CBC (hemoglobin, WBC, platelets)
  - Follow up two weekly for hemoglobin tests.
  - More frequent review for patients who will start with borderline hemoglobin.
This section will highlight the management of patients who are infected with other diseases in addition to HIV.

**HIV-TB co-infection**

TB is one of the most common opportunistic infections in Guyana, and the major cause of death in persons who are HIV-infected. Patients who are co-infected with TB and HIV and receiving HAART have a lower TB relapse rate. This is the justification for starting HAART at higher CD4 lymphocyte count. Treating TB for at least 2 months will ensure sufficient mycobacterial clearance before initiation of HAART.

Table 3.3 contains the recommendations for managing patients with HIV-TB co-infection in Guyana—where CD4 lymphocyte counts are available.

**Table 3.3 HIV-tuberculosis co-infection: recommendations for management**

<table>
<thead>
<tr>
<th>CD4 lymphocyte count</th>
<th>General recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>All TB HIV patients</td>
<td>Offer cotrimoxazole to all.</td>
</tr>
<tr>
<td>&gt;350 cells/mm³</td>
<td>Treat TB first for 6–9 months, then review for HAART.</td>
</tr>
<tr>
<td>&lt;350 cells/mm³</td>
<td>Treat TB for 2 months, and then start HAART.</td>
</tr>
</tbody>
</table>

See Appendix 3–B for recommendations on co-administering PIs and NNRTIs with rifampicin.

In summary:

- Patients who are co-infected with TB and HIV are classified as WHO Stage 3 and thus all of these patients with CD4 lymphocyte count <350 mm³ need treatment for HIV.
- TB should always be treated according to the Guyana National TB Treatment Guidelines.
- Rifampicin reduces nevirapine levels by about 37% and these drugs should generally not be used together. Efavirenz should preferably be used with a rifampicin-based TB regimen.
- Nevirapine should only be used when there is no alternative drug and close clinical and virologic monitoring are available. Liver function should be carefully monitored as both nevirapine and rifampicin cause hepatotoxicity.
- Lopinavir/ritonavir may be used with rifampicin under special circumstances with additional boosting with ritonavir. (See Appendix 3–B.) In the absence of efavirenz, or when efavirenz toxicity or another contraindication is present, physicians may be compelled to use a triple NRTI regimen including abacavir.
- Direct observed therapy (DOT) for HAART along with TB medication should be explored as a treatment method for co-infected patients (The Modified DOT HAART strategy).
- Thiacetazone is not recommended for use for TB treatment in patients co-infected with HIV because of the risk of severe hypersensitivity reactions such as Stevens-Johnson syndrome.
Part 3 – Antiretroviral Therapy in Special Circumstances

- Isoniazid preventive therapy (IPT) can be given to HIV-positive patients who are PPD-positive (>5mm in adults) with no evidence of active tuberculosis infection. Isoniazid is compatible with ARV drugs.

- In view of the high incidences of immune reconstitution inflammatory syndrome (IRIS) as a result of undiagnosed TB disease in persons with low CD4 lymphocyte counts, there was consensus to treat all persons with CD4 lymphocyte count <350/mm³ for 2 months on the usual 4 drug TB regimen for effective mycobacterial clearance before HAART is initiated. Persons with CD4 lymphocyte count >350/mm³ will be treated for at least 9 months before being re-evaluated for HAART except if they become eligible on clinical grounds (Stage 4 OI) or their CD4 lymphocyte count drops to the eligible range before the end of the 9 months.
HIV-hepatitis B or hepatitis C co-infection

The prevalence of hepatitis infection in Guyana is not documented and serology testing is not readily available. In view of this, certain considerations should be borne in mind when managing patients who are HIV-infected:

- When the tests are available, baseline hepatitis serology should be performed before starting HAART, and caution used when choosing HAART regimens for those who have Hepatitis A, B, or C co-infection.
- There may be accelerated liver damage in patients who are receiving HAART and are co-infected with HIV and hepatitis.
- Nelfinavir is the least hepatotoxic of the PIs.
- Lamivudine and tenofovir have antiviral effects in patients with hepatitis B, but hepatitis B viral resistance may occur in patients receiving only one of the drugs. This resistance may worsen liver damage in patients who are co-infected with HIV and hepatitis and are receiving these drugs.
HIV-malaria co-infection

Malaria is endemic in certain parts of Guyana; therefore, clinicians will encounter patients with HIV-malaria co-infection. The following should be noted:

- HIV infection appears to increase the severity of malaria infection.
- Pregnant women who are HIV-infected appear to be more susceptible to acquiring malaria, and people who are immunosuppressed seem to have more frequent symptomatic episodes.
- Malaria infection appears to increase viral load, which could result in an increased risk of transmitting HIV as well as an increased risk of HIV disease progression.
- Malaria may cause severe anaemia in women and children. Thus, increased vigilance is warranted in patients who are HIV-infected and at risk for malaria, and in patients who follow a HAART regimen containing drugs that may cause anaemia, particularly zidovudine.
- A patient who is HIV-infected and presents with unexplained anaemia and fever should be evaluated for malaria.
- Infants born to mothers who are co-infected with HIV and malaria are more likely to die and are approximately twice as likely to be infected perinatally with HIV if a high placental burden of malaria is present in the mother.
- Cotrimoxazole has strong anti-malarial activity and is used commonly for malaria prophylaxis in patients who are HIV-infected. As more and more of these patients take cotrimoxazole, there is a theoretical danger of patients with malaria developing resistance to cotrimoxazole and pyrimethamine/sulfadoxine (related to cotrimoxazole).
HIV-dengue fever co-infection

The Caribbean is a dengue fever-endemic area with outbreaks of virus types 1, 2 and recently 3 reported. Patients who are co-infected with HIV and dengue fever, and who are taking ARV drugs that may cause anaemia or hemorrhagic reactions should be monitored carefully.
HIV-sickle cell disease

Sickle cell disease (SCD) is a genetic disorder characterised by chronic anaemia, vaso-occlusive events, recurrent infections, and functional asplenia. Especially in children, functional asplenia causes recurrent infections that may be exacerbated by the immunocompromised state. The following should be noted when treating patients with HIV-sickle cell co-infection:

- Anaemia and recurrent infections are common to both conditions. Thus, extra vigilance must be mounted to investigate and proactively manage anaemia and infections. In view of the risks of anaemia and jaundice with ARV drugs, caution should be exercised when prescribing ARV drugs.
- Prophylactic antibiotics, pneumococcal vaccine, early identification and treatment of serious bacterial infections, and general prophylaxis are crucial.
HIV TYPE-2

HIV type-2 is found most often in West Africa, but as a result of migration is becoming more prevalent in Western Europe and other places. It is thought to be less virulent and transmissible than the more common HIV type-1 and to run a less aggressive course with slower disease progression.

It is important to note that all NNRTIs and Nelfinavir are ineffective against HIV type-2. Nevirapine is in the first-line PMTCT and HAART regimens for Guyana. Because the prevalence and clinical significance of HIV-2 in Guyana are unknown, the implications of the drug's being ineffective against type-2 are unclear.
INJECTION DRUG USERS

In Guyana HIV is transmitted mainly through unprotected heterosexual intercourse with an infected partner. Injection drug use is emerging as a public health problem and a growing route for HIV transmission. The following should be borne in mind when treating injection drug users who are HIV-infected:

- The treatment protocol for injection drug users is the same as for other patients.
- In addition, issues about lifestyle instability, drug dependence, adherence problems, and ARV drug interactions with addictive drugs must be addressed in the treatment programme.
- Direct observed therapy (DOT) should be considered for this group of patients.

