ANTIRETROVIRAL THERAPY (ART) & OPPORTUNISTIC INFECTION (OI) MANAGEMENT IN RVD PATIENTS

DIAMS Quick Guide

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Only for internal circulation (HSgB)
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Disclaimer: This guide provides general advice based on published evidence and expert opinion for standardization of practice in HSgB. This guide may not cover all aspects of clinical practice, thus healthcare practitioners are encouraged to review patient details and professionally assess the relevance of this guide to each clinical situation. This guide is subject to periodic updates. We assume no responsibility for any party who referred to an outdated version of this protocol.

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DISCLAIMER

This guide provides general advice based on published evidence and expert opinion for hospital-wide standardization of practice. This guide may not cover all aspects of clinical practice, thus healthcare practitioners are encouraged to review patient details and professionally assess the relevance of this protocol to each clinical situation.

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SECTION 1: ANTIRETROVIRAL THERAPY (ART)

ART AVAILABLE IN HSGB

NRTI (Nucleoside/Nucleotide Reverse Transcriptase Inhibitors)

Backbone for 1st or 2nd line treatment

- **AZT** = Zidovudine *(only available as combination tablet with 3TC)*
- **TDF** = Tenofovir Disoproxil Fumarate
- **TAF** = Tenofovir Alafenamide
- **ABC** = Abacavir

Paired with:

- **3TC** = Lamivudine
- **FTC** = Emtricitabine *(only available as combination tablet with TDF)*

Combination tablet:

- **Combivir** = Zidovudine + Lamivudine
- **Tenvir-EM** = Tenofovir DF + Emtricitabine
- **Kivexa** = Abacavir + Lamivudine

NNRTI (Non-Nucleoside Reverse Transcriptase Inhibitors):

Part of 1st line treatment

- **EFV** = Efavirenz
- **NVP** = Nevirapine
- **ETR** = Etravirine (Intelence)

Combination tablet:

- **Atripla / Viraday** = Tenofovir DF + Emtricitabine + Efavirenz

Protease Inhibitors (PIs):

Part of 2nd line treatment

- **LPV** = Lopinavir *(only available as combination tablet with RTV)*
- **ATV** = Atazanavir
- **DRV** = Darunavir (Prezista) *(In HSgB: reserved for salvage therapy)*

Boosted with:

- **RTV** = Ritonavir (Norvir) [Booster]

Combination tablet:

- **Kaletra** = Lopinavir + Ritonavir

Integrase Inhibitors (INSTI):

Alternative for NNRTI for 1st line or alternative for PIs for 2nd line treatment

1st line:

- **RAL** = Raltegravir (Isentress)

1st line/2nd line:

- **DTG** = Dolutegravir (Tivicay)

Combination tablet:

- **Teldy** = Tenofovir DF + Lamivudine + Dolutegravir

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Antiretroviral Therapy (ART) & Opportunistic Infections (OI) Management in RVD Patients

Launched: March 2025 Latest Update: -

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ART COMPONENT IN A TREATMENT REGIMEN

ART Regimen: Combination usually consists of 3 ART from 2 different classes					
Usual Combination	**1st Line** (3 Agents therapy):	**2 NRTIs:** • Tenvir-Em **or** • Combivir **or** • Kivexa **or** • TAF + 3TC*	+	**1 NNRTI** • Efavirenz **or** • Nevirapine **or** **1 INSTI** • Raltegravir **or** • Dolutegravir	* **TAF + 3TC:** *Only for RVD patients with Hep B co-infection & unable to receive Tenvir-EM due to renal impairment.*
	2nd Line (for VIROLOGICAL/TREATMENT FAILURE) (3 Agents therapy):	**2 NRTIs:** • Tenvir-Em **or** • Combivir **or** • Kivexa **or** • TAF + 3TC*	+	**1 INSTI** • Dolutegravir **or** **1 Boosted PI** • Kaletra **or** Atazanavir + Ritonavir	* **TAF + 3TC:** *Only for RVD patients with Hep B co-infection & unable to receive Tenvir-EM due to renal impairment.*
Other Combination	**Dual therapy – 1st line / 2nd Line:** (2 Agents therapy)	Lamivudine	+	Dolutegravir	Usually given in patients with renal impairment, while waiting for HLA-B*5701 test before starting Abacavir. Refer to: **LAMIVUDINE (3TC) + DOLUTEGRAVIR (DTG) DUAL-THERAPY CRITERIA** table below
	Dual therapy - 2nd line: (2 Agents therapy)	**Boosted PIs** • Kaletra **or** • Atazanavir + ritonavir	+	Dolutegravir	For patients unable to tolerate any NRTI.
			or		
		Kaletra 3 tabs BD	+	Efavirenz	This regimen is being phased out due to high incidence of metabolic side effects.
	4 Agents therapy:	**3 NRTIs:** • Combivir **plus** • Tenofovir*	+	**Boosted PIs** • Kaletra **or** • Atazanavir + ritonavir	This regimen is only for RVD patients with **Hep B co-infection** (Tenofovir (TDF) is added for Hep B).
	Salvage Therapy:	**2 NRTIs.** Eg: • Tenvir-Em **or** • TAF + 3TC* **AND/OR** • Dolutegravir	+	Darunavir + Ritonavir	Regimen is decided based on the result of the **HIV resistance test**. * **TAF + 3TC**: *Only for RVD patients with Hep B co-infection & unable to receive Tenvir-EM due to renal impairment.*

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LAMIVUDINE (3TC) + DOLUTEGRAVIR (DTG) DUAL-THERAPY CRITERIA

Criteria for Initiating DTG+3TC in ART-naive patients:

- HIV VL < 500,000 copies/ml (BHIVA 2022, EACS 2022, DHHS 2022, IAS-USA 2022)
- CD4 > 200 cells/mm^3 (BHIVA 2022)
- No Hep B co-infection (BHIVA 2022, EACS 2022, DHHS 2022, IAS-USA 2022)
- No history of PrEP failure (EACS 2022)

Criteria for Switching to DTG+3TC in ART-experienced patients:

- HIV VL < 50 copies/mL (EACS 2022, DHHS 2022, IAS-USA 2022)
- No history of prior virological failure or resistance (EACS 2022, DHHS 2022, IAS-USA 2022)
- For patients with active Hep B infection, patient needs to be on specific HBV active regimen (EACS 2022, DHHS 2022, IAS-USA 2022)

If criteria not fulfilled, please revert back to the ID Physician

PREFERRED & ALTERNATIVE OPTIONS FOR 1ST LINE ART REGIMEN

Table 5.1 • Preferred and Alternative ARV Options for patients who are ARV naive

NRTI Backbone		NNRTI		INSTI		Protease Inhibitor (PI)****
(Preferred) TDF/FTC TDF + 3TC TAF/FTC**	PLUS	(Preferred) EFV 400/600	OR	(Preferred) DTG	OR	Special Situation ATV/r
(Alternative) AZT# + 3TC ABC* + 3TC		(Alternative) NVP RPV***		(Alternative) RAL		

* Perform HLA-B*5701 testing before initiating ABC; if result is positive, do not start ABC and add ABC to allergy list. If using ABC/3TC in a patient with HIV VL>100,000 copies/ml, combination with DTG is preferred over NNRTI
\# AZT should not be initiated in patients with baseline Hb < 8.0g/dl.
** TAF regime is preferred over TDF in renal impairment and bone disease.
*** RPV as an alternative when intolerant to EFV/DTG, with VL<100,000 copies/ml.
**** This should only be chosen in special situations and should be discussed with an ID Physician.

Source: Malaysian Consensus Guideline on Antiretroviral Therapy 2022

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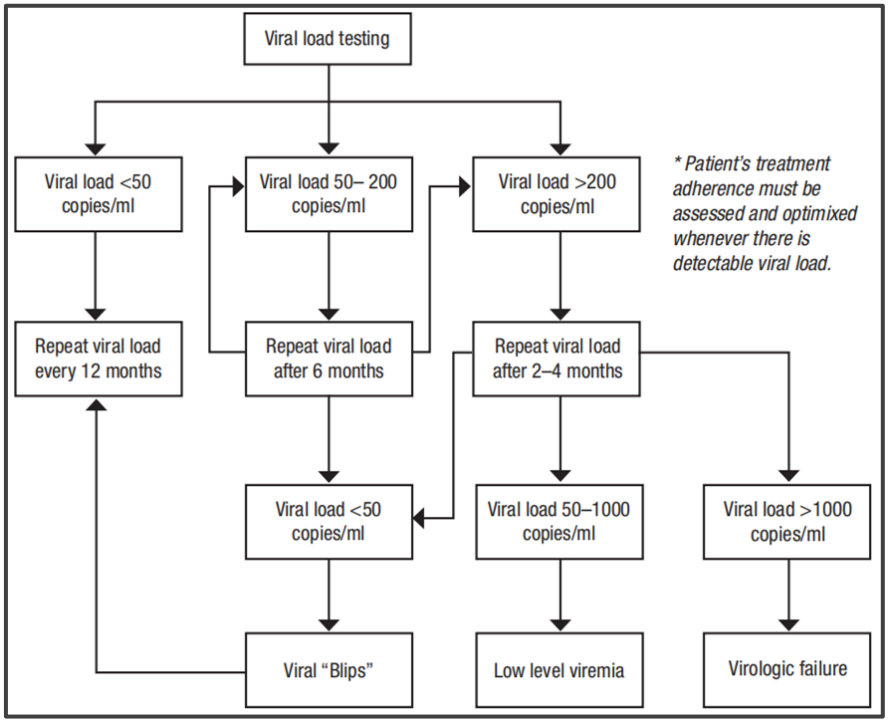
VIROLOGICAL/TREATMENT FAILURE

- **Definition:**
  Persistent high Viral Load (VL > 1000 copies/mL) in two consecutive tests within 3 months, despite adherence support & after at least 6 months on a new ART regimen.
- **Genotypic Resistance Testing:** Conducted to detect drug resistance mutations in viral genes, and done only when VL > 1000 copies/mL.
- **Timing of Resistance Testing:**
  It should be done while the patient is on ART or within 4 weeks of stopping therapy. If ART is stopped for more than 4 weeks, the test might miss resistance mutations due to the lack of drug-selective pressure.



Source: Malaysian Consensus Guideline on Antiretroviral Therapy 2022

PREFERRED & ALTERNATIVE OPTIONS FOR 2ND LINE ART REGIMEN

Failing First Line Regimen	Preferred Second Line Regimen	Alternative Second Line Regimens
TDF + FTC (or 3TC) + EFV (or NVP) ABC + 3TC + EFV (or NVP)	TDF + FTC (or 3TC) + DTG#	AZT + 3TC + DTG AZT + 3TC + LPV/r (or ATV/r or DRV/r) TDF + FTC (or 3TC) + DRV/r#
AZT + 3TC + EFV (or NVP)	TDF + FTC (or 3TC) + DTG ABC + 3TC + DTG	TDF + FTC (or 3TC) + LPV/r (or ATV/r or DRV/r) ABC + 3TC + LPV/r (or ATV/r or DRV/r)
TDF + FTC (or 3TC) + DTG (or RAL) ABC + 3TC + DTG (or RAL)	AZT + 3TC + LPV/r	AZT + 3TC + DRV/r (or ATV/r)
AZT + 3TC + DTG (or RAL)	TDF + FTC (or 3TC) + LPV/r ABC + 3TC + LPV/r	TDF + FTC (or 3TC) + DRV/r (or ATV/r) ABC + 3TC + DRV/r (or ATV/r)

Based on evidence from the NADIA trial.

