Pharmaceutical Services Division
Ministry of Health Malaysia

Protocol
Medication Therapy Adherence Clinic:
RETROVIRAL DISEASE
(Adult & Paediatric)

2nd Edition 2014

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PREFACE

Pharmacy Practice, which was traditionally product-centered, has now shifted towards patient care. Pharmaceutical care, which is comprehensive and patient focused, is vital in ensuring that patient receive rational, safe and effective treatment. By adopting pharmaceutical care to Human Immunodeficiency Virus (HIV) patients, a pharmacist needs to cooperate with the patient and other health professionals (e.g. infectious disease consultants, physicians, medical officers, nurses and social workers) in the management of patients, focusing on the medication therapy.

Due to the vast development in the field of HIV medicines over the last few years, the first edition of the Retroviral Disease (RVD) Protocol that was published in 2010 has been revised. This second edition protocol combines the management of the adult & paediatric HIV patients. This protocol is meant for pharmacists in Ministry of Health (MOH) in providing their expertise in Retroviral or Pediatric Retroviral Medication Therapy Adherence Clinic (RVD or PRVD MTAC). This protocol will ensure the standardisation of practice and also enable the pharmacists to fully contribute as part of the healthcare team throughout Minsitry Of Health's facilities.

I would like to thank the Clinical Pharmacy Working Committee (Retroviral Disease-RVD Subspecialty) Pharmaceutical Services Division, MOH for their contribution and commitment to the publication of this protocol.

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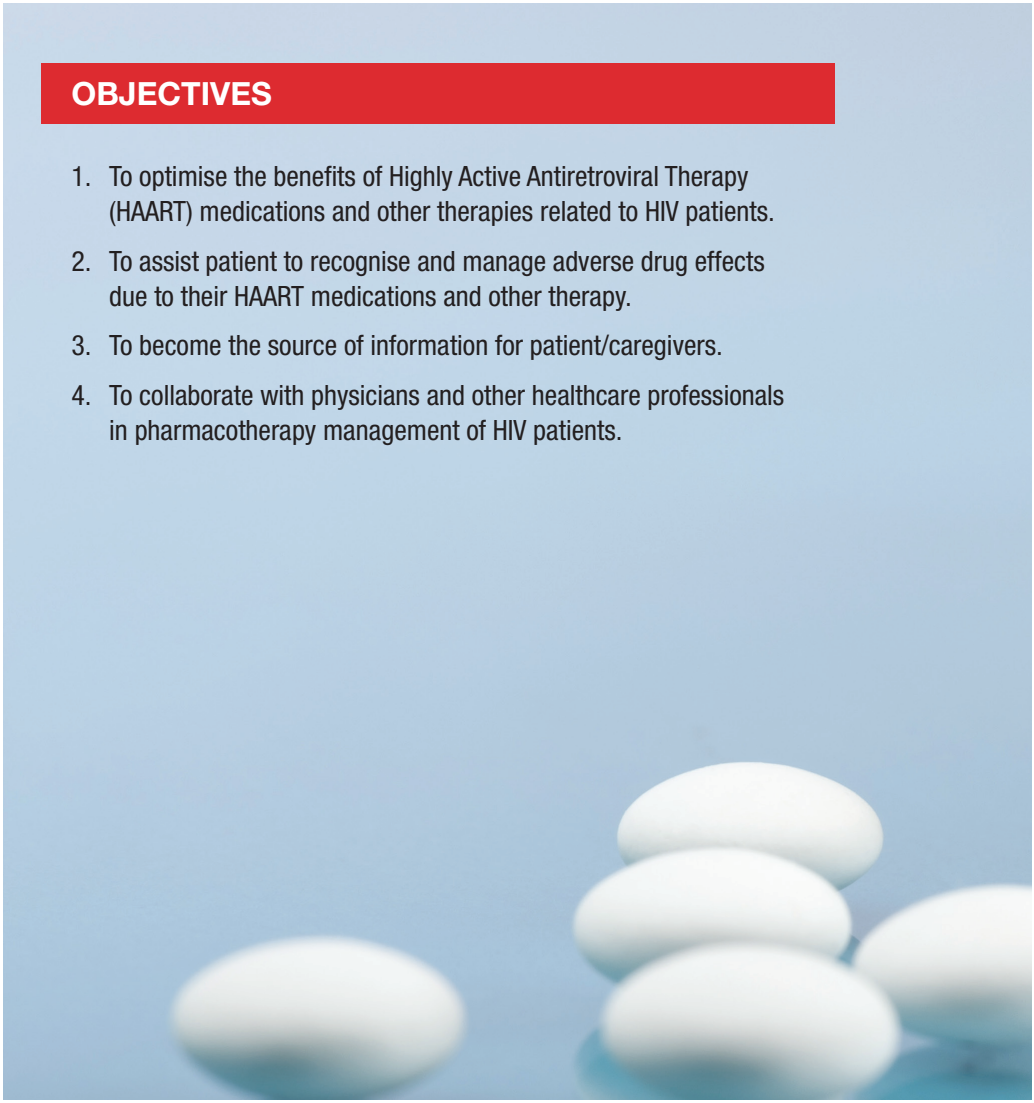
PROTOCOL

PHARMACIST IN HIV MANAGEMENT (ADULT & PAEDIATRIC PATIENTS)

OBJECTIVES

1. To optimise the benefits of Highly Active Antiretroviral Therapy (HAART) medications and other therapies related to HIV patients.
2. To assist patient to recognise and manage adverse drug effects due to their HAART medications and other therapy.
3. To become the source of information for patient/caregivers.
4. To collaborate with physicians and other healthcare professionals in pharmacotherapy management of HIV patients.



A. RETROVIRAL/PAEDIATRIC RETROVIRAL DISEASE MEDICATION THERAPY ADHERENCE CLINIC (RVD MTAC) PROTOCOL

1 INTRODUCTION

Infection of HIV leads to progressive immune destruction as a result of persistent viral replication. Therefore, antiretroviral treatment has been shown to improve CD4 cell count, reduce viral replication, reduce the frequency of opportunistic infection, improve quality of life and hence, prolong life expectancy of HIV infected patients. Through collaboration with other healthcare providers, pharmacists could play an important role in providing pharmaceutical care to HIV patients in order to achieve a better therapeutic outcome. By adopting pharmaceutical care, a pharmacist needs to cooperate with the patient and other health professionals in planning specific therapeutic outcomes for the patient.

1.1 HIV Infection in Paediatric

The pathogenesis of HIV infection and the general virologic and immunologic principles underlying the use of antiretroviral therapy in paediatrics are similar to adults. However, there are some unique considerations for HIV-infected infants, children and adolescents as stipulated below:

- Acquisition of infection through perinatal exposure for many infected children.
- In utero, intrapartum and/or postpartum neonatal exposure to zidovudine and other antiretroviral medications in most perinatally infected children.
- Requirement for the use of HIV virologic tests to diagnose perinatal HIV infection in infants under the age of 18 months.
- Age-specific differences in CD4 cell counts.
- Changes in pharmacokinetic parameters with age caused by the continuing development and maturation of the organ systems involved in drug metabolism and clearance.

- Differences in the clinical and virologic manifestations of perinatal HIV infection secondary to the occurrence of primary infection in growing, immunologically immature persons.
- Special considerations associated with adherence to antiretroviral treatment for infants, children and adolescents.

Different from adult HIV patients, children living with HIV infections are, as a group, growing older, bringing new challenges in medication adherence, drug resistance, and management of multiple drugs.

1.1.1 Disease Disclosure Status

Disease disclosure status in children living with HIV is one of the crucial factors that affect medication adherence in paediatric patients. Thus, the pharmacist should be aware of the importance of maintaining patient confidentiality throughout the counselling session. At the clinic, PRVD MTAC pharmacist should assess not only the patient readiness (in older children) to adhere to medication therapy, but also the willingness of the caregiver to make sure medications are served correctly and discuss other medication related factors.

Disclosure of HIV infection status to children and adolescents should take into consideration of their age, psychosocial maturity, the complexity of the family dynamics and the clinical context. The paediatrician will discuss and plan the process for disclosure with the parents/family members and access the child's knowledge and coping capacity. The process of disclosure will be individualised to include child's cognitive ability, developmental stage, clinical status and social circumstances.

Disclosure of the disease status may lead to stigmatisation, discrimination or ostracism toward the child and other family members. Hence, pharmacists should be aware of the child's disease disclosure status while conducting counselling sessions and concern about the impact of the disclosure on the child's emotional health.

1.1.2 Partial Disclosure and Full Disclosure of RVD Status

	Partial Disclosure	Full Disclosure
Age	■ ≥ 7 years old. ■ Depends on the child's psychosocial maturity.	■ ≥ 12 years old. ■ Depends on the child's cognitive and emotional understanding of illness and dying. ■ Also depends on parent's/ caregiver's readiness.
Introduce the child to	■ Germs ~Virus. ■ Germs fighters ~ CD4. ■ Pharmacist MUST NOT mention 'HIV'/'AIDS' during the counselling session.	■ HIV.

