Paediatric Dolutegravir (DTG) 10 mg Dispersible, Scored Tablet

Paediatric ART Training for Health Care Workers

Outline

- Introduction of Paediatric DTG & Benefits
- Eligibility Criteria
- Transition & Implementation Considerations
- Paediatric DTG Administration and Dosage Recommendations
- Use in TB/HIV Co-infection & Drug-Drug Interactions
- Paediatric DTG 10 mg Associated Side Effects
- 2021 Paediatric Optimization Acceleration Plan
- Key points
- Supplemental Dosage Slide

Introduction of Paediatric DTG 10 mg dispersible tablet (DT)

- Paediatric dolutegravir 10 mg dispersible, scored tablets (pDTG) is a new generic formulation of DTG suitable for infants and CLHIV who are
  - ≥ 4 weeks of age and,
  - Weigh at least 3 kg up to less than 20 kg
- Paediatric DTG 10 mg exists as a simpler formulation, much easier to administer
- The introduction of Paediatric DTG 10 mg DT will allow all eligible infants and CLHIV to benefit from DTG

Benefits of DTG use for children <20 kg

Improves adherence

- DTG is taken once daily, whereas LPV/r is twice daily
- DTG dispersible tablet is easily dissolved in water and allows easier administration versus LPV/r formulations
- DTG dispersible tablet has a strawberry cream taste and is more palatable in comparison to LPV/r's bitter taste

Tolerability in patients

- Better side effect profile and improved tolerability over LPV/r, which has been associated with GI upset, hyperlipidaemia and decreased bone density*
- In the entirety of the IMPAACT P1093 study, not a single child discontinued DTG dispersible tablets due to intolerance or toxicity

Clinically Superior

- Demonstrated superior clinical efficacy
- Increasing NNRTI resistance necessitates transition away from EFV and NVP-based regimens
- DTG's genetic barrier to resistance is an advantage over NNRTIs
- Versatile for use in second-line and third-line as well

*Precaution must still be taken where needed, e.g., in concomitant use with other medicines such as TB (See Slide 14 - 15)

Preferred 1st line Paediatric Treatment Regimens:2021

Populations	Preferred 1st line regimen	Alternative 1st line regimen(s)
Neonates <2 weeks old, premature, or low birth weight	AZT/3TC/NVP - Seek HIV experienced provider or clinical mentor advice	
Neonates 2 to <4 weeks old	AZT/3TC/LPV+r[a] If infant anaemic, seek HIV clinical mentor or specialist advice	
Infants ≥3kg and 4 weeks to <3 years old	ABC/3TC/DTG1[b]	ABC/3TC/LPV+r[a]
Children 3 years and 10 to <20 kg	ABC/3TC/DTG1[b]	ABC/3TC/LPV+r[a], or ABC/3TC/ATV+r
Adolescents 20 to <30 kg	ABC/3TC/DTG1(50mg)[b,c,d]	ABC/3TC/ATV+r if SEs with DTG
For adolescents at least 30 kg, same as adults		