Source: Malaysian Consensus Guideline on Antiretroviral Therapy 2022

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STANDARD & RENAL DOSAGES FOR ART

Drug	Standard Dose	Renal Adjusted Dose
Combivir (AZT + 3TC)	1 tab BD	• **CrCl <50:** Co-formulated tablet is not recommended
Tenvir-EM (TDF + FTC)	1 tab ON	• **CrCl 30-49:** 1 tab EOD • **CrCl <30 or HD:** Co-formulated tablet is not recommended
Kivexa (ABC + 3TC)	1 tab OD	• **CrCl <50:** Co-formulated tablet is not recommended
Abacavir (ABC)	600 mg OD (preferred) / 300 mg BD	• No dose adjustment required
Tenofovir Disoproxil Fumarate (TDF)	300 mg OD	• **CrCl 30-49:** 300 mg EOD • **CrCl <30:** 300 mg q72-96H • **CrCl <10 (not on HD):** Use not recommended • **HD:** 300 mg once weekly
Tenofovir Alafenamide Fumarate (TAF)	25 mg OD	• **CrCl <15 (not on HD):** Use not recommended • **CrCl <15 (on HD):** No dose adjustment required
Lamivudine (3TC)	300 mg OD (preferred)/ 150 mg BD	• **CrCl <50:** 150 mg OD • **CrCl <15 or HD:** 150 mg OD x 1 dose, then 75 mg OD
Efavirenz (EFV)	600 mg ON / 400 mg ON *(for pts with CNS s/e)*	• No dose adjustment required
Nevirapine (NVP)	200 mg OD x 2/52, then 200 mg BD *(Check for Black Box Warning)*	• No dose adjustment required
SLN (D4T + 3TC + NVP)	1 tab BD	• **CrCl <50:** Co-formulated tablet is not recommended
Kaletra (LPV + RTV)	2 tabs BD	• No dose adjustment required
Atazanavir (ATV)	300 mg OD *(together with Ritonavir 100 mg OD)*	• No dose adjustment required
Darunavir (DRV)	600 mg BD *(together with Ritonavir 100 mg BD)*	• No dose adjustment required
Ritonavir (RTV)	Only as booster • 100 mg OD (with Atazanavir) • 100mg BD (with Darunavir)	• No dose adjustment required
Raltegravir (RAL)	400 mg BD	• No dose adjustment required
Dolutegravir (DTG)	50 mg OD ***or*** 50 mg BD • *If on Rifampicin, or* • *If suspected/confirmed RAL resistance, or* • *If switching from EFV with unsupressed VL (BD for 2 weeks, then OD)*	• No dose adjustment required

For further info on renal dose adjustment, refer to:
DIAMS - HSgB Antimicrobial Standard & Renal Adjusted Dose Quick Guide

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COMMON ADVERSE EFFECTS OF ART - OVERVIEW

Drug	Side Effects
Zidovudine	Anaemia, **nausea, vomiting**, nail pigmentation, lipodystrophy *Click here [Zidovudine (AZT) Side Effects - Myelosuppresion] for more info.*
Abacavir	Systemic Hypersensitivity *(positive HLA-B*5701 test strongly increases risk of hypersensitivity)* *Click here [Abacavir (ABC) Adverse Effects – Hypersensitivity Reaction (HSR)] for more info.*
Tenofovir Disoproxil Fumarate (TDF)	AKI, Fanconi's syndrome, ↓ bone marrow density *Click here [Tenofovir (TDF) Side Effects - Nephrotoxicity] for more info.*
Tenofovir Alafenamide Fumarate (TAF)	Weight gain
Lamivudine (3TC) or Emtricitabine (FTC)	Lactic acidosis with hepatic steatosis
Stavudine (d4t)	Peripheral neuropathy, lipodystrophy, lactic acidosis
Efavirenz	**CNS side effects** (eg: headache, giddiness, nightmares, sleep disturbance & depression), hepatotoxicity, rashes, gynecomastia *Click here [Efavirenz (EFV) Side Effects – CNS Disturbance] for more info.*
Nevirapine	Systemic hypersensitivity *(eg: rashes, mouth ulcer, fever, hepatitis, Stevens-Johnson Syndrome (SJS))*
Kaletra	**Nausea, diarrhoea**, hyperglycemia, **dyslipidemia**, transaminase elevation
Atazanavir	**Unconjugated hyperbilirubinemia** *(increase in indirect bilirubin),* GI intolerance
Darunavir	GI intolerance, headache, hyperglycemia, hyperlipidemia, transaminase elevation
Raltegravir	**Weight gain**, LFT elevation, rash
Dolutegravir	**Weight gain**, ↑ Creatinine *(due to inhibition of renal tubular creatinine secretion without affecting glomerular filtration itself. Consider new set point after 1-2 months)*

- In **Bold**: "Frequent effects" *(events expected in at least 10% of treated pts)*
- In Red: "Severe effects" *(events that can put a person's life at risk and require medical attention)*

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ADVERSE EFFECTS OF SPECIFIC ART

Tenofovir (TDF) Side Effects - Nephrotoxicity

Tenofovir induced nephrotoxicity:

Risk factors:

1. Underlying kidney disease (avoid if eGFR <50mL/min)
2. Older age
3. BMI < 18.5 kg/m2 (or body weight < 50kg)
4. Untreated Diabetes Mellitus & uncontrolled Hypertension
5. Concomitant use of nephrotoxic drugs or boosted PIs
6. Prolonged NSAIDS use

Counseling point:

- Drink at least 1.5 - 2 L of non-Caffeinated fluid per day (preferably water)
- Avoid NSAIDs

Fanconi Syndrome:

Proximal tubulopathy with any combination of:

- Proteinuria: urine dipstick ⩾ 1, or confirmed increase in UP/C > 15 mg/mmol
- Progressive decline in eGFR and eGFR ⩽ 90 mL/min
- Phosphaturia: confirmed hypophosphatemia secondary to increased urine phosphate leak
- Glucosuria in non-diabetics

Management:

- Replace TDF with non-tenofovir drug or TAF
- Refer Protocol for Initiation and Monitoring of Tenofovir → put in link

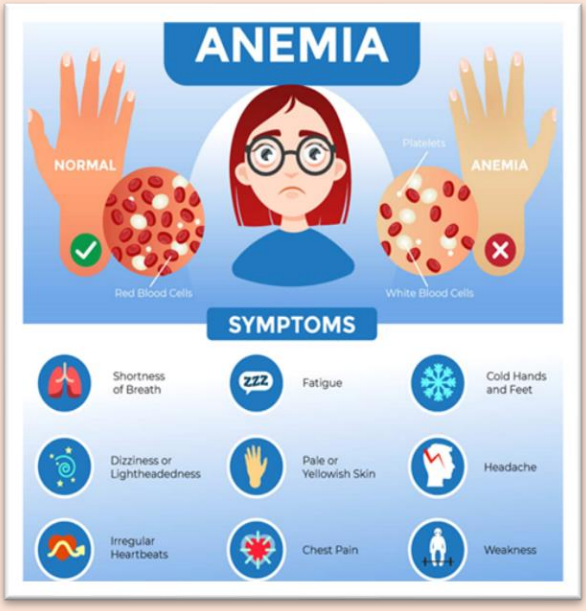
Zidovudine (AZT) Side Effects - Myelosuppresion

- Side effects: Anemia, leukopenia, GI intolerance
- Avoid concurrent bone marrow suppressants
- Monitor FBC with differential –
  At weeks 4, 8, 12 (more frequently in patients at risk)

Management:

- Discontinue AZT and substitute with TDF / ABC if:
  - Hb has dropped ⩾ 25% of baseline or is < 8.0 g/dL

    or
  - When the patient develops symptomatic anaemia and/or leukopenia
- If Hb is dropping and AZT is continued, closely monitor Hb and advice the patient on symptoms of anaemia.



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Efavirenz (EFV) Side Effects – CNS Disturbance

EFV CNS/Neuropsychiatric Side Effects:

- Headache,
- Giddiness,
- Nightmares,
- Sleep disturbance,
- Depression,
- Hallucination
- Suicidal ideation

Risk Factors:

- History of psychiatric illness
  - Monitor for depression
  - Prolonged or severe depression should prompt a change in regime, especially if the patient has other risk factors for depression.
- Concomitant use of substances with Neuropsychiatric effects
- Genetic factor resulting in high serum EFV concentration
- Increased EFV absorption with food.

Counseling Points:

- Take EFV at bedtime
- Take on an empty stomach or avoid fatty meals 2 hours before taking EFV
- Inform the doctor or counselor if severe side effects occur

Management if patient is unable to tolerate CNS side effects:

- **Mild-moderate Side Effects:**
  - Reduce Efavirenz to 400 mg ON
  - If keen to continue in mild depression, closely monitor for deterioration of depression (caretakers are advised to monitor for deterioration of depression).
- **Moderate-Severe Side Effects:**
  - Switch EFV to INSTI (Raltegravir or Dolutegravir) – quota item, to d/w ID consultant

Abacavir (ABC) Adverse Effects – Hypersensitivity Reaction (HSR)

Abacavir HSR Symptoms:

Fever and/or rash with multi-organ involvement:

- Respiratory: shortness of breath, cough, sore throat
- Gastrointestinal: nausea, vomiting, diarrhea, abdominal pain
- Constitutional: lethargy, malaise, headache, achiness

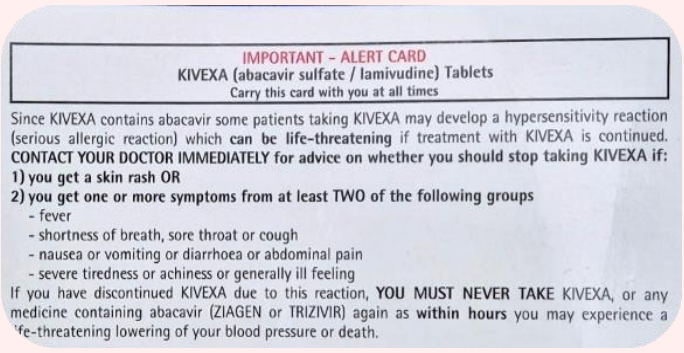
Onset:
Usually within the first 6 weeks of treatment (median 9 days), but can occur anytime. Symptoms typically improve 48 hours after stopping Abacavir

Risk Factor:
Positive HLA-B*5701 allele increases the risk

Management:

- Immediate Action:
  Stop Abacavir and switch to another NRTI without delay, regardless of HLA-B*5701 status. Delaying can lead to a life-threatening reaction.
- Differential Diagnosis:
  Rule out other causes of symptoms (e.g., viral infections, other skin rashes).
- Symptomatic Support:
  Provide antipyretics, fluids, and pressure support if necessary.
- Rechallenge Contraindication:
  Never re-initiate Abacavir in patients with HSR. Rechallenge can cause rapid and severe, potentially fatal reactions (symptoms return within hours, often more severe, including life-threatening hypotension and respiratory distress).

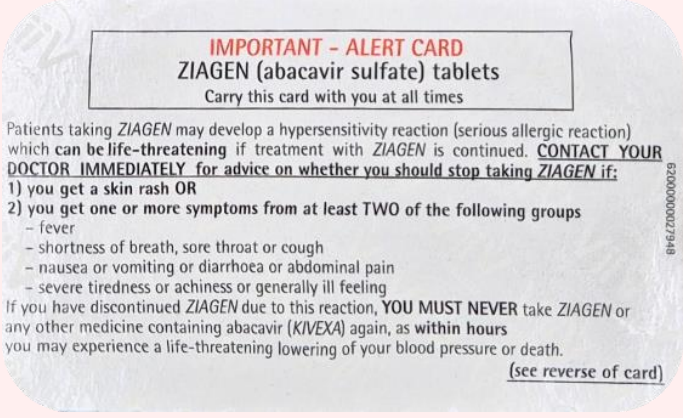
ABACAVIR ALERT CARD available in every Kivexa/Abacavir Medicine Box:



IMPORTANT – ALERT CARD
KIVEXA (abacavir sulfate / lamivudine) Tablets
Carry this card with you at all times

Since KIVEXA contains abacavir some patients taking KIVEXA may develop a hypersensitivity reaction (serious allergic reaction) which **can be life-threatening** if treatment with KIVEXA is continued. **CONTACT YOUR DOCTOR IMMEDIATELY for advice on whether you should stop taking KIVEXA if:**
1) you get a skin rash OR
2) you get one or more symptoms from at least TWO of the following groups
- fever
- shortness of breath, sore throat or cough
- nausea or vomiting or diarrhoea or abdominal pain
- severe tiredness or achiness or generally ill feeling

If you have discontinued KIVEXA due to this reaction, **YOU MUST NEVER TAKE** KIVEXA, or any medicine containing abacavir (ZIAGEN or TRIZIVIR) again as **within hours** you may experience a life-threatening lowering of your blood pressure or death.