2 PHARMACIST'S ROLE AND RESPONSIBILITY

The pharmacist will educate and counsel:

- New patients on Highly Active Antiretroviral Therapy (HAART) medications.
- Patients requiring changes in HAART medications.
- Patients with long-standing adherence problems.

Responsibilities of the pharmacist include the following:

- Assess patient's readiness to adhere to medication therapy.
- Provide ongoing monitoring of drug adherence and evaluate the presence of social stressors that may impair adherence.
- Patient assessment for medication-related factors.
- Interpret laboratory results to monitor outcomes of medication therapy and identify potential drug toxicities.

- Identify potential and actual drug-drug interactions and make appropriate recommendations for dosage modification or alternative therapies.
- Document the care provided in the patient's records and maintain patient's confidentiality at all times.
- Identify any instances of non-adherence to medication therapy and work with patients to uncover any barriers to adherence.
- Communicate to prescribers any known instances of non-adherence to medication therapy and propose strategies to the prescriber and/or patients to help overcome the barriers and improve the likelihood for success in current or subsequent regimens.
- Impart the counselling skills required when handling an RVD patient e.g. empathy, acceptance, good listening skills and non-biased.

3 LOCATION/SETTING

The RVD/PRVD MTAC service should be conducted at the Medical/ Infectious Disease/Paediatric Outpatient Clinic of the hospital or health clinic area (within reach of patient's case notes, physicians and other healthcare personnel involved in the management of the patients) during clinic days.

4 MANPOWER REQUIREMENTS

At least one pharmacist should be placed in the clinic. The pharmacist shall spend an average of 10 to 15 minutes per case but longer time (around 30 minutes) will be needed for newly-referred cases.

Additional pharmacist may be required in center where dispensing and pill count activities are performed.

5 COUNSELLING TOOLS

The RVD/PRVD MTAC should have suitable counselling tools (such as pamphlet, flipchart & medication chart) at the clinic to provide a comprehensive counselling to the patients.

6 APPOINTMENT

All appointments will be scheduled by pharmacists or other healthcare providers participating in the clinic.

7 HAART IN ADULT AND PAEDIATRIC

Refer to *Appendix C1: Drug Dosing Chart.*

8 DISCHARGE CRITERIA

Patients will be discharged from RVD/PRVD MTAC only if they are transferred out to other MOH facilities for follow-up.

9 DOCUMENTATIONS FOR RVD/PRVD MTAC

Refer to Appendices:

- Appendix A1 : RVD MTAC Monitoring Record
- Appendix A2 : RVD MTAC Follow-Up Monitoring Record
- Appendix A3 : PRVD MTAC Monitoring Record
- Appendix A4 : PRVD MTAC Follow-Up Monitoring Record

- Appendix A5 : RVD/PRVD MTAC Medication Count Chart
- Appendix B1 : Pre-HAART Counselling Checklist
- Appendix B2 : Initiating HAART Counselling Checklist
- Appendix B3 : Follow-Up HAART Counselling Checklist
- Appendix C1 : HAART Guidance Chart
- Appendix C2 : HAART Drug Interaction Chart
- Appendix C3 : HAART Adverse Effects Chart

10 WORK PROCESS FOR RVD/PRVD MTAC

(Refer *Appendix 1*).

10.1 Pre-HAART: Assess Readiness for HAART

(Refer *Appendix B1* and document information in Patient Monitoring Record as in *Appendix A1 – RVD* or *Appendix A3 – PRVD*).

Pre-HAART counselling is usually conducted once patient is diagnosed with HIV infection.

10.1.1 Evaluate knowledge and educate patient

- HIV/AIDS, CD4, viral load and the association of CD4 and viral load to the disease
  (use flipchart, pamphlet and other educational tools if necessary).

10.1.2 Evaluate patient's readiness and belief to adhere to medication therapy

10.1.2.1 Assess and evaluate patient's:

- Beliefs & perception about HAART medications.

- Readiness to be on HAART medications.
- Caregiver support.

10.1.2.2 Explain and emphasize the importance of:

- Lifelong commitment towards HAART Medications.
- First-line HAART medications.
- Presence of psychosocial stressor and other barriers that may impair medication adherence.

10.1.3 HAART Medications

10.1.3.1 Emphasize and explain:

- Combination of HAART medications regime.
- Role of HAART medications in suppressing viral and improving CD4 count.
- Duration of time when HAART medications will show its effect (usually 4 months after starting HAART medications).
- HAART medications does not cure the disease, it will only suppress the virus.
- Importance of adherence and how drug resistance and drug cross-resistance can occur.
- Common side effects of HAART medications.
- Ministry of Health (MOH)'s policy in supplying HAART medications.

10.1.4 Educate caregivers and family members (when necessary) and obtain their additional information

10.1.5 Possible drug interactions

- Assess patient's medication history (including other medications, supplements and traditional medicines).

10.1.6 Provide patients with written material about HAART

10.1.7 Additional information for PRVD MTAC

Disclosure of RVD status-need to fill up once the status disclosed according to the phase (*Appendix A3*).

10.1.8 Re-evaluate patient's understanding and document accordingly

**The patient's beliefs and perceptions about HAART as well as adherence should be reassessed after pre-HAART session.*

- Request patient to let us know their understanding on HAART.
- Evaluate patient's understanding and give additional necessary information (if any).

10.1.9 Re-evaluate patient's understanding and document accordingly

**The patient's beliefs and perceptions about HAART medications as well as adherence should be reassessed after pre-HAART session.*

- Request patient to let us know their understanding on HAART medications.
- Evaluate patient's understanding and give additional necessary information (if any).

10.2 Initiating HAART: HAART-Naive Patient and Regimen Change

(Refer *Appendix B2* and document further informations in Patient Follow-Up Monitoring Record as in *Appendix A2 – RVD* and *Appendix A4 – PRVD* and complete necessary information on *Appendix A1 – RVD* and *Appendix A3 – PRVD* accordingly).

Once initiated on HAART medications or changing into new HAART regime, the patient (and their caregiver for PRVD) should be scheduled for a 'start HAART' session.

10.2.1 Reassess patient's readiness to start HAART

10.2.1.1 Reassess on patient's:

- Readiness to start HAART medications.
- Medication history (including other medications, supplements and traditional medicines).
- Beliefs & perception about HAART medications.
- Knowledge about HIV/AIDS, CD4, viral load and the association of CD4 and viral load to the disease.

10.2.1.2 Reemphasize & explanation on:

- Lifelong commitment towards HAART medications.
- Reason of changing HAART regime such as adverse effects reaction or treatment failure.

10.2.2 Educate patient on their medication today

10.2.2.1 Explain to patient:

- Show & tell on his/her medications and make sure patient understands how medications work & remember their medications (at least colour and shape).
- Drug name, dosage, frequency, possible side effects and contraindications, formulation, dose adjustment, administration advice and storage (*refer Appendix C1*).
- Precautions, possible drug interactions including with traditional medicine, adverse effects of antiretroviral therapy and how to manage them (*refer Appendix C2* and *C3*).
- Purpose of trimethoprim/sulfamethoxazole (Bactrim®) in preventing Opportunistic Infections(OIs).

10.2.3 Reinforce importance of adherence

- Stress the importance of proper timing and implication of non-adherence, including occurrences of drug resistance.
- Provide medication administration schedule/timetable guide and suggest adherence tools to increase adherence (pill box, alarm clock or hand phone alarm and calendar).
- Action to be taken in the event of late/missed dose/vomiting after taking HAART medications.
- Always bring sufficient supply when travelling and timing during travelling.
- Adherence issue during fasting month.
  - Not to fast until CD4 is high enough and viral load undetectable.
- Intervene when the patient states or indicates that he or she cannot or will not adhere to treatment.
- Stress the need for regular check-ups and blood tests.

10.2.4 IRIS (Immune Reconstitution Inflammatory Syndrome)

- Explain what is IRIS (when CD4 count <100 cells/µl, patient has potential for IRIS) commonly TB, MAC, CMV retinitis, Cryptococcal Meningitis.
- Explain that it is a transition period before getting better (warn patient that they may get worse before getting well).
- HAART medications are working even though there is an infection.

10.2.5 Discuss the effects of high-risk behaviours and activities, including alcohol or drugs abuse (e.g. recommend methadone maintenance therapy programme, if needed.)

10.2.6 Advise patient to come for every appointment given by pharmacist and clinic for consultation – do not stop medication before consulting doctor, pharmacist or nurse. Therefore, provide patients with clinic's telephone number for any emergency query and or appointment

10.3 Follow-up HAART: During Subsequent Visits

(Refer *Appendix B3* and document information on *Appendix A1-A2 – RVD*, *Appendix A3-A4 – PRVD* and *Appendix A5 – RVD and PRVD*)

Patients will be scheduled to return for a 'medication check' session **two to four** weeks after initiation/regime changing which medication adherence is assessed by pill count and/or patient report. This visit gives the pharmacist an opportunity to detect and address any problems in adherence or drug related issues and to optimise drug therapy. Patient who have shown a good adherence profile after four visits can be scheduled for follow-up session every 8 weeks.