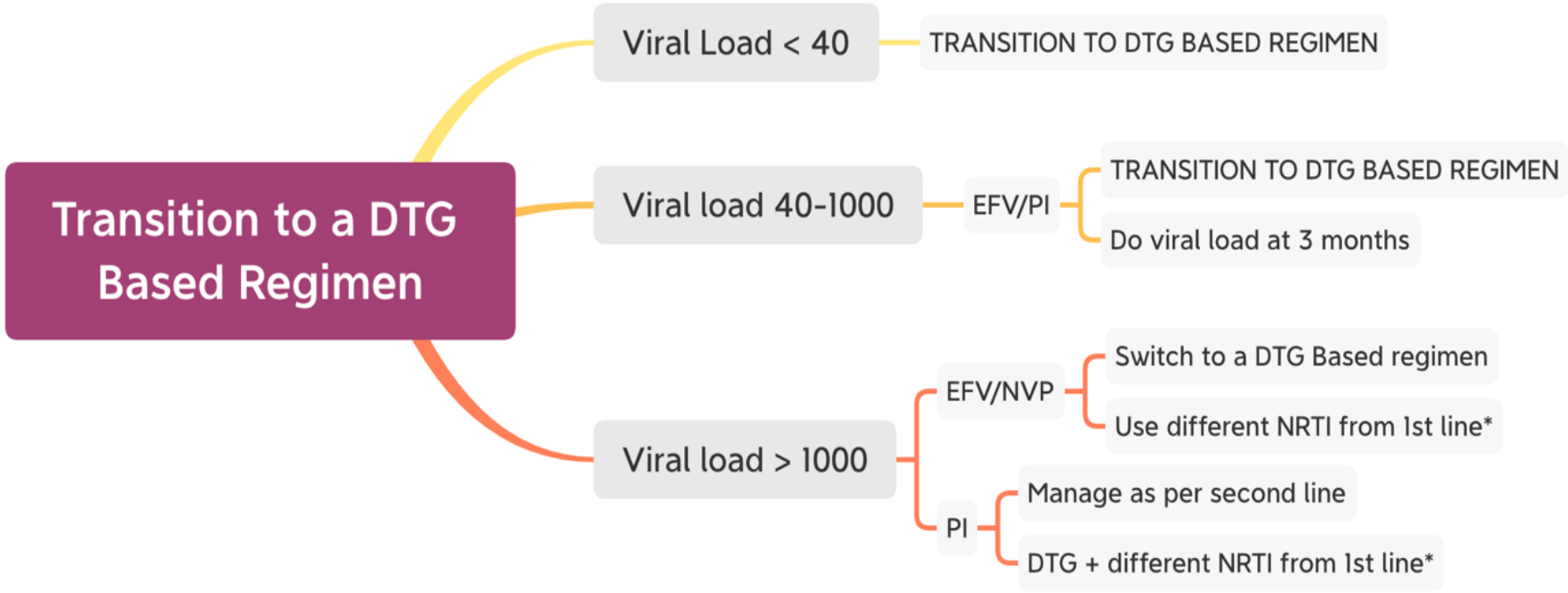
[a] LPV+r granules starting at 2 weeks or LPV+r solution starting 42 weeks following the start of mother's LMP until 3 months old; when 10 kg and if can swallow tablets whole, can change to LPV+r 100/25mg
[b] DTG as a single dose formulation
[c] When TAF is available for lower weight children this would be preferred over ABC
[d] DTG 50mg adult formulation used at this weight

Source: Namibia HIV Clinical Guidelines, 2021

Eligibility Criteria for Paediatric DTG 10mg DT

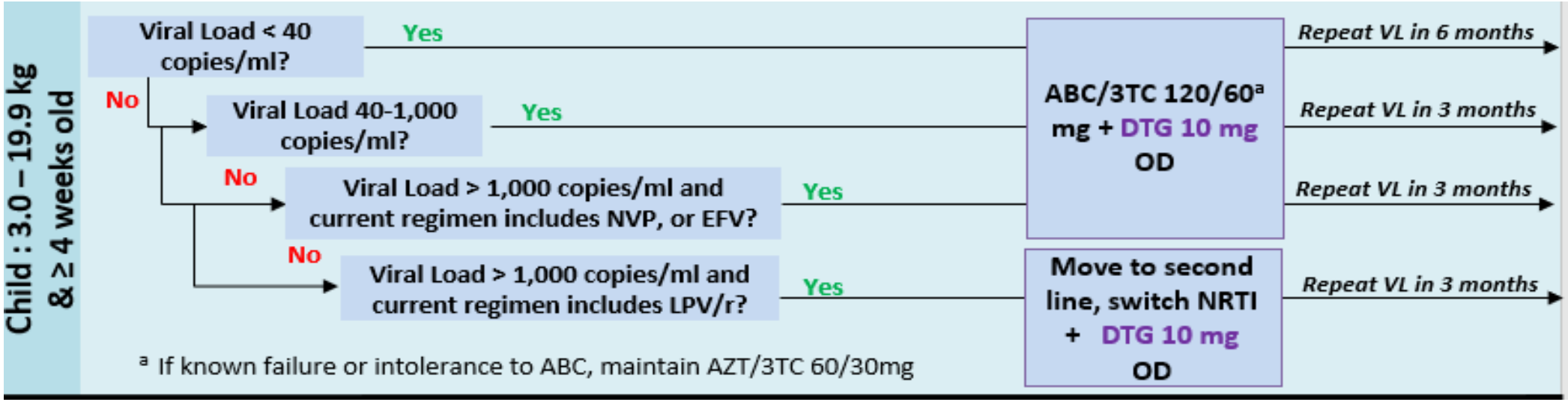
- All infants and CLHIV ≥ 4 weeks of age and, weigh at least 3 kg up to less than 20 kg