IMPORTANT – ALERT CARD
ZIAGEN (abacavir sulfate) tablets
Carry this card with you at all times

Patients taking *ZIAGEN* may develop a hypersensitivity reaction (serious allergic reaction) which **can be life-threatening** if treatment with *ZIAGEN* is continued. **CONTACT YOUR DOCTOR IMMEDIATELY for advice on whether you should stop taking *ZIAGEN* if:**
1) you get a skin rash OR
2) you get one or more symptoms from at least TWO of the following groups
- fever
- shortness of breath, sore throat or cough
- nausea or vomiting or diarrhoea or abdominal pain
- severe tiredness or achiness or generally ill feeling

If you have discontinued *ZIAGEN* due to this reaction, **YOU MUST NEVER** take *ZIAGEN* or any other medicine containing abacavir (*KIVEXA*) again, as **within hours** you may experience a life-threatening lowering of your blood pressure or death.

(see reverse of card)

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PEP (POST-EXPOSURE PROPHYLAXIS)

Post-Exposure Prophylaxis (PEP) is an emergency medical intervention taken within 72 hours **after potential HIV exposure** to prevent infection.

Indication of PEP:

- Exposure to blood, tissue or other body fluids that may risk a HCW for HIV, HBV or HCV infection
- PEP should start within 2 hours of exposure.

Transmission can occur through:

- Percutaneous injury
- Contact of mucosal membrane
- Non-intact skin

Immediate Management of Individuals with Known or Suspected Exposure to HIV

1. Wash wound or skin sites that have been in contact with blood or body fluids with soap and water
2. Irrigate mucous membranes and eyes (remove contact lens) with saline and water
3. Do not inject antiseptics or disinfectants into wound
4. Do not squeeze the wound as it may promote hyperaemia and inflammation at the wound site, thus potentially increasing the risk of systemic exposure to HIV if present in the contaminating fluid.

PEP Recommendations When Exposed to HIV Positive Source Patient

Type of exposure with known HIV positive patient	PEP recommendation	
	Source already on HIV treatment and recent viral load (VL) is undetectable/ < 20 copies/ml	Source not on HIV treatment, or on HIV treatment but recent viral load (VL) is still detectable, or no recent viral load (VL) available
Needle stick injury or other sharps exposure *(penetrating injury to the skin with a sharp instrument containing fresh blood)*	**2 drugs basic regimen**	**3 drugs expanded regimen**
Mucous membrane or non-intact skin exposure	**Consider 2 drugs basic regimen**	**3 drugs expanded regimen**

PEP Regimen in HSgB	Basic Regimen: *(2 drugs regimen)*	Expanded Regimen: *(3 drugs regimen)*
Preferred:	**Tenvir-EM 1 tab OD**	**Tenvir-EM 1 tab OD** plus **Dolutegravir 50 mg OD**
Alternative:	**Combivir 1 tab BD**	**Tenvir-EM 1 tab OD** plus **Kaletra 2 tabs BD**
Duration of Treatment for Basic/Expanded PEP Regimen:	**28 days**	

Supply of PEP in HSgB:

- PEP is only for HCWs in contact with high-risk sources, as determined by the **OSH department** and in consultation with an ID Physician.
- The **STAT dose** of PEP must be obtained from **Ward 4C** within 2 hours by the HCW, regardless of office hours or after office hours. The remaining one-month supply should be ordered by OSH clinic & supply obtained from the OPD pharmacy.

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PrEP (PRE-EXPOSURE PROPHYLAXIS):

Pre-Exposure Prophylaxis (PrEP) is a medicine for individuals at high risk of HIV, to significantly reduce the likelihood of infection **prior to exposure.**

Click here for Gov Clinics with PrEP

Option 1: Tenvir-EM On-demand* (2:1:1)

Can be used only by:

Cisgender man/trans & gender diverse people assigned male at birth (AMAB)

AND

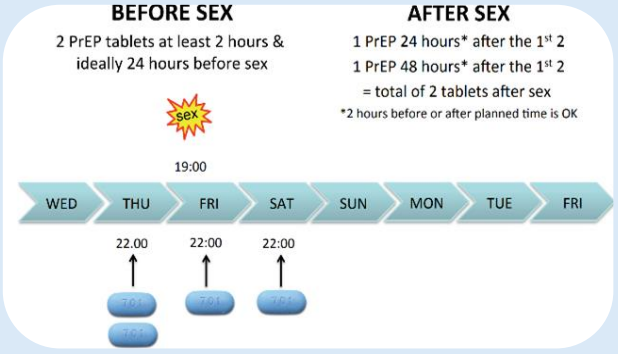
are NOT taking exogenous estradiol-based hormones.

Regimen:

Take Tenvir-Em **loading dose of 2 tabs** (taken 2-24 H before sex), followed by **1 tab at 24H** and **1 tab at 48H** after the loading dose

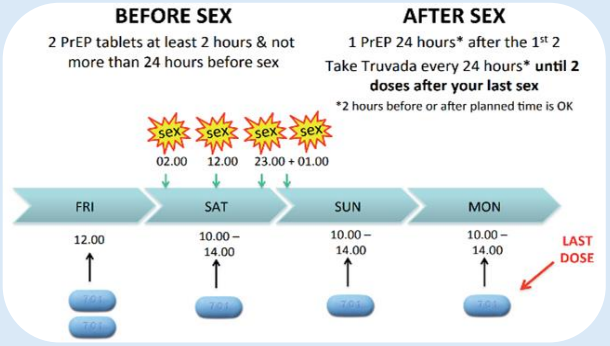
Example 1:

On-demand dosing - If you have sex **once a week**



Example 2:

On-demand dosing - Sex **several times over a few days**



Option 2: Tenvir-EM 1 tab once daily dosing

Can be used by:

Cisgender man/trans & gender diverse people assigned female at birth (AFAB)

OR

Cisgender man/trans & gender diverse people assigned male at birth who are taking exogenous estradiol-based hormones

OR

People who inject drugs (PWID) to prevent HIV acquisition from injecting practices

Regimen:

Take Tenvir-EM (TDF/FTC) **1 tab daily** for **7 days before** potential exposure and continue **1 tab daily during** exposure and for **7 days after** the last potential exposure

Refer to Malaysian Consensus Guideline on Antiretroviral Therapy 2022 for more info

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BACK

RVD WITH HEP B CO-INFECTION: ART REGIMEN

Goals of Hep B Treatment :

- Prevent progression of the diseases to cirrhosis, end stage liver disease reducing the risk of hepatocellular carcinoma and liver-related mortality
- **HBeAg Positive Patient target:**

  Seroconversion from HBeAg to anti-HBe antibody Achieve a sustained suppression of HBV DNA
- **HBeAg Negative Patient target:**

  Achieve a sustained suppression of HBV DNA

Drugs active against both HBV & HIV:

3TC (Lamivudine)

FTC (Emtricitabine)

TDF (Tenofovir Disoproxil Fumarate)

TAF (Tenofovir Alafenamide Fumarate)

- HBV develops rapid resistance to 3TC and FTC therefore monotherapy is discouraged.
- **TDF + FTC (Tenvir-Em)** is the preferred first-line treatment for RVD patients with Hep B co-infection.
- **TAF + 3TC** can replace Tenvir-EM for treating RVD patients with Hepatitis B co-infection who have renal impairment, making them unable to receive Tenvir-EM.

*In HSgB, Hepatitis B without HIV co-infection is not managed by the ID Team, such patients will be referred to Hospital Selayang.

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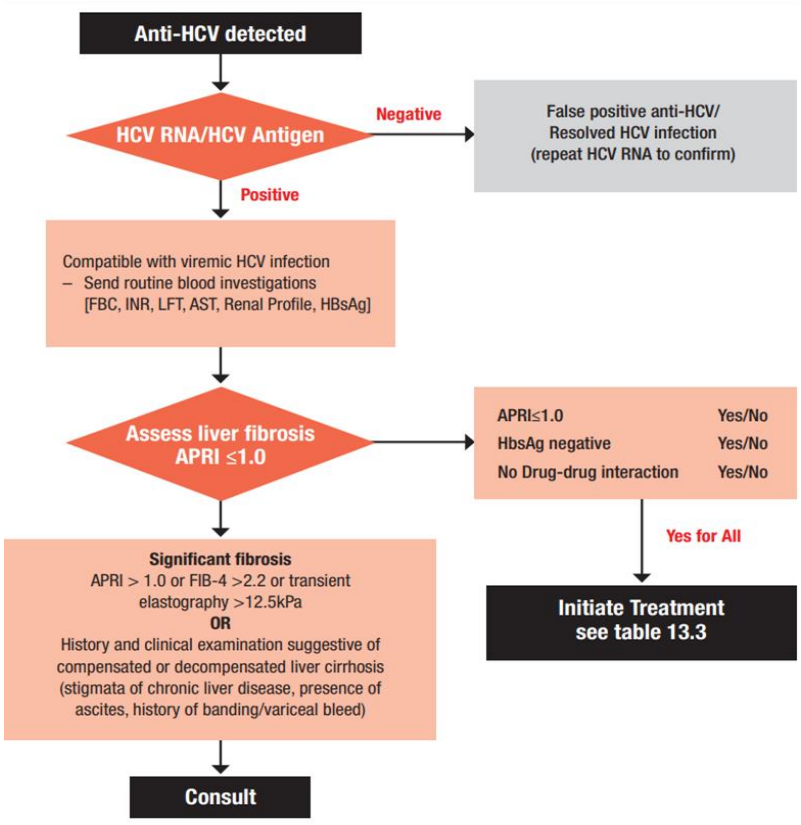
RVD WITH HEP C CO-INFECTION: HEP C REGIMEN

Goals of Hep C Treatment:

- To eradicate Hepatitis C virus (HCV) & CURE the infection.
- To reduce all-cause mortality and liver-related complications including fibrosis, cirrhosis, end-stage liver disease and hepatocellular carcinoma (HCC).
- To prevent transmission of HCV infection.
- To improve quality of life including physical, emotional, and social health.

HCV/HIV Co-infection Treatment Algorithm:

Source: Malaysian Consensus Guideline on Antiretroviral Therapy 2022



***APRI Score:**

$$APRI = \frac{(AST\ level/AST\ ULN) \times 100}{Platelet\ count\ (10^9/L)}$$

Click here for
APRI Score Calculator

Hep C Treatment Regimen in HSgB:

- Sofosbuvir (SOF) 400 mg OD
- **plus** Daclatasvir (DCV) 60 mg OD **or** Ravidasvir (RDV) 200 mg OD
- **plus/minus** Ribavirin (RBV) 600 mg OD

Common Side Effects:

- **Sofosbuvir + Daclatasvir :** Headache , Fatigue (>10%)
- **Sofosbuvir + Ribavirin :** Headache, Fatigue (>20%)
- **Sofosbuvir + Peg-Interferon alpha + Ribavirin :** Fatigue, headache, nausea, anaemia, insomnia, flu-like illness, rash, low appetite, chills

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Choice of DAA, dose & duration of treatment according to HIV Treatment Regimen:

HIV Treatment Regimen	Choice of DAA, dose & duration of treatment according to HIV Treatment Regimen			
	Without cirrhosis			With compensated cirrhosis
NNRTI: • Efavirenz (EFV), or • Nevirapine (NVP)	SOF 400 mg OD **plus** RDV 200 mg OD	**or**	SOF 400 mg OD **plus** DCV 90 mg OD	SOF 400 mg OD **plus** RDV 200 mg OD
Integrase Inhibitors (INSTI): • Dolutegravir	SOF 400 mg OD **plus** RDV 200 mg OD	**or**	SOF 400 mg OD **plus** DCV 60 mg OD	SOF 400 mg OD **plus** RDV 200 mg OD
Protease Inhibitors (PI): • Lopinavir/ritonavir (Kaletra) or • Darunavir/ritonavir	SOF 400 mg OD **plus** DCV 60 mg OD			Consult
Protease Inhibitors (PI): • Atazanavir/ritonavir	SOF 400 mg OD **plus** DCV 30 mg OD			Consult
Duration of treatment:	**12 weeks**			**24 weeks**

