National Centre for Infectious Diseases

Recommendations for the Use of Antiretroviral Therapy in Adults Living with HIV in Singapore: 2021 Updates

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Overview

- Need for national ART recommendations
- Recommendations workgroup & process
- What's new in the guidelines?
- What to start?
- Switch strategies
- Monitoring while on ART

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NHIVP ROLES & FUNCTIONS

National Centre for Infectious Diseases

- Formulate national strategic approach to achieve UNAIDS 90-90-90 targets & beyond
  - ✓ Ending HIV in Singapore
  - ✓ 4th 90 – living well with HIV
- Consult & coordinate with key stakeholders across the continuum of HIV prevention, testing & treatment services
- Develop evidence-based guidelines & best practices on HIV prevention, testing & treatment
- Assess impact of international & locally conducted research on national policies
- Monitor epidemiological trends in national registries & inform solutions

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IMPORTANCE OF “GLOCALIZATION”

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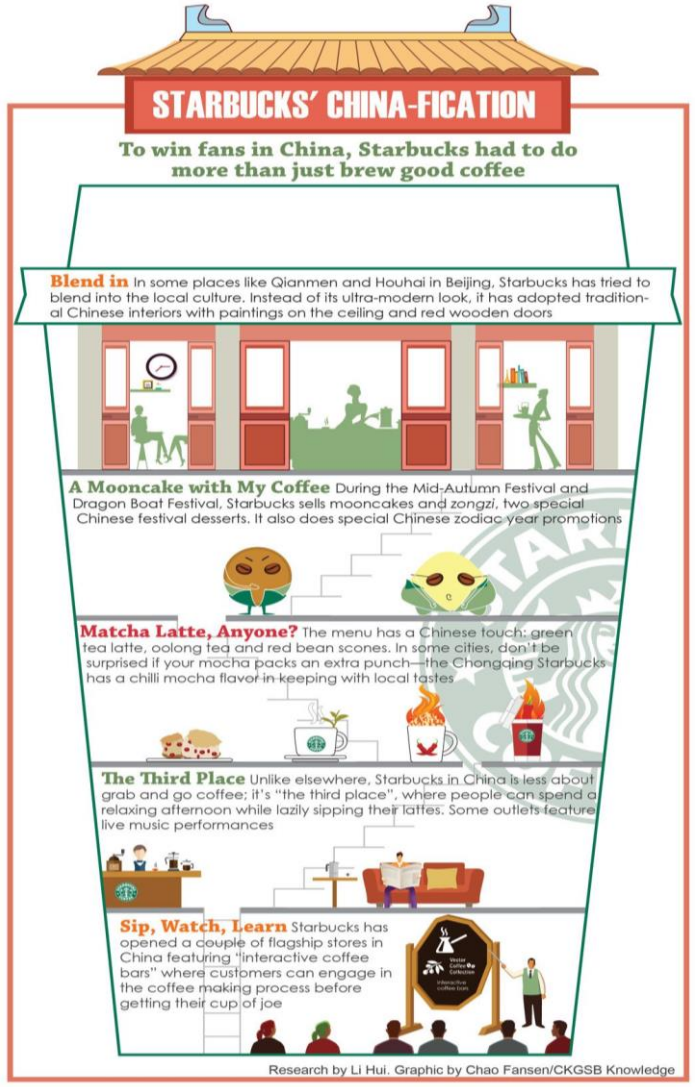
- International recommendations & benchmarks must be applied with local context in mind
- Of particular importance for ART:
  - Transmitted drug resistance trends
  - Health economics



RESULTS FOR HIV MOLECULAR SURVEILLANCE, 2014-2018

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HIV molecular surveillance	2014	2015	2016	2017	2018
Total number of samples tested	118	116	245	160	130
Recent infections (%)	17.8	22.4	20.4	23.8	16.9
Circulating subtypes (%)					
CRF01_AE	60.0	61.5	64.0	52.6	63.6
Subtype B	40.0	34.6	24.0	34.2	27.3
Transmitted Drug Resistance					
Any drug class (%)	3.4	7.0	3.7	3.1	3.8
NRTI (%)	1.7	0.9	0.8	1.3	0.8
NNRTI (%)	1.7	2.6	3.3	1.9	2.3
PI (%)	0	3.5	0.8	1.3	0.8

MOH, Communicable Diseases Surveillance 2018

Antiretroviral therapies

for treating Human Immunodeficiency Virus type 1 (HIV-1) infection

Technology Guidance from the MOH Drug Advisory Committee

Guidance recommendations

The Ministry of Health's Drug Advisory Committee has recommended the following antiretroviral therapies (ARTs):