Support systems must be identified to help with drug adherence, and coordination is required with community-based AIDS organizations and drug treatment programmes.
POST-EXPOSURE PROPHYLAXIS

Post-exposure prophylaxis (PEP) refers to using antiretroviral agents to reduce the risk of HIV transmission following a potentially infectious exposure—occupational exposure in a healthcare setting or sexual assault.

For Guyana’s national guidelines on PEP, please see Appendix 3-C.

Occupational exposure

- The average risk of HIV transmission due to percutaneous (needle stick) injury is 0.3%, while the risk due to a mucocutaneous exposure is estimated at 0.09%.
- Potentially infectious body fluids include blood, spinal fluid, pleural fluid, pus, and amniotic fluid. Urine, sweat, and faeces are not considered infectious unless visibly bloody.
- The following should be considered serious risk factors for transmission:
  - deep injury
  - visible blood on device
  - large bore hollow needle
  - exposure of device to source patient’s vein or artery
  - high viral titer in the source patient
- Studies have shown that PEP – when initiated as early as possible with AZT alone – reduces the risk of HIV transmission by about 80%.
- Everyone who is exposed to potentially-infected body fluids should receive PEP.
- PEP should be taken as soon as possible after exposure, preferably within 2 hours. PEP after 72 hours of exposure is not recommended.

Assessing the need for PEP and determining the recommended regimen

1. Evaluate the exposure.
   - Document the exposure and report to supervisor
   - High risk: exposure to large quantity of body fluids or secretions from a potential source of HIV infection with deep mucocutaneous penetration

2. Evaluate the HIV status of the source patient.
   - If possible, the source patient should have a rapid test done after counselling. If source cannot be tested or refuses testing, manage exposed person as if source was HIV-positive.

3. Determine the PEP regimen.
   - Determine if the patient needs the basic regimen or the expanded regimen.
Guyana PEP regimen

Zidovudine (AZT) or tenofovir (TDF) + lamivudine (3TC) or emtricitabine (FTC) + efavirenz (EFV) for 4 weeks

*Nevirapine should not be used in PEP regimens because of unacceptably high rates of life-threatening toxicity reported in HIV-negative healthcare workers taking nevirapine-containing PEP regimens.*

*Lopinavir/ritonavir can be used in healthcare workers who are intolerant to efavirenz, where the source patient is already on first line therapy or where the index case is pregnant.*

General principles

- Universal precautions guidelines and practices should be actively promoted in all healthcare facilities. Infection control designees can be identified to monitor and oversee universal precautions, PEP drug availability, and documentation.
- The basic ARV regimen for PEP should be available 24 hours a day, including nights and weekends, in all healthcare facilities.
- Nevirapine should not be used in PEP regimens because of unacceptably high rates of life-threatening toxicity reported in healthcare workers taking nevirapine-containing PEP regimens.
- A confidential log book should be maintained to record all cases of exposure, the specific circumstances of the exposure, and the drugs prescribed.
- After counselling, a rapid HIV test should be offered to any healthcare worker who has been exposed. (People who refuse HIV testing or are HIV-infected should not take PEP.)
- The fact that the healthcare worker was offered counselling and testing should be documented in writing. If the patient refuses testing, that should be documented as well.
- If the healthcare worker’s test results are negative, continue PEP. To ascertain whether seroconversion has occurred, repeat the test at 6 weeks and at 3 and 6 months. If there is seroconversion, refer the healthcare worker to an HIV treatment center for follow up.
- Post-traumatic stress counselling for the healthcare worker is also important.
- The exposed healthcare worker should also be tested for hepatitis B and have a liver function test and full blood count. Hepatitis B PEP should be provided, as the risk of hepatitis B transmission is as high as 30%—more than 100 times the risk of HIV transmission.
- If ARV drug resistance is suspected in the source patient, an expert opinion should be sought from an HIV clinician. At least one or more drugs in a class to which the source patient’s HIV is likely to be sensitive should be included.
Sexual assault

- The risk of HIV transmission in a single sexual assault is comparable to the risk associated with occupational exposure. However, the risk may be higher if the assault caused physical trauma (a rape) or if the source or the exposed individual had genital ulcerative lesions.
- In cases of sexual assault, administering PEP after 72 hours of exposure is not recommended.
- If rape is reported or suspected, the police should be informed.
- In all cases of sexual assault, post coital contraception, STI prophylaxis and trauma counseling should be offered.
APPENDICES
Appendix 3–A Recommendations for co-administering non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors (PIs) with rifampin

NNRTIs should always be listed first.

<table>
<thead>
<tr>
<th>NNRTIs</th>
<th>ARV dose change</th>
<th>Rifampin dose change</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efavirenz (EFV)</td>
<td>None</td>
<td>None (600 mg once daily)</td>
<td>Efavirenz AUC↓ by 22%. May reduce efavirenz to 600 mg once daily if 800 mg dose not well tolerated.</td>
</tr>
<tr>
<td>Nevirapine (NVP)</td>
<td>200 mg twice daily</td>
<td>None (600 mg once daily)</td>
<td>Nevirapine AUC↓ by 37%–58%.</td>
</tr>
</tbody>
</table>

Nevirapine should only be used if no other option exists and clinical and virologic monitoring is possible.

<table>
<thead>
<tr>
<th>PIs</th>
<th>ARV dose change</th>
<th>Rifampin dose change</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ritonavir (RTV)</td>
<td>None</td>
<td>None (600 mg once daily)</td>
<td>Ritonavir AUC↓ by 35%. No change in rifampin concentration.</td>
</tr>
<tr>
<td>Saquinavir (SQV)</td>
<td>Rifampin and saquinavir should not be used together. Saquinavir 400 mg twice daily when boosted with ritonavir 400 mg twice daily</td>
<td>None (600mg once daily)</td>
<td>Saquinavir AUC↓ by 84%. Limited clinical experience, data</td>
</tr>
<tr>
<td>Lopinavir + ritonavir (LPV+RTV)</td>
<td>Rifampin and lopinavir/ritonavir should not be used together.</td>
<td>Lopinavir AUC↓ by 75% and Cmin↓ by 99%.</td>
<td></td>
</tr>
</tbody>
</table>

AUC = area under the curve.

Appendix 3–B Exposure to Blood and Body Fluids

The Following Guidelines are Hereby Recommended, When Managing Percutaneous Exposure to Blood and Body Fluids.

THE ADOPTED GUIDELINES SHOULD BE WIDELY DISSEMINATED TO ALL MEMBERS OF STAFF.

RESPONSIBILITIES

THE HEALTHCARE WORKER
Any healthcare workers (HCW) who has been accidentally injured should take the following steps immediately:

1. WASH SITE THOROUGHLY WITH SOAP AND WATER.
2. IMMEDIATELY INFORM THE SUPERVISOR OF THE ACCIDENT.

THE SUPERVISOR
The supervisor upon being informed must immediately:

- Make arrangements for the healthcare worker to be seen by the physician on duty at the accident and emergency department.
- Inform the patient of the injury of the healthcare worker and of the need to obtain a blood sample for HIV testing.
- Have blood sample (5ml clotted specimen) taken off from the patient, as soon as the patient’s physician is informed of the accident and document the request for the patient to be tested for HIV.
- Have 5ml of blood (clotted specimen) taken from the healthcare worker.
- Have both samples sent to the laboratory for HIV testing.