Hep C Treatment Duration:

Genotype	Treatment naive/experienced	Non-cirrhosis	Compensated cirrhosis	Decompensated cirrhosis
1a, 4, 5, 6	Treatment naive	12 weeks	12 weeks	12 weeks with RBV or 24 weeks without RBV *1, 4: 24 weeks without RBV
	Treatment experienced	12 weeks with RBV or 24 weeks without RBV	12 weeks with RBV or 24 weeks without RBV	
1b	Treatment naive	12 weeks	12 weeks	12 weeks with RBV
	Treatment experienced			
2	Treatment naive	12 weeks	12 weeks	12 weeks plus/minus RBV
	Treatment experienced			
3	Treatment naive	12 weeks	24 weeks with RBV	24 weeks with RBV
	Treatment experienced	12 weeks with RBV or 24 weeks without RBV		

Hep C Treatment Protocol in HSgB:

1	**Week 0**	○ ○	**See Doctor.** Start Hep C treatment as per algorithm. **See Pharmacist** for Hep C Counseling
2	**Week 4**	○	**See Pharmacist.** Perform blood tests (urgent LFT & RP) on TCA & assess adherence and adverse effects
3	**Week 12:** End of Therapy (EOT)	○	**See Doctor.** Perform blood test (urgent LFT & RP) on TCA.
4	**12 Weeks Post-EOT**	○	**Perform blood test** (HCV RNA)
5	**16 weeks Post-EOT**	○	**See Doctor.** Perform blood test (urgent LFT, RP) on TCA

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WHEN TO INITIATE ART IN PATIENTS WITH OPPORTUNISTIC INFECTIONS (OI)

- For newly diagnosed RVD, ART should be started within 7 days of diagnosis irrespective of CD4 count.
- However, in the presence of certain opportunistic infections, ART can be initiated within 2 weeks of the OI treatment after the patient has been clinically assessed.

Type of Opportunistic Infections (OI)	When to initiate ART
CMV *(strongly consider starting in 2nd week)*	**Start ART as soon as possible**
MAC	
Histoplasmosis	
PCP	**Start ART within 2 weeks of OI treatment**
Talaromycosis / Penicilliosis	
Salmonellosis	
Toxoplasmosis	
TB with CD4 <50 *(except TB Meningitis)*	
Cryptococcal Meningitis *(delayed until after completion of induction/ consolidation phase)*	**Delay initiation**
TB Meningitis *(delayed until 2 months of antiTB initiation)*	

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SECTION 2: OPPORTUNISTIC INFECTIONS (OI) MANAGEMENT

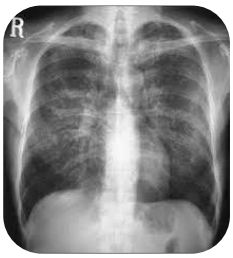
Important cut-offs for CD4 T cells, above which particular AIDS illnesses are improbable.
These **CD4 counts** are only reference values; exceptions are always possible.

- **No cut-off:** Kaposi's sarcoma, pulmonary tuberculosis, HZV, bacterial pneumonia, lymphoma, HSV
- **< 250/µl:** PCP, oesophageal candidiasis, PML, HIV encephalopathy
- **< 100/µl:** Cerebral toxoplasmosis, cryptococcosis, miliary tuberculosis
- **< 50/µl:** CMV end organ disease, cryptosporidiosis, atypical mycobacteriosis

The treatment regimens are based on drugs available in the Ministry of Health National Formulary and hence in some instances may vary from internationally accepted treatments. Some regimes are chosen as preferred regimes due to cost considerations.

1. PNEUMOCYSTIS JIROVECI (CARINII) INTERSTITIAL PNEUMONIA (PJP/PCP)

<table>
<tr><th rowspan="2">Infection/Condition & Likely Organism</th><th colspan="2">Suggested Treatment</th><th rowspan="2">Comments</th></tr>
<tr><th>Preferred</th><th>Alternative</th></tr>
<tr>
<td>Treatment

  </td>
<td>Bactrim (Trimethoprim/ sulfamethoxazole) 15-20 mg/kg/day [of TMP component] IV/PO in 3-4 divided doses

*DIAMS - IV to PO
Tab. Bactrim & Cap. Clindamycin have excellent bioavailability (~90%).
*Change to oral formulation after clinical improvement and once patient can tolerate orally</td>
<td><u>For mild to moderate cases:
(PO_2 70-80 mmHg)</u>

Clindamycin 600 mg IV/PO q8h
PLUS
Primaquine 30 mg (base) PO q24h

OR

Dapsone 100 mg PO q24h*
PLUS
Trimethoprim 15 mg/kg/day PO in 3-4 divided doses

<u>For severe cases:
(PO_2 < 70 mmHg)</u>

Pentamidine (UKK) 4 mg/kg/day IV (in 1 pint D5% or NS run over 1-2 hours)

OR

Clindamycin 600 mg IV q6h or 900 mg IV q8h
PLUS
Primaquine 30 mg (base) PO q24h
(Patient should be tested for G6PD deficiency)</td>
<td>Duration: 21 days

Patients with severe disease should receive adjunctive corticosteroids as soon as possible (within 72 hours of starting PCP treatment):

Prednisolone dose:
• 40 mg PO q12h for 5 days, then
• 40 mg PO q24h for 5 days, then
• 20 mg PO q24h for 11 days
(Total duration is 21 days)</td>
</tr>
<tr>
<td>Prophylaxis (primary & secondary)

<u>Indications:</u>
• CD4 count < 200 cells/µL
• CD4 count 200-250 cells/µL if ART cannot be initiated</td>
<td>Bactrim (Trimethoprim/ sulfamethoxazole) 80-160 mg TMP/ 400-800 mg SMX (= 1–2 tablets) PO q24h</td>
<td>Dapsone 100 mg PO q24h
(Patient should be tested for G6PD deficiency)

OR

Aerosolized Pentamidine (UKK) 300 mg monthly via ultrasonic nebulizer</td>
<td>Discontinuation:
Can consider when CD4 100-200 cells/µL if HIV RNA is suppressed for 3-6 months with ART.

Restarting prophylaxis:
• CD4 count falls to < 200 cells/µL or
• PCP occurs at a CD4 > 200 cells/µL (lifelong prophylaxis should be considered).

Patients receiving Sulfadiazine/ Pyrimethamine or Sulfadoxine/ Pyrimethamine for treatment or suppression of toxoplasmosis do not require additional prophylaxis for PCP.</td>
</tr>
</table>

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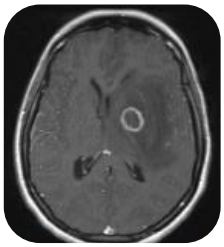
2. TOXOPLASMA GONDII ENCEPHALITIS

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Acute Infection Up to 97% patients are Toxo IgG +ve 	Bactrim (Trimethoprim/ sulfamethoxazole) 10 mg/kg/day [of TMP component] IV/PO* in 2 divided doses *DIAMS - IV to PO **Tab. Bactrim & Cap. Clindamycin** have excellent bioavailability (~90%). *Change to oral formulation after clinical improvement and once patient can tolerate orally	**If Bactrim unavailable/intolerable:** Pyrimethamine **(UKK)** 200 mg PO loading dose followed by Pyrimethamine: • 50 mg PO q24h (if BW ≤ 60kg) • 75 mg PO q24h (if BW > 60kg) **PLUS** Folinic acid 10-25 mg IV q24h **or** Folinic acid 15 mg PO q24h **PLUS** Clindamycin 600 mg IV/PO* q6h *(additional therapy must be added for primary prophylaxis for PCP)*	**Duration:** At least 6 weeks Longer duration if clinical and radiologic disease is extensive or response is incomplete in 6 weeks. **Adjunctive corticosteroids** (E.g.: dexamethasone) should be administered when clinically indicated to treat mass effect associated with focal lesions or associated oedema but should be discontinued as soon as clinically feasible. In the case of sulfa allergy and pyrimethamine is not available, sulfa desensitization should be attempted in those without a history of severe reaction (E.g.: SJS).
Suppressive Therapy/ Maintenance Therapy/ Secondary Prophylaxis	Bactrim (Trimethoprim/ sulfamethoxazole) 160/800 mg (= 2 tablets) PO **q12h** CAUTION **Common mistake:** For **Toxoplasmosis maintenance therapy,** the correct dose is **T. Bactrim 2 tabs BD**. This differs from PCP maintenance therapy, which uses T. Bactrim 2 tabs OD.	Dapsone 100 mg PO q24h **PLUS** Pyrimethamine **(UKK)** 50 mg PO twice weekly* **PLUS/MINUS** Folinic acid 15 mg PO twice weekly* **OR** Clindamycin 600 mg PO q8h **PLUS** Pyrimethamine **(UKK)** 50 mg PO twice weekly* **PLUS/MINUS** Folinic acid 15 mg PO twice weekly*	**Discontinuation:** Consider when CD4 >200 cells/µL if HIV RNA is suppressed for 6 months with ART. *Recommendation is based on the consensus of HSgB ID Consultants, based on expert opinion.
Primary Prophylaxis Indications: Toxoplasma IgG +ve with CD4<100	Bactrim (Trimethoprim/ sulfamethoxazole) 160/800 mg (= 2 tablets) PO **q24h**	Dapsone 50 mg PO q24h **PLUS** Pyrimethamine **(UKK)** 50 mg PO once weekly **PLUS** Folinic acid 30 mg PO once weekly **OR** Dapsone 200 mg PO once weekly **PLUS** Pyrimethamine **(UKK)** 75 mg PO once weekly **PLUS** Folinic Acid 25 mg PO once weekly	**Discontinuation:** • CD4 > 200 cells/µL for > 3 months, or • CD4 > 100 cells/µL if HIV viral load suppressed for 3 to 6 months

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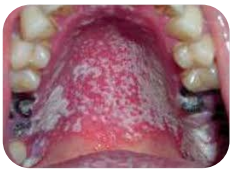
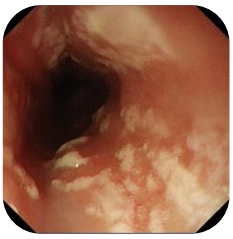
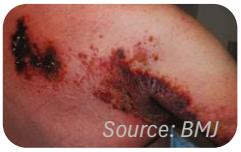
3. MUCOCUTANEOUS CANDIDIASIS

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Oropharyngeal candidiasis (oral thrush) 	Fluconazole 100 mg PO q24h **OR** Nystatin suspension 500,000 units PO 4-times daily	Itraconazole 200 mg PO q24h *Itraconazole's absorption depends on gut acidity. Take the Itraconazole capsule with food and acidic beverages (e.g., Cola drinks). Avoid Proton Pump Inhibitors (PPIs).*	**Duration:** 7-14 days Chronic suppressive therapy is usually not recommended. **CAUTION** **Drug-drug Interaction (Azole):** Check for drug-drug interactions for every patient on azole antifungals
Oesophageal candidiasis 	Fluconazole 200-400 mg PO/IV* q24h **DIAMS - IV to PO** **Oral Fluconazole** has excellent bioavailability (>90%). *Change to Cap. Fluconazole once patient can tolerate orally	Itraconazole 200 mg PO q24h *Itraconazole's absorption depends on gut acidity. Take the Itraconazole capsule with food and acidic beverages (e.g., Cola drinks). Avoid Proton Pump Inhibitors (PPIs).* **CAUTION** **Drug-drug Interaction (Azole):** Check for drug-drug interactions for every patient on azole antifungals	**Duration:** 14-21 days Infection with other pathogens (E.g.: CMV, HSV that causes esophagitis) can result in symptoms that mimic oesophageal candidiasis, a diagnostic and therapeutic trial of antifungal therapy is usually warranted before endoscopy. Endoscopy is required with unusual presentations or lack of response to azole within several days.