10.3.1 Review patient's/caregiver's understanding on medications

- Identification of medications.
- Administration of medications (including time of administration).
- Patient's understanding on CD4 and viral load.
- Lifestyle and hygiene practice (refer to Additional Counselling Notes for RVD/PRVD MTAC Patients).
- Storage of medications.

10.3.2 Review patient's adherence to medication (in a non-judgmental way)

- Acknowledge the difficulty in taking medications exactly as prescribed.

- Ask about any recent missed/delayed doses (yesterday/last one week/passed one month).
- Enquire about specific reasons why doses were missed/delayed (if any).
- Keep track of patient's adherence issues from patient's previous records.
- Use this information to identify solutions to the adherence problems (if any).
- Do pill count (for patient with doubtful compliance).

10.3.3 Review patient's tolerability and drug toxicities

- Assess patient's well-being.
- Ask if patient had any experience of side effects and how he/she managed it.
- Identify, address and monitor any drug-related issues.

10.3.4 Positive reinforcement

- Share CD4 and viral load results and reinforce the relationship with adherence by explaining the role of HAART medications in viral suppression and improvement of CD4 count.
- Explain on how drug resistance and drug cross-resistance can occur.
- Emphasize on the importance of adherence towards HAART medications which includes taking the medications at the scheduled time daily.
- Recommend strategies to overcome drug-related issues

11 ADDITIONAL COUNSELLING NOTES FOR RVD/PRVD MTAC PATIENTS

- For PRVD patients/caregiver, remind them to avoid mixing HAART medications into milk.
- Advise patients to eat only fully-cooked meat and boiled water- bacteria may be present in half-cooked meals.
- Maintain good general hygiene.
- Encourage and motivate patients to be positive thinking.
- Advise patients to avoid pet feces (dog/cat etc.).
- Proper storage of HAART medications.

B. RVD WARD PHARMACY PROTOCOL

1 INTRODUCTION

Most HIV-infected patients are warded due to Opportunistic Infections (OIs) or HAART-related adverse events. The pharmacist is involved in the care of HIV-infected patients by collaborating with other members of the healthcare team (e.g. physicians, medical officers, nurses and social workers) in the management of the patients, focusing on the medication therapy.

In the ward, the pharmacist should perform the following (**Refer Appendix 2**):

- Take medication history (using CP1 form).
- Review medications and case progression (using CP2 and CP3 forms).
- Participate in ward rounds, give feedback and recommendations relating to medication therapy.
- Counsel the patient at bedside and/or upon discharge:
  - HAART-naive patient - Refer A (Work Process 10.2).
  - Regimen change - Refer A (Work Process 10.2).
  - Post HAART patient - Refer A (Work Process 10.3).
  - For discharged patients that need further counselling, use CP4 form.
- Monitor and report adverse drug reactions (ADRs).
- Detect and overcome drug-related problems (DRPs).

2 LOCATION/SETTING

This ward pharmacy service shall operate in the Medical/Infectious Disease/Paediatric ward.

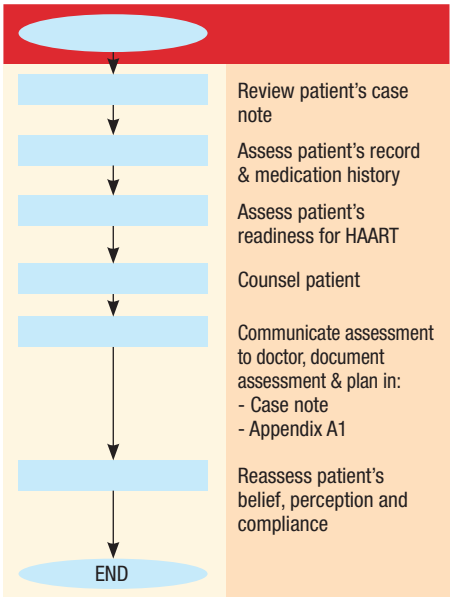
REFERENCES

1. Guidelines for the Use of Antiretroviral Agents in Paediatric HIV Infection. The Working Group on Antiretroviral Therapy and Medical Management of HIV-Infected Children, National Resource Centre at Francois-Xavier Bagnoud Center, UMDNJ, Health Resources and Services Administration (HRSA), and National Institutes of Health (NIH); November 2012.
2. Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection. WHO; June 2013.
3. Clinical Practice Guidelines: Management of HIV Infection in Children. Ministry of Health Malaysia; February 2008.
4. Protocol: Retroviral Disease (Medication Therapy Adherence Clinic & Ward Pharmacy). Pharmaceutical Services Division, Ministry of Health; 2010.

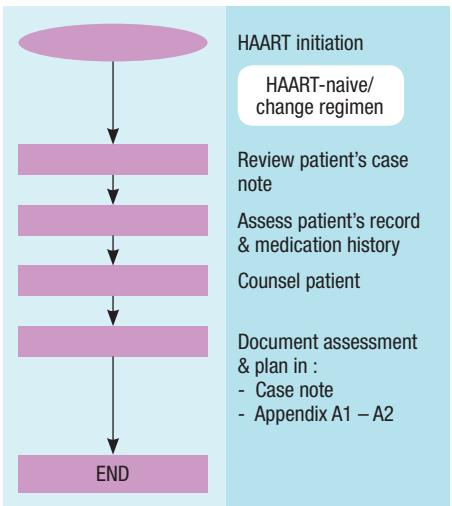
C. APPENDICES

WORKFLOW OF RVD/PRVD MTAC

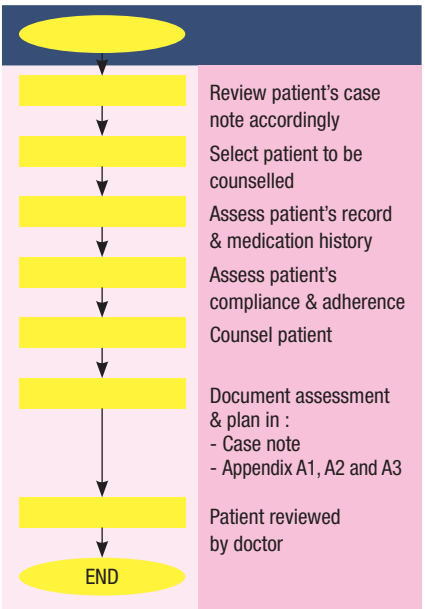
1. Pre-HAART



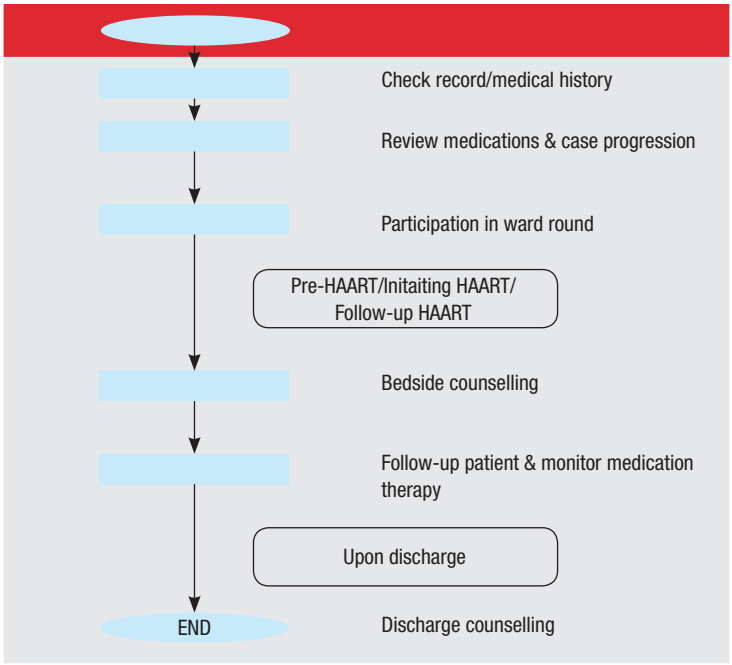
2. Initiating HAART



3. Follow-up HAART



WORKFLOW OF RVD/PRVD WARD PHARMACY



RVD MTAC MONITORING RECORD

HOSPITAL/HEALTH CLINIC .....

MTAC RN:
.....

FILING DATE: .....

PATIENT INFORMATION					
Name:					
IC No.:		**Date of Birth:**		**Age :**	
Address:					
Gender:	[ ] Male [ ] Female	**Race:**	[ ] Malay [ ] Chinese [ ] India [ ] Others:		
Tel. No. (House):		**Tel. No. (Mobile):**			
Marital Status	[ ] Single [ ] Married [ ] Divorced [ ] Widow	**No. of child :**			
		Occupation :			
Staying :	[ ] Family [ ] Partner/Friend(s) [ ] Alone [ ] NGO Shelter/Social Welfare, please specify: ..... [ ] Others, please specify:				
Habit :	[ ] Smoking: ..... sticks/day [ ] Alcohol: ..... consumption/day/week [ ] Illicit Drug, please specify:				

ALLERGIES/INTOLERANCE
[ ] No Known Drug Allergy [ ] Yes, please specify: .....