The supervisor should ascertain the type of exposure that occurred and record the following information on the prescribed surveillance form:

- TIME OF ACCIDENT
- TYPE OF INJURY
  - Solid or Hollow Bore Instrument
  - Whether Blood was Exchanged
- TYPE OF PROCEDURE THAT WAS BEING UNDERTAKEN, WHEN INJURY OCCURRED
  - Both the healthcare worker and the patient must be sent for HIV counselling as soon as possible after the exposure has occurred.
  - Samples must be sent to the National Infectious Diseases (NLID) at the National Blood Transfusion Centre.
Appendix 3–B Exposure to Blood and Body Fluids (continued)

THE PHYSICIAN (EMERGENCY ROOM)
The physician at emergency room of the new ambulatory care and diagnostic centre will:
- Request rapid HIV test of blood specimen (5ml clotted) extracted from the healthcare worker.
- Document incident.
  - Prescribe drug treatment according to the National Regime.
    Select one of two (2) regimens depending on the risk related to the injury:
    **Expanded regimen**
    1. Zidovudine 300mg twice daily / tenofovir 300mg daily
    2. Lamivudine 150mg twice daily
    **Plus**
    1. Efavirenz 600mg daily for 4 weeks (28 days) (Lopinavir/ritonavir can be used if the healthcare worker cannot take efavirenz or in cases where the source patient is already on first line therapy.
    2. 6
    3. Refer the healthcare worker to the nearest HIV treatment centre.

THE PHARMACY MANAGER (ESS)
The Pharmacy Manager (ESS) must ensure that:
- The medication can be dispensed on demand.
- A continuous supply of the medication is maintained in the office of the Director of Nursing Services to facilitate dispensing of the first dose (by the corporation’s Nursing Supervisor); whenever the dispensary is closed.

THE DIRECTOR OF NURSING SERVICES
The Director of Nursing Services shall ensure that the stock of the medication is adequate.

THE OCCUPATIONAL SAFETY AND HEALTH OFFICER
The Occupational Safety and Health Officer shall:
- Be informed of the accident within 48 (forty-eight) hours of its occurrence.
- Document the following information in the accident report:
  - Date, time and place of the accident
  - Cause of accident
  - Nature and location of injury
  - Action taken after the accident
  - Description of events leading up to the accident
POST-EXPOSURE PHOPHYLAXIS (PEP)
- In all cases of accidental injuries, regardless of whether the patient’s HIV status is known, PEP must be started within 2 (two) hours of the injury.
- In addition, the healthcare worker must be followed up for at least 6 (six) months.
- Referral to the nearest ARV treatment site for follow-up management and care is advisable.

POST-EXPOSURE MANAGEMENT (PEM)
- The healthcare worker must be counselled to either abstain from sexual intercourse or use condoms, for at least 6 (six) months after the exposure.
- The healthcare worker should have the HIV test repeated at 6 (six) weeks, 3 (three) months, and 6 (six) months, after the exposure has occurred.

RECORD KEEPING/ REPORTING
As part of our surveillance for these types of injuries, a record must be made of all accidental exposures on the prescribed reporting form and a copy must be sent to the National AIDS Programme Secretariat (NAPS).

REVIEW
This Policy and its Guidelines will be subjected to a yearly review or update as warranted.
Prevention of opportunistic infections

Prophylaxis should be provided for the following conditions:

- **Tuberculosis (TB) prophylaxis**: Provide when purified protein derivative (PPD) result is positive (> 5mm for adults), with negative chest x-ray and sputum, at any CD4 lymphocyte count. In children, do not give INH prophylaxis to those who are symptomatic because of the difficulty of excluding the diagnosis of TB in infants and children.

- **Pneumocystis jiroveci (formerly carinii) pneumonia (PCP) prophylaxis**: In adults, provide when CD4 lymphocyte count <200 cells/mm3. Do not start PCP prophylaxis with cotrimoxazole at the same time as starting nevirapine as both cause rashes.

- **In HIV exposed infants and children**, give cotrimoxazole beginning at age 4–6 weeks (or when first seen) until confirmed HIV-negative. See Table 4.1 for detailed information on prophylaxis in children with documented HIV infection.

In adults and children, begin cotrimoxazole at least 2 weeks before starting ART.

- **Toxoplasmosis prophylaxis**: Provide prophylaxis when Toxoplasma IgG is positive and CD4 lymphocyte count <100 cells/mm³.

- **Mycobacterium avium complex (MAC) prophylaxis**: Provide when CD4 lymphocyte count <50 cells/mm³ as long as active TB and MAC have been ruled out.

For recommendations on discontinuation of prophylaxis, readers will note that criteria vary by such factors as duration of CD4 lymphocyte count increase above 200 and—in the case of secondary prophylaxis—duration of treatment of the initial episode of disease. These differences reflect the criteria used in specific studies. Therefore, some inconsistency in the format of these criteria is unavoidable. Please consult with an experienced HIV clinician before discontinuing prophylaxis.
# Table 4.1 Prophylaxis of selected opportunistic infections

## Pneumocystis jiroveci (formally Pneumocystis carinii) pneumonia prophylaxis

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Eligibility</th>
<th>Regimen(s)</th>
<th>Discontinuation</th>
</tr>
</thead>
</table>
| **Primary Pneumocystis jiroveci (formally Pneumocystis carinii) pneumonia in adults** | CD4 <200 cells/mm<sup>3</sup>  
Symptomatic HIV infection  
WHO Stage 3 or 4 (including oropharyngeal candidiasis, and TB irrespective of CD4) | Trimethoprim-sulfamethoxazole (TMP-SMX) 960mg once daily*  
Alternative dapsone 2 mg/kg body weight by mouth once daily (in case of allergy or intolerance to cotrimoxazole) | CD4 lymphocyte >200 cells/mm<sup>3</sup> for >3 months in response to HAART |
| **Secondary PCP prophylaxis in adults**                                   | History of PCP                                                              | Trimethoprim-sulfamethoxazole (TMP-SMX) 960 mg once daily* OR  
Alternative: dapsone 100 mg once daily                                      | Continue until CD4 >200 mm<sup>3</sup> while on HAART.  
Should be re-started if CD4 decreases to <200 mm<sup>3</sup> or if PCP recurs at CD4 >200 mm<sup>3</sup>. |

*TMP-SMX 960 mg once daily is the preferred dose but in patients with anaemia, skin rash, or liver problems, the 480 mg dose is preferably given and has been found to be efficacious.*

---

**PCP prophylaxis may be given to eligible pregnant women after 1<sup>st</sup> trimester.**

**HIV exposed infants and children:**
- All HIV-exposed children from 4–6 weeks (or when first seen) until confirmed HIV-negative
- Infants of any age who are breastfeeding and continue prophylaxis until HIV can be excluded by HIV antibody testing at least 6 weeks after complete cessation of breastfeeding

**Infants and children with documented HIV infection**
- < 1 yr: prophylaxis indicated regardless of CD4 count or clinical status
- 1-4 yrs: WHO Stages 1, 3, and 4 regardless of CD4 count OR Any WHO Stage and CD4 < 25%
- ≥5 yrs Follow adult recommendations

**Children <5 yrs of age,** who started prophylaxis during infancy, should continue receiving it, irrespective of whether they are receiving ARV therapy.

**Children ≥ 5 yrs of age,** who started prophylaxis after infancy should follow recommendations for adults.

---

**Secondary PCP prophylaxis in children**

**History of PCP**

Same as in primary prophylaxis

**Children <5 yrs of age,** who started prophylaxis during infancy, should continue receiving it, irrespective of whether they are receiving ARV therapy.

