2018

Clinical Management of HIV In Children and Adults

2019 Policy Updates

Addendum to the 4th Edition of the Malawi Integrated Guidelines and Standard Operating Procedures for Clinical HIV Services

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Foreword

This addendum includes detailed policy updates for the **2018 Clinical Management of HIV in Children and Adults guidelines**.

The updates apply **from April 2019** until publication of the next guideline edition which is scheduled for late 2020.

This addendum does not fully replace the 4th edition of Clinical Management of HIV in Children and Adults guidelines for Malawi of 2018, but it should be used side-by-side with the 2018 guidelines. Updated content is shown using the same section numbering as in the main guideline document and this replaces the respective section.

Oral Pre-Exposure Prophylaxis for HIV (PrEP) has been included as it relates to the prescription and monitoring of ARVs in Malawi. However, a detailed PrEP implementation guideline will be published as a separate document.

Acronyms and Abbreviations

3TC	Lamivudine
3HP	3 months short course of isoniazid rifapentine TB preventive therapy
6MD	6 month dispensing / ART clinic appointment spacing
ABC	Abacavir
ART	Antiretroviral therapy
ARV	Antiretroviral medicines
ATV/r	Atazanavir and ritonavir fixed dose combination
AZT	Zidovudine
DBS	Dried blood spot
DSD	Differentiated service delivery
DTG	Dolutegravir
FeFol	Iron and folate supplement
EFV	Efavirenz
H	Isoniazid
HIV	Human immunodeficiency virus
IAC	Intensive adherence counseling
INH	Isoniazid
IPT	Isoniazid preventive therapy
LDL	Lower detection limit (for viral load)
LPV/r	Lopinavir and ritonavir fixed dose combination
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside reverse transcriptase inhibitor
NVP	Nevirapine
PI	Protease inhibitor
PLHIV	People living with HIV
PMTCT	Prevention of mother to child transmission
PrEP	Pre-exposure prophylaxis for HIV using antiretroviral medicines
RAL	Raltegravir
RFP	Rifapentine (used in 3HP)
TDF	Tenofovir disoproxil fumarate
TPT	Tuberculosis (TB) preventive therapy
TST	Tuberculin skin test
VL	Viral load

Summary of Policy Updates

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	TPT transition Phase 2 (from mid-2020): Once available, give a single short course of isoniazid and rifapentine (3HP) to all new patients on ART in all districts. Take one weekly dose of isoniazid + rifapentine (every 7 days) for 3 months, completing a total of 12 doses. Exempt patients who have already completed 6 months or more of IPT. 3HP is currently not given to children, pregnant women and patients on PI-based ART.	
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8 HIV-related diseases

8.1 Routine urine LAM and serum CrAg screening

- Serum CrAg
    - **Positive:** Do Lumbar Puncture (LP), treat for active meningitis if CSF testing (CrAg, Indian ink, Xpert) result is positive. If CSF testing result is negative, give pre-emptive anti-fungal therapy for cryptococcaemia (see **section 8.2.2**)

8.2 Management of HIV-related diseases

8.2.1 Cryptococcal meningitis (CM)

Key Facts: Cryptococcal meningitis (CM)

- Early diagnosis and treatment are life-saving.
- Liposomal amphotericin B has much lower toxicity than the regular amphotericin B deoxycholate. This means it can be given at higher doses which is more effective.
- Liposomal amphotericin B will be distributed to central, district and large mission hospitals from early 2020. Call the HIV Department logistics hotline for ad-hoc supplies.

Primary Management

Admit

Daily therapeutic spinal tap if high intracranial pressure, severe headache or vomiting is present (up to 30 ml per puncture).
If not already on ART, start ART only 5 weeks after antifungal treatment initiation.

Induction phase

Do not give adjunctive corticosteroids during induction treatment.

Option 1: Liposomal Amphotericin[1] + Flucytosine for 7 days

Preferred option if both meds are available

Liposomal Amphotericin B[1]

Adult: 3 – 4 mg/kg IV over 6 hours 24-hourly. Use up to 6 mg/kg for treatment failure or serious disease.
Child: 6mg/kg IV over 6 hours 24-hourly.

Flucytosine tabs

100mg/kg/day divided into 4 doses (6-hourly)

Option 2: Fluconazole + Flucytosine for 14 days

This option requires FBC monitoring: at baseline and 2-3 times in the second week of treatment.

Fluconazole tabs

Adult: 1200mg 24-hourly
Child: 12mg/kg (max 800mg) 24-hourly

Flucytosine tabs

100mg/kg/day divided into 4 doses (6-hourly)

[1] Before giving **Liposomal** Amphotericin B: Pre-hydrate and supplement electrolytes: 1000ml NS (weight-based for children) + Potassium 2 tabs 12-hourly + Magnesium trisilicate 1 tabs 24-hourly in the evening.

Do not combine **Liposomal Amphotericin B** with **TDF-based** ART (5A, 6A, 7A, 10A, 13A). Substitute for ABC-based regimen if already on ART.

Option 3: Liposomal Amphotericin B[1] + Fluconazole for 14 days

This option requires FBC, Creatinine and K+ monitoring: at baseline and 2-3 times in the second week of treatment.

Liposomal Amphotericin B[1]

3 – 4 mg/kg IV over 6 hours 24-hourly
Use up to 6 mg/kg for treatment failure or serious disease.

Fluconazole tabs

Adult: 1200mg 24-hourly
Child: 12mg/kg (max 800mg) 24-hourly

8.2.2 Cryptococcaemia

Clinical signs

Often no clinical signs. Note: the lack of meningitis signs does not rule out active CM

Diagnosis/investigations

Serum CrAg test positive but CSF is negative for CrAg and/or microscopy (Indian ink).