Transitioning children safely to the new preferred regimen



Note: Prior to transitioning, a viral load test should be done ≤ 6 months, otherwise a new viral load test is recommended. However, a viral load test should not delay the transition to DTG. Take a viral load test the same day as initiating DTG.

DTG Prescribing Algorithms for Children & Adolescents (3.0 – 19.9 kg)

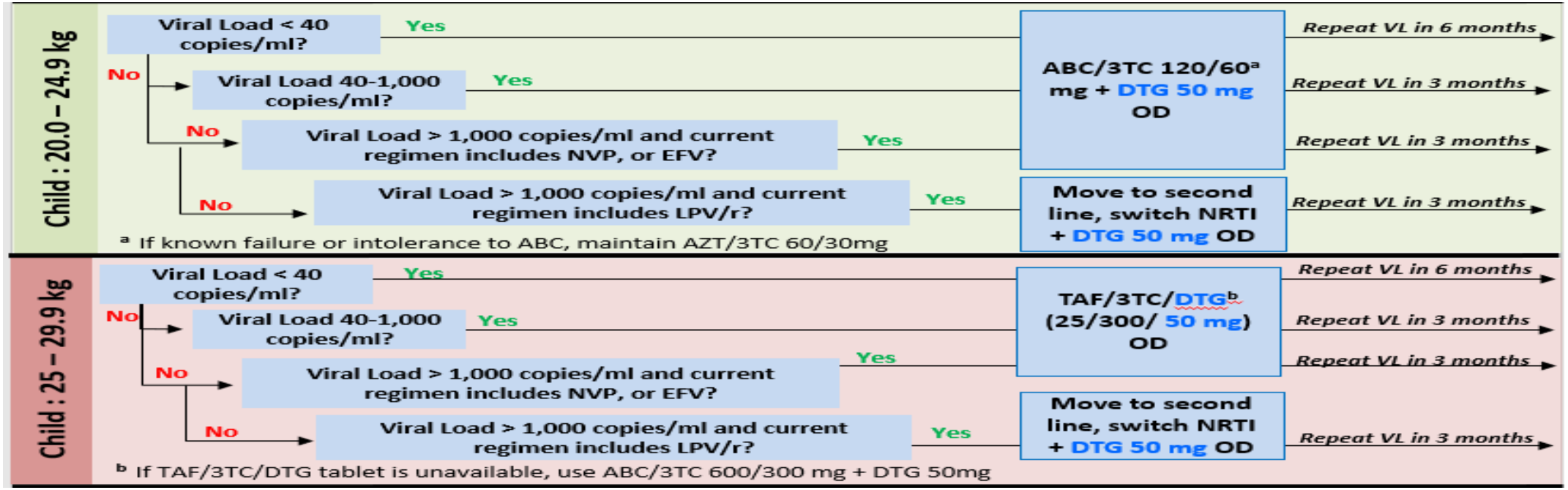


IMPORTANT: Follow national guidance for precise weight-based dosing of each product

Key Points:

- Transition all to DTG containing regimen (**10 mg**)
- ABC/3TC 120/60 mg is preferred first-line but if known failure or intolerance to ABC, maintain AZT/3TC 60/30mg
- VL is repeated in 3 months for those with VL ≥ 40 copies/ml
- Intensify adherence counselling for children with a VL ≥ 40 copies/ml
- If VL >1,000 and child has been on LPV/r, NVP, or EFV > 2 years, move to second line and switch their NRTI.