**Children ≥ 5 yrs of age,** who started prophylaxis after infancy should follow recommendations for adults.
Table 4.1 Prophylaxis of selected opportunistic infection (continued)

<table>
<thead>
<tr>
<th>Mycobacterium tuberculosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Conditions</strong></td>
</tr>
<tr>
<td>TB prophylaxis in adults and children</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Toxoplasmosis gondii</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Conditions</strong></td>
</tr>
<tr>
<td>Primary toxoplasmosis prophylaxis in adults</td>
</tr>
<tr>
<td>Primary toxoplasmosis prophylaxis in children</td>
</tr>
<tr>
<td>Secondary toxoplasmosis prophylaxis in adults</td>
</tr>
<tr>
<td>Secondary toxoplasmosis prophylaxis for children</td>
</tr>
</tbody>
</table>

† Dose of INH for TB prophylaxis in HIV-infected children

<table>
<thead>
<tr>
<th>Weight</th>
<th>Dosage of INH</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-10 kg</td>
<td>50 mg</td>
</tr>
<tr>
<td>11-20 kg</td>
<td>100 mg</td>
</tr>
<tr>
<td>21-30 kg</td>
<td>200 mg</td>
</tr>
</tbody>
</table>
### Table 4.1: Prophylaxis of selected opportunistic infection (continued)

**Mycobacterium avium complex (MAC)**

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Eligibility</th>
<th>Regimens</th>
<th>Discontinuation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary MAC prophylaxis for adults</strong></td>
<td>CD4 &lt;50 cells/mm³ and active MAC and TB ruled out</td>
<td>▪ Azithromycin* 1200 mg po once weekly OR</td>
<td>▪ Discontinue when CD4 &gt;100 cells/mm³ for &gt;3 months on HAART.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▪ Clarithromycin 500 mg po twice daily</td>
<td>▪ Re-start if CD4 falls to &lt;50–100 cells/mm³.</td>
</tr>
<tr>
<td><strong>Primary MAC prophylaxis for children</strong></td>
<td>&lt;1 yr and CD4 &lt;750 cells/mm³</td>
<td>Azithromycin* 20 mg/kg (max 1200 mg) once weekly OR</td>
<td>▪ Not well evaluated</td>
</tr>
<tr>
<td></td>
<td>1–2 yrs and CD4 &lt;500 cells/mm³</td>
<td>clarithromycin 7.5mg/kg (max 500mg) twice daily</td>
<td>▪ Consult with an experienced HIV clinician before starting primary prophylaxis.</td>
</tr>
<tr>
<td></td>
<td>2–6 yrs and CD4 &lt;75 cells/mm³</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;6 yrs and CD4 &lt;50 cells/mm³</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Secondary MAC prophylaxis for adults</strong></td>
<td>Diagnosis of disseminated MAC</td>
<td>If patient has disseminated MAC, consult an experienced HIV clinician for duration and discontinuation of treatment.</td>
<td>Secondary prophylaxis for disseminated MAC may be discontinued in patients with a sustained (eg, &gt;6 months) increase in CD4 lymphocyte count to &gt;100 cells/µL in response to HAART after 12 months of MAC therapy and no symptoms or signs attributable to MAC.</td>
</tr>
<tr>
<td><strong>Secondary MAC prophylaxis for children</strong></td>
<td>Diagnosis of disseminated MAC</td>
<td>Same as above</td>
<td>Same as above</td>
</tr>
</tbody>
</table>

* Azithromycin is preferred over clarithromycin because it has fewer interactions with HAART than clarithromycin.


**Source:** Adapted from: Lynen L. and Biot M (Eds.). 2006. *Clinical Aids Care Guidelines for Resource-Poor Settings*. Brussels, Belgium. Médecins Sans Frontières.


SYNDROMIC CARE OF HIV RELATED ILLNESSES

Most of the algorithms in this section were adapted from Lynen L. and Biot M (Eds.). 2000. Clinical AIDS Care Guidelines for Resource-Poor Settings. Brussels, Belgium. Médecins Sans Frontières.
Chronic diarrhoea in adults

Chronic diarrhoea: annotations
(A) Definition: liquid stools three (3) or more times daily, continuously or episodically for more than one month in a patient with HIV infection.

It is important to obtain the following history in a patient with diarrhoea:
- fever
- blood or mucus in the stools
- drug history
- previous antibiotic use
- hospitalisation

Conduct a physical examination to assess the patient’s degree of hydration and nutritional status.

Nutritional support is very important to avoid wasting. Try giving regular small meals as tolerated by the patient. At least 2500 kcal once daily are needed.
At all levels of care, time must be taken to instruct the patient’s family about how to handle soiled bed linen and the disposal of faeces. It may be necessary to give them appropriate material (gloves, buckets, etc.).

**Chronic diarrhoea**

Continued from flowchart 1

Treat with TMF-SMX, 480 mg (SS)
2 tablets 2 x daily for 5 days.
If no response,
metronidazole, 500 mg 3 x daily
for 7 days (A)

Improvement?

Yes

Relapse within 4 weeks of therapy?

Yes

Retreat with drug as in box 1 for 3 weeks
(B)

No

Follow up as needed

No

Give constipating and anti-haemorrhagic agents
(C)

Improvement within one week of maximal dosage

Yes

Continue treatment

No

Stop treatment; refer (D)

Level A
Chronic diarrhoea: annotations (level A)

(A) TMP-SMX. Any patient who is HIV-infected, and has an episode of diarrhoea lasting longer than 5 days should receive empirical treatment with antibiotics, in association with oral rehydration solution (ORS). If there is no response, a course of metronidazole should be administered. These drugs cover common bacterial infections and bacterial overgrowth.

(B) It is possible that the initial course of treatment was too brief. A prolonged course of therapy (3 weeks) is justified.

(C) For example, loperamide 4 mg initially, followed by 2 mg after each liquid stool. The maximum daily dose should not exceed 16 mg.

(D) An alternative treatment is codeine phosphate 30 mg to 60 mg 3 to 6 times daily or oral (liquid) morphine starting with 2.5 mg 4 hourly. Constipating agents should not be given to patients with bloody diarrhoea.

(E) An antihelminthic drug should be given first. Mebendazole 100 mg 3 times daily for 7 days is partially effective against strongyloidiasis. Albendazole 400 mg once daily for 3 days is a broader spectrum antihelminthic but not often available for the homecare setting.

(F) When diarrhoea is disabling, refer to the nearest district or the tertiary care hospital – Georgetown Public Hospital Corporation.
**Chronic diarrhoea: annotations (level B)**

(A) If the patient has not been treated, a trial with antibiotics is justified, always associated with ORS and feeding instructions. Avoid repeating a treatment that did not lead to improvement. If the patient has already received an unsuccessful treatment for this episode of diarrhoea, a stool examination should be performed to detect specific pathogens. Three stool samples may increase the diagnostic yield of parasites.

(B) A fresh stool examination (direct and after concentration) and a lugol-stained wet mount is necessary at this level.

(C) In the case of a helminthic infection, treat accordingly:

- **Strongyloidiasis** can be successfully treated with ivermectin 12 mg once daily for 3 days. An alternative treatment is albendazole 400 mg twice daily for 5 days. Monthly maintenance therapy is necessary (Albendazole 400 mg or ivermectin 6 mg).

- **Trophozoites of *Entamoeba histolytica*** should be treated with metronidazole 750 mg 3 times daily for 10 days followed by a contact amoebicide:
  - Diloxanide furoate 500 mg 3 times daily for 10 days or
  - Paromomycin 500 mg 3 times daily for 7 days.
  - *Giardia lamblia* is treated with metronidazole 750 mg 3 times daily for 5 days.
  - *Isospora belli* is treated with higher than usual doses of TMP-SMX:
    - 1 double strength (DS) 4 times daily for 10 days followed by 1 DS twice daily for 3 weeks. Single doses are not recommended in patients who are HIV-infected because of unreliable gastric absorption.

(D) As in patients who are not HIV-infected, 5%–30% of patients with *Clostridium* associated diarrhoea relapse. The treatment with metronidazole should be repeated.

(E) In long-lasting or severe diarrhoea with fever, a combination of metronidazole with an antibiotic effective against the local strains of bacterial enteric pathogens is warranted. Empiric therapy with quinolones is most likely to be effective:

- Nalidixic acid 1 g 4 times daily for 10 days or
- Ciprofloxacin 500 mg twice daily for 10 days or ofloxacin 400 mg twice daily for 10 days.