Assess for meningitis signs. If positive, do full investigation and treatment for active CM (see **section 8.2.1**). If negative, but patient is symptomatic treat for active CM

Primary management

Fluconazole tablets

800 mg 24-hourly for 2 weeks *then*
400 mg 24-hourly for 8 weeks *then*
200mg 24-hourly for life

Consolidation phase

Fluconazole tabs for 8 weeks

Adult: 800mg 24-hourly
Child: 12mg/kg (max 800mg) 24-hourly

Maintenance phase

Fluconazole tabs, lifelong

Adult: 200mg 24-hourly
Child: 6mg/kg 24-hourly

10 Preventive Services for HIV patients

10.3 TB Preventive Therapy

Key Facts: TB Preventive Therapy (TPT)

- A single course of TPT can prevent active TB in people who are at high risk. Give TPT to:
  - HIV infected children and adults regardless of TST status (if known).
  - Children under 5 years – regardless of HIV status - who live with a patient being treated for TB (sputum positive or negative, or LAM positive): give 6 months course of IPT.
- HIV patients who have completed 6 months of IPT in the past (during pre-ART or ART) do not need another course of TPT.
- Do not give TPT to a patient who has any signs suggestive of active TB: such patients need full investigation for TB and combination TB treatment to avoid TB drug resistance.
  - New patients: Start TPT together with ART and CPT.
  - Already on ART: Start TPT regardless of the time on ART.
  - Give TPT regardless of previous TB treatment.
- Two alternative TPT options are similarly effective:
  - **6H**: 6-month course of daily dose of isoniazid:
    - Immediately available, suitable for children, not suitable for pregnant women
    - Can be combined with all ART regimens
  - **3HP**: 3-month course of weekly doses of isoniazid + rifapentine
    - Available from mid-2020
    - Easier to complete due to short duration.
    - Not suitable for children under 20kg and pregnant women, cannot be combined with PI-based ART regimens
    - Women on hormonal contraception need to use condoms while on 3HP. Rifapentine reduces contraceptive effectiveness.
- TPT is well tolerated by 95% of patients. Most side effects are mild and disappear within 3 months. Serious side effects are rare: hypersensitivity, neuropathy and severe hepatitis.
- Stop TPT if any of the following are seen:
  - Nausea, vomiting, loss of appetite
  - Pellagra-type skin rash in sun-exposed areas and other severe skin rash
  - Yellow eyes
  - Dizziness / confusion / convulsions
  - Severe numbness/burning pain and muscular weakness of legs and/or arms

10.3.1 Dispensing TPT

- Patients who have already completed 6 months or more of IPT in the past are exempt.
- Emphasize adherence during treatment.
- Ensure proper documentation on patient card.
- Always give pyridoxine to prevent neuropathy. Don't prescribe TPT if pyridoxine is not available.
- Stop immediately if clients develop severe peripheral neuropathy, hypersensitivity reactions, gastrointestinal intolerance and hepatotoxicity.
- Report to the health facility immediately with nausea and loss of appetite. These are early warning signs of hepatotoxicity.

IPT: (TPT Phase 1) Start from October 2019

- Once sufficient stocks of INH and pyridoxine have been distributed, give a single 6 month course of IPT to all new and all current patients on ART in all districts.
- Give 1 daily dose of INH and pyridoxine for 6 months (cumulative total of at least 168 daily doses).
- Give 1 daily tablet of pyridoxine 24-hourly. **Adults:** 25 or 50mg. **Children <20kg**: about 1mg/kg
- Review patients at **month 1, 3 and 6** after starting IPT for any side effects and monitor adherence.

3HP: (TPT Phase 2) Start from mid-2020

- Once rifapentine is available, give a single course of 12 weekly doses of isoniazid and rifapentine (3HP) as TB preventive therapy to all new patients on ART in all districts.
- All clients newly initiated on ART in all districts who are 20kg+ and can swallow tablets whole without crushing/chewing are eligible for 3HP.
- Give weekly doses of rifapentine + isoniazid for 12 weeks based on weight (see **Table 12 on page 15**).
- Give 1 daily tablet of pyridoxine 24-hourly. **Adults:** 25 or 50mg. **Children <20kg**: about 1mg/kg
- Advise women on hormonal contraceptives to use condoms while on 3HP.
- Review patients at **month 1**, **2** and **3** after starting 3HP for any side effects and monitor adherence.

TPT Contraindications

Table 1: Contraindications for IPT and 3HP

IPT and 3HP	3HP
• Suspected or confirmed active TB • Prior adverse events or hypersensitivity to INH • Active hepatitis, liver damage, heavy alcohol use • Severe peripheral neuropathy • Pregnant women or women planning to become pregnant during treatment	• Prior adverse events or hypersensitivity to rifapentine or rifampicin. • Children under 20kg: almost all will now be on LPV/r based regimens, which cannot be combined with 3HP. • Unable to swallow a tablet without crushing/chewing. • PI-based ART regimens

11 Understanding ART regimens and formulations

Key Facts: Dolutegravir (DTG)

- The general benefits of DTG are now thought to outweigh any potential risks, including for **women who may get pregnant** while on ART:
    - Faster and more durable viral suppression
    - Lower risk of maternal OIs and death
    - Reduced risk of HIV transmission to sexual partners and to the child
    - The potential risk of neural tube defects is now considered very low.
- Start / transition all children from 20kg+ to a DTG-based regimen. However, **note that regimen 13A can only be used from 30kg+** because the dose of TDF is too high for smaller children. Use:
    - **15P** for **20.0 – 24.9 kg**
    - **15A** for **25.0 – 29.9kg**
    - Monitor weight and routinely move children to **13A** once they have reached **30kg+**
        - Confirm undetectable VL in the last 6 months before making this transition.
- DTG may be associated with increased risk of obesity in some patients.