PAST MEDICAL HISTORY			
	Date of Diagnosis	**Disease**	**Treatment**
1			
2			
3			
4			
5			
6			

RETROVIRAL DISEASE HISTORY			
Mode of Transmission :	[ ] Heterosexual [ ] Homosexual/Bisexual [ ] IVDU [ ] Blood transfusion [ ] Unknown [ ] Others, please specify:		
Date of Diagnosis :			
CD4 Upon Diagnosis :	**Cells/µl**	**CD4 Before Treatment :**	**Cells/µl**
Viral Load Baseline :	**Copies/ml**		

OPPORTUNISTIC INFECTION			
	Date of Diagnosis	**Opportunistic Infection**	**Treatment**
1			
2			
3			
4			
5			

HAART REGIME HISTORY				
	Date Start	**Date Stop**	**HAART Regime**	**Reason for Changing (If Any)**
1				
2				
3				
4				
5				
6				
7				

OTHER MEDICATIONS (Including OTC, Traditional, Hormonal Etc.)				
	Date Start	**Medication**	**Indication**	**How Often/Last Use**
1				
2				
3				
4				
5				
6				

RVD MTAC FOLLOW-UP MONITORING RECORD

HOSPITAL/HEALTH CLINIC .....

PATIENT NAME: .....

Date	HAART Regimen	Timing & Reminder	Weight (kg)	CD4		Viral Load (copies/ml)	Laboratory Results					*Adherence (good/ moderate/poor)	Side Effect	Remarks	Pharmacist's Plan
				Count (cells/µl)	%		Hb (g/100mL)	SCr (umol/L)	LDL (mmol/L)	TG (mmol/L)	Other				
															Sign. & Stamp
															Sign. & Stamp
															Sign. & Stamp
															Sign. & Stamp
															Sign. & Stamp

**Use any adherence tool*

RVD MTAC MONITORING RECORD

HOSPITAL/HEALTH CLINIC .....

MTAC RN: ..... **FILING DATE:** .....

PATIENT INFORMATION					
Name:					
IC No.:		**Date of Birth:**		**Age :**	
Address:					
Gender:	[ ] Male [ ] Female	**Race:**	[ ] Malay [ ] Chinese [ ] India [ ] Others:		
Tel. No. (House):		**Tel. No. (Mobile):**			
Caregiver (Name):	[ ] Parent: Mother/Father/Both [ ] Extended family/Adopted/Foster care [ ] NGO Shelter/Social Welfare, please specify: ..... [ ] Others, please specify:				
Family/Social History	**Father:**				
	Mother:				
	Siblings:				

ALLERGIES/INTOLERANCE
[ ] No Known Drug Allergy [ ] Yes, please specify: .....

PAST MEDICAL HISTORY			
	Date of Diagnosis	**Disease**	**Treatment**
1			
2			
3			
4			
5			
6			

RETROVIRAL DISEASE HISTORY			
Mode of Transmission :	[ ] Vertical transmission [ ] Blood transfusion [ ] Unknown [ ] Others, please specify:		
Date of Diagnosis :			
CD4 Upon Diagnosis :	**Cells / µl**	**CD4 Before Treatment :**	**Cells / µl**
Viral Load Baseline :	**Copies / ml**		

DISCLOSURE OF RVD STATUS	
Partial: Phase I – CD4	Date:
Partial: Phase II – Virus	Date:
Full Disclosure	Date:

OPPORTUNISTIC INFECTION			
	Date of Diagnosis	**Opportunistic Infection**	**Treatment**
1			
2			
3			
4			
5			

HAART REGIME HISTORY				
	Date Start	**Date Stop**	**Haart Regime**	**Reason for Changing (If Any)**
1				
2				
3				
4				
5				
6				
7				

OTHER MEDICATIONS (Including OTC, Traditional, Hormonal Etc.)				
	Date Start	**Medication**	**Indication**	**How Often/Last Use**
1				
2				
3				
4				
5				
6				

PRVD MTAC FOLLOW-UP MONITORING RECORD

HOSPITAL/HEALTH CLINIC .....

PATIENT NAME: .....

Date	HAART Regimen	Timing & Reminder	Weight (kg)	CD4		Viral Load (copies/ml)	Laboratory Results					*Adherence (good/ moderate/poor)	Side Effect	Remarks	Pharmacist's Plan
				Count (cells/µl)	%		Hb (g/100mL)	SCr (µmol/L)	LDL (mmol/L)	TG (mmol/L)	Other				
															Sign. & Stamp
															Sign. & Stamp
															Sign. & Stamp
															Sign. & Stamp
															Sign. & Stamp

**Use any adherence tool*

RVD/PRVD MTAC MEDICATION COUNT CHART*

HOSPITAL/HEALTH CLINIC .....

PATIENT NAME : .....

Date	ARV Agent	Prescribed Regime	No. of Pills Dispensed	Name & Sign.	Visit Date	[a]No. of Pills to be taken	[b]No. of pills taken	Pill balance	Adherence (%) (b/a) x 100%	Adherence Remarks	Sign. & Stamp
starting date					visit date 1						
visit date 1					visit date 2						
visit date 2					visit date 3						
visit date 3					visit date 4						
visit date 4					visit date 5						

**For new patient or suspected non-adherence case only. Not compulsory for all cases.*

PRE-HAART COUNSELLING CHECKLIST
HOSPITAL/HEALTH CLINIC .....

PATIENT NAME: .....

NO.	COUNSELLING CHECKLIST
1	**Knowledge about HIV** 1. HIV/AIDS. 2. CD4. 3. Viral load (VL).
	Pharmacist's Notes ....
2	**Evaluate patient's readiness, belief and perception to adhere to medication therapy** 1. Assess patient's beliefs & perception about HAART. 2. Is patient ready to be on HAART? 3. Evaluate caregiver support. 3. Lifelong commitment – *even when CD4 count is high, HAART cannot be stopped.* 4. First regimen is always the best. 5. Presence of psychosocial stressor and other barriers that may impair medication adherence.
	Pharmacist's Notes ....
3	**HAART** 1. Combination of 3 or more drugs. May give example of HAART drugs. 2. Explain the role of HAART in suppressing viral and improving CD4 count. 3. Required duration to see positive outcome (usually 4 months after starting HAART). 4. HAART medications are drugs to supress the viral and not to cure the disease. 5. The importance of adherence and the possible development of drug resistance. Explain on how drug resistance and drug cross-resistance can occur. 6. Some of the common side effects of HAART. 7. Ministry of Health (MOH)'s policy with regard to the supply of HAART.
	Pharmacist's Notes ....
4	Educate caregivers and family members (when necessary) and obtain their additional information.
	Pharmacist's Notes ....

5	**Possible drug interactions** 1. Is patient taking any other medications? 2. Is patient taking any supplements/traditional medications? 3. Not to mix HAART into milk for PRVD .
	Pharmacist's Notes ....
6	**Educate about healthy lifestyle** 1. Eat only full cooked meat, vegetable and boiled water – bacteria may be present in half cooked meals. 2. Maintain good general hygiene. 3. Positive thinking. 4. Avoid pets feces (dog/cat etc).
	Pharmacist's Notes ....
7	**Provide patients with written material about HAART.**
	Pharmacist's Notes ....
8	**Additional information for PRVD MTAC** 1. Disclosure of RVD status-need to fill up once the status disclosed according to the phase (appendix A3).
	Pharmacist's Notes ....
9	**Re-evaluate patient's understanding on HAART** 1. Request patient to let us know their understanding on HAART. 2. Evaluate patient's understanding and give additional necessary information (if any).
	Pharmacist's Notes ....

Pharmacist : ..... **Date :** .....

INITIATING HAART COUNSELLING CHECKLIST
HOSPITAL/HEALTH CLINIC .....

PATIENT NAME: .....

NO.	COUNSELLING CHECKLIST
1.	**Reassess patient's readiness to start HAART** 1. Is patient ready? 2. Does patient understand that HAART is a lifelong commitment? 3. Is patient taking any supplements/traditional medications? 4. Reassess patient's beliefs & perception about HAART. 5. Reassess patient's knowledge about HIV/AIDS, CD4, Viral load and the association of CD4 and viral load to the disease. 6. For HAART regime change, explain to patient the reason of changing such as adverse effects reaction or treatment failure.
	Pharmacist's Notes ....
2.	**Educate patient on their medication today** 1. Explain to patient (show & tell) on his/her medication and make sure patient understand how medications work & remember their medication (at least colour and shape). 2. Drug name, dosage, frequency, possible side effect and contraindication, formulation, dose adjustment, administration advice and storage (refer *Appendix C1*). 3. Precautions, possible drug interactions including with traditional medicine, adverse effects of antiretroviral therapy and how to manage them (refer *Appendix C2* and *C3*). 4. Purpose of trimethoprim/sulfamethoxazole (Bactrim®) in preventing OIs.
	Pharmacist's Notes ....
3.	**Reinforce importance of adherence** 1. Stress the importance of proper timing and implication of non-adherence including occurences of drug resistance. 2. Provide medication administration schedule/timetable guide and suggest adherence tools to increase adherence (pill box, alarm clock or hand phone alarm and calendar). 3. Action to be taken in the event of late/missed dose/vomiting after taking HAART. 4. Always bring sufficient supply when travelling and timing during travelling. 5. Adherence issue during fasting month. Not to fast until CD4 is high enough and viral load undetectable. 6. Intervene when the patient states or indicates that he or she cannot or will not adhere to treatment. 7. Stress the need for regular check-ups and blood tests.