Although chloramphenicol has become unacceptable for use in certain countries, it remains a valuable drug for severe Gram-negative infections, and it is more readily available at level B. If there is no response, bacterial resistance or the presence of a parasite not responding to metronidazole must be considered. At this point, a course of erythromycin might be tried—500 mg twice daily for 5 days for *Campylobacter* dysentery.

(F) For example, loperamide 4 mg initially, followed by 2 mg after each liquid stool. The maximum daily dose should not exceed 16 mg. An alternative is codeine phosphate 30–60 mg 3 to 6 times daily. Constipating agents should not be given to patients with bloody diarrhoea.

(G) At level C, special stains or stool cultures may be performed to identify remaining treatable conditions. If referral is not possible, a treatment trial for remaining treatable causes should be started.
Part 4 – Prophylaxis And Management of Common Opportunistic Infections

- Resistant bacteria: it is important to obtain information on prevailing resistance patterns in your region, eg, in some areas; most of the salmonellae and shigellae are resistant to cotrimoxazole, amoxicillin, and chloramphenicol. However, they remain sensitive to quinolones and nalidixic acid.
- *Isospora belli*: a parasite sometimes encountered, will respond to higher than usual doses of CTX (1 DS 4 times daily for 10 days followed by 1 DS twice daily for 3 weeks) This infection is less likely to occur, however, in patients who are taking TMP-SMX prophylaxis.
- Albendazole will be effective against strongyloides and may have an effect on microsporidia.
Chronic diarrhoea (2)

Continued from flowchart 1 level C

- WBC +++ RBC +++ in stools
  - Yes: History of antibiotic use?
    - Yes: Treat with metronidazole, 500 mg x 3/day for 7 days (I)
    - No: Improvement?
  - No: Fever?
    - Yes: Empiric antibiotics +/- metronidazole 10 days (J)
    - No: Metronidazole 7 days
      - Improvement?
        - Yes: Follow up as needed
        - No: Empiric therapy (L)
          - Improvement?
            - Yes: Follow up as needed
            - No: Symptomatic treatment (M)

- Follow-up as needed

Treat remaining treatable causes that are epidemiologically most likely in your setting (K)

Improvement?
Chronic diarrhoea: annotations (level C)

(A) A trial of antibiotics is only justified if this is a new case of diarrhoea. Always consider previous treatment in order to avoid re-running the same algorithms every time without success. If your patient was referred from level B, start immediately with the stool examination.

(B) Stool microscopy: fresh examination and after concentration. Multiple stool samples may be necessary.

(C) Stool culture: if available, will be useful to detect resistant enteropathogens.

(D) Systematic stool culture at this level may also be helpful for orienting empiric therapy at the lower levels of care.

(E) See annotation C, level B.

(F) Cryptosporidium and Isospora belli are identified in the stool with a modified acid-fast stain.

(G) Isospora cysts are much larger than those attributable to Cryptosporidium species (20–30 µm vs. 4–6 µm). The distinction between them is important because Isospora belli usually responds well to high-dose TMP-SMX (1 DS 4 times daily for 10 days, followed by 1 DS twice daily for 3 weeks, then chronic suppression with 1 DS per day (PCP prophylaxis dose).

(H) There is no good treatment for cryptosporidiosis. Often symptomatic control with antidiarrhoeal agents is the only recourse. Sometimes there is a partial response with paromomycin (500 mg 4 times daily). If there is a response, treatment should be continued for 2–4 weeks, after which it is often necessary to maintain the patient on suppressive therapy with paromomycin 500 mg twice daily.

(I) Loperamide or codeine phosphate: Treatment is often not successful, especially for cryptosporidiosis and microsporidiosis. Do not continue an ineffective treatment. Switch to symptomatic treatment.

(J) On rare occasions, Cyclospora, another protozoan, can be detected on the stains for Cryptosporidium. The Cyclospora oocysts are a bit bigger (8–9 µm) than cryptosporidium oocysts (5 µm). Cyclospora can be treated with TMP-SMX 1 DS 4 times daily for 10 days, followed by secondary prophylaxis with TMP-SMX.

(K) Microsporidia: Thin smears of stool-formaline suspension that has not been concentrated or of duodenal aspirates stained with Weber's modified trichrome method.

(L) Frequent hospitalisation of patients who are HIV-infected and exposure to antibiotics puts them at high risk of infection with the toxin-producing strain of Clostridium difficile. Five percent (5%) to 30% of patients with Clostridium-associated diarrhoea relapse. The same treatment with metronidazole should be repeated.

(M) When no specific pathogens are identified, or when stool culture is not available, empiric antibiotherapy is justified. For watery diarrhoea: high dose TMP-SMX for isosporiasis; for dysenteric stools (WBC + RBC): nalidixic acid, or another quinolone (ciprofloxacin or ofloxacin) for resistant shigellae and salmonellae. If not yet treated with metronidazole, it may be added at this point; giardiasis and amoebiasis are then treated as well.
If the patient does not respond, bacterial resistance or the presence of a parasite not responding to metronidazole must be considered. A trial with albendazole (effective against Microsporidia and Strongyloidiasis) or a higher-than-usual dose of TMP-SMX (effective against Isospora belli) may be tried. The choice will depend on the epidemiology of gastrointestinal pathogens in the region.

See annotation (J). Giardiasis should have responded. If Campylobacter was diagnosed from stool culture, the first-line treatment is now erythromycin 500 mg twice daily for 5–10 days.

Once this flowchart has been followed without result, untreatable conditions remain: cytomegalovirus (CMV), Cryptosporidium, atypical mycobacteria, etc. Continue with palliative care.
Respiratory problems

Respiratory infections are the most common infections in patients who are HIV-infected. Differential diagnoses in order of importance include tuberculosis, *Pneumocystis* pneumonia, pyogenic bacterial infections, fungal infections such as Cryptococcal infection, and helminthic infections. Tuberculosis should be treated according to the information on HIV-TB co-infection in this guideline (above) as well as in the *Guyana National TB Treatment Guidelines*.

**Pneumocystis jiroveci (formerly carinii) pneumonia**

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Diagnosis</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-acute onset of fever, cough and dyspncea</td>
<td>Chest x-ray: bilateral interstitial and alveolar infiltrates</td>
<td>TMP 20 mg/kg and SMX 100 mg/kg once daily divided into 4 doses per day IV or PO for 21 days (2 double strength tablets 3 times a day)</td>
</tr>
<tr>
<td>Exertional dyspncea usually present</td>
<td>Nodule, cavities and pneumothorax sometimes present. All patients with pneumothorax should be treated empirically for PCP.</td>
<td>Prednisolone 40 mg twice a day for 5 days, then 40 mg once daily for hypoxic patients (pO2 &lt;70 mmHg) [pO2 can be measured with a pulse oximeter in district and tertiary hospitals].</td>
</tr>
<tr>
<td>Decrease in oxygen (O2) saturation, especially during effort.</td>
<td>Sputum smear and broncho-alveolar lavage with methenamine silver staining.</td>
<td>Alternative to TMP-SMX regimen:</td>
</tr>
<tr>
<td></td>
<td>High lactate dehydrogenase (LDH)</td>
<td>- Primaquine 15-30 mg qd + Clindamycin 600-900 mg IV q 6-8h (or clindamycin 300–450 mg po q 6–8hr),</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Dapsone 10 mg + Trimethoprim 20 mg/kg PO once daily x 21 days</td>
</tr>
</tbody>
</table>

**Pyogenic bacterial pneumonia**

This is similar to pneumonia seen in patients who are not HIV-infected but is more severe, acute, and caused by organisms that are less common. It should be managed aggressively using the known sensitivity patterns. For bacterial pneumonia in patients not receiving PCP prophylaxis, amoxicillin, amoxyclovulanic acid, second-generation cepahlosporins, and cotrimoxazole are all drugs of choice.
Part 4 – Prophylaxis And Management of Common Opportunistic Infections