DTG Prescribing Algorithms for Children & Adolescents (20.0 – 29.9 kg)

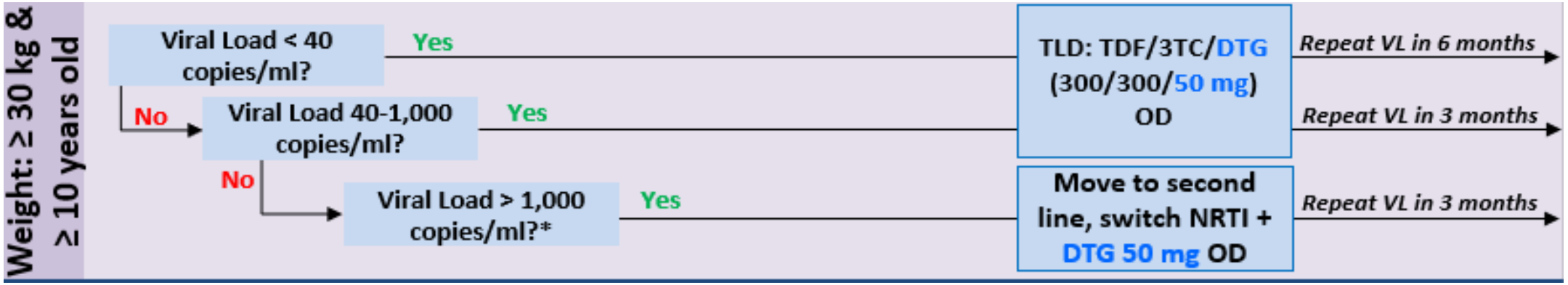


IMPORTANT: Follow national guidance for precise weight-based dosing of each product

Key Points:

- Transition all to DTG containing regimen (**50 mg**)
- **< 25 kg** use **ABC/3TC** but if known failure or intolerance to ABC, maintain AZT/3TC
- **25-29.9 kg** use **TAF/3TC/DTG** is preferred over ABC/3TC when available
- VL is repeated in 3 months for those with VL ≥ 40 copies/ml
- Intensify adherence counselling for children with a VL ≥ 40 copies/ml
- If VL >1,000 and child has been on LPV/r, NVP, or EFV > 2 years, move to second line and switch their NRTI

DTG Prescribing Algorithms for Children & Adolescents (≥ 30 kg)



IMPORTANT: *Follow national guidance for precise weight-based dosing of each product*

Key Points:

- Transition all to DTG containing regimen (50 mg)
- VL is repeated in 3 months for those with VL ≥ 40 copies/ml
- Intensify adherence counselling for children with a VL ≥ 40 copies/ml

Differences between the DTG 50 mg film-coated tablets and Paediatric DTG 10 mg DT

DTG 50 mg Film-Coated Tablets

- **Administration:** The adult 50 mg tablet is a small, film coated tablet (FCT) that should be swallowed whole
  - While 50 mg is the adult dose, it can also be used for children who weigh 20kg or more

DTG 10 mg Dispersible Tablets

- **Administration:** The Paediatric DTG 10 mg scored, dispersible tablet (DT) can be swallowed whole, but is meant to be dissolved in water

Paediatric DTG 10 mg DT is a priority commodity and should not be used in children/adults weighing ≥ 20kg as a replacement for DTG 50 mg FCT!

Clinicians and Pharmacist **should not** switch between 50 mg DTG FCT and 10 mg DTG DT
- the product dosing is not 1:1 (i.e. 5 x 10 mg DT is *not* equivalent to 1 x 50 mg FCT).

Dosage recommendations according to weight and age for DTG 10 mg

Paediatric DTG dosing based on a child's weight

Weight	Recommended Dose	Number of Tablets
≥ 4 weeks and 3 to < 6 kg	5 mg once daily	1/2
6 to < 10 kg	15 mg once daily	1 and 1/2
10 to < 14 kg	20 mg once daily	2
14 to < 20 kg	25 mg once daily	2 and 1/2

Source: WHO Policy Brief (July 2020) For Introducing New ARVs For Children; *Switch only if child can swallow pills.