11.2 Choosing ART regimen, formulation and dosage

Key Facts: NVP-resistance in children

- About half of all children no longer achieve viral suppression on NVP-based ART (regimen 2P)
    - This is mainly due to increasing NNRTI-resistance (NVP, EFV) among children who are getting infected by their mothers.
- Start / transition all children **under 20kg** to regimen **9P** (ABC/3TC + LPV/r)
    - Use LPV/r granules or pellets for children who can't swallow paediatric LPV/r tablets whole.
    - **Caution:** LPV/r tablets are not properly absorbed when crushed, chewed or dissolved. This will lead to development of LPV/r resistance.
    - Move to paediatric LPV/r tablets when the child's ability for swallowing whole has been confirmed.
    - Children and their caregivers may initially struggle to take LPV/r granules due to the relatively large amount and the bitter taste if not quickly swallowed.
    - Probe patiently and thoroughly at every visit to understand if the child is actually swallowing the full dose twice daily as prescribed. Review step-by-step how the granules are opened, prepared and administered.
    - Offer an alternative regimen if the child is not able to reliably take the prescribed dose.
    - Consult the Department of HIV and AIDS for alternative regimens for children on LPV/r-based regimens who need TB treatment.

11.2.3 Start regimen

- Select one of the 3 standard regimens to start patients on ART, based on weight.
- Use alternative 1st line regimens if the patient has any contraindications for the standard regimen.

Table 10: Selection of standard ART regimen for initiation

Weight (kg)	Regimen	Conditions / Instructions
Under 3kg	-	No routine ART. Consult DHA in special cases.
3 – 20kg	**9P**	Use LPV/r granules for children unable to swallow whole paediatric LPV/r tabs. LPV/r tabs must not be broken, crushed or dissolved.
20.0 – 24.9kg	**15P**	Use paediatric ABC/3TC tablet + regular (adult) dose DTG 50mg. Use paediatric patient card (blue)
25.0 - 29.9kg	**15A**	Use adult ABC/3TC tablet + regular (adult) dose DTG 50mg. Use adult patient card (yellow)
30kg +	**13A**	

11.2.10 Use of DTG or EFV in women of reproductive age

- The benefits of DTG outweigh the potential, very low risk of neural tube defects for **women who may get pregnant** while on ART.
- Use DTG-based regimens as standard 1st line regimens for all patients 20kg+, including girls and women who may get pregnant.
    - Explain the general benefits vs. the potential, very low risks of birth defects to all women who want to become pregnant. Offer **5A** or alternative regimens if women chose to avoid DTG.
    - **Note** that **13A** can only be used from **30kg**+. Use **15P** from 20-24.9kg and **15A** from 25-29.9kg

11.2.12 How to give LPV/r granules

- LPV/r granules contain the same medication and dose as the LPV/r pellets (in capsules), but the granules are much smaller and a packed in sachets.

1. Take the required number of sachets according to weight (see **Table 12** on **page 15**).
2. Shake the sachet gently to ensure all granules settle towards bottom of packet.
3. Tear open the required number of sachets one after the other and empty granules into a dry cup or bowl. Make sure all granules empty out of packet.
4. Put a small amount of food or expressed breast milk in a separate clean bowl
    - Babies 0-5 months: add some granules to spoonful of breastmilk, mix to prevent clumping, nurse after giving each spoonful.
    - Children 6+ months: mix some granules with soft food (mashed banana, avocado, sweet potato, Irish potato, yoghurt, porridge, etc.), feed to the child immediately. Then give the child a small bite of food without medicine.
    - For all: repeat this process until the whole amount of granules has been taken.
5. Don't forget to give the other part of the regimen (e.g. ABC/3TC)
6. **Switch foods often, do not always give with the same food.**
7. **Bitter taste comes after sitting in liquid/food for several seconds, so give as quickly as possible and follow up with nursing or sweet food to help remove taste.**
8. Throw away the empty sachet.

Table 11: Standard ART Regimens (all strengths in mg)

Regi-men	Paed. Formulation	Adult Formulation	Used for ART initiation 'Start regimen'	Line	Prescriber level	'Tail' needed	Contraindications	Possible adverse reaction	If confirmed, use Alt 1	If confirmed, use Alt 2
4	**AZT** 60 / **3TC** 30 + **EFV** 200	**AZT** 300 / **3TC** 150 + **EFV** 600	**No**	1st	1	**Yes**	• Anaemia <8g/dl • History of psychosis	• Anaemia, vomiting, appetite loss	5, 17	13, 15
								• Lipodystrophy, lactic acidosis	5, 17	13, 15
								• Hepatitis, rash [a], psychosis, gynaecomastia [b]	14	13, 15, 11
								• Treatment failure	13	15, 9, 10
5		**TDF** 300 / **3TC** 300 / **EFV** 600	Alternative for patients with (relative) DTG contraindications	1st	1	**Yes**	• History of psychosis • Uncontrolled BP↑/ diabetes, renal failure	• Renal failure	17 [c]	4, 15 [c], 14
								• Hepatitis, rash [a], psychosis, gynaecomastia [b]	7	13, 15, 14
								• Persistent dizziness, visual disturbances	13	7, 15, 14
								• Treatment failure	14	8, 11
7		**TDF** 300 / **3TC** 300 + **ATV/r** 300/100	**No**	2nd	2	**No**	• Uncontrolled BP↑/ diabetes, renal failure • Patient on rifampicin [d] • Pre-existing jaundice or suspected hepatitis [e]	• Renal failure	15 [c]	11, NS
								• Jaundice [f]	13	10, NS
								• Treatment failure [g]	(12)	
8		**AZT** 300 / **3TC** 150 + **ATV/r** 300/100	**No**	2nd	2	**No**	• Anaemia <8g/dl • Patient on rifampicin [d] • Pre-existing jaundice or suspected hepatitis [e]	• Anaemia, vomiting, appetite loss	15	9, 13, NS
								• Lipodystrophy, Lactic acidosis	15	9, 13, NS
								• Jaundice [f]	11	14, 13
								• Treatment failure [g]	(12)	
9	**ABC** 120 / **3TC** 60 + **LPV/r** 100/25	**ABC** 600 / **3TC** 300 + **LPV/r** 200/50	**New standard for children under 20kg**	1st or 2nd	1	**No**	• ABC hypersensitivity	• Fever, body pains, vomiting, cough [h]	10, 11	14, 13, 8
								• Diarrhoea, vomiting, dizziness, headache	15	7
								• Treatment failure [g]	(12)	
10		**TDF** 300 / **3TC** 300 + **LPV/r** 200/50	**No**	2nd	2	**No**	• Uncontrolled BP↑/ diabetes, renal failure	• Renal failure	9 [c]	14, 15 [c], 8
								• Diarrhoea, vomiting, dizziness, headache	7	13, 14, 15
								• Treatment failure [g]	(12)	
11	**AZT** 60 / **3TC** 30 + **LPV/r** 100/25	**AZT** 300 / **3TC** 150 + **LPV/** 200/50	**No**	2nd	2	**No**	• Anaemia <8g/dl	• Anaemia, vomiting, appetite loss	9	13, 15
								• Lipodystrophy, lactic acidosis	9	13, 15
								• Diarrhoea, vomiting, dizziness, headache	8	14
								• Treatment failure [g]	(12)	
12		**DRV** 600 + **r** 100 + **DTG** 50 (± NRTIs)	**No**	3rd	2	**No**	• Epilepsy [i]	• Diarrhoea, vomiting, headache, dizziness, insomnia	NS	
								• Neuropathy	NS	
								• Rash, jaundice	NS	