NO.	COUNSELLING CHECKLIST
	Pharmacist's Notes ....
4.	**IRIS (Immune Reconstitution Inflammatory Syndrome)** 1. Explain what is IRIS (when CD4 count<100 cells/µl, patient has potential for IRIS) commonly TB, MAC, CMV retinitis, cryptococcal meningitis. 2. Explain that it is a transition period before getting better (warn patient that they may get worse before getting well. 3. HAART is working even though when there is an infection.
	Pharmacist's Notes ....
5	**Educate about healthy lifestyle** 1. Eat only full cooked meat, vegetable and boiled water – bacteria may present in half cooked meals. 2. Maintain good general hygiene. 3. Positive thinking. 4. Avoid pets feces (dog/cat etc).
	Pharmacist's Notes ....
6.	Discuss the effects of high-risk behaviours and activities, including alcohol or drugs abuse, (e.g. recommend methadone maintenance therapy programme if needed).
	Pharmacist's Notes ....
7.	Advise patient to come for every appointment given by pharmacist and clinic for consultation – do not stop medications before consulting doctor, pharmacist or nurse. Therefore, provide patient clinic's telephone number for any emergency query and for appointment.
	Pharmacist's Notes ....

Pharmacist : ..... **Date :** .....

FOLLOW-UP HAART COUNSELLING CHECKLIST
HOSPITAL/HEALTH CLINIC .....

PATIENT NAME:
MTAC R/N:

No.	Topic
1	**Review patient's/caregiver's understanding** a) Can patient identify the medications? b) How does patient take his/her medications? c) What does the patient know about his/her CD4 and viral load (VL)? d) Patient's hygiene practices and lifestyle. e) Storage.
	Pharmacist's Notes ....
2	**Review patient's adherence to medication** a) Ask about the most recent missed/delayed dose (yesterday, last 1 week/and passed month). b) Use any suitable assesment tools to measure adherence. c) Enquire about specific reasons why doses were missed. d) Who will monitor patient to take medications? e) Pill count (*Appendix B5*). f) Keep track from the medication record. g) Review on Medication Dosing Schedule and make amendment accordingly – is the time of administration convenient?
	Pharmacist's Notes ....
3	**Review patient's tolerability and drug toxicities** a) How does patient feel now? b) Interpretation of laboratory results. c) Is patient experiencing any side effects? d) How does patient manage the side effects?
	Pharmacist's Notes ....
4	**Positive reinforcement** a) Share CD4 count and VL results and reinforce the relationship to adherence. b) Emphasise the importance of adherence to HAART .
	Pharmacist's Notes ....

Counselled by : ..... **Date :** .....

HAART GUIDANCE CHART

<table>
<tr><th>Agent</th><th>Recommended Dosage, Side Effects and Contraindications</th><th>Formulation</th><th>Dose Adjustment</th><th>Intake Advice</th></tr>
<tr><td colspan="5">Nucleoside Reverse Transcriptase Inhibitors (NRTI): lactic acidosis, lipoatrophy, steatosis (manifestations of mitochondrial toxicity)</td></tr>
<tr><td>Lamivudine
(3TC)</td><td>Neonate/infant (age <4weeks):
2mg/kg BD
Child: 4mg/kg BD or 8mg/kg OD (well- tolerated roundup doses)
<table><tr><th>Body Weight (kg)</th><th>AM Dose</th><th>PM Dose</th><th>Total Daily Dose (mg)</th></tr><tr><td>14-21</td><td>½ tab (75mg)</td><td>½ tab (75mg)</td><td>150</td></tr><tr><td>>21-30</td><td>½ tab (75mg)</td><td>1 tab (150mg)</td><td>225</td></tr><tr><td>≥30</td><td>1 tab (150mg)</td><td>1 tab (150mg)</td><td>300</td></tr></table>Max. dose: As for adults.
Adult: 150mg BD or 300mg OD
S/E: Peripheral neuropathy, nausea, diarrhoea, headache.</td><td>Tab: 150mg (white)
Soln: 10mg/ml</td><td>For adult patients:
CrCl 30–49mL/min.: 150mg OD;
CrCl 15–29mL/min.: 150mg first dose then 100mg OD;
CrCl 5–14mL/min.: 150mg first dose then 50mg OD;
CrCl <5mL/min.: 50mg first dose then 25mg OD
Paediatric patients: Dose adjustment and/or an increase in the dosing interval should be considered.</td><td>Can be taken with or without food.</td></tr>
<tr><td>Zidovudine
(AZT, ZDV, RetrovirÒ)</td><td>Child: (<6 weeks): 4mg/kg BD
(≥6 weeks – 18 years):
180-240mg/m² BD
Max. dose as for adults.
Adult: 300mg BD
S/E: Granulocytopenia and/or anaemia, nausea, headache, myopathy, hepatitis, nail pigmentation, neuropathy.</td><td>Cap: 100mg (white)
Soln: 10mg/ml (sugar- free)</td><td>Not to be used with d4T.
Dosage adjustment in severe renal impairment: 300-400mg/day
ESRF, maintained on haemodialysis/ peritoneal dialysis: 100mg q6-8hrs
Hb 7.5-9g/dl: Dose reduction/ interruption may be necessary.</td><td>Can be taken with or without food.</td></tr>
</table>

<table>
<tr>
<td>Stavudine
(d4T)</td>
<td>Neonate/infant (birth to 13 days): 0.5mg/kg BD
Child (>14 days and <30kg): 1mg/kg BD
Max. dose: As for adults.
Adult: 30mg BD;
S/E: Lipodystrophy (especially in combination with ddI), peripheral neuropathy, pancreatitis, hepatitis, GI disturbances, headache, rash.</td>
<td>Cap: 30mg (white)</td>
<td>Not to be used with AZT.
Interrupt administration if peripheral neuropathy develops.
Dosage adjustment in renal impairment & patients on haemodialysis.</td>
<td>Can be taken with or without food.</td>
</tr>
<tr>
<td>Didanosine
(ddI)</td>
<td>Neonate/infant (2 weeks-<3 months): 50mg/m2 BD
Infant (≥3 months-8months): 100mg/m2 BD
Child (>8 months): 120mg/m2 BD (dose range 90-150mg/m2 BD, Max: 200mg/dose BD)
Adolescent/Adult (<60kg): 125mg BD; (≥60kg): 200mg BD
Didanosine EC
<table>
<tr><th>Body Weight (kg)</th><th>Dose (mg)</th></tr>
<tr><td>20-<25</td><td>200mg OD</td></tr>
<tr><td>25-<60</td><td>250mg OD</td></tr>
<tr><td>≥60</td><td>400mg OD</td></tr>
</table>
S/E: Peripheral neuropathy, pancreatitis, nausea, diarrhoea. Lipodystrophy enhanced in combination with d4T.</td>
<td>Tab: 25mg chewable/ dispersible buffered
Soln: 2g paediatric powder for 10mg/ml oral soln (VIDEX®)
Cap: 250mg (white) enteric coated, delayed release cap (VIDEX EC®)</td>
<td>Dosage adjustment in renal impairment. Therapy should be suspended if confirmed occurrence of pancreatitis.</td>
<td>Food decreases absorption of all ddI preparations.
Should be taken on an empty stomach (30 minutes before or 2 hours after food).
ddI oral solution contains antacids that interfere with the absorption of other medications: PIs.
ddI in combination with TDF should be avoided because of enhanced ddI toxicity.</td>
</tr>
<tr>
<td>Tenofovir (TDF)</td>
<td>Child (≥2 years – 12 years): 8mg/kg OD
Max. dose: As for adults.
Adult (aged ≥12 yrs and ≥35kg): 300mg OD
S/E: Headache, diarrhoea, nausea, vomiting, renal tubular dysfunction, bone demineralisation. Important to do blood monitoring (and TDF urine if available).</td>
<td>Tab: 300mg (blue) film-coated tab. as tenofovir disoproxil fumarate (= 245mg tenofovir disoproxil)</td>
<td>Significant changes in C_{max} of ddI when co-administered with TDF.
Dosage adjustment in renal impairment (≥50ml/min q24h; 30-49ml/min q48h; 10-29ml/min twice a week).</td>
<td>Can be taken with or without food, although absorption is enhanced when administered with a high-fat meal.</td>
</tr>
</table>