Administration guidance for Paediatric DTG 10 mg DT and ABC/3TC 120/60 mg DT

1

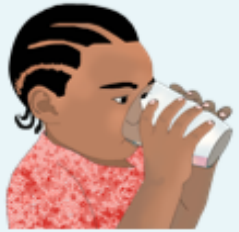
Add the correct number of DTG10 and ABC/3TC tablets to a clean, empty glass based on your child's weight. (See Dosing Table).

Weight	No. of DTG Daily Tablets	No. of ABC/3TC 120/60 mg Daily Tablets
3 to < 6 kg	0.5	1
6 to < 10 kg	1.5	1.5
10 to < 14 kg	2	2
14 to < 20 kg	2.5	2.5

2

Add 10-20 mL (2-4 teaspoons) of clean water into the glass and stir until the tablets dissolve. If the tablets do not dissolve completely (i.e., they lump together), stir and slowly add a small amount of extra water until the tablets fully dissolve.

3



Give the medicine to your child to drink. Make sure they drink all the medicine right away or within a maximum of 30 minutes.

4

If any medicine remains in the glass, add a little more water to the glass and give to your child. Repeat until no medicine remains in the glass.

Reminders

- Remember to give Paediatric DTG 10 mg (and other ARVs) at the same time everyday.
- Use other liquids or foods for mixing if your child is unable to take the tablets in water. Follow the same volume recommendations as above to avoid spills and to ensure the child takes the full dose.
- Crushing, chewing, or mixing with other foods or liquids can be considered as long as the entire tablet is ingested.
- Give the child another full dose of Paediatric DTG 10 mg if they vomit within 30 minutes of taking their initial dose. If they vomit after 30 minutes, you do not need to give them another dose.

Paediatric DTG 10mg: TB and HIV coinfection

- DTG interacts with the TB medicine rifampicin (RIF). (rif induces UGT 1A1 & CYP 3A)
- Children receiving TB treatment containing RIF should be given double their daily standard dose of DTG 10 mg for the duration of TB treatment (one dose in the morning and one dose in the evening).
  - Children >20 kg should increase dose of DTG 50 mg twice daily
- Health Care workers should switch back to standard doses 2 weeks after a child completes TB therapy.

Source: WHO Policy Brief (July 2020) For Introducing New ARVs For Children

Drug-Drug Interactions

- Iron, aluminium, magnesium, and calcium-containing medicines or multivitamins bind with and reduce absorption of DTG.
  - If co-administered, DTG should be taken with food to enhance DTG absorption or taken at alternate times (2 hours before or at least 6 hours after).
- Drugs that are metabolic inducers may decrease the plasma concentrations of DTG. This includes some anticonvulsants such as carbamazepine, phenytoin or phenobarbital.
  - Co-administration with these anticonvulsants is not recommended with DTG. Consult expert opinion or consider use an alternative anticonvulsant agent (valproic acid or gabapentin).
- For more information on drug interactions, please see the latest national guidelines.

Source: WHO Policy Brief (July 2020) For Introducing New ARVs For Children

Side Effects

- **In clinical studies, no participants permanently discontinued DTG due to adverse events from Paediatric DTG 10 mg.** Possible side effects include:
  - **Insomnia**
  - **Fatigue**
  - **Headache**

  These tend to be most common on first taking DTG and tend to improve with time (approximately 1-2 months)
- Weight gain has been a common side effect of DTG 50 mg in adults and while there is no current evidence to suggest a problem with weight gain in children, it must be monitored regularly.
- Incidence of high blood sugar following DTG has also been reported in ART experienced adults. Related symptoms such as polyuria, polydipsia should also be monitored routinely.