Respiratory problems (A)

History and physical examination

Severe dyspnoea and/or respiratory distress

Yes

Refer with supportive therapy (B)

No

Choose appropriate level

Level A
Diagnosis is based on history and physical examination only

Level B
Level A + limited laboratory + microscope + (chest X-ray)

Level C
Level B + chest X-ray + complete CBC + oxygen saturation + LDH + sputum stains and culture
Respiratory problems: annotations

(A) Definition: persistence or worsening of cough and/or chest pain and/or dyspnoea in a patient with symptomatic HIV infection

Possible aetiologies include (in order of frequency):

- **Infections**
  - pyogenic bacteria: *Streptococcus pneumoniae, Haemophilus influenzae*
  - tuberculosis (TB)
  - *Pneumocystis pneumonia* (PCP)
  - fungal infections: cryptococcosis, penicilliosis, aspergillosis, histoplasmosis, etc.
  - (atypical mycobacteria): rarely
  - (CMV, toxoplasmosis): rarely

- **Malignancies**
  - Kaposi’s sarcoma
  - lymphoma

- **Others**: lymphoid interstitial pneumonitis

- **Associated problems**
  - pleural effusion/empyema (often TB)
  - pericardial effusion (often TB)
  - pneumothorax (associated with TB, PCP, pneumonia or cancer)

- **Heart failure, pulmonary embolism, asthma, severe anaemia**

(B) If clinically diagnosed hypoxaemia is present (dyspnoea, cyanosis), oxygen therapy is indicated. A patient with a respiratory rate of more than 30 beats/minute while resting will need hospitalisation and oxygen, and must be referred to a clinician at the appropriate level.

---

**Respiratory problems**

- **Cough >3 weeks and/or haemoptoe?**
  - Yes: Start amoxicillin and refer to exclude TB
  - No

- **Patient on TMP/SMX prophylaxis?**
  - Yes: Treat with amoxicillin (A)
  - No: Treat with TMP/SMX, 450 mg, 2 x 2 tablets daily (B)

- **Improvement after 3 days?**
  - Yes: Complete treatment for 10 days (A)
  - No: Further diagnostic evaluation is needed. Refer (C)
Respiratory conditions: annotations (level A)
If drugs are available for the homecare setting, this algorithm may be followed. If not, the patient must go to the clinic.

(A) In most developing countries, bacterial pathogens are the most probable cause of infection. A trial with antibiotics to treat pneumococcal pneumonia is justified. In patients who were taking TMP-SMX prophylaxis, it is better to prescribe amoxycillin 500 mg to 1 g, 3 times daily for 10 days.

(B) For patients who are not taking TMP/SMX prophylaxis, the first choice is treatment with TMP-SMX, as it covers the most common respiratory pathogens: S. pneumoniae, H. influenzae, Moraxella cattharalis and Klebsiella pneumoniae. The dose is TMP-SMX 960 mg twice daily.

(C) Excluding tuberculosis is now a priority. Every HIV-infected patient with respiratory symptoms must be screened for TB.
Respiratory conditions: annotations (level B)

(A) It is important to screen patients and do sputum examination for patients with chronic cough (duration >3 weeks).

(B) In countries with a high prevalence of TB, sputum examination for AFB is essential. The highest yield of AFB in smear and culture is with expectorated early-morning sputum. Induced sputum should be used only in people who cannot expectorate. The sensitivity of sputum examination is decreased in HIV-positive patients.

(C) In many countries, pyogenic bacteria will be the most probable cause of bacterial pneumonia. If the patient is already taking TMP-SMX prophylaxis, the drug of choice is amoxycillin. If available, amoxyclovulanic acid or cefuroxime has a broader spectrum and could be the first choice at level B.

(D) For patients who are not yet receiving TMP-SMX prophylaxis, TMP-SMX is preferred over amoxycillin because of the broader spectrum of the former. If available, amoxyclovulanic acid or cefuroxime is the best choice for empirical therapy for respiratory infections.

(E) If there is no improvement after a 5-day course of antibiotics, the patient should be re-evaluated. Repeat the history and physical examination thoroughly. Look for additional signs that may help in the differential diagnosis. Skin lesions are present in Kaposi's sarcoma, disseminated cryptococcosis, or penicilliosis. Pyomyositis and cellulites point toward staphylococcal infection. High fever, pleuritic-type chest pain, and productive cough are suggestive of bacterial pneumonia. Lymph nodes are usually seen in TB and lymphoma. A chest X-ray and a sputum AFB and Gram stain should be carried out. Direct sputum examination may reveal Strongyloides stercoralis larvae or eggs of Paragonimus species. Other lab tests may also be included, eg, a white blood cell (WBC) count or Gram stain of pus from other sites.
### Oral problems

<table>
<thead>
<tr>
<th>Condition</th>
<th>Presentation</th>
<th>Diagnosis</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral candidiasis</td>
<td>▪ Pseudomembranous</td>
<td>▪ Clinical appearance; KOH</td>
<td><strong>Topical therapy:</strong></td>
</tr>
<tr>
<td></td>
<td>▪ Erythematous</td>
<td>preparation on scrapings</td>
<td>▪ Nystatin 100,000 unit 3 times daily OR</td>
</tr>
<tr>
<td></td>
<td>▪ Hyperplastic</td>
<td></td>
<td>▪ Clotrimazole 100–150 mg twice daily dissolved in the mouth and swallowed OR</td>
</tr>
<tr>
<td></td>
<td>▪ Angular cheilitis</td>
<td></td>
<td>▪ Amphotericin B lozenges 10 mg three times daily</td>
</tr>
<tr>
<td></td>
<td>This can all result in</td>
<td></td>
<td><strong>Systemic therapy:</strong></td>
</tr>
<tr>
<td></td>
<td>white patches and pain in</td>
<td></td>
<td>▪ Fluconazole 50–100 mg once daily OR</td>
</tr>
<tr>
<td></td>
<td>the oral cavity.</td>
<td></td>
<td>▪ Ketoconazole 200 mg once daily OR</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>▪ Itraconazole 100–200 mg once daily Treat for 7–14 days.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Both ketoconazole and itraconazole are contraindicated in patients receiving INH or rifampicin and require gastric acidity for maximum absorption. They are not to be given with ddI.</td>
</tr>
<tr>
<td>Oesophageal candidiasis</td>
<td>▪ Difficulty</td>
<td>▪ Clinical appearance</td>
<td>Always use systemic treatment.</td>
</tr>
<tr>
<td></td>
<td>▪ Pain on swallowing</td>
<td>Oesophagoscopy</td>
<td>Fluconazole 200 mg loading dose and 100 mg once daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Barium meal</td>
<td>Ketoconazole 200–400 mg once daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Showing filling defects</td>
<td>Itraconazole 100 mg twice daily up to 400 mg once daily.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Both ketoconazole and itraconazole are contraindicated in patients receiving INH or rifampicin and require gastric acidity for maximum absorption. They are not to be given with ddI.</td>
</tr>
</tbody>
</table>
### Part 4 – Prophylaxis And Management of Common Opportunistic Infections