Tenofovir (TDF) + **Emtricitabine** (FTC)	**Child**: Individual TDF & FTC dose OD Max. dose: As for adults. **Adult**: 1 tab. OD **S/E**: As for TDF. SE for FTC included nausea and diarrhoea, hyperpigmentation/ skin discolouration on palms/soles, predominantly observed in non-white patients.	**Tab**: TDF 300mg/ FTC 200mg	Do not use in patient with CrCl <30ml/ min or in patient requiring dialysis.	Can be given without regard to food.
Abacavir (ABC, Ziagen®)	**Child (aged ≥3 months)**: 8mg/kg BD Max. dose : As for adults. **Adult**: 300mg BD or 600mg OD **S/E**: Hypersensitivity, LOA, respiratory symptoms such as sore throat, cough, SOB.	**Tab**: 300mg scored tablet **Soln**: 20mg/ml	Dosage adjustment in hepatic insufficiency. Do not use in patient with CrCl <50ml/ min, patients on dialysis or patients with impaired hepatic function.	Can be given without regard to food. Test patients for the HLA B*5701 allele before starting therapy to predict risk of hypersensitivity.
AZT + 3TC (Combivir®)	**Child**: Individual AZT & 3TC dose BD Max. dose: As for adults. **Adult**: 1 tab. BD	**Tab**: AZT 300mg/ 3TC 150mg (white)	Dose adjustment for AZT in hepatic impairment, or if Hb level <9g/dl, or neutrophil count <1 x 109. Dose adjustment for 3TC if CrCl <50ml/ min.	Can be taken with or without food.
ABC + 3TC (Kivexa®)	**Child**: Individual ABC & 3TC dose OD Max. dose: As for adults. **Adult**: 1 tab. OD	**Tab**: ABC 600mg/ 3TC 300mg (orange)	Do not use ABC in patient with CrCl <50ml/min, patients on dialysis or patients with impaired hepatic function.	Can be taken with or without food.

Non-Nucleoside Analogue Reverse Transcriptase Inhibitors (NNRTI)				
Efavirenz (EFV, Stocrin®)	**Child (≥3 yrs and body weight ≥10kg)**: 10-<15kg: 200mg ON; 15-<20kg: 250mg ON; 20-<25kg: 300mg ON; 25-<32.5kg: 350mg ON; 32.5-<40kg: 400mg ON **Adolescent/Adult or ≥40kg**: 600mg ON **S/E**: Mood changes, vivid dreams (common but usually short-lived), hypercholesterolaemia, rash.	**Tab**: 50mg (yellow) **Tab**: 200mg (yellow) **Tab**: 600mg (yellow)		Should be taken on an empty stomach, preferably at bedtime. Bioavailability is increased following a high-fat meal. Tablet can be cut.
Nevirapine (NVP)	**Child**: (<8years): 200mg/m2 BD (Max: 200mg BD) (≥8 years): 120-150mg/m2 BD (Max: 200mg BD) Max. dose: 200 mg BD **Adult**: 200mg OD 2/52, then 200mg BD **S/E**: Rash, hepatitis, Stevens-Johnson syndrome – usually first 12 weeks. Hepatic function at 2, 4 and 8 weeks.	**Tab**: 200mg (white) **Susp**: 10mg/ml	Discontinue if patient experiences rash/ severe rash. Interrupt administration if LFT abnormalities develop.	Can be taken with or without food.
Protease Inhibitors (PI)				
Atazanavir (ATV, Reyataz®)	**Child (>6 years); treatment-naive:** 15 - <20kg: 150mg + ritonavir 100mg OD 20 - <32kg: 200mg + ritonavir 100mg OD 32 - <40kg: 250mg + ritonavir 100mg OD ≥ 40kg: 300mg + ritonavir 100mg OD **Adult boosted dose:** 300mg OD	**Cap**: 300mg (white)	Renal impairment (not on haemodialysis): no dose adjustment. Haemodialysis: Treatment-naive patient: 300mg OD; treatment-experienced patient should not receive atazanavir.	Should be taken with food to enhance absorption. Omeprazole and all other PPIs are contraindicated.

Darunavir (DRV, Prezista®)	**Child (3 - <18 yrs and BW ≥10kg):** 10 -<11kg: DRV 200mg + RTV 32mg BD 11 -<12kg: DRV 220mg + RTV 32mg BD 12 -<13kg: DRV 240mg + RTV 40mg BD 13 -<14kg: DRV 260mg + RTV 40mg BD 14 -<15kg: DRV 280mg + RTV 48mg BD 15 -<30kg: DRV 375mg + RTV 50mg BD 30 -<40kg: DRV 450mg + RTV 60mg BD ≥40kg: DRV 600mg + RTV 100mg BD **Adolescent (aged >18yrs)/ Adult:** (treatment-naive/ARV-experienced with no DRV resistance-associated mutations) : DRV 800mg + RTV 100mg OD (treatment-naive / ARV-experienced with at least one DRV resistance associated mutations) : DRV 600mg + RTV 100mg BD **S/E**: Skin rash, including SJS and erythema multiforme, hepatotoxicity, diarrhoea, nausea, headache, fat maldistribution.	**Tab**: 300mg (orange)		DRV should not be used without RTV. To be taken with food. DRV contains a sulphonamide moiety. Use with caution in patients with known sulphonamide allergy.
Indinavir (IDV, Crixivan®)	**Adult**: IDV 800mg + 100/200mg RTV BD **S/E**: Nausea, abdominal pain, headache, metallic taste, dizziness, asymptomatic hyperbilirubinaemia (10%), lipid abnormalities.	**Cap**: 400mg (white)	Decreased metabolism in mild to moderate hepatic impairment.	Should be taken on an empty stomach 1 hour before or 2 hours after food (or can be administered with a light meal). Adequate hydration is required to minimise risk of nephrolithiasis.

Lopinavir/ ritonavir (LPV/r, Kaletra®)	**Infant** (14 days-12 months): 300mg LPV/75mg RTV per m2 BD **Child** (>1 year): 230mg LPV/75mg RTV per m2 BD Max. dose: As for adults. **Adult**: 400 mg/100mg LPV/r BD or 800mg/200mg LPV/r OD **S/E**: Cautious use with hepatic insufficiency. Diarrhoea, headache, nausea, vomiting.	**Tab**: 100mg LPV/25mg RTV and 200mg LPV/50mg RTV **Soln**: 1ml = 80mg LPV/20mg RTV		Tabs. can be taken with or without food. Caps. & soln. should be administered with food. Absorption is increased following a high-fat meal. LPV/r soln. can be kept at room temperature if used within 2 months.
Ritonavir (RTV, Norvir®)	**Child (for boosting other PI's):** <1.3 m2: 75mg/m2 BD (up to 100mg) BD or OD **Adult:** 100mg BD or 100mg OD with atazanavir.	**Caps**: 100mg (white)		Give with or after food.
Integrase Inhibitors				
Raltegravir (RAL, Isentress®)	**Child** (aged 2-<12 years) Chewable tablet 10-<14kg: 75mg BD 14-<20kg: 100mg BD 20-<28kg: 150mg BD 28-<40kg: 200mg BD ≥40kg: 300mg BD Film-coated tablet **Adult and adolescent ≥12years**: 400mg BD S/**E**: rash, nausea, diarrhoea, headache, fever.	**Tab**: 400mg (pink)	Renal impairment: No dosage adjustment is necessary. Co- administration with rifampicin: 800mg BD.	Can be taken with or without food. Film-coated tablets and chewable tablets are NOT interchangeable. Chewable tablets have better bioavailability than film-coated tablets.
Fixed Dose Combinations				
d4T + 3TC + NVP (SLN 30)	**Adult (30-60kg)**: 1 tab. BD	**Tab**: d4T 30mg/ 3TC 150mg/NVP 200mg (blue)	Interrupt administration in moderate to severe LFT abnormalities.	Can be taken with or without food.

HAART–DRUG INTERACTION CHART

A. NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTIS)

	Abacavir	Didanosine (ddI)	Emtricitabine (FTC)	Lamivudine (3TC)	Stavudine (d4T)	Tenofovir	Zidovudine (AZT/ZDV)
Antiinfectives							
Acyclovir	*	*	*	*	*	#	*
Adefovir	*	*	*	*	*	X	*
Amikacin	*	*	*	*	*	#	*
Amoxicillin	*	*	*	*	*	*	*
Amphotericin B	*	#	#	#	#	#	#
Azithromycin	*	*	*	*	*	*	*
Ciprofloxacin	*	*	*	*	*	*	*
Dapsone	*	*	*	*	*	*	#
Fluconazole	*	*	*	*	*	*	#
Flucytosine	*	#	#	#	#	#	#
Ganciclovir	#	#	#	#	*	#	#
Itraconazole	*	*	*	*	*	*	*
Isoniazid	*	*	*	*	#	*	*
Oseltamivir	*	*	*	*	*	*	*
Pentamidine	*	#	#	#	#	#	#
Penicillins	*	*	*	*	*	*	*
Pyrimethamine	*	#	#	#	#	#	#
Rifabutin	*	*	*	*	*	*	*
Rifampicin	#	*	*	*	*	*	#
Streptomycin	*	*	*	*	*	#	*
Trimethoprim/Sulfamethoxazole	*	*	#	#	#	#	#