Regi-men	Paed. Formulation	Adult Formulation	Used for ART initiation 'Start regimen'	Line	Prescriber level	'Tail' needed	Contraindications	Possible adverse reaction	If confirmed, use Alt 1	If confirmed, use Alt 2
13		**TDF** 300 / **3TC** 300 / **DTG** 50	**Standard for all patients 30 kg+**	1st or 2nd	1	No	• Renal failure • Uncontrolled BP↑, uncontrolled diabetes • Epilepsy [i] • (Hepatitis B or C) [k]	• Renal failure	15 [c]	14
								• Insomnia, headache, nausea, diarrhoea [j]	5	7
								• Hepatitis [k]	10	5, NS
								• Treatment failure [g]	(8)	(11)
14	**AZT** 60 / **3TC** 30 + **DTG** 50	**AZT** 300 / **3TC** 150 + **DTG** 50	**No**	1st or 2nd	1	No	• Anaemia <8g/dl • Epilepsy [i] • (Hepatitis B or C) [k]	• Anaemia, vomiting, appetite loss, lipodystr., lactic acidosis	13	15
								• Renal failure	15 [c]	17 [c]
								• Insomnia, headache, nausea, diarrhoea [j]	4	8, 11
								• Hepatitis [k]	4	11
								• Treatment failure [g]	(7)	(9, 10)
15	**ABC** 120 / **3TC** 60 + **DTG** 50	**ABC** 600 / **3TC** 300 + **DTG** 50 [l]	**Standard for children 20 – 29.9 kg**	1st or 2nd	1	No	• ABC hypersensitivity • Epilepsy [i] • (Hepatitis B or C) [k]	• Fever, body pains, vomiting, cough [h]	13	14
								• Insomnia, headache, nausea, diarrhoea [j], hepatitis [k]	17	4, 9, NS
								• Treatment failure [g]	(8)	(11, 7)
16	**ABC** 120 / **3TC** 60 + **RAL** 25	**ABC** 600 / **3TC** 300 + **RAL** 400		1st	1	No	• ABC hypersensitivity • (Hepatitis B or C) [k]	• Fever, body pains, vomiting, cough	TDF/3TC + RAL	
								• Insomnia, headache, nausea, diarrhoea [j]	15	7
								• Treatment failure [g]	(8)	(11)
17	**ABC** 120 / **3TC** 60 + **EFV** 200	**ABC** 600 / **3TC** 300 + **EFV** 600		1st	1	Yes	• ABC hypersensitivity • History of psychosis	• Fever, body pains, vomiting, cough [h]	5	13, 4, 14
								• Hepatitis, rash [a], psychosis, gynaecomastia [b]	15	16, 9, 7, 8
								• Treatment failure	14	8, 11

[a] Mild skin rash and/or dizziness and nightmares are common after starting EFV. This usually resolves by itself and is not usually a reason to interrupt or change regimen.
[b] EFV can cause breast enlargement in children and men (one side or both sides). This may resolve spontaneously while continuing EFV, but substitution is usually needed (and effective).
[c] Patients with CrCl <50 ml/min need lower dose 3TC but full dose ABC. Combine ABC/3TC paed tabs and ABC (single) tabs for the correct dose. Call HIV Dept. logistics hotline for ABC single tabs.
[d] Do not combine ATV/r with rifampicin (TB treatment).
[e] Do not start patients with pre-existing jaundice or suspected hepatitis on ATV/r. Use LPV/r instead.
[f] ATV/r can cause jaundice. Mostly, this is only of cosmetic concern. Refer jaundice to a specialist for LFT. If only indirect bilirubin is raised, continue ATV. Stop ATV/r if LFT cannot be done.
[g] Treatment failure on 2nd line ART and DTG-based regimens need confirmation of resistance mutations by genotyping before switch can be considered.
[h] Fever, body pains, vomiting, cough / sore throat and breathing problems can be due to life-threatening ABC hypersensitivity (rare). Stop all ARVs immediately. Never re-start ABC.
[i] DTG should not be combined with standard antiepileptic drugs: carbamazepine, phenobarbital, phenytoin. Use non-DTG based regimen if possible. Else, consider phenobarbital or carbamazepine with double dose of DTG. Check VL 6-monthly to confirm suppression.
[j] DTG and RAL are very well tolerated. Mild headache, insomnia, nausea and diarrhoea usually subside without regimen change.
[k] DTG and RAL may worsen liver damage (alcohol, viral Hepatitis B or C, etc.) and rarely cause hepatotoxicity. Check transaminases before and after starting DTG in patients with known Hep B/C.
[l] ABC/3TC/DTG 600/300/50mg will become available as fixed-dose combination in 2020.