Report all side effects and adverse events to the **Therapeutics Information and Pharmacovigilance CENTER (TIPC).**

Namibia Medicines Regulatory Council
- Tel: (061) 203 2406/203 2312
- Fax: (061) 226 631
- Fax2email: 0886606781
- Email: info.TIPC@mhss.gov.na

Use the yellow "*Adverse Medicine Reaction Reporting Form*"

2021 Paediatric Optimization Acceleration Plan (POAP)

- Using the arrival of Paediatric DTG 10 mg to catalyze the scaling up optimal antiretroviral therapy for infants and children living with HIV

Goal 1 by December 31, 2021

- 100% of all CHLHIV <6 years on DTG 10 mg
- 100% of all CLHIV between 6-9 on DTG 50 mg
- 100% of all CLHIV between 10-15 on TLD

Goal 2 by December 31, 2021

- 80% of all CLHIV <6 years on 3-month MMD
- 80% of all CLHIV between 6-9 on 4–6-month MMD
- 80% of all CLHIV between 10-15 on 6-month MMD

Key points for Paediatric DTG 10 mg

- Paediatric DTG 10mg
  - also known as pDTG.
  - It is much simpler to administer and well tolerated.
  - Can be given from ≥ 4 weeks of age and, weight of at least 3 kg up to less than 20 kg.
  - Can be used for clients initiating 1st, 2nd and 3rd line treatment.
- For clients transitioning to DTG 10mg, VL monitoring is important, but results returned should not delay the transition to the new regimen.
- Always refer to the dosage recommendation for appropriate dosing according to the weight.
- Clinicians should be aware of the potential “Drug to Drug” interactions related to DTG 10mg
- Clinicians should watch out for any possible side effects and if any, they should be reported.

Paediatric Dosage Recommendations According to Weight and Age for Preferred First-line Regimens per day

Formulation	3 – 5.9 kg	6 – 9.9 kg	10 – 13.9 kg	14 – 19.9 kg	20 – 24.9 kg	25 – 29.9 kg	≥ 30 kg + ≥ 10 years
1a - ABC/3TC 120/60mg scored dispersible tablet (*OD*)	1	1.5	2	2.5	3	[transition to TAF]	–
1b - AZT/3TC 60/30mg scored dispersible tablet (*AM/PM*)	1 | 1	1.5 | 1.5	2 | 2	2.5 | 2.5	3 | 3	[transition to TAF]	–
DTG 10mg scored dispersible tablet (*OD*)	0.5	1.5	2	2.5	*[transition to 1 DTG 50mg]*	[transition to TAF]	–
DTG 50 mg tablet (OD)	–	–	–	–	1	[transition to TAF]	–
TAF/3TC/DTG 25/300/50 mg tablet aka TAF (*OD*)	–	–	–	–	–	1	*[transition to TLD]*
TDF/3TC/DTG 300/300/50 mg tablet aka TLD (*OD*)	–	–	–	–	–	–	*1*

- Children 3 – 24.9 kg will either be on 1a) ABC/3TC or 1b) AZT/3TC; ABC-3TC is preferred unless known failure or intolerance to ABC.
- If TAF is unavailable, use ABC/3TC (or AZT/3TC is known failure or intolerance to ABC) – see table below.

Formulation	3 – 5.9 kg	6 – 9.9 kg	10 – 13.9 kg	14 – 19.9 kg	20 – 24.9 kg	25 – 29.9 kg	≥ 30 kg + ≥ 10 years
1a - ABC/3TC 600/300 mg tablet [Fixed dose pill] (*OD*)	–	–	–	–	–	1	*[transition to TLD]*
1b - AZT/3TC 300/150 mg tablet [Fixed dose pill] (*AM/PM*)						1 | 1	*[transition to TLD]*
1c- ABC 300mg tablets (*OD*)	–	–	–		–	2	*[transition to TLD]*
1c - 3TC 150mg tablets (*OD*)	–	–	–	–	–	2	*[transition to TLD]*

- Children 25-29.9 kg should on TAF but if unavailable, choose 1a, 1b or 1c; ABC is preferred over AZT unless known failure or intolerance to ABC.

Morning Evening

PEPFAR

U.S. President's Emergency Plan for AIDS Relief

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