	Abacavir	Didanosine (ddI)	Emtricitabine (FTC)	Lamivudine (3TC)	Stavudine (d4T)	Tenofovir	Zidovudine (AZT/ZDV)
Antiretrovirals (NNRTI)							
Efavirenz	*	*	*	*	*	*	*
Nevirapine	*	*	*	*	*	*	*
Antiretrovirals (PI)							
Atazanavir	*	#	*	*	*	#	*
Darunavir	*	#	*	*	*	#	*
Fosamprenavir	*	#	*	*	*	#	*
Indinavir	*	#	*	*	*	#	*
Lopinavir	#	#	*	*	*	#	*
Nelfinavir	*	#	*	*	*	*	*
Ritonavir	*	#	*	*	*	#	*
Saquinavir	*	#	*	*	*	#	*
Tipranavir	#	#	*	*	*	*	#

Note:

X - Should not be co-administered

\# - Potential interaction (Requires close monitoring, dosing and timing alteration)

* - No clinically significant interaction expected

B. NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTIS)

	Efavirenz	Nevirapine
Antiinfectives		
Acyclovir	#	#
Adefovir	#	#
Amikacin	*	*
Amoxicillin	*	*
Antemisinin	#	#
Amphotericin B	*	*
Caspofungin	#	#
Azithromycin	*	*
Ciprofloxacin	*	*
Clarithromycin	#	#
Clavulanic acid	*	*
Clindamycin	*	*
Dapsone	*	*
Erythromycin	*	#
Fluconazole	*	#
Flucytosine	*	*
Ganciclovir	*	*
Ethambutol	*	*
Itraconazole	#	X
Isoniazid	*	*
Mefloquine	*	*
Metronidazole	*	*
Moxifloxacin	*	*
Ofloxacin	*	*
Oseltamivir	*	*
Pentamidine	*	*
Penicillins	*	*
Primaquine	n/a	n/a
Pyrimethamine	*	*
Pyrazinamide	*	*
Quinine	#	#
Rifabutin	#	#
Rifampicin	#	X
Streptomycin	*	*
Sulfadoxine/ pyrimethamine	*	*

	Efavirenz	Nevirapine
Tetracyclines	*	*
Trimethoprim/Sulfamethoxazole	*	*
Voriconazole	#	#
Antiretrovirals (NRTI)		
Abacavir	*	*
Didanosine (ddI)	*	*
Emtricitabine (FTC)	*	*
Lamivudine (3TC)	*	*
Stavudine (d4T)	*	*
Tenofovir	*	*
Zidovudine (AZT/ZDV)	*	*
Antiretrovirals (PI)		
Atazanavir	#	X
Darunavir	#	*
Fosamprenavir	#	#
Indinavir	#	#
Lopinavir	#	#
Nelfinavir	#	#
Ritonavir	#	*
Saquinavir	#	#
Tipranavir	*	*

Note:

X - Should not be co-administered

\# - Potential interaction (Requires close monitoring, dosing and timing alteration)

* - No clinically significant interaction expected

n/a - No data

C. PROTEASE INHIBITORS (PI)

	Atazanavir	Darunavir	Fosamprenavir	Indinavir	Lopinavir	Nelfinavir	Ritonavir	Saquinavir	Tipranavir
Antiinfectives									
Acyclovir	*	*	*	*	*	*	*	*	*
Adefovir	*	*	*	*	*	*	*	*	*
Amikacin	*	*	*	*	*	*	*	*	*
Amoxicillin	*	*	*	*	*	*	*	*	*
Antemisinin	#	#	#	#	*	#	#	#	#
Amphotericin B	*	*	*	*	*	*	*	*	*
Caspofungin	#	#	#	*	#	*	#	*	#
Azithromycin	*	#	*	*	*	*	#	*	*
Ciprofloxacin	*	*	*	*	*	*	*	*	*
Clarithromycin	#	#	*	*	#	*	#	*	#
Clavulanic acid	*	*	*	*	*	*	*	*	*
Clindamycin	*	*	*	*	*	*	#	*	*
Dapsone	*	*	#	*	*	*	*	#	#
Erythromycin	*	#	#	#	#	*	#	*	#
Fluconazole	*	*	*	*	*	*	*	*	#
Flucytosine	*	*	*	*	*	*	*	*	*
Ganciclovir	*	*	*	*	*	*	*	*	*
Ethambutol	*	*	*	*	*	*	*	*	*
Itraconazole	#	#	#	#	#	*	#	*	#
Isoniazid	*	*	*	*	*	*	*	*	*

	Atazanavir	Darunavir	Fosamprenavir	Indinavir	Lopinavir	Nelfinavir	Ritonavir	Saquinavir	Tipranavir
Mefloquine	#	#	#	#	#	#	#	#	#
Metronidazole	#	#	*	*	#	*	#	*	#
Moxifloxacin	#	*	*	*	#	*	*	*	*
Ofloxacin	#	*	*	*	#	*	*	*	*
Oseltamivir	*	*	*	*	*	*	*	*	*
Pentamidine	*	*	*	*	*	*	#	*	*
Penicillins	*	*	*	*	*	*	*	*	*
Primaquine	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Pyrimethamine	*	*	*	*	*	*	#	*	*
Pyrazinamide	*	*	*	*	*	*	*	*	*
Quinine	#	#	#	#	#	#	#	#	#
Rifabutin	#	#	#	#	#	#	#	#	#
Rifampicin	X	X	X	X	X	X	X	X	X
Streptomycin	*	*	*	*	*	*	*	*	*
Sulfadoxine/ pyrimethamine	*	*	*	*	*	*	#	*	#
Tetracyclines	*	*	*	*	*	*	*	*	*
Trimethoprim/ Sulfamethoxazole	*	*	*	*	*	*	*	*	#
Voriconazole	#	#	#	#	#	#	X	#	#
Antiretrovirals (NRTI)									
Abacavir	*	*	*	*	#	*	*	*	#
Didanosine (ddI)	#	#	#	#	#	#	#	#	#
Emtricitabine (FTC)	*	*	*	*	*	*	*	*	*
Lamivudine (3TC)	*	*	*	*	*	*	*	*	*

	Atazanavir	Darunavir	Fosamprenavir	Indinavir	Lopinavir	Nelfinavir	Ritonavir	Saquinavir	Tipranavir
Stavudine (d4T)	*	*	*	*	*	*	*	*	*
Tenofovir	#	#	#	#	#	*	#	#	*
Zidovudine (AZT/ ZDV)	*	*	*	*	*	*	*	*	#
Antiretrovirals (NNRTI)									
Efavirenz	#	#	#	#	#	#	#	#	*
Nevirapine	X	*	#	#	#	#	*	#	*

Note:

X - Should not be co-administered

\# - Potential interaction (Requires close monitoring, dosing and timing alteration)

* - No clinically significant interaction expected

n/a - No data

D. POTENTIAL METHADONE DRUG INTERACTIONS

Medication	Effect on Methadone	Effect on HIV-Related Medications	Potential Significance/ Recommendation
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)			
Zidovudine (AZT)	None	May increase AZT AUC 40%	No dose adjustment. Watch for signs/ symptoms of AZT-adverse effects (e.g., headache, muscle aches, fatigue, and irritability).
Didanosine (ddI), buffered tablet	Unknown	May decrease ddI AUC 57%	No dose adjustment. Monitor CD4 and viral load to ensure the effectiveness of ddI.
Didanosine (ddI), enteric coated capsule (EC)	Unknown	No significant change in ddI AUC	-
Stavudine (d4T)	Unknown	May decrease d4T AUC 23%	No dose adjustment. Monitor CD4 and viral load to ensure the effectiveness of d4T.
Lamivudine (3TC)	Unknown	Unknown	No significant change when given as AZT-3TC (Combivir).
Emtricitabine	No clinically significant interaction expected		-
Abacavir (ABC)	May increase 23% methadone clearance	Decreased abacavir peak concentration 34%	Monitor for signs/symptoms of withdrawal.
Nucleotide Reverse Transcriptase Inhibitor (NtRTI)			
Tenofovir disoproxil fumarate	Unknown	No significant changes	No dose adjustment.
Non Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)			
Nevirapine	May decrease methadone level 51%	Unknown	May need to increase methadone dose ~16%.
Efavirenz	May decrease methadone level 57%	Unknown	May need to increase methadone dose ~22% (15-30mg).
Delavirdine	May increase methadone levels (predicted)	Unknown	May need to decrease methadone dose.