4. HERPES ZOSTER (HZ) DISEASES

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Shingles (Herpes Zoster)  *Source: BMJ*	**Immunocompetent** Acyclovir 800 mg PO 5 times/day*		Advisable to start treatment early within 48 hours. **Duration: 7 days** ***Oral Acyclovir 5 times/day administration:** • Please ensure there is at least a 4-hour interval between doses. • Example of administration times: 7 AM, 11 AM, 3 PM, 7 PM & 11 PM. ****IV Acyclovir Dose in Obese Patients:** • Obesity class 1 & 2 (BMI 30-39.9 kg/m^2): Use Ideal Body Weight (IBW) • Obesity class 3 (BMI ≥ 40 kg/m^2): Use Adjusted Body Weight (AdjBW)
	Immunocompromised **Acyclovir 10 mg/kg IV q8h** *(change to oral once there is an improvement)* **Oral Therapy:** Acyclovir 800 mg PO 5 times/day*		

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5. VARICELLA-ZOSTER VIRUS (VZV) DISEASES

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Chicken Pox (*Varicella zoster*)  Source: Wikipedia	**Immunocompetent** Acyclovir 800 mg PO 5 times/day*		Advisable to start treatment early within 48 hours. **Duration: 7 days** ***Oral Acyclovir 5 times/day administration:** • Please ensure there is at least a 4-hour interval between doses. • Example of administration times: 7 AM, 11 AM, 3 PM, 7 PM & 11 PM.
	Immunocompromised Acyclovir 10 mg/kg IV q8h** *(change to oral once there is an improvement)* **Oral Therapy:** Acyclovir 800 mg PO 5 times/day*		
Viral Pneumonia (*Varicella zoster*)	Acyclovir 10 mg/kg IV q8h** **Duration: 7 days**		** **IV Acyclovir Dose in Obese Patients:** • Obesity class 1 & 2 (BMI 30-39.9 kg/m^2): Use Ideal Body Weight (IBW) • Obesity class 3 (BMI ≥ 40 kg/m^2): Use Adjusted Body Weight (AdjBW)
Viral Encephalitis (*Varicella zoster*)	*Acyclovir 10 mg/kg IV q8h** **Duration: 14-21 days**		

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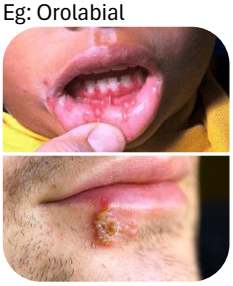
6. HERPES SIMPLEX VIRUS (HSV) INFECTIONS

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Non-genitalia Eg: Orolabial  *Ref: BMC ID Biomed Cental*	Acyclovir 400 mg PO q8h		**Duration: 7 days**
Genital Herpes Physical supportive measures (saline bathing, analgesia, local anaesthetics) are recommended. Topical antivirals are less effective than oral agents and not recommended, due to the association with acyclovir resistant strain. Addition of topical antivirals to oral treatment is of no benefit.	**First Episode (in non-pregnant petients):** Acyclovir 400 mg PO q8h *Oral antiviral drugs indicated within 5 days of the start of the episode and while new lesions are still forming.* **Duration: 7-10 days**	**First episode (in pregnancy):** Acyclovir 400 mg PO q8h **Duration: 7-10 days.** **For 3rd trimester acquisition:** **Continue treatment till delivery**	
	Recurrent Episode (in non-pregnant petients): **Short course:** Acyclovir 800 mg PO q8h for **2 days** **5-day course:** Acyclovir 800 mg PO q12h for **5 days**	**Recurrent episode (in pregnancy):** Acyclovir 400 mg PO q8h *Treatment recommended starting at 36 weeks' gestation.*	
	Suppressive therapy *(if ⩾ 6 recurrences/year, severe, prolonged or with psychosocial problems):* Acyclovir 400 mg PO q12h **Duration:** Up to 1 year, then reassess **If break-through recurrences occur:** **Increase to:** Acyclovir 400 mg PO q8h **Duration:** 7-10 days	-	
Viral Encephalitis	*Acyclovir 10 mg/kg IV q8h **Duration: 14-21 days**		***Dose in Obese Patients:** • Obesity class 1 & 2 (BMI 30-39.9 kg/m^2): Use Ideal Body Weight (IBW) • Obesity class 3 (BMI ≥ 40 kg/m^2): Use Adjusted Body Weight (AdjBW)

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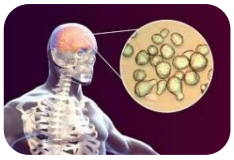
7. CRYPTOCOCCAL MENINGITIS OR MENINGOENCEPHALITIS (CRYPTOCOCCUS NEOFORMANS)

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Induction therapy 	Amphotericin B deoxycholate 1 mg/kg IV q24h **PLUS** Flucytosine 25 mg/kg PO q6h (**Duration:** 1 week) **Followed by:** Fluconazole 1200 mg IV/PO q24h *(may be given in divided dosing)* (**Duration:** 1 week) **OR** **Liposomal Amphotericin B **(UKK)** 10 mg/kg **(single high dose)** **Followed by:** Fluconazole 1200 mg IV/PO q24h *(may be given in divided dosing)* **PLUS** Flucytosine 25 mg/kg PO q6h (**Duration:** 2 weeks) **Followed by Consolidation Therapy**	Amphotericin B deoxycholate 0.7 - 1 mg/kg IV q24h **PLUS** • Flucytosine 25 mg/kg PO q6h **OR** • Fluconazole 800 - 1200 mg IV/PO q24h *(may be given in divided dosing)* (**Duration:** 2 weeks) **OR** Fluconazole 1200 mg IV/PO q24h **PLUS** Flucytosine 25 mg/kg PO q6h (**Duration**: 2 weeks) **Followed by Consolidation Therapy**	*Lipid formulation of Amphotericin B may be used to replace Amphotericin B deoxycholate if renal impairment occurs while patient is on Amphotericin B deoxycholate. 2 types of lipid formulation Ampho B available in HSgB: • Amphotericin B Lipid Complex (ABLC) **(UKK)** 5 mg/kg IV q24h **OR** • Liposomal Amphotericin B **(UKK)** 3 mg/kg IV q24h For severe/recurrent infection, please refer to ID physician. **DIAMS - IV to PO** **Oral Fluconazole** has excellent bioavailability (>90%). *Change to Cap Fluconazole once patient can tolerate orally
Consolidation therapy Continued after successful induction therapy; defined as substantial clinical improvement and negative CSF culture after repeat LP.	*Fluconazole 400 - 800 mg PO/IV q24h **Consider weight-based dosing for Obesity Class 1, 2, or 3 (BMI ≥30 kg/m2)* *Use actual body weight (ABW) for weight-based dose calculations: 6 mg/kg once daily (maximum dose not well established: 800-1600 mg)* **Followed by Maintenance Therapy**	Itraconazole 200 mg PO q12h *Itraconazole's absorption depends on gut acidity. Take the Itraconazole capsule with food and acidic beverages (e.g., Cola drinks). Avoid Proton Pump Inhibitors (PPIs).* **CAUTION** **Drug-drug Interaction (Azole):** Check for drug-drug interactions for every patient on azole antifungals **Followed by Maintenance Therapy**	(Duration: 8 weeks) ***Fluconazole dose** can then be reduced to 400 mg/day to complete the 8-week consolidation phase if all of the following criteria are met: (i) The patient received induction therapy with amphotericin B plus flucytosine for 2 weeks. (ii) CSF cultures obtained after 2 weeks of induction therapy are negative. (iii) ART has been started.
Maintenance Therapy Continued after consolidation therapy.	Fluconazole 200 mg PO q24h	Itraconazole 200 mg PO q24h *For patients intolerant or failed fluconazole (however less effective and higher relapse rate)* **CAUTION** **Drug-drug Interaction (Azole):** Check for drug-drug interactions for every patient on azole antifungals	**Discontinuation:** • Completed initial (induction, consolidation) therapy **AND** • At least 1 year on maintenance therapy **AND** • Remains asymptomatic from cryptococcal infection **AND** • CD4 count ≥ 100 cells/μL and suppressed HIV RNA in response to effective ART for ≥ 6 months
Secondary prophylaxis	Fluconazole 200 mg PO q24h	-	**Restarting secondary prophylaxis:** CD4 count < 100 cells/μL

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8. CRYPTOCOCCOSIS (LOCALIZED NON-MENINGEAL DISEASE)

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Mild-moderate pulmonary infection or extra-pulmonary non-CNS disease **or** **Asymptomatic with positive lung/blood culture or positive antigen test (no CNS disease)**	*Fluconazole 400 - 800 mg PO q24h **Duration:** 10 weeks. **Consider weight-based dosing for Class 1, 2, or 3 obesity (BMI ⩾ 30 kg/m²) patients.* *Use actual body weight (ABW) for weight-based dose calculations: 6 mg/kg once daily (maximum dose not well established: 800-1600 mg)* **Followed by Maintenance Therapy (secondary prophylaxis)**	**Itraconazole 200 mg PO given q8h **Duration:** 3 days Then, consolidation: Itraconazole 200 mg PO given q12h **Duration:** 8 weeks. *Itraconazole's absorption depends on gut acidity. Take the Itraconazole capsule with food and acidic beverages (e.g., Cola drinks). Avoid Proton Pump Inhibitors (PPIs).* **Followed by Maintenance Therapy (secondary prophylaxis)**	⚠ **CAUTION** **Drug-drug Interaction (Azole):** Check for drug-drug interactions for every patient on azole antifungals
Maintenance Therapy (secondary prophylaxis)	Fluconazole 200 mg PO q24h	Itraconazole 200 mg PO q24h *Itraconazole's absorption depends on gut acidity. Take the Itraconazole capsule with food and acidic beverages (e.g., Cola drinks). Avoid Proton Pump Inhibitors (PPIs).*	**Discontinuation of maintenance:** At least 1 year of treatment **AND** CD4 count ≥ 100 cells/μL and suppressed HIV RNA in response to effective ART for ≥ 6 months In the case of treatment failure, all patients initially treated with fluconazole should have their therapy changed to amphotericin B until clinical response is achieved.
Severe pulmonary or extra-pulmonary non-CNS disease	Treat as per **7. CRYPTOCOCCAL MENINGITIS OR MENINGOENCEPHALITIS (CRYPTOCOCCUS NEOFORMANS)**		

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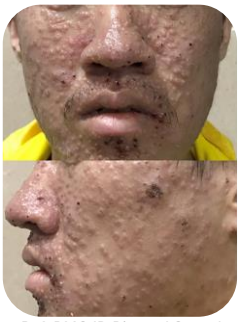
9. PENICILLIOSIS (PENICILLIUM/TALAROMYCES MARNEFFEI)