Table 12: Standard pack sizes and dosing of Paediatric and Adult formulations of ARVs, TPT and CPT

Drug	Tablets per tin		3 – 3.9 kg		4 – 5.9 kg		6 – 9.9 kg		10 – 13.9 kg		14 – 19.9kg		20 – 24.9kg		25 – 29.9kg		30 – 34.9 kg		35 – 39.9 kg		40 – 49.9 kg		50 kg +	
	Paed.	Adult	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
AZT / 3TC	60	60	1	1	1	1	1 ½	1 ½	2	2	2 ½	2 ½	3	3	1	1	1	1	1	1	1	1	1	1
ABC / 3TC	60	60	1	0	1	0	1 ½	0	2	0	2 ½	0	3	0	1	0	1	0	1	0	1	0	1	0
ABC / 3TC / DTG		60													1	0	1	0	1	0	1	0	1	0
LPV / r liquid / tabs	60	120	*1ml*	*1ml*	*1.5ml*	*1.5ml*	2	1	2	1	2	2	2	2	3	3	3	3	2	2	2	2	2	2
LPV/r granules (sachets)	120		2	2	2	2	3	3	4	4	5	5	6	6										
EFV	90	30							0	1	0	1 ½	0	1 ½	0	2	0	2	0	1	0	1	0	1
ATV / r		30															0	1	0	1	0	1	0	1
TDF / 3TC		30															0	1	0	1	0	1	0	1
TDF / 3TC / EFV		30																	0	1	0	1	0	1
TDF / 3TC / DTG		30/90															1	0	1	0	1	0	1	0
DTG 50		30											0	1	0	1	0	1	0	1	0	1	0	1
DRV		60																	1	1	1	1	1	1
r	60	60							2	1	2	2	2	2	3	3	3	3	1	1	1	1	1	1
ETV		120																	2	2	2	2	2	2
RAL	60	60	1	1	2	2	3	3	4	4	4	4	6	6	1	1	1	1	1	1	1	1	1	1
CTX 120	1000		0	1	0	1	1	1	1	1	2	2	2	2										
INH 100	100		0	½	0	½	0	1	0	1 ½	0	2	0	2 ½										
CTX 480		1000					0	½	0	½	0	1	0	1	0	2	0	2	0	2	0	2	0	2
CTX 960		1000									0	½	0	½	0	1	0	1	0	1	0	1	0	1
INH 300 (daily for IPT)		672									0	½	0	½	0	1	0	1	0	1	0	1	0	1
INH 300 (weekly for 3HP)		672											0	1	0	1 ½	0	1 ½	0	2	0	2	0	3
RFP 150 (weekly for 3HP)		24											0	3	0	4	0	5	0	5	0	5	0	6

14 Combining ART and TB treatment

- DTG- and RAL-based regimens (13, 14, 15 and 16) are a good combination with TB 1st line treatment.
    - However, the daily dose of DTG and RAL needs to be doubled while on rifampicin-containing TB treatment:
        - Take the regular DTG-containing regimen in the morning and one additional tablet of DTG 50mg in the evening (after 12 hours).
        - Take double the regular RAL-dose regimen in the morning and in the evening.
        - The doubling of DTG and RAL also applies to children.
    - Continue with double-dose DTG and RAL for 7 days after the last dose of rifampicin.

15 Continuing ART

15.7 Achieving optimal adherence

15.7.3 Supporting children on LPV/r granules

- Try to identify 2 or more guardians to ensure uninterrupted and reliable adherence support. Small children are completely reliant on a guardian to take their ARVs.
- Teach the guardians how to give LPV/r granules. Use the standard national job aid and education material.
    - LPV/r granules taste bitter when kept in the mouth for more than a few seconds. Give quickly after mixing with food.
    - Make sure guardians understand that both parts of the regimen have to be given together at the same time (e.g. ABC/3TC + LPV/r).
- Carefully check the child's weight at each visit and adjust the dose based on **Table 12** on **page 15**.
- Offer alternative regimens if the family is not able to cope with LPV/r granules and if additional support has not resulted in good adherence.
- Consult the DHA for any paediatric treatment challenges, including children suspected to be failing on PI- or DTG-based regimens.

15.10 Monitoring for treatment failure / HIV drug resistance

15.10.2 Viral load (VL) testing

Key Facts: Viral load testing

- The VL monitoring schedule is designed to detect ART failure early while avoiding unnecessary tests to save cost.
- Collect the first scheduled VL **after 6 months** on ART. Normally, patients are expected to have an undetectable VL at this time. If the VL is detectable, investigate:
    - Patients who were infected with drug-resistant HIV.
    - Patients who developed drug-resistance from previous ARV use (e.g. infants who received NVP prophylaxis).
    - Otherwise, a high VL at 6 months can be an important sign for poor adherence.
- After that, patients who are adherent and clinically well have a low risk of ART failure. Therefore, routine VL monitoring is scheduled approximately **every 12 months** from the last test.
- Collect missed VL tests at the next regular visit.
- Do additional targeted VL tests outside of this schedule when suspecting ART failure.
- Explain the standard VL monitoring schedule to every patient. Ask the patient to help remember when VL is due.
    - Explain (example): "You had your viral load drawn in November. Therefore, every November ASK your provider for your viral load test to be done."
- Actively communicate (phone / home visit) any detectable VL results (above detection limit, even if <1000) to patients as soon as the result is received at the site. Call for an early appointment.
- **DBS** and **plasma** VL samples produce different results in the low ranges below 839 copies/ml:
    - DBS results are usually not quantifiable below 839 copies/ml. (Some labs may produce an actual readout above 400 copies/ml from DBS). A DBS result <839 copies/ml means that some virus has been detected, but it is not possible to determine if this VL is in the very low range below 40 copies/ml or higher.
    - Plasma results are usually quantified above 40 copies/ml.
    - Both DBS and plasma results of <LDL mean that no virus has been detected, i.e. the VL is undetectable or fully suppressed.
    - Plasma is the gold-standard for viral load testing. Collect plasma samples if possible.