#### Neurologic problems

<table>
<thead>
<tr>
<th>Condition</th>
<th>Features</th>
<th>Diagnosis</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryptococcosis</td>
<td>▪ Meningeal or extra-meningeal in patients with</td>
<td>▪ Lumbar puncture showing increased opening pressure, occasional lymphocytosis.</td>
<td>1st choice: amphotericin B (IV) 0.7 mg/kg once daily + flucytosine 100 mg/kg x 2 weeks followed by fluconazole 400 mg once daily for 8 weeks, reduced to 200 mg once daily as a maintenance therapy for life.</td>
</tr>
<tr>
<td></td>
<td>▪ CD4 &lt;50 cells/mm³</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>▪ Fever, subacute onset, headache are present.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>▪ Neck stiffness and meningeal signs may be absent.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>▪ Behavioural changes and confusion may be present.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>▪ Extra meningeal should be treated as meningeal.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2nd choice: Fluconazole po 400 mg once daily x 8 weeks, followed by 200 mg once daily.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Itraconazole can be used, provided there is no rifampicin, rifabutin, antiseizure medications, achlorrhydria, or malabsortion.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>With either of the above regimens, regular spinal taps + acetazolamide to reduce spinal hypertension</td>
</tr>
</tbody>
</table>
### Neurologic problems (continued)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Features</th>
<th>Diagnosis</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Toxoplasmosis</strong></td>
<td>Fever, headache, focal neurologic symptoms, seizures</td>
<td>CSF findings are non-specific.</td>
<td><em>Induction therapy</em> for 4–6 weeks:</td>
</tr>
<tr>
<td></td>
<td>May be focal necrotising encephalitis or occasionally chorioretinitis and pneumonitis</td>
<td>Delayed double dose contrast CT scan will reveal lesions.</td>
<td>(a) High dose TMP-SMX 10/50 mg/kg once daily for 4 weeks OR 960 mg 8 hourly or 1440 mg 12 hourly for 21 days</td>
</tr>
<tr>
<td></td>
<td>Signs of a cerebral space-occupying lesion, hemiparesis or cognitive disorders should warrant a work up for toxoplasmosis, especially in patients with</td>
<td>Toxoplasmosis IgG can be useful as it has a high negative predictive value: 15% of people with cerebral Toxoplasmosis will be negative on Toxoplasma IgG.</td>
<td>(b) Pyrimethamine 100 mg loading dose followed by 50 mg once daily PLUS sulfadiazine 1–2 g 4 times daily (100 mg/kg once daily) PLUS folinic acid 10 mg once daily OR</td>
</tr>
<tr>
<td></td>
<td>CD4 &lt;100 cells/mm³.</td>
<td></td>
<td>(c) Clindamycin 600 mg 3 times daily PLUS pyrimethamine 100 mg once daily loading dose followed by 50 mg once daily + folinic acid 10 mg once daily.</td>
</tr>
<tr>
<td></td>
<td>All HIV patients with focal brain disease or cognitive impairment should be treated empirically for toxoplasmosis.</td>
<td></td>
<td>Fansidar is discouraged because of toxicity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Phenytoin 100 mg 2–3 daily in cases of seizures</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Maintenance therapy for life:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TMP-SMX 960 mg once daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Monitor BUN, creatinine, and CBC while on treatment.</td>
</tr>
<tr>
<td><strong>Tuberculous meningitis</strong></td>
<td>Gradual onset of headache, decreased consciousness and low-grade fever.</td>
<td>LP: CSF with high lymphocyte count, protein (40–100 mg/dl), and low glucose (&lt;20 mg/dl). CSF microscopy seldom shows AFB. Centrifuge to increase yield.</td>
<td>National protocol for TB meningitis should be followed. Steroids should be used when severe neurological symptoms are present.</td>
</tr>
<tr>
<td></td>
<td>Neck stiffness and positive Kernig's sign Cranial nerve palsies.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

National Guidelines for Management of HIV-Infected and HIV-Exposed Adults and Children 121
Skin lesions (1)

- Vesicles, crusts, painful, burning, non itchy
  - Yes: Anogenital/oral lesions (Herpes simplex)
    - Yes: Topical treatment + pain medication (A)
    - No: Extensive, big painful ulcers
      - Topical treatment + pain medication (B)
      - Yes: Acyclovir 200 mg x 5/day for 7 days + pain medication (B)
      - No: Zoster or extensive neurotic skin lesions
        - Topical treatment + pain medication (C)
        - Yes: Acyclovir 800 mg x 5/day for 7 days + pain medication (C)
        - No: Localised disease
          - Topical treatment + pain medication (D)

- Tinea corporis, tinea cruris, tinea pedis
  - Yes: Whitfield's ointment/gentian violet
    - Yes: Improvement after 10 days
      - Yes: Continue for 4 weeks
      - No: Miconazole/ clotrimazole/ketoconazole cream
        - Yes: Improvement after 10 days
          - Yes: Continue
          - No: Griseofulvin + local imidazole cream or Whitfield's (E)
        - No: Griseofulvin 12-18 months or itraconazole pulse therapy 4 months (E)
  - No: Tinea capitis
    - Yes: Griseofulvin + local imidazole cream or Whitfield's (E)
    - No: Onychomycosis (F)
      - Yes: KOH (+)
        - Yes: Griseofulvin 12-18 months or itraconazole pulse therapy 4 months (E)
        - No: Dystrophic nails
      - No: Go to the next page
SKIN LESIONS (3)

Part 4 – Prophylaxis And Management of Common Opportunistic Infections

1. Papular pruriginous eruption (P)
   - Yes: Miconazole cream/local antiseptic
   - No: Xerosis (ichthyosis)

2. Xerosis (ichthyosis)
   - Yes: Thict scales?
     - Yes: Whitfield’s ointment + chlorpheniramine
     - No: Dry skin lotion (catalamine lotion) + chlorpheniramine
   - No: Dry skin lotion (catalamine lotion) + chlorpheniramine

3. No treatment/ selenium sulphide or ketoconazole cream 2%
   - If no improvement, give ketoconazole 400 mg single dose or 200 mg during 5 days.

4. Seborrhoeic dermatitis
   - Yes: Topical treatment (Q)
   - No: Drug rash (R)

5. Psoriasis
   - Yes: Localised?
     - Yes: UVB topical treatment (Q)
     - No: UVB + topical treatment + etretinate (+ AZT) (P)
   - No: Diffuse erythematous, maculo-papular rash + pruritis + oedema of the skin +/- fever
     - Yes: Mucositis? conjunctivitis? ophthalmia?
       - Yes: Stevens-Johnson (Q)
       - No: Drug rash (R)

6. Pityriasis versicolor
   - Yes:
     - No: No treatment/ selenium sulphide or ketoconazole cream 2%
     - Improvement after 2 weeks?
       - Yes: Continue until 2 weeks after disappearance of symptoms
       - No: Ketoconazole 200 mg/day for 7-14 days

National Guidelines for Management of HIV-Infected and HIV-Exposed Adults and Children 124
Skin lesions: annotations

Care remains the same at all levels.

(A) Nonsteroidal anti-inflammatory drug (NSAID), or paracetamol and gentian violet or polyvidone iodine

(B) Pain medication: stepwise analgesia. If recurrences are frequent, give suppressive therapy: acyclovir 200 mg twice daily or 400 mg twice daily.

(C) In addition to acyclovir, use topical antiseptics, NSAID, and carbamazepine 200–600 mg once daily or clomipramine 25–75 mg once daily in the evening

(D) Gentian violet + NSAID + carbamazepine or clomipramine

(E) Tinea capitis requires treatment with griseofulvin 10 mg/kg once daily for at least 6 weeks. Addition of imidazole ointment or Whitfield's ointment will clear scalp scales more rapidly. Severe dermatophytosis or ringworm infection resistant to local therapy may be treated with griseofulvin 10 mg/kg once daily for 4 weeks.

(F) Dermatophytosis of the nail (onychomycosis) has to be distinguished from infection of the nail wall or nail bed, which is usually due to Candida (paronychia).

(G) Not all patients with dystrophic nails have a fungal infection. Because the treatment is long, it is important to confirm the diagnosis. Direct microscopic examination of a KOH preparation of subungual scrapings will show the presence of hyphae in onychomycosis. In that case, treat with griseofulvin 10 mg/kg once daily for 12–18 months. If available, pulsed therapy with itraconazole (200 mg twice daily for the first 7 days of each month for 4 months) is also effective. Lamictil or terbinafine may also be used.