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Acute infection Mild disease Only skin involvement; no fungaemia	Loading dose *Itraconazole 200 mg PO q8h for 3 days, then reduce to: *Itraconazole 200 mg PO q12h *Itraconazole's absorption depends on gut acidity. Take the Itraconazole capsule with food and acidic beverages (e.g., Cola drinks). Avoid Proton Pump Inhibitors (PPIs).* **Followed by Maintenance Therapy (secondary prophylaxis)**		**Duration:** at least 8-12 weeks **CAUTION** **Drug-drug Interaction (Azole):** All triazole antifungals have the potential to interact with certain ARV agents and other anti-infectives. Check for drug-drug interactions for every patient on azole antifungals
Acute infection Moderate to severe disease  *Ref: BMC ID Biomed Cental*	**Induction Therapy:** *Amphotericin B deoxycholate 0.7 - 1.0 mg/kg/day IV **Followed by Consolidation Therapy.**	**If unable to tolerate Amphotericin B deoxycholate:** Voriconazole 6 mg/kg IV q12h on Day 1, then 4 mg/kg IV q12h for at least 3 days, then 400 mg PO q12h **OR** **If IV Voriconazole is not available:** Voriconazole 600 mg PO q12h on Day 1, then 400 mg PO q12h **OR** **If Voriconazole is Contraindicated:** Amphotericin B Lipid Complex (ABLC) **(UKK)** 5 mg/kg IV q24h, **OR** Liposomal Amphotericin B **(UKK)** 3 mg/kg IV q24h **Followed by Consolidation Therapy.**	**Duration:** 2 weeks ***DIAMS - IV to PO** **Oral Voriconazole** has excellent bioavailability (96%). *Change to Tab Voriconazole once patient can tolerate orally **CAUTION** **Drug-drug Interaction (Azole):** Check for drug-drug interactions for every patient on azole antifungals
	Consolidation Therapy: (Preferred) Itraconazole 200 mg PO q12h *Absorption depends on gut acidity. Take the Itraconazole capsule with food and acidic beverages (e.g., Cola drinks). Avoid Proton Pump Inhibitors (PPIs).* **Followed by Maintenance Therapy (secondary prophylaxis)**	**Consolidation Therapy:** (If unable to tolerate Itraconazole) Voriconazole 200 mg PO q12h **OR** **Consolidation Therapy:** (If on concurrent Rifampicin or Rifabutin) Fluconazole 400 mg PO q12h **Followed by Maintenance Therapy (secondary prophylaxis)**	**Duration:** 10 weeks **CAUTION** **Drug-drug Interaction (Azole):** Check for drug-drug interactions for every patient on azole antifungals
Maintenance therapy **or** **Secondary prophylaxis**	Itraconazole 200 mg PO q24h *Absorption depends on gut acidity. Take the Itraconazole capsule with food and acidic beverages (e.g., Cola drinks). Avoid Proton Pump Inhibitors (PPIs).*	**Maintenance Therapy:** (If on concurrent Rifampicin or Rifabutin) Fluconazole 400 mg PO q24h	**Discontinuation:** CD4 count > 100 cells/μL for ≥ 6 months on ART

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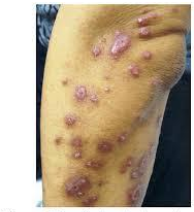
10. HISTOPLASMOSIS (HISTOPLASMA CAPSULATUM)

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Mild disseminated disease (Blood culture positive but patient is asymptomatic)	**Induction & maintenance therapy:** *Itraconazole 200 mg PO q8h for 3 days, then 200 mg PO q12h **Itraconazole absorption depends on gut acidity. Take capsule with a full meal. Avoid PPIs and H2 blockers.*	**Induction & maintenance therapy:** (For patients intolerant to Itraconazole) Fluconazole 800 mg/day PO in 1-2 divided doses	**Duration:** At least 12 months ⚠ CAUTION **Drug-drug Interaction (Azole):** Check for drug-drug interactions for every patient on azole antifungals
Moderate to severe disseminated disease  Figure 1: Skin papules located on the arm in a patient with PDH associated with AIDS. *Image Source: Messina FA, Negroni R, Romero MLM, Santiso MG. AIDS Related Histoplasmosis, Treatment and Prophylaxis: the Mycology Unit of FJ Muñiz Hospital Experience. J AIDS HIV Treat. 2020; 2(2): 57-62.*	**Induction therapy:** Amphotericin B deoxycholate 0.7-1.0 mg/kg IV q24h **Duration:** At least 2 weeks **Followed by Maintenance therapy**	**Induction therapy** (if unable to tolerate Amphotericin B Deoxycholate)*: Amphotericin B Lipid Complex (ABLC) **(UKK)** 5 mg/kg IV q24h **OR** Liposomal Amphotericin B **(UKK)** 3 mg/kg IV q24h **Duration:** for 2 weeks or until clinically improved **Followed by Maintenance therapy**	*Lipid formulation of Amphotericin B may be used to replace Amphotericin B deoxycholate if renal impairment occurs while patient is on conventional Amphotericin B until improvement in renal function is seen. All triazole antifungals have the potential to interact with certain ARV agents and other anti-infective agents. ⚠ CAUTION **Drug-drug Interaction (Azole):** Check for drug-drug interactions for every patient on azole antifungals
	Maintenance therapy: Itraconazole 200 mg PO q8h for 3 days, then 200 mg q12h *Absorption depends on gut acidity. Take the Itraconazole capsule with food and acidic beverages (e.g., Cola drinks). Avoid Proton Pump Inhibitors (PPIs).* **Duration:** At least 12 months **Followed by Chronic Suppressive Therapy (Secondary prophylaxis)** for patients with severe disseminated disease or CNS Infection	**Maintenance therapy** (For patients intolerant to Itraconazole or on concurrent Rifampicin or Rifabutin): Fluconazole 800 mg/day PO in 1-2 divided doses **Duration:** At least 12 months **Followed by Chronic Suppressive Therapy (Secondary prophylaxis)** for patients with severe disseminated disease or CNS Infection	
Chronic Suppressive therapy (Secondary prophylaxis) Indication: • Severe disseminated or CNS infection after completion of at least 12 months of treatment. • Relapsed despite appropriate initial therapy.	Itraconazole 200 mg PO q24h *Itraconazole absorption depends on gut acidity.* *Take the Itraconazole capsule with food and acidic beverages (e.g., Cola drinks).* *Avoid Proton Pump Inhibitors (PPIs).*	**For patients intolerant to Itraconazole or on concurrent Rifampicin or Rifabutin:** Fluconazole 400 mg PO q24h	**Discontinuation:** • Received azole for > 1 year **AND** • Negative fungal blood cultures **AND** • CD4 count > 150 cells/µL for ≥ 6 months on ART **Restarting secondary prophylaxis:** CD4 count < 150 cells/µL

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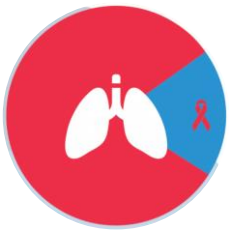
11. MYCOBACTERIUM TUBERCULOSIS (TB) INFECTION AND DISEASES

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	**Alternative**	
Treatment of tuberculosis **(Intensive Therapy)** 	**Fixed Dose Combination (FDC):** **Tab. Akurit-4/Forecox:** *(Each tablet contains: Rifampicin 150mg, Isoniazid* 75mg, Pyrazinamide 400mg & Ethambutol 275mg)* • 30 - 37 kg: 2 tablets PO q24h • 38 - 54 kg: 3 tablets PO q24h • 55 - 70 kg: 4 tablets PO q24h • > 70 kg: 5 tablets PO q24h **PLUS** Pyridoxine (**Vit B6**) 20-30 mg PO q24h *(All patients on Isoniazid (H) should be given Tab. Pyridoxine for prevention of neuropathy)* **Followed by Maintenance Therapy**	**Loose Pills:** Ethambutol (**E**) 15 mg/kg PO q24h *(Range: 15 – 20 mg/kg)* *(Round the dose to the nearest 200 mg)* *(Max dose: 1600 mg)* **PLUS** Isoniazid* (**H**) 5 mg/kg PO q24h *(Range: 4 – 6 mg/kg)* *(Round the dose to the nearest 50 mg)* *(Max dose: 300 mg)* **PLUS** Rifampicin (**R**) 10 mg/kg PO q24h *(Range: 8 - 12 mg/kg)* *(Round the dose to the nearest 150 mg)* *(Max dose: 600 mg)* **PLUS** Pyrazinamide (**Z**) 25 mg/kg PO q24h *(Range: 20 - 30 mg/kg)* *(Round the dose to the nearest 250 mg)* *(Max dose: 2000 mg)* **PLUS** Pyridoxine (**Vit B6**) 20-30 mg PO q24h *(All patients on Isoniazid (H) should be given Tab. Pyridoxine for prevention of neuropathy)* **Followed by Maintenance Therapy**	**Duration:** 2 months (56 doses) *Duration can be prolonged to 3 months in cases such as:* • *Pneumonia with cavitation* • *Persistently +ve sputum AFB* Refer to **Ministry of Health CPG on Management of Tuberculosis 4th Edition (2021)** for more info.
Treatment of tuberculosis **(Maintenance Therapy)**	**Fixed Dose Combination (FDC):** **Tab. Akurit-2:** *(Each tablet contains: Rifampicin 150mg & Isoniazid* 75mg)* • 30 - 37 kg: 2 tablets PO q24h • 38 - 54 kg: 3 tablets PO q24h • 55 - 70 kg: 4 tablets PO q24h • > 70 kg: 5 tablets PO q24h **PLUS** Pyridoxine (**Vit B6**) 20-30 mg PO q24h *(All patients on Isoniazid (H) should be given Tab. Pyridoxine for prevention of neuropathy)*	**Loose Pills:** Isoniazid* (**H**) 5 mg/kg PO q24h *(Range: 4 – 6 mg/kg)* *(Round the dose to the nearest 50 mg)* *(Max dose: 300 mg)* **PLUS** Rifampicin (**R**) 10 mg/kg PO q24h *(Range: 8 - 12 mg/kg)* *(Round the dose to the nearest 150 mg)* *(Max dose: 600 mg)* **PLUS** Pyridoxine (**Vit B6**) 20-30 mg PO q24h *(All patients on Isoniazid (H) should be given Tab. Pyridoxine for prevention of neuropathy)*	**Duration:** Based on indication • **4 months (126 doses)** *For pulmonary TB* • **7 months (217 doses)** *For bone & joint TB* *or* *For pulmonary/ extrapulmonary TB with:* ○ *Slow / suboptimal response* ○ *Sputum culture still positive after 2 months of intensive phase provided sensitive to 1st line regime* ○ *No PZA in intensive phase* • **10 months (309 doses)** *For TB meningitis*

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12. LATENT TUBERCULOSIS INFECTION (LTBI) TREATMENT

Latent tuberculosis infection (LTBI) signifies that a person harbors Mycobacterium tuberculosis bacteria, but these bacteria are dormant, resulting in no symptoms and no risk of infecting others. However, there is a possibility of reactivation in the future, potentially leading to illness and transmission. Treatment for LTBI is recommended to prevent the development and progression from dormant to active tuberculosis disease.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Latent tuberculosis (LTBI)	**6H Regimen:** Isoniazid* (**H**) 5 mg/kg PO q24h *(Range 4–6 mg/kg)* *(Round the dose to the nearest 50 mg)* *(Max dose: 300 mg)* **PLUS** Pyridoxine (**Vit B6**) 20-30 mg PO q24h *(All patients on Isoniazid (H) should be given Tab. Pyridoxine for prevention of neuropathy)* **Duration:** 6 months (180 doses)	**3HR Regimen:** Isoniazid* (**H**) 5 mg/kg PO q24h *(Range: 4 – 6 mg/kg)* *(Round the dose to the nearest 50 mg)* *(Max dose: 300 mg)* **PLUS** Rifampicin (**R**) 10 mg/kg PO q24h *(Range: 8- 12 mg/kg)* *(Round the dose to the nearest 150 mg)* *(Max dose: 600 mg)* **PLUS** Pyridoxine (**Vit B6**) 20-30 mg PO q24h *(All patients on Isoniazid (H) should be given Tab. Pyridoxine for prevention of neuropathy)* **Duration:** 3 months (90 doses) **OR** **4R Regimen:** Rifampicin (**R**) 10 mg/kg PO q24h *(Range: 8- 12 mg/kg)* *(Round the dose to the nearest 150 mg)* *(Max dose: 600 mg)* **Duration:** 4 months (120 doses)	⚠ **CAUTION** **Drug-drug Interaction (Rifampicin):** Check for drug-drug interactions before starting Rifampicin based regimen.