When to do VL

- Routinely collect the next VL sample when 11 months or more have elapsed since the last VL sample was collected.
- Don't delay a scheduled/routine or targeted viral load sample collection because of (suspected) poor adherence.
- Ascertain good adherence in the last 3 months before taking the follow-up sample after a high VL.
    - Review pill counts and doses missed carefully. Discuss openly to understand the true circumstances.
    - Trust the patient if they insist that adherence was good. Do not rely on pill count alone.
- Delay collection of follow-up sample after IAC ONLY if poor adherence is confirmed and if the patient is still clinically stable.
- See **Figure 6** on **page 22** for the alignment of the VL monitoring schedule and 6 month dispensing.

Interpreting and acting on VL results

- See **Figure 5** on **page 21** for indication, interpretation and action for VL testing.

Table 13 (new): Classification of DBS and plasma VL results

Sample type	Suppressed	Low-level viraemia	Viraemia 1000+
DBS	<LDL	<400 <550 <839 Any value 400-999	1000+
Plasma	<LDL <20 <40 <150 Any value 20-199	Any value 200-999	1000+

Successful ART

Finding	**Routine** or **targeted / repeat** VL "*suppressed*"
Interpretation	Successful ART
Action	Praise the patient and encourage further good adherence. Continue on the same regimen. Offer 6 month dispensing if otherwise eligible. Next routine VL after 12 months.

Potential treatment failure

Finding	**Routine, Targeted/ repeat or Follow-up** VL: *"low-level viraemia"*
Interpretation	Potential treatment failure
Action	Deliver one quality session of intensive adherence counselling at the same visit when returning the result to the patient. Provide additional IAC sessions at 1 month intervals for patients with specific adherence problems. Enter in "*Detectable Viral Load*" register (green cover, prev. "High VL register"). Continue same ART regimen. Give a regular 3-month appointment. Collect repeat VL sample after 3 months of good adherence. Repeat the cycle if follow-up result is *"low-level viraemia"*.

Confirmed treatment failure

Finding	**Targeted / repeat** VL: *"viraemia 1000+" AND* Patient is **on NNRTI-based regimen (0, 2, 4, 5, 6, 17)** *AND* **good adherence** in the 3 months before sample collection
Interpretation	The virus is likely resistant to the current ART regimen.
Action	Deliver one quality session of intensive adherence counselling at the same visit when returning the result to the patient. Provide additional IAC sessions at 1 month intervals for patients with specific adherence problems. Enter in "*Detectable Viral Load*" register (green cover, prev. "High VL register"). Consult certified 2nd Line Prescriber for initiation of 2nd line ART without delay. 'Reset the clock' for routine VL monitoring: **6 months** after switch to 2nd or 3rd line and **every 12 months** thereafter.

