Thai National List of Essential Medicines: What needs?

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	จำนวน	เข้าใหม่	
Antibacterial	53	0	
Anti-TB	18	0	
Antifungal	13	2	Flucytosine, micafungin
Antiviral-non-HIV	14	5	Cidofovir, peramivir, entegavir, sofosbuvir, sofosbuvir+ledipasvir
Antiviral-HIV	20	1	raltegravir
Antiparasitic	16	1	ivermectin
Vaccine	24	1	

DHHS, IAS-USA, EACS, WHO Guidelines: Recommended Regimens for First-line ART

Class	DHHS (2018)[1]	IAS-USA(2018)[2]	EACS (2017)[3]	WHO (2018)[4]	Thailand 2017
INSTI	• BIC/TAF/FTC • DTG/ABC/3TC* • DTG + TDF/FTC or TAF/FTC • EVG/c/TDF/FTC or EVG/c/TAF/FTC • RAL + TDF/FTC or TAF/FTC	• BIC/TAF/FTC • DTG + ABC*/3TC • DTG + TAF/FTC	• DTG/ABC*/3TC • DTG + TDF/FTC or TAF/FTC • EVG/c/TAF(TDF)/FTC • RAL + TAF/FTC or TDF/FTC	• TDF/3TC/DTG • TAF/FTC/DTG	
Boosted PI			• DRV/r or DRV/c + TAF/FTC or TDF/FTC		
NNRTI			• RPV + TAF/FTC or TDF/FTC**	• TDF + 3TC (or FTC) + EFV	• TDF + 3TC (or FTC) + EFV • TDF + 3TC (or FTC) + RPV provided CD4 >350 cells/mm3 or baseline VL <500000

* ABC: If HLA B*5701 negative
** Only if CD4 count >200 cells/mm^3 and HIV-VL <100,000 copies/mL

1.DHHS guidelines May 2018; 2. Saag MS, et al. JAMA. 2018;320:379-396.; 3.European AIDS Clinical Society. http://www.eacsociety.org/files/guidelines_8.2-english.pdf. Accessed Oct 2017;4. World Health Org

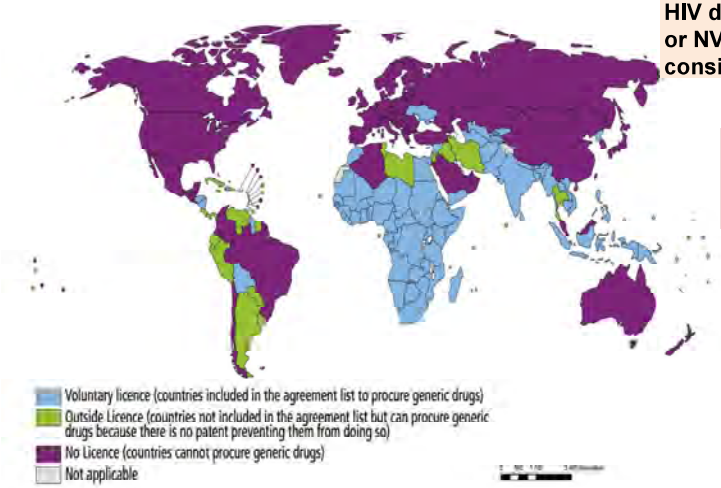
DTG: High efficacy, high genetic barrier, less drug interaction

Clinical trial [ref]	Treatment arms	HIV RNA <50 copies/ml	Virological failure	Discontinuation for adverse events
First-line treatment				
SINGLE, $n=833$	ABC/3TC/DTG	71%	9%	3%
Week 144 [14]	TDF/FTC/EFV	63%	8%	11%
ARIA, $n=495$	ABC/3TC/DTG	82%	6%	4%
Week 48 [15]	TDF/3TC with ATV/r	71%	14%	7%
FLAMINGO, $n=484$	2NRTI with DTG	80%	8%	2%
Week 96 [16]	2NRTI with DRV/r	68%	12%	2%
SPRING-2, $n=822$	2NRTI with DTG	81%	5%	2%
Week 96 [17]	2NRTI with RAL	76%	10%	2%
Gilead 1489, $n=631$	ABC/3TC/DTG	93%	3%	1%
Week 48 [18]	TAF/FTC/BIC	92%	1%	0%
Gilead 1490, $n=657$	TAF/FTC/DTG	93%	1%	0%
Week 48 [19]	TAF/FTC/BIC	89%	4%	1%
INSPIRING, $n=113$	TDF/XTC/DTG	81%	10%	0%
Week 24 [42]	TDF/XTC/EFV	89%	7%	2%
HIV RNA <50 copies/ml (Switch studies)				
NEAT 022, $n=415$	2NRTI with DTG	93%	2%	3%
Week 48 [48]	2NRTI with PI/r	95%	0.5%	1%
STRIIVING, $n=553$	2NRTI with DTG	85%	1%	4%
Week 24 [46]	Current treatment	88%	1%	0%
SWORD 1 and 2, $n=1024$	DTG with RPV	95%	0.6%	3%
Week 48 [47]	Current treatment	95%	1%	0.6%
Treatment-experienced patients				
SAILING, $n=715$	OB with DTG	71%	20%	3%
Week 48 [65]	OB with RAL	64%	28%	4%
DAWNING, $n=627$	2NRTIs with DTG	82%	12%	1%
Week 24 [56]	2NRTIs with LPV/r	69%	25%	4%

3TC, lamivudine; BIC, bictegravir; DRV, darunavir; DTG, dolutegravir; EFV, efavirenz; FTC, emtricitabine; LPV/r, lopinavir/ritonavir; NRTI, nucleoside reverse transcriptase inhibitor; RIF, rifampicin; TAF, tenofovir alafenamide; XTC =3TC or FTC.