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13. MYCOBACTERIUM AVIUM COMPLEX (MAC) DISEASE

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Treatment	**Three-drug therapy** **Macrolide:** • Azithromycin 500 mg PO q24h **OR** • Clarithromycin 500 mg PO q12h **PLUS** **Ethambutol** 15 mg/kg PO q24h **PLUS** **Rifamycin:** • Rifabutin 5 mg/kg PO q24h **OR** • Rifampicin 10 mg/kg PO q24h *Concomitant tuberculosis needs to be ruled out if monotherapy rifampicin is used.* ⚠ **CAUTION** **Drug-drug Interaction (Rifampicin/Rifabutin):** Check for drug-drug interactions before starting Rifampicin or Rifabutin based regimen	**MAY ADD:** Addition of 4th drug should be considered for patients with disseminated disease, requiring IV/IM **Fluoroquinolones*:** • Levofloxacin 500 mg PO q24h **OR** • Ciprofloxacin 500-750 mg PO q12h **OR** • Moxifloxacin 400 mg PO q24h **AND/OR:** **Part of combination therapy if oral therapy has been ineffective or is not feasible:** Amikacin 10-15 mg/kg IV q24h	**Duration:** At least 12 months Treatment of choice shall be tailored according to culture and susceptibility testing results. **Discontinuation:** Consider if patient is on ART **AND** CD4 >100 cells/µL **AND** undetectable HIV viral load **AND** clinical improvement with culture conversion **AND** completed ≥ 12 months of MAC treatment *Fluoroquinolone Administration **Fluoroquinolones (FQ)** such as **Levofloxacin, Ciprofloxacin & Moxifloxacin** can bind to multivalent cations (eg: Ca, Fe, Al, Mg, Zn), thus reducing absorption. Allow a **2-6 hours gap** between taking FQ and consuming **dairy products / multivitamins / antacids / NG tube feeds** to avoid concurrent exposure. Hold NG tube feeds 1H before & 2H after FQ is administered.
Maintenance Therapy	Same as the treatment regimen (oral drugs only)		
Secondary Prophylaxis	Same as the maintenance therapy		**Restarting secondary prophylaxis:** CD4 < 100 cells/µL again
Primary Prophylaxis Indications: • CD4 < 50 cells/µL • Ruled out active MAC and TB	Azithromycin 1250 mg PO once weekly	Clarithromycin 500 mg PO q12h	**Discontinuation:** • Consider if patient is on ART **AND** • Viral load is suppressed, CD4 > 100 cells/µL > 3 months

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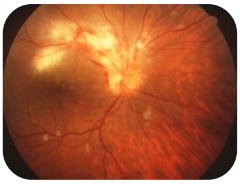
14. CYTOMEGALOVIRUS (CMV) DISEASE

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
CMV Retinitis  *Ref: www.hiv.uw.edu*	**Systemic therapy:** Ganciclovir 5 mg/kg IV q12h **Duration:** 2-3 weeks **Followed by Maintenance Therapy/ Secondary prophylaxis**	**Systemic therapy** (If patient well, tolerating orally & planned for discharge): Valganciclovir 900 mg PO q12h **Duration:** 3 weeks **Followed by Maintenance Therapy/ Secondary prophylaxis**	Systemic therapy is indicated in all cases. **HSgB PRACTICE** • May consider switching IV Ganciclovir to PO Valganciclovir once pt tolerate orally & fit to be discharged • Start ART ASAP (within 2 weeks if possible).
	Intravitreal therapy: (Indicated in zone 1 and 2 lesions Intravitreal Ganciclovir 2 mg/0.1ml biweekly	**Intravitreal therapy: (Indicated in zone 1 and 2 lesions** Intravitreal Foscarnet **(UKK)** 2.4 mg/0.1ml (1-2 weekly)	Intravitreal therapy to be tapered according to clinical response. Ganciclovir implant 4.5 g is an option for prolonged usage of intravitreal ganciclovir.
Extraocular CMV diseases Eg: Oesophagitis, colitis, interstitial pneumonitis, neurological disease	Ganciclovir 5 mg/kg IV q12h, Once patient tolerate orally, may consider switch to: Valganciclovir 900 mg PO q12h *(in CMV oesophagitis and colitis only)* **Followed by Maintenance Therapy/ Secondary prophylaxis**		**Duration:** 3 – 6 weeks or until signs and symptoms have been resolved. **HSgB PRACTICE** • May consider switching IV Ganciclovir to PO Valganciclovir once pt tolerate orally & fit to be discharged • Start ART ASAP (within 2 weeks if possible).
Maintenance Therapy/ Secondary prophylaxis Indications: • CD4 <100 cells/μL	Ganciclovir 5 mg/kg IV q24h 5–7 times weekly	Valganciclovir 900 mg PO q24h	**Discontinuation:** Consider if patient is on ART and viral load well suppressed, CD4 > 100 cells/μL > 3 months and after 3-6 months of CMV treatment. **Maintenance therapy is generally not necessary; ART offers best hope for prevention of relapses.** **HSgB PRACTICE** May consider discontinuing maintenance Ganciclovir/ Valganciclovir once ART started

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15. RHODOCOCCUS INFECTIONS (RHODOCOCCUS EQUI, FORMERLY *CORYNEBACTERIUM EQUI*)

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Induction Treatment	Azithromycin 500 mg STAT, then 250 mg IV/PO q24h **OR** *Fluoroquinolones: • Levofloxacin 500-750 mg IV/PO q24h **OR** • Ciprofloxacin 500-750 mg PO q12h or 400 mg IV q8-12h **PLUS** Rifampicin 600 mg PO q24h *Concomitant tuberculosis needs to be ruled out with use of rifampicin monotherapy.* ⚠ CAUTION **Drug-drug Interaction (Rifampicin):** Check for drug-drug interactions before starting Rifampicin based regimen **Followed by Maintenance Therapy/ Secondary prophylaxis**	**For severe/disseminated disease:** **CONSIDER ADDING:** Injectables: • Vancomycin 15-20 mg/kg weight) IV q8-12H; *Refer to DIAMS – HSgB Vancomycin Protocol for more dosing info* **OR** • Imipenem/Cilastatin 500 mg IV q6h **Followed by Maintenance Therapy/ Secondary prophylaxis**	**Duration:** Immunocompromised – at least 2 months (Duration will depend on the extent of the diseases). Adjust antibiotics according to susceptibility data. Use at least two or more susceptible agents. For CNS involvement, to consider antibiotics with good CNS penetration. ⚠ CAUTION ***Fluoroquinolone Administration:** Allow a 2-hour **gap between taking Ciprofloxacin/Levofloxacin and consuming dairy products, multivitamins, antacids or NG tube feeding** to avoid concurrent exposure to multivalent cation (e.g Ca, Fe, Al, Mg, Zn) – cations can bind to the drug & prevent absorption.
Maintenance Therapy/ Secondary prophylaxis	Azithromycin 250 mg PO q24h **PLUS** *Fluoroquinolones: • Levofloxacin 500-750 mg PO q24h **OR** • Ciprofloxacin 500-750 mg PO q12h	**Rifampicin 600 mg PO q24h *Concomitant tuberculosis needs to be ruled out with use of rifampicin monotherapy.* **PLUS** Azithromycin 250 mg PO q24h **OR** **Rifampicin 600 mg PO q24h *Concomitant tuberculosis needs to be ruled out with use of rifampicin monotherapy.* **PLUS** *Fluoroquinolones: • Levofloxacin 500-750 mg PO q24h **OR** • Ciprofloxacin 500-750 mg PO q12h	**Duration:** Until CD4 > 200 cells/μL Choice to be based on susceptibility test. ⚠ CAUTION ***Fluoroquinolone Administration:** Allow a 2-hour **gap between taking Ciprofloxacin/Levofloxacin and consuming dairy products, multivitamins, antacids or NG tube feeding** to avoid concurrent exposure to multivalent cation (e.g Ca, Fe, Al, Mg, Zn) – cations can bind to the drug & prevent absorption. ⚠ CAUTION ****Drug-drug Interaction (Rifampicin):** Check for drug-drug interactions before starting Rifampicin based regimen

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16. BACTERIAL ENTERIC INFECTIONS – EMPIRICAL TREATMENT

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Empirical Treatment (Pending Diagnostic Studies and Culture & Sensitivity)	Ceftriaxone 2 g IV q24h		Antibiotic is indicated for patients with **advanced HIV disease** with **fever** or **infective diarrhoea** **Duration:** • Therapy and its duration should be adjusted depending on stool microbiology results and antibiotic sensitivity testing • If no pathogen is identified and the patient recovers quickly, **5 days** of therapy is reasonable.

17. BACTERIAL ENTERIC INFECTIONS – SALMONELLOSIS (SALMONELLA NON-TYPHI)

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Salmonellosis (Non-Typhoidal Salmonella spp.) *Refer to Hospital Sungai Buloh Guideline > Tropical Infection > Typhoid Fever for Treatment of* ***Salmonella typhi***	Ciprofloxacin 500-750 mg PO or 400 mg IV q12h **OR** Ceftriaxone 2 g IV q24h **DIAMS - IV to PO** **Oral Ciprofloxacin** has good bioavailability (>70%). *Change to Tab. Ciprofloxacin once patient can tolerate orally	Ampicillin 2 g IV q4-6h **OR** Trimethoprim/Sulfamethoxazole (Bactrim) 160 mg/800 mg (= 2 tablets PO or 2 ampoules IV) q12h ***DIAMS - IV to PO** **Oral Bactrim** has excellent bioavailability (~90%). *Change to Tab. Bactrim once patient can tolerate orally	Susceptibility profile may help guide final choice. **Duration:** • **If CD4 ≥ 200: 7-14 days.** • **If CD4 ≥ 200 and with bacteraemia: 14 days** is appropriate provided documented clearance of bacteraemia. • **If CD4< 200 and with bacteraemia: 6 weeks.** Longer course with debridement and drainage needed for persistent bacteraemia or metastatic disease.

18. ENTERIC INFECTIONS – CRYPTOSPORIDIOSIS & MICROSPORIDIOSIS

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Cryptosporidium sp.	Symptomatic treatment of diarrhoea		Effective ART (to increase CD4 > 100 cells/μL) can result in complete, sustained clinical, microbiological and histologic resolution.
Microsporidium sp .	Albendazole 400 mg PO q12h **PLUS** Symptomatic treatment of diarrhoea (the best treatment option is ART and fluid support)		**Duration:** for 2-4 weeks Effective ART (to increase CD4 > 100 cells/μL) can result in complete, sustained clinical, microbiological and histologic resolution.

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19. ENTERIC INFECTIONS – CYSTOISOSPORA/ISOSPORA BELLI

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Initial Therapy	Bactrim (Trimethoprim/ sulfamethoxazole) 160/800 mg (=2 tablets PO or 2 ampoules) IV q6h *DIAMS - IV to PO **Oral Bactrim** has excellent bioavailability (~90%). *Change to Tab. Bactrim once patient can tolerate orally	**If sulfa-intolerant** Pyrimethamine **(UKK)** 50-75 mg PO q24h **PLUS** Folinic acid 10-25 mg PO q24h **OR** Ciprofloxacin 500 mg PO q12h	**Duration:** 10 days For patients whose symptoms persist after 10 days, the treatment duration can be extended to 3-4 weeks. **Discontinuation:** CD4 count > 200 cells/µL for ≥ 6 months on ART
Secondary prophylaxis	Bactrim (Trimethoprim/ sulfamethoxazole) 160/800 mg (= 2 tablets) PO q24h	**If sulfa-intolerant** Pyrimethamine **(UKK)** 25 mg PO q24h **PLUS** Folinic acid 5-10 mg PO q24h **OR** Ciprofloxacin 500 mg PO three times a week	

20. BARTONELLOSIS

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Bacillary Angiomatosis, Peliosis Hepatis, Bacteraemia, and Osteomyelitis	Doxycycline 100 mg PO q12h **OR** Erythromycin 500 mg PO/IV q6h	Azithromycin 500 mg PO q24h **OR** Clarithromycin 500 mg PO q12h	**Duration:** At least 3 months If relapse occurs after initial (> 3 month) course of therapy, long-term suppression with doxycycline or a macrolide is recommended as long as CD4 <200 cells/µL.
Other Severe Infections (or CNS involvement)	Doxycycline 100 mg PO/IV* q12h **OR** Erythromycin 500 mg PO/IV q6h **MAY ADD** Rifampicin 300 mg PO/IV* q12h	-	**Duration:** At least 3 months If relapse occurs after initial (> 3 month) course of therapy, long-term suppression with doxycycline or a macrolide is recommended as long as CD4 <200 cells/µL. *IV Doxycycline and IV Rifampicin requires DG's approval (UKK).
Confirmed *Bartonella* endocarditis	Doxycycline 100 mg PO q12h **Duration:** For 6 weeks **PLUS** Gentamicin 3 mg/kg IV q24h **Duration:** For 2 weeks	-	

21. PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)

- Caused by Polyoma virus JC virus (JCV)
- No effective therapy exists.
- With ART, some patients improve and others stabilize. Few may deteriorate due to immune reconstitution.