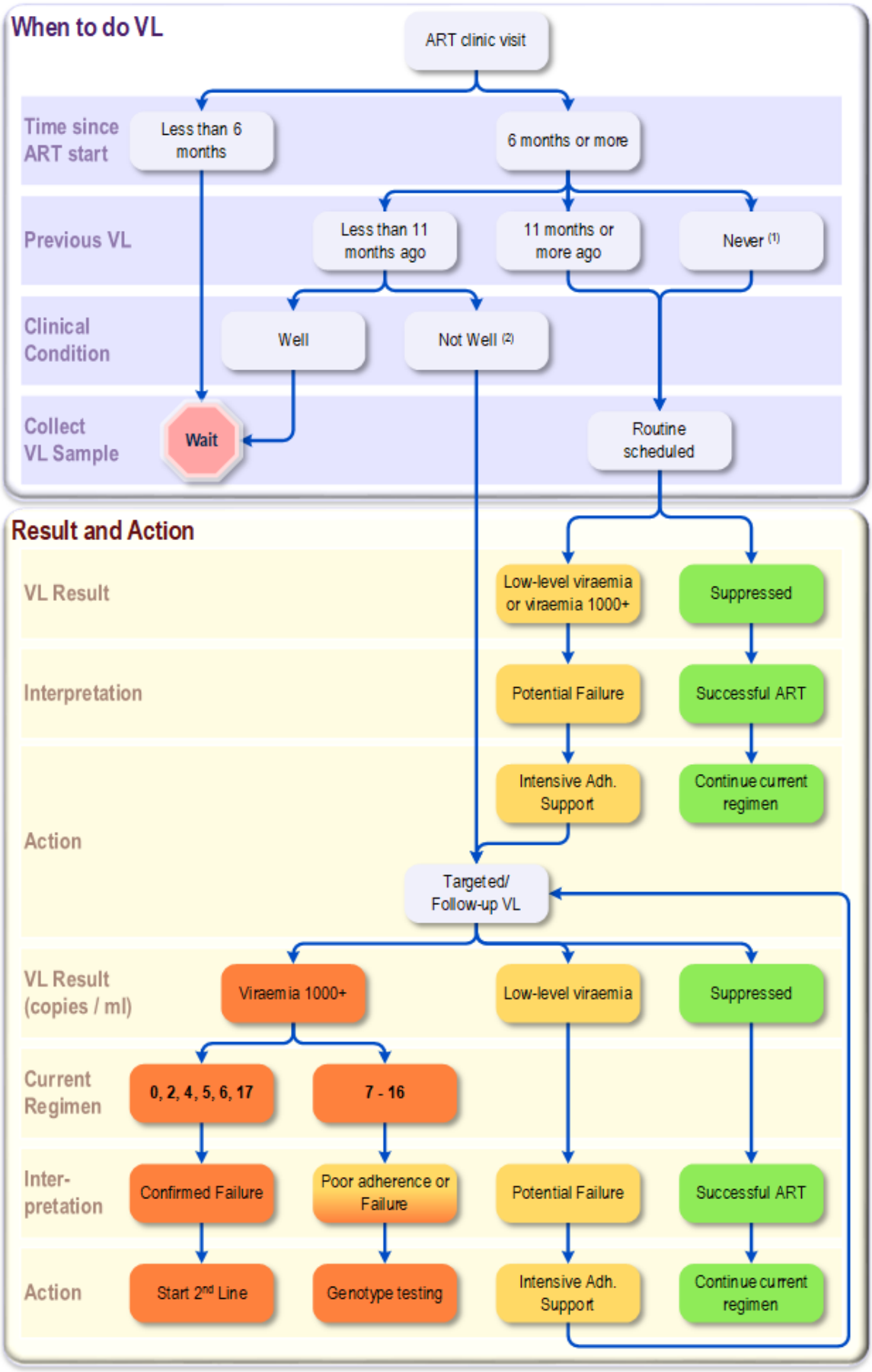
Poor adherence or treatment failure

Finding	**Targeted / repeat** VL: *"viraemia 1000+" AND* Patient is **on PI- or DTG-based regimen (7, 8, 9, 10, 11, 12, 13, 14, 15, 16)**
Interpretation	High VL on these regimens can be adherence problems / poor absorption or drug-resistant virus. Need genotype to confirm resistance before changing regimen.
Action	Deliver one quality session of intensive adherence counselling at the same visit when returning the result to the patient. Provide additional IAC sessions at 1 month intervals for patients with specific adherence problems. Enter in "*Detectable Viral Load*" register (green cover, prev. "High VL register"). Collect DBS or plasma sample for genotying. Consult certified 2nd Line Prescriber and/or call the HIV Dept. hotline to organize resistance testing. Continue on current regimen until genotyping results are available. Give a regular 3-month appointment. Select ART regimen based on resistance profile. 'Reset the clock' for routine VL monitoring: **6 months** after switch to 2nd or 3rd line and **every 12 months** thereafter.

Updating VL results in the electronic medical record system

- Enter as "839" for <839 copies/ml if the system does not provide qualifiers (<, >, =)
- Enter at "40" for <40 copies/ml if the system does not provide qualifiers (<, >, =)

Figure 5: Indication, interpretation and action for routine scheduled and targeted VL testing



(1) Includes: VL never tested, sample rejected, lost, or declared missing.
(2) Any of the following: Significant unintended weight loss, failure to thrive, new / worsening HIV-related disease (suspected or confirmed)

16 Differentiated ART services

16.1 Six months ARV dispensing (6MD) visits

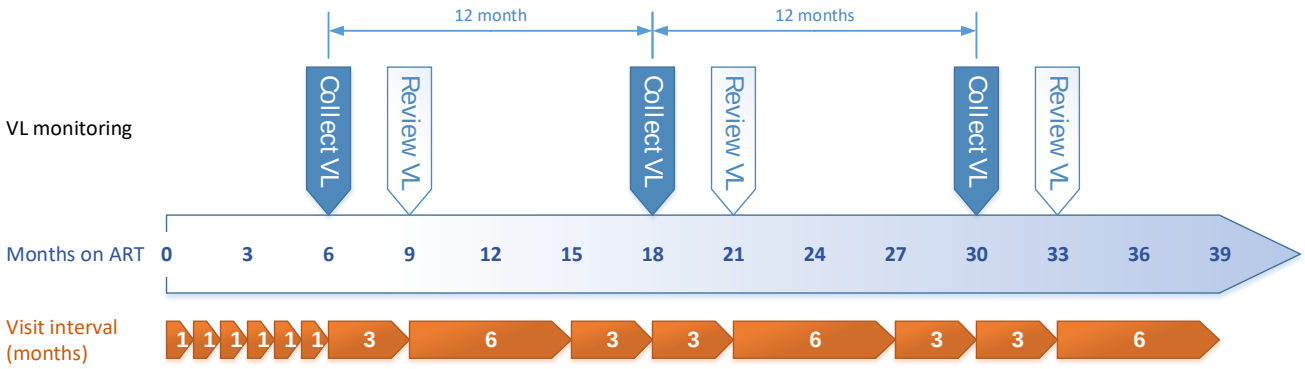
Facility criteria

- Sites can provide 6MD when they meet the **facility criteria**:
    - Stable and reliable stock management for all HIV related commodities.
    - Secure storage space for additional large volumes of commodities: identify and organize room for storage in advance before the stocks arrive.
    - Ample current stocks for each ARV and other drugs needed (CPT, fluconazole, etc.) to avoid the need for rationing supplies for other patients.

Patient criteria

- Routinely give 6MD appointments for stable and adherent patients. Patients must meet all of the following criteria:
    - At least 24 years old; ages 18-24 are eligible if they have a dedicated treatment supporter recognised by the clinic.
    - On ART treatment for at least 6 months
    - On the current ART regimen for at least 3 months
    - Not on TPT (IPT or 3HP)
    - No current ARV side effects
    - No opportunistic infections
    - Suppressed VL in the last 12 months (<LDL or <40 copies/ml)
    - No pending VL result
    - Not pregnant or breastfeeding
- **Figure 6** shows how to align 6MD appointments with the standard VL monitoring schedule.
- Plan ahead: give potentially a shorter appointment to maintain around 12 months between collection of VL samples.

Figure 6: Alignment of 6 months dispensing with 12-monthly VL monitoring



19 Transition to new ART regimen

Key Facts: 2nd Phase of regimen transition

- The 2nd Phase of regimen transition is for children previously on NNRTI-based regimens and for patients on PI-based 1st and 2nd line regimens.
- All **NVP-based regimens** (0P, 0A, 2P, 2A, 6A) will be **phased out completely** by 2nd half of 2020.
- **Transition of existing patients** from other 1st and 2nd line regimens to DTG-based regimens:
    - Early experience from the DTG transition has shown that it is safer to confirm viral load suppression on the previous regimen before moving to a DTG-based regimen.
    - See updates in **Section 19.2**