Medication	Effect on Methadone	Effect on HIV-Related Medications	Potential Significance/ Recommendation
Protease Inhibitors			
Indinavir	No significant change in methadone AUC	Non-significant change in Indinavir's AUC; Increased Indinavir Cmin 50%-100%; Decreased Indinavir Cmax 16%-36%	Interactions are unlikely to be clinically significant.
Ritonavir	May decrease methadone AUC by 36%	Unknown	May need to increase methadone dose. Monitor for signs/symptoms of methadone withdrawal.
Saquinavir	Unknown	Unknown	Unknown
Lopinavir/ Ritonavir (Kaletra)	Unknown, but contains ritonavir so may decrease methadone AUC 36%	Unknown	May need to increase methadone dose.
Darunavir	May decrease methadone AUC by 16%; Decreased methadone Cmin 15%; decreased methadone Cmax 24%	Unknown	Monitor for signs/symptoms of methadone withdrawal. To titrate methadone dose to effect although it is not routinely recommended.
Nelfinavir	May decrease methadone AUC 40%	Unknown	Methadone dose usually stays the same.
Entry and Integrase Inhibitor			
Raltegravir	No clinically significant interaction expected		

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HAART ADVERSE EFFECTS CHART

A. Nucleoside Reverse Trascriptase Inhibitors (NRTI)

NRTI damages the cellular mitochondria function, which is believed to cause many, if not all, side effects associated. Clinical manifestations of mitochondrial toxicity are lactic acidosis, hepatitic steatosis, pancreatitis, peripheral neuropathy, lipoatrophy (fat loss), skeletal myopathy/ cardiomyopathy, and HIV associated neuromuscular weakness.

Table 1: Known and expected Adverse Drug events associated with NRTIs

Drug	Adverse Events
Abacavir (ABC)	■ Hypersensivitiy syndrome (usually occurs in first 6 weeks of therapy) which can be characterized by fever, rash, progressive nausea, malaise, diarrhea, respiratory symptoms such as sore throat, cough and shortness of breath. ■ Nausea, headache ■ Rare lactic acidosis and hepatitic steatosis
Didanosine (ddI)	■ Pancreatitis ■ Peripheral neuropathy ■ Nausea, diarrhea ■ Lactic acidosis with hepatic steatosis is a rare but potentially life-threatening toxicity associated with use of NRTIs, particularly stavudine
Emtricitabine (FTC)	■ Minimal toxicity ■ Diarrhea, nausea, headache ■ Hyperpigmentation/skin discoloration of palms and soles
Lamivudine (3TC)	■ Minimal toxicity ■ Headache, dry mouth
Stavudine (d4T)	■ Peripheral neuropathy ■ Lactic acidosis ■ Pancreatitis ■ Lipodystrophy ■ Dyslipidaemia *Warning: Concomitant use with ddI appears to have increased risk of fat distribution, peripheral neuropathy, pancreatitis and lactic acidosis.*
Tenofovir (TDF)	■ Flatulence, abdominal discomfort, headache, nausea, diarrhea, vomiting ■ Asthenia ■ Acute renal insufficiency, Fanconi syndrome ■ Decrease bone mineral density (BMD) particularly of the lumbar spine
Zidovudine (AZT)	■ Bone marrow suppression: ■ Macrocytic anemia (may be seen as early as 2 to 6 weeks after initiation of therapy; avoid initiating AZT in those with Hgb<9) ■ Neutropenia (Usually occurs after 12-24 weeks) ■ Gastrointestinal intolerance, headache, nausea, ■ Asthenia ■ Hyperpigmentation of skin and nails

B. Non-Nucleoside Reverse Trascriptase Inhibitors (NNRTI)

NNRTIs are associated with hypersensitivity reactions, commonly characterized by skin rash, usually begins within 1 – 3 weeks of therapy. Rare cases of Stevens - Johnson Syndrome (SJS) have been reported with the use of all four NNRTIs, the highest incidence seen associated with nevirapine use.

Table 2: Known and expected Adverse Drug events associated with NNRTIs

Drugs	Adverse Events
Delaviridine (DLV)	■ Rash ■ Elevated liver transaminase levels, hepatitis ■ Headache, nausea, diarrhea
Efavirenz (EFV)	■ Low incidence of rash ■ Central Nervous System (CNS) symptoms ■ Dizziness, somnolence, insomnia, abnormal dreams, confusion, abnormal thinking, impaired concentration, amnesia, agitation, hallucinations, and euphoria ■ Severity usually decreases within 2 – 4 weeks after initiation of efavirenz ■ Elevated liver transaminase levels, hepatoxicity (rare) ■ Dyslipidemia
Etravirne (ETV)	■ Elevated liver transaminase levels ■ Rash ■ Nausea
Nevirapine (NVP)	■ 33% incidence of rash, 5% of persons with rash will develop SJS. Usually develops within first 6 weeks of therapy ■ Hepatitis ▶ Women who start NVP therapy with CD4 cell counts greater than 250 (and men with CD4 counts>400) have a 12 times greater risk of hepatitis. ■ Elevated liver transaminase levels. Hepatotoxicity is more common at higher CD4 cell counts, in women and in patients with hepatitis B or C. ■ Dyslipidemia

C. Protease Inhibitors (PI)

All PIs are associated with lipodystrophy syndrome.

Lipodystrophy is:

- An abnormal fat distribution refers to fat wasting (lipoatrophy) and fat accumulation (lipohypertrophy). Generally, PIs raise the problem of fat accumulation at the abdomen, neck, breasts.
- Metabolic disturbances such as raised triglycerides or cholesterol, impaired glucose tolerance/diabetes.

Table 3: Known and expected Adverse Drug events associated with PIs

Drug	Adverse Events
Atazanavir (ATV)	■ Indirect hyperbilirubinemia ■ Prologed PR interval – 1st degree symptomatic AV block in some patients ■ Hyperglycemia ■ Fat maldistribution ■ Possible increased bleeding episodes in patients with hemophilia ■ Nephrolithiasis
Darunavir (DRV)	■ Skin rash (7%) ■ Diarrhea, nausea, headache ■ Hyperlipidemia ■ Hyperglycemia ■ Elevated liver transaminase levels ■ Fat maldistribution ■ Possible increased bleeding episodes in patients with hemophilia
Fosamprenavir (FPV)	■ Skin rash (19%) ■ Diarrhea, nausea, vomiting, headache ■ Hyperlidemia ■ Elevated liver transaminase levels ■ Hyperglycemia ■ Fat maldistribution ■ Possible increased bleeding episodes in patients with hemophilia
Indinavir	■ Nephrolithiasis ■ GI intolerance ■ Indirect Hyperbilirubinemia ■ Hyperlipidemia ■ Headache, asthenia, blurred vision, dizziness, rash, metallic taste, thrombocytopenia, alopecia and hemolytic anemia ■ Hyperglycemia ■ Fat maldistribution ■ Possible increased bleeding episodes in patients with hemophilia

Drug	Adverse Events
Lopinavir/Ritonavir	■ GI intolerance, nausea, vomiting, diarrhea (increased in OD than BD dosing) ■ Asthenia ■ Hypertriglyceridemia ■ Elevated liver transaminase levels ■ Hyperglycemia ■ Fat maldistribution ■ Possible increased bleeding episodes in patients with hemophilia
Nelfinavir (NFV)	■ Diarrhea (50%) ■ Hyperlipidemia ■ Elevated liver transaminase levels ■ Hyperglycemia ■ Fat maldistribution ■ Possible increased bleeding episodes in patients with hemophilia
Ritonavir (RTV)	■ GI intolerance, nausea, vomiting, diarrhea ■ Paresthesias – circumoral and extremities ■ Hypertriglyceridemia ■ Hepatitis ■ Asthenia ■ Taste perversion ■ Hyperglycemia ■ Fat maldistribution ■ Possible increased bleeding episodes in patients with hemophilia
Saquinavir (SQV)	■ GI intolerance, nausea and diarrhea ■ Headache ■ Elevated liver transaminase levels ■ Hyperlipidemia ■ Hyperglycemia ■ Fat maldistribution ■ Possible increased bleeding episodes in patients with hemophilia
Tipranavir (TPV)	■ Hepatotoxicity – clinical hepatitis including hepatic decompensation has been reported ■ Skin rash (14% females, 8 – 10% males) ■ Rare cases of fatal and nonfatal intracranial hemorrhages have been reported ■ Hypertriglyceridemia ■ Hyperglycemia ■ Fat maldistribution ■ Possible increased bleeding episodes in patients with hemophilia

D. Fusion Inhibitors

Table 4: Known and expected Adverse Drug events associated with Fusion Inhibitors

Drug	Adverse Events
Enfuvirtide (T20)	■ Local injection site reaction: mild to moderate pain and discomfort, induration, erythema, nodules and cysts, pruritus, and ecchymosis. May be minimized by good injection technique ■ Increased bacterial pneumonia ■ Hypersensitivity rash

E. Chemokine Coreceptor Antagonis

Table 5: Known and expected Adverse Drug events associated with Chemokine Co-receptor Antagonists

Drug	Adverse Events
Maraviroc (MVC)	■ Abdominal pain, dizziness, diarrhea, pyrexia, nausea ■ Musculoskeletal symptoms, ■ Upper respiratory infections, cough ■ Hepatitis, elevated liver transaminase levels ■ Orthostatic hypotension

F. Intergrase Inhibitors

Table 6: Known and expected Adverse Drug events associated with Integrase Inhibitors

Drug	Adverse Events
Raltegravir (RAL)	■ Nausea, diarrhea, flatulence ■ Headache ■ Dizziness, abnormal dreams ■ Pyrexia ■ Elevated amylase and liver transaminase levels ■ Pruritis, rash ■ Fatigue, muscle pain

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