health
Department:
Health
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NOTICE: UPDATED GUIDANCE FOR THE USE OF DOLUTEGRAVIR IN PREGNANCY

The National Essential Medicines List Committee has reviewed the evidence for dolutegravir (DTG) compared with efavirenz (EFV) in pregnancy, and has determined that the benefits outweigh the risks[1]. DTG is therefore recommended as part of the preferred first line ART regimen for all adults and adolescents living with HIV, including pregnant women and women of child-bearing potential. .

Evidence of benefit

- Two randomised controlled trials conducted in pregnant women found that DTG caused more rapid virological suppression than EFV, resulting in more women being virologically suppressed at delivery.
- In a surveillance study in Botswana, rates of vertical transmission were low, and were similar for DTG and EFV (8/999 and 8/883 respectively, risk difference 0.11%, 95% CI -0.79 to 1.06%).
- DTG has a higher virological barrier to resistance than EFV.

Evidence of harms

- The 2020 update of the Botswana Tsepamo study found no significant difference in neural tube defect (NTD) prevalence between DTG- and EFV-exposure at conception (7/3 591 and 8/10 958 respectively, risk difference 0.12%; 95%CI -0.001% to 0.33%).
- In a randomised controlled trial, mean weight gain during pregnancy was similar amongst women on DTG/TDF/FTC (0.319 kg/week) and EFV/TDF/FTC regimens (0.291 kg/week).

The Primary Healthcare (2020 edition) and Adult Hospital Level (2019 edition) Standard Treatment Guidelines and Essential Medicine List will be updated accordingly:

Indications in the Primary Healthcare STGs and EML, 2020	Current recommendations			Updated recommendations		
SECTION 6.8: HIV IN PREGNANCY *- First-line ART regimens – 1st ANC visit*	» Pregnant women ≥6 weeks gestation » Breastfeeding women not actively wishing to conceive » Those who make an informed choice to use DTG	• TDF, oral 300 mg daily. **AND** • 3TC, oral, 300 mg daily **AND** • DTG, oral, 50 mg daily *Note:* Provide as a FDC	» Contraindication to TDF: renal insufficiency, other nephrotoxic medicines e.g. aminoglycosides. » Contraindication to DTG: pregnant women <6 weeks gestation or actively wanting to conceive or intolerance to DTG	Pregnant women	• TDF, oral 300 mg daily. **AND** • 3TC, oral, 300 mg daily **AND** • DTG, oral, 50 mg daily *Note:* Provide as a fixed dose combination (FDC)	Contraindication to TDF: renal insufficiency, other nephrotoxic medicines e.g. aminoglycosides.
	Pregnant women <6 weeks gestation or actively wanting to conceive	• TDF, oral, 300 mg daily. **AND** • 3TC, oral, 200 mg daily **AND** • EFV, oral, 600 mg at night *Note:* Provide as a FDC	Contraindication to EFV: active psychiatric illness.			
	Contraindications to EFV and DTG	• TDF, oral, 300 mg daily. **AND**	» Contraindication to EFV: active psychiatric illness.			

[1] National Department of Health: Affordable Medicines, EDP-PHC/Adult Hospital level. Medicine Review: Dolutegravir in pregnancy, June 2021

		• 3TC, oral, 300 mg daily **AND** • LPV/r, oral, 400/100 mg 12 hourly	» High-risk pregnancy: doctor consult or refer immediately if acute psychiatric illness.			

Indications in the Adult Hospital Level STGs and EML, 2019	Current recommendations		Updated recommendations	
SECTION 6.7: HIV IN PREGNANCY *- 1st ANC visit*	Pregnant women >6 weeks gestation - not on ART, with normal renal function, **without** TB, with no desire for more children and who chooses to use DTG after understanding the risk and benefits. (DTG associated with NTDs, ≤6 weeks gestation)	• TDF, oral, 300 mg daily. **AND** • 3TC, oral, 300 mg daily. **AND** • DTG, oral, 50 mg daily. » Provided as a FDC	Pregnant women not on ART, with normal renal function, **without** TB.	• TDF, oral, 300 mg daily. **AND** • 3TC, oral, 300 mg daily. **AND** • DTG, oral, 50 mg daily. Provided as a FDC
	Pregnant women >6 weeks gestation - not on ART, with normal renal function, **with** TB, with no desire for more children and who chooses to use DTG after understanding the risk and benefits. (DTG requires boosting with TB treatment)	• TDF, oral, 300 mg daily. **AND** • 3TC, oral, 300 mg daily. **AND** • DTG, oral, 50 mg daily. Provided as a FDC **WITH** • DTG, oral 50 mg 12 hours later.	Pregnant women not on ART, with normal renal function, **with** TB. (DTG requires boosting with TB treatment)	• TDF, oral, 300 mg daily. **AND** • 3TC, oral, 300 mg daily. **AND** • DTG, oral, 50 mg daily. Provided as a FDC **WITH** • DTG, oral 50 mg 12 hours later.
	» Pregnant women ≤6 weeks gestation, or planning a pregnancy after this one.	• TDF, oral, 300 mg daily. **AND** • FTC, oral, 200 mg daily. **AND** • EFV, oral, 600 mg at night. » Provided as a FDC	Pregnant woman on TDF + FTC + EFV.	Switch to TDF+3TC+DTG: **Switch only if VL is <50 copies/mL in the last 6 months**
	Pregnant woman already on TDF+3TC+DTG and understands the risk and benefits of DTG. (Document in the antiretroviral pregnancy register http://www.APRegistry.com/)	Chooses to remain on TDF+3TC+DTG: » Enter in antiretroviral pregnancy register http://www.APRegistry.com/		

3TC=lamivudine, DTG=dolutegravir, EFV=efavirenz, FDC=fixed dose combination, FTC=emtricitabine, LPV/r=lopinavir/ritonavir, TB=tuberculosis, TDF=tenofovir

The National Consolidated Guidelines for the Management of HIV in Adults, Adolescents, Children and Infants and Prevention of Mother-to-Child Transmission will also be updated.

Provinces and Health Care Facilities are requested to distribute and communicate this information in consultation with their Pharmaceutical and Therapeutics Committees.

Queries may be submitted to:

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Kind regards

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