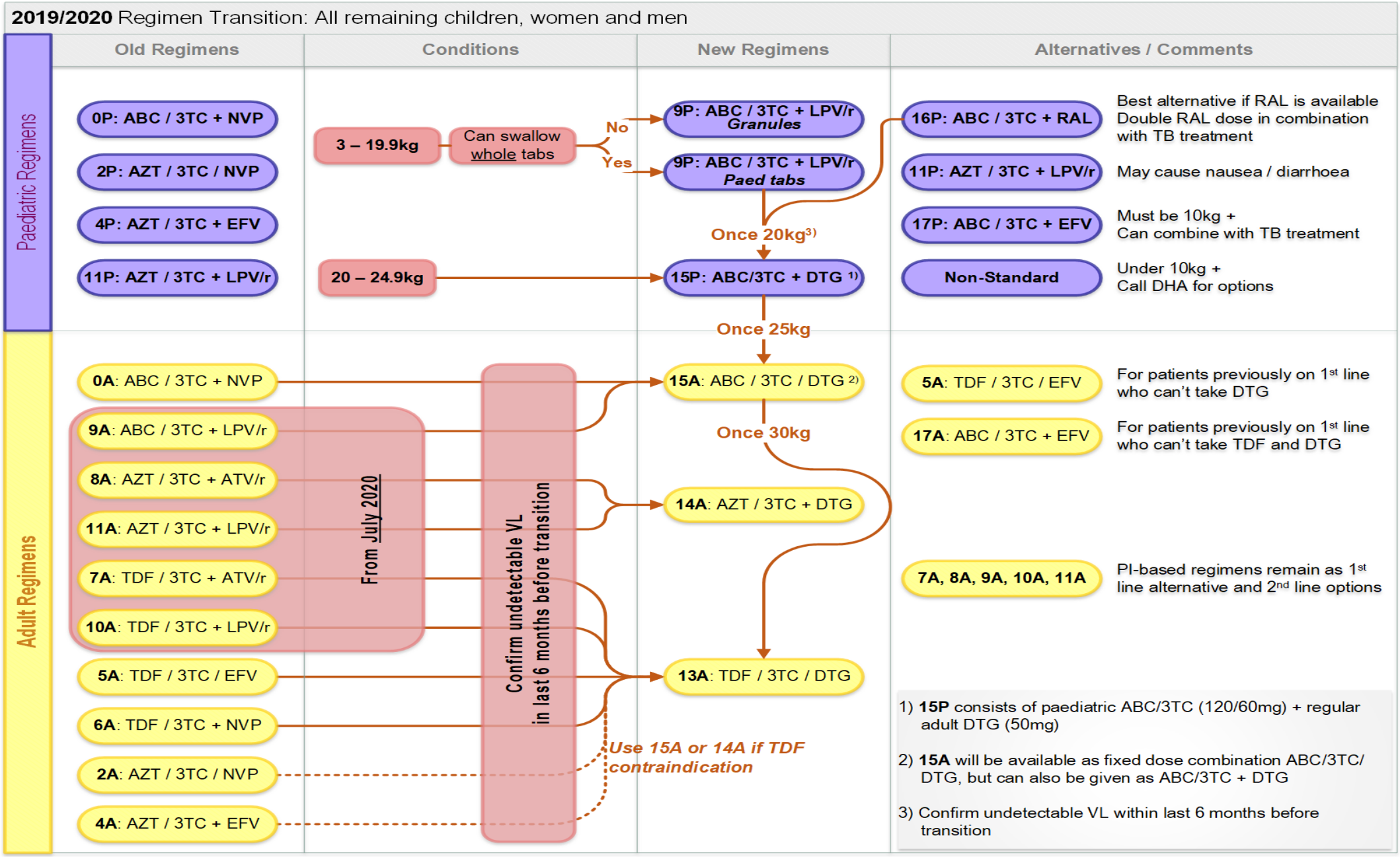
19.2 Transition for patients currently on ART

- Explain to all patients the *Key Facts* about DTG
- Emphasize that other medicines and **supplements containing cations** (calcium, magnesium, zinc, iron, aluminium) **must not be taken at the same time as DTG-based ART regimens** (13, 14, 15) because this reduces DTG absorption. Such medicines include FeFol, antacids, multivitamin supplements.
    - Take DTG-based ARVs **2 hours before or 6 hours after** such medicines.
- Patients who are yet to be transitioned need a ***suppressed*** **VL result from within 6 months before transition to the new regimen**.
    - Provide intensive adherence support and follow-up (FUP) VL for patients with potential or confirmed failure.
    - Proceed with routine transition **only** if the follow-up VL is *suppressed*.
    - Follow normal VL interpretation and switch to appropriate 2nd line if failure is confirmed.

Routine transition of children to 13A once they reach 30kg+

- Monitor weight at each visit
- When the child has reached **30kg+**:
    - Collect extraschedular VL sample (unless VL from the last 6 months is already available).
        - VL is *suppressed*: move to **13A**
        - VL is *low-level viraemia* or *viraemia 1000+*: provide intensive adherence support, follow up for suspected failure.
- See **Figure 7** for details of the 2019 / 2020 regimen transition strategy.

Figure 7: Regimen transition for all remaining children, women and men in 2019/2020



20 Pre-exposure prophylaxis (PrEP)

- PrEP is now approved for roll-out as a public health intervention for HIV prevention in Malawi.
- Offer PrEP as an additional primary prevention method for HIV negative persons at substantial risk of acquiring HIV (see separate PrEP guidelines)
    - Emphasize the need for combination with other prevention methods such as consistent condom use, VMMC, etc.
- PrEP involves:
    - Taking one daily fixed-dose combination tablet of ARVs.
    - Quarterly HIV testing
    - Quarterly STI screening
    - Quarterly adherence support
    - Renal function monitoring
- Eligibility criteria for PrEP:
    - Confirmed HIV negative status
    - At substantial high risk of HIV acquisition
    - Body weight 30kg+
- TDF/3TC is the preferred PrEP regimen for Malawi.
    - Tenofovir/emtricitabine (TDF/FTC) can be given as an alternative.
- More details on PrEP are included in the upcoming PrEP guidelines for Malawi to be released this year.