(H) In case of scabies with secondary infection, it is better to treat this secondary infection first. Start some days later with benzyl benzoate.

(I) Apply benzyl benzoate 25% on the entire body, except the face, for 3 consecutive days. Clean clothes and bed linen. Treat family members with symptoms.

(J) In a patient with nodular skin lesions, ulcers, papules, and lymphadenopathy who is severely ill, the differential diagnosis between disseminated deep fungal infections and disseminated mycobacterial disease has to be made. In the absence of a skin biopsy and appropriate staining, this may be challenging. Try to find other arguments for mycobacterial disease (miliary TB, AFB on lymph node aspirate, etc). In the case of meningeal involvement, perform Indian ink stain on CSF. In case of productive cough, do AFB and Gram stain, or Cotton-blue stain.

(K) Molluscum contagiosum usually is asymptomatic. Treating for aesthetic reasons may be an option.

(L) Genital warts should only be treated if they are large and causing symptoms. Apply podophyllotoxin 0.5% twice daily on the wart only. Protect the surrounding healthy skin. Ask the patient to wash off the podophyllotoxin 1–4 hours later. Repeat once daily for 3 consecutive days per week for 4 weeks maximum. Do not use with pregnant women.

(M) Because it is sometimes difficult to distinguish clinically between bacillary angiomatosis and Kaposi's sarcoma, a trial with erythromycin is justified. If no response after 14 days, doxycycline may be tried. If there is still no response, stop treatment and give palliative care.

(N) Very suggestive for secondary syphilis. Check VDRL (rarely negative in secondary syphilis). Patients sometimes do not remember that they had a primary chancre.
Follow up VDRL at 3, 6, 12, and 24 months. If no decline in VDRL, treat the patient again.

(O) Symptoms suggestive of psoriasis.

(P) Diffuse erythematous or maculopapular rash, fever and mucositis (oral and vaginal lesions, conjunctivitis, inability to swallow), are suggestive of Stevens-Johnson syndrome. This is a life-threatening disease and requires hospitalisation in an intensive care unit (ICU) if available. It is most often associated with the intake of sulphonamides (TMP/SMX and dapsone) or thiacetazone. Stop the offending drug. If epidermolysis is not yet present, corticosteroids may reverse the inflammatory process (prednisolone 40–60mg once daily for one week). In case of extensive skin breakdown, steroids enhance the risk of secondary infections. The patient should be treated as a burn patient. Use aseptic techniques to clean and cover the wounds, give aggressive IV rehydration, and provide feeding via nasogastric (NG) tube. In case of high fever and/or chills, start broad-spectrum antibiotics (ceftriaxone/amikacin). Stevens-Johnson syndrome has a mortality rate of 50%.

(Q) Drug rash: Stop the drug and give symptomatic treatment: chlorpheniramine 4 mg 3–4 times daily and hydrocortisone or betamethasone cream. In case of a non-life-threatening rash due to TMP/SMX, consideration may be given to re-trying the therapy after two weeks, using gradual dose escalation as discussed below. The reason for doing this is that TMP/SMX is such a valuable drug for prophylaxis of PCP, toxoplasmosis, and bacterial infections in people living with HIV/AIDS (PLWH/A).

Example of a regimen of gradual dose escalation:
TMP/SMX suspension (40 mg TMP + 200 mg SMX/5 ml):
- 1 ml 3 times daily for 3 days
- 2 ml 3 times daily for 3 days then 5 ml daily for 3 days
- 10 ml once daily for 3 days
- 20 ml once daily for 3 days
- 1 DS tab once daily or 1 single strength (SS) tablet once daily (if DS is not supported).

In selected patients, desensitisation under surveillance is possible, with up to 70% of patients regaining their tolerance for TMP-SMX.

(R) Topical treatment that is effective for seborrhoeic dermatitis:
- Gentian violet
- Whitfield's ointment
- Miconazole or clotrimazole cream
- Ketoconazole cream

Apply treatment twice daily and, if effective, continue treatment for 2 weeks after all symptoms have disappeared. In case of severe inflammation, the miconazole cream or the ketoconazole cream may be mixed with a topical steroid.

(S) Chronic symmetric papular eruption, often with secondary infection. Underlying causes may be scabies, fungal, and bacterial disease. These need to be treated first.
1. Malassezia folliculitis will respond to miconazole and bacterial folliculitis to antiseptic topical treatment.
2. For all pruriginous lesions that do not respond to antifungal therapy, the patient should have a trial with benzyl benzoate.
3. When there is no response to ARV drugs and anti-scabies treatment, provide symptomatic treatment.
The following are guidelines for prophylaxis of opportunistic infections in infants and children:

- All HIV-exposed children should receive PCP prophylaxis from 6 weeks of age until HIV infection is ruled out. This may be up to 18 months, if PCR DNA cannot be performed before this time.
- It is advisable to start cotrimoxazole about 2 weeks before starting nevirapine, as both can cause rashes.
- All HIV-infected children should receive PCP prophylaxis when the CD4 <200 cells/mm³ or CD4% is <15%.
- For HIV-infected children receiving HAART and PCP prophylaxis, PCP prophylaxis may be discontinued when the CD4% is >20% for >3 months.
Viral load testing

- Viral load testing is currently not routinely available in the public sector in Guyana. It may initially be used to confirm failure of first line therapy.
- PCR DNA may likely be available in the near future and will help exclude HIV infection as early as 6 weeks in HIV-exposed children.

Drug resistance surveillance

- With the implementation and scale-up of antiretroviral therapy in Guyana—and the complexity and life-long duration of ARV treatment—resistance to ARV drugs will surely emerge with the possibility of compromising treatment regimens.
- Resistance to available drugs will lead to treatment failure, and will increase direct and indirect healthcare costs, transmission of resistant HIV strains to treatment naïve subjects, and the need for continuously new antiretroviral drugs.
- Currently resistance testing is not available in Guyana. However, to assess the level of baseline resistance to ARVs, the most common types of resistance patterns, and the drug resistance trend over time, Guyana will be involved in the World Health Organization Surveillance of HIV Drug Resistance Network.

Continuing medical education

There is a crucial need for medical education in HIV management, in order to train health workers in the use of ARVs. A strategic National HIV Management Training Plan is recommended to provide systematic training to different health cadres about ARVs and HIV management, using the National Treatment Guidelines as a template. This training, which will be approved by the MOH and the Guyana Medical Council and implemented through the National AIDS Program Secretariat, will include state-of-the art lectures, case discussions, group work, preceptorships, evaluation assessment and certification from the Guyana Medical Council. Physicians thus certified will be approved to prescribe ARVs and receive free government ARV supplies with accountability.

There will be pre-service training targeting medical, nursing, and laboratory technology; and student and in-service training targeting physicians, nurses, pharmacists, and laboratory technicians both in government and private practice.

Local operational research questions

As the ARV program scales up rapidly across the country, it is important to answer certain crucial operational research questions relevant to program refinement. These include but are not limited to:
- Baseline CD4 count profile in sero-negative Guyanese
- Prevalence of TB, HBV, and HCV in the HIV-infected population receiving treatment.
- Characteristics of patients in the ARV program
- Local adherence strategies that work best
- Prevalence and presentation of opportunistic infections, etc


### Additional resources

- [http://www.aids-etc.org/](http://www.aids-etc.org/)
- [http://www.carec.org/](http://www.carec.org/)
- [http://www.fxbcenter.org](http://www.fxbcenter.org)
- [http://www.mtctplus.org/](http://www.mtctplus.org/)
- [http://www.womenchildrenhiv.org/](http://www.womenchildrenhiv.org/)