Vitoria, Marco AIDS32(12):1551-1561, July 31, 2018.

Fig. 3.4. Current status of DTG generic licence in countries (March 2017)



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Information Evidence and Research (IER)
World Health Organization

WHO July 2017 : Countries with national pretreatment HIV drug resistance to EFV or NVP ≥10% should consider a transition to DTG

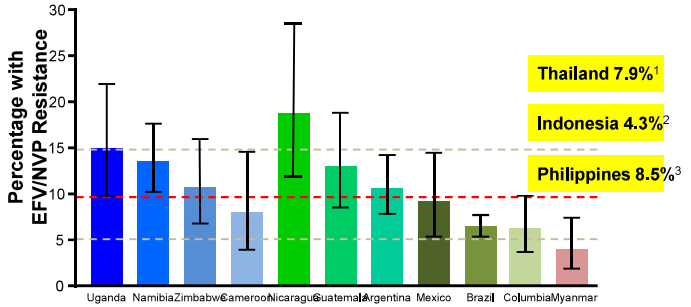
TLD = TDF/3TC/DTG

75 USD/person/yr

TAFED = TDF/FTC/D

TAFLD = TDF/3TC/D

Pretreatment HIV drug resistance to EFV or NVP among first-line ART initiators in selected countries



Transition to new ART in HIV program WHO July 2017[4]
HIV Drug Resistance Report 2017[5]

1. Kiertiburanakul S, et al. 2016 Feb 1;11(2):e0147945. Kotaki T, et al. AIDS Research and Therapy 2015:12:5 DOI 10.1186/s12981-015-0046-y 3. Salvana E, et al. Open Forum Infectious Diseases 2017: 4(suppl 1): S423 4. WHO Guidelines 2017. Transition to new ART in HIV program, WHO July 2017. Available at: http://www.who.int/hiv/pub/toolkits/transition-to-new-arv-technical-update/en/. Accessed Jan 2018 5. HIV Drug Resistance Report 2017. Available at: http://www.who.int/hiv/pub/drugresistance/hivdr-report-2017/en/. Accessed Jan 2018

WHO 2018 : DTG for 1st, 2nd, 3rd line

Population	First-line regimens	Second-line regimens	Third-line regimens
Adults and adolescents (including women and adolescent girls who are of childbearing potential or are pregnant)[a]	Two NRTIs + DTG[b]	Two NRTIs + (ATV/r or lopinavir/ritonavir (LPV/r))	Darunavir/ritonavir (DRV/r)[c,d] + DTG[e] + 1–2 NRTIs (if possible, consider optimization using genotyping)
	Two NRTIs + EFV[c]	Two NRTIs + DTG[b]	
Children	Two NRTIs + DTG	Two NRTIs + (ATV/r[d] or LPV/r)	
	Two NRTIs + LPV/r	Two NRTIs + DTG[e]	
	Two NRTIs + NNRTI	Two NRTIs + DTG[f]	

[a] An optimized NRTI backbone should be used such as zidovudine (AZT) following TDF or abacavir (ABC) failure and vice versa.
[b] Women and adolescent girls of childbearing potential with consistent and reliable contraception and who are fully informed of the benefits and risks can use DTG.
[c] If population-level pretreatment resistance to EFV or NVP is ≥10%, the choice of alternative options to EFV needs to be made weighing the drug availability and toxicity profile. DTG (with consistent and reliable contraception among adolescent girls and women of childbearing potential) or ATV/r are the drug options to be considered.
[d] ATV/r can be used as an alternative to LPV/r among children older than three months, but the limited availability of suitable formulations for children younger than six years, the lack of a fixed-dose formulation and the need for separate administration of a ritonavir booster should be considered when choosing this regimen.
[e] This applies to children for whom approved DTG dosing is available. RAL should remain the preferred second-line regimen for the children for whom approved DTG dosing is not available.
[f] ATV/r or LPV/r should remain the preferred second-line treatment for the children for whom approved DTG dosing is not available. This applies to children for whom approved DTG dosing is available.
[g] For PI-experienced people, the recommended DRV/r dose should be 600 mg/100 mg twice daily.
[h] Children younger than three years should not use DRV/r.
[i] DTG-based third-line ART following the use of integrase inhibitors must be administered with DTG twice daily.

Knowledge gaps on clinical use of dolutegravir : neuropsychiatric AE in Asia

CNS side effects: higher than expected rate of DTG discontinuation due to neuropsychiatric (NP) AE in observational studies (compared w

N=1950 German	Discontinuation due to any AE (12m rate)	Discontinuation due to neuropsychiatric (12 m rate)
dolutegravir	7.6%	5.6%
elvitegravir	7.6%	0.7%
raltegravir	3.3%	1.9%

High CNS toxicity in woman HR 2.64
Older>60 vrs HR 2.86
Hoffmann C HIV Med 2017

- **Clinical trial : low rates of DTG discontinuation because of AE at wk 96(2% Spring2, 3% Flamingo) , 4% at wk 144 Single**
- **"Real-life" settings: rate of DTG discontinuation**
  - **7.0% French** (Johann C AIDS 2017) : ABC (10.2%), non ABC (4.7%), NP-AE was higher in ABC user (5.1% vs 1.5%)
  - **8 % of 157 in Belfast** (Todd S Int J STD AIDS 2017)
  - **10.2%, Italian cohort** (Bonfanti P AIDS 2017)
  - **10.6%, Europe** (Menard A AIDS 2017)
  - **14.5%** (Borghetti A AIDS 2017)
  - **15.3%** (de Boer M AIDS 2016) : ABC