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22. SYPHILIS (*TREPONEMA PALLIDUM* INFECTION)

- Sexually transmitted infections (STIs) which have similar signs and symptoms are grouped into syndromes:
  - Anogenital ulcer disease (syphilis, herpes simplex, chancroid, lymphogranuloma venereum (LGV), donovanosis, Mpox)
  - Urethral discharge (gonorrhoea, chlamydia, non-gonococcal urethritis, epididymo-orchitis)
  - Vaginal discharge (trichomoniasis, bacterial vaginosis, candidiasis, cervicitis)
  - Anorectal discharge (gonorrhoea, chlamydia, LGV)
- Syndromic approach is essential to ensure appropriate, prompt and effective treatment.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	**Alternative**	
Primary syphilis or **Secondary syphilis** or **Early latent syphilis** (history of syphilis infection within the last 2 years)	Benzathine Penicillin 2.4 MU IM **STAT** **OR** Procaine Penicillin 600,000 units IM q24h **for 10 days**	**For penicillin allergy** (in non-pregnant patients): Doxycycline 100 mg PO q12h **Duration: 14 days** **For penicillin allergy** (in pregnant patients): Desensitize and treat with penicillin as there are no proven alternatives. *(The benefit of treatment outweighs the risk of allergic reaction in skin test and desensitization. Refer to HSgB penicillin desensitization protocol)* **If failed desensitization:** Ceftriaxone 500 mg IM q24h **Duration: 10 days** **OR** *Azithromycin 2 g PO **STAT** **OR** *Erythromycin ethylsuccinate (EES) 800 mg PO q6h **Duration: 14 days**	**Treatment of sexual partner:** • Sexual partner(s) should be examined, investigated and treated epidemiologically. • Abstain from sex for 1 week after the patient and partner(s) have completed treatment. **Treatment interruption:** If drug administration is interrupted for ⩾ 1 day at any point during the treatment course, the entire course may need to be restarted. Patients should be warned of possible reactions to treatment: - Jarisch-Herxheimer reaction - Anaphylaxis/allergy ***Macrolide use in Pregnancy:** If macrolide is used, for neonate assessment and treatment at birth
Late latent syphilis or **Gumma (benign tertiary) syphilis** or **Cardiovascular syphilis**	Benzathine Penicillin 2.4 MU IM weekly **for 3 weeks** **(Day 1, 8, and 15)** **OR** Procaine penicillin 600,000 units IM q24h **for 14 days**	**For penicillin allergy** (in non-pregnant patients): Doxycycline 100 mg PO q12h **Duration: 28 days** **For penicillin allergy (in pregnant patients):** Erythromycin ethylsuccinate (EES) 800 mg PO q6h ***Macrolide use in Pregnancy:*** *If macrolide is used, for neonate assessment and treatment at birth* **Duration: 28 days**	**Treatment of sexual partner:** • Sexual partner(s) should be examined, investigated and treated epidemiologically. • Abstain from sex for 1 week after the patient and partner(s) have completed treatment. **Cardiovascular syphilis:** Consider prednisolone 40-60 mg PO q24h for 3 days starting 24 hours before the antibiotics. **Treatment interruption:** If benzathine penicillin is interrupted by ⩾ 2 weeks in between the weekly doses, the entire course needs to be restarted

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Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Neurosyphilis or **Ocular Syphilis (syphilitic uveitis)**	Benzylpenicillin 4 MU q4h IV **for 14 days** **FOLLOWED BY:** Benzathine penicillin G 2.4 million units IM **x 1** after completion of Benzylpenicillin	**For penicillin allergy without anaphylaxis (in pregnant/non-pregnant patients):** Ceftriaxone 2 g IV/IM q24h **Duration: 14 days** **If anaphylaxis to penicillin** (in non-pregnant patients): Doxycycline 200 mg PO q12h **Duration: 28 days**	Consider Prednisolone 40-60 mg PO q24h for 3 days starting 24 hours before the antibiotics.

SYPHILIS CLASSIFICATION

Primary Syphilis

Development of **chancre (usually genital ulcer)** - usually firm, round, and painless, approx. 21 days after exposure, at the location where syphilis entered the body (e.g., the vagina or anus).

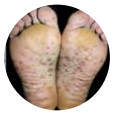
The chancre lasts 3-6 weeks & heals regardless of whether treated or not. However, untreated infection progresses to secondary stage.

Secondary Syphilis

Skin rashes (red, or reddish-brown spots both on the palms of the hands & the bottoms of the feet, & usually does not cause itching) +/- mucous membrane lesions (sores in the mouth, vagina, or anus). Can appear when the primary chancre is healing or several weeks after the chancre has healed.

Symptoms may include fever, swollen lymph glands, sore throat, patchy hair loss, headaches, weight loss, muscle aches, and fatigue.

Symptoms will go away with or without treatment. However, untreated infection progresses to latent or tertiary stage.



Latent Syphilis

Latent (hidden) stage has **no visible signs or symptoms** of syphilis (**asymptomatic infection**). Without treatment, the infected person will continue to have syphilis in their body & can last for years.

- **Early-latent syphilis:** infection occurred within the past 12 months.
- **Late-latent syphilis:** infection occurred more than 12 months ago (if sudden rise in RPR titre despite given treatment, to do LP and check CSF VDRL to look for neurosyphilis)

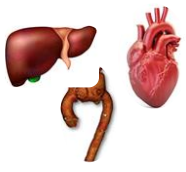
Asymptomatic

Tertiary Syphilis

Rare & develops in a subset of untreated syphilis infections; it can appear 10–30 years after infection was first acquired and can be fatal.

Can affect **multiple organ systems, including the brain, nerves, eyes, heart, blood vessels, liver, bones, and joints**.

Symptoms vary depending on the organ system affected.



Neurosyphilis & Ocular Syphilis

Invasion of the nervous system (neurosyphilis), visual system (ocular syphilis), or auditory system (otosyphilis) at any stage of infection.

Cause a wide range of symptoms such as:

- **Neurosyphilis:** neurologic symptoms (cranial nerve dysfunction, meningitis, stroke, acute or chronic altered mental status, or motor or sensory deficits)
- **Ocular syphilis:** isolated ocular abnormalities (eg; posterior uveitis and panuveitis) or with neurologic manifestations
- **Otosyphilis:** sensorineural hearing loss (unilateral or bilateral - sudden onset, and progress rapidly & may result in permanent hearing loss), tinnitus, or vertigo

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SYPHILIS TESTS

Treponemal test:	• **TPHA:** Used as a confirmatory test for syphilis infection. TPHA tests for syphilis patient will remain positive for the rest of the patient's life.
Non-treponemal test:	• **RPR** (blood sample): Used to screen for syphilis & track the progress of the disease over time/response to therapy. RPR should reduce 4-fold 6 months after treatment (Eg: 1:32 ➔ 1:8). • **VDRL** (CSF sample): Lumbar puncture (LP) is indicated if pt has ocular/otologic symptoms, neurological symptoms at any stage, sudden rise in RPR titre despite given treatment.

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SECTION 3: DRUG -ART INTERACTIONS

ART – METHADONE INTERACTION

ART	EFFECTS	REMARKS
Zidovudine (AZT)	↑ AZT AUC by 40%	Watch out for marrow toxicity i.e. anaemia
Nevirapine (NVP)	↓ Methadone level by 46%	Clinical opiate withdrawal may occur, usually seen 7 days after co-administration. Adjust Methadone dosages : 5-10 mg daily until patient is comfortable.
Efavirenz (EFV)	↓ Methadone levels by 43%	
Lopinavir/Ritonavir (Kaletra)	Significant ↓ in Methadone levels	

ART - HMG COA REDUCTASE INHIBITOR (STATINS) INTERACTION

- Most of the statins undergo metabolism via CYP3A4 in the liver.
- **Lovastatin > Simvastatin > Atorvastatin = Rosuvastatin > Pravastatin**
- Adverse Effects: **myalgias, rhabdomyolysis, hepatic dysfunction**

ART	ACTION	EFFECTS
NRTI	Not Affected	Not Affected
NNRTI	Induce CYP3A4	↓ The Level Of Statins (↓ 40 %)
Protease Inhibitors	**Inhibit CYP3A4**	**↑↑↑ The Level Of Statins (↑ 70 - 800 %)**

Statins	Usual Dose	Advice on use of lipid lowering therapy together with ART		Adverse Effects of statins
		Patients on boosted PI	Patients on NNRTI	
Atorvastatin	10 - 80 mg/day	**Start with a low dose.** [max daily dose: 10mg (ATV/r); 20mg (LPV/r); 40mg (DRV/r)]	Consider a higher dose. Increase dose gradually to achieve expected benefit.	Gastrointestinal symptoms, headache, insomnia, rhabdomyolysis (rare) & toxic hepatitis
Pravastatin	20 - 80 mg/day	Consider a higher dose. Increase dose gradually to achieve expected benefit. *(Exception: If used with DRV/r, start with a lower dose of pravastatin)*		
Rosuvastatin	5 - 40 mg/day	**Start with a low dose.** [max daily dose: 10mg (ATV/r or LPV/r); 20mg (DRV/r)]	Start with a low dose	
Simvastatin	10 – 40 mg/day	**Contraindicated**		

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ART – ANTI TB INTERACTIONS

ANTI TB	ART	INTERACTION DESCRIPTION	MANAGEMENT
Rifampicin (RIF) *(potent **INDUCER** of CYP3A4)*	**Protease Inhibitors (PI)**	Significant reduction in antiretroviral concentration (up to 90%)	• **AVOID** combination of **Rifampicin with all Protease Inhibitors** • Substitute Rifampicin with **Rifabutin 150 mg OD** → Induction effect on CYP3A4 may last up to 2 weeks → A **2 weeks "washout period"** is recommended between the last dose of Rifampicin & the 1st dose of Protease Inhibitors
	Efavirenz (EFV)	20% ↓ in EFV level	• Unlikely to have a significant effect ➔ Cont the same dose
	Nevirapine (NVP)	20-60% ↓ in NVP level	• Skip lead-in dosing
	Integrase Inhibitors (INSTI) *Eg: RAL/DTG*	40-60% ↓ in INSTI level	• **Raltegravir (RAL):** Increase RAL dose to **800 mg BD** • **Dolutegravir (DTG):** Increase DTG dose to **50 mg BD**
Rifabutin (RFB)	**Efavirenz (EFV)**	36% ↓ in Rifabutin level	• Increase **Rifabutin to 450 mg OD**

OTHER ART INTERACTIONS

ART	Interacts with:	Interaction Description	Management
Dolutegravir (DTG)	**Polyvalent cations containing drugs (eg: Mg, Al, Fe or Ca) in antacids, laxative or supplements**	74% ↓ in DTG concentration	• Avoid co-administration • Take DTG 2 hrs before or 6 hrs after taking medications containing polyvalent cations. • Ca & Fe containing products can be given simultaneously if given with food
	Metformin	Metformin Cmax ↑ by 66% and AUC ↑ by 79%	• **Limit Metformin total daily dose to 1000 mg** when starting metformin or DTG
Raltegravir (RAL)	**Antacids**	RAL AUC ↓ by 24% and Cmin ↓ by 67%	• Avoid co-administration • Administer RAL 2-4 hrs before antacids administration
Atazanavir (ATV)	**Proton Pump Inhibitors (PPIs)** • **Omeprazole,** • **Esomeprazole,** • **Pantoprazole**	PPI **decreases absorption of Atazanavir (ATV)** by 75%	• **Co-administration of PPI & ATV** is **NOT RECOMMENDED.** • **ATV/r + Omeprazole (20mg max*)** separated by 12 hours may be considered, but **NOT recommended** (46% ↓ in ATV level). • ***PPI Equivalence:** Omeprazole 20mg ≈ Esomeprazole 20mg = Pantoprazole 40mg
Efavirenz (EFV) with Kaletra (LPV+RTV)		Reductions in LPV/r levels when used concurrently (39% ↓ in LPV level)	• If given concurrently, increase **Kaletra dose to 3 tabs BD**

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