- ✓ **Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs):** lamivudine 150 mg tablet, tenofovir disoproxil fumarate 300 mg tablet, zidovudine 100 mg capsule;
- ✓ **Non-nucleoside reverse transcriptase inhibitors (NNRTIs):** efavirenz 200 mg and 600 mg tablets, etravirine 200 mg tablet, nevirapine 200 mg and 400 mg tablets, rilpivirine 25 mg tablet;
- ✓ **Protease inhibitors (PIs):** atazanavir 200 mg and 300 mg capsules, darunavir 600 mg and 800 mg tablets, lopinavir 200 mg/ritonavir 50 mg tablet and lopinavir 80 mg/ritonavir 20 mg oral solution, ritonavir 100 mg tablet;
- ✓ **Integrase strand transfer inhibitors (INSTIs):** dolutegravir 50 mg tablet, raltegravir 400 mg and 600 mg tablets; and
- ✓ **Fixed-dose combinations:** abacavir 600 mg/lamivudine 300 mg tablet, abacavir 600 mg/dolutegravir 50 mg/lamivudine 300 mg tablet, emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg tablet

in line with their registered indications for the treatment of Human Immunodeficiency Virus type 1 (HIV-1) infection.

Subsidy status

Raltegravir 400 mg and 600 mg tablets, and emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg tablet are recommended for inclusion on the Medication Assistance Fund (MAF) in combination with other antiretroviral agents for the treatment of HIV-1 infection.

All other abovementioned ARTs are recommended for the inclusion on the MOH Standard Drug List (SDL).

SDL subsidy or MAF assistance **do not** apply to any other ARTs that are not listed above.

Details of all recommendations are provided in the Annex.

Published on 1 September 2020

- ✓ Inclusion of 16 antiretroviral drugs on MOH Standard Drug List on 1 September 2020
- ✓ Greatly reducing the cost of ART for patients

https://www.ace-hta.gov.sg/docs/default-source/drug-guidances/antiretroviral-therapies-for-treating-hiv-1-infection-(1-sept-2020).pdf

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WORKGROUP

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- Aim
  - Provide guidance to HIV care practitioners on the optimal use of ART for the treatment of HIV infection in adults and adolescents in Singapore
- Composition
  - Directors of HIV clinical programmes
  - Private ID practitioners who treat PLHIV
  - HIV pharmacists
  - HIV medical social workers

PROCESS

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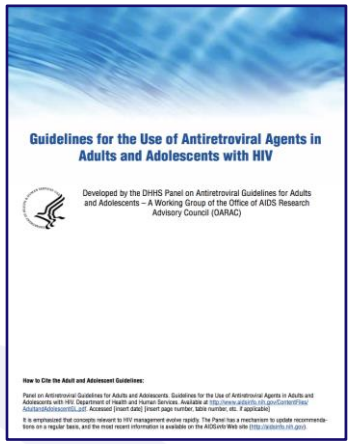
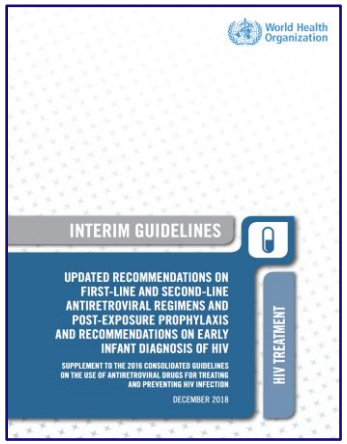
1) Review of select benchmark international guidelines and updates





2) Adaptation to Singapore context
   - ✓ Inclusion of interim local studies & data such as transmitted resistance trends, cost-effectiveness

3) Consultation & feedback
   - ✓ ID Chapter, College of Physicians, Singapore
   - ✓ NHIVP Community Advisory Board
   - ✓ MOH Communicable Diseases Division

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WHAT'S NEW IN THE GUIDELINES?

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- Changes to first-line regimens, with a greater emphasis on integrase inhibitors in view of the advantages they provide
- Changes to ART switch therapy in the setting of virologic suppression
- Changes to baseline laboratory investigations for people newly diagnosed with HIV infection

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WHAT TO START: KEY POINTS

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1) DTG- and BIC-based regimens are the preferred first line regimens:
   a) **TDF/TAF + FTC/3TC based regimens**: combined with DTG. BIC is currently only available as a combination tablet with TAF/FTC (Biktarvy®) *
   b) **ABC + 3TC based regimens**: A combination tablet consisting of ABC, 3TC and DTG is available (Triumeq®) *
   c) **NRTI-sparing regimens**: DTG + 3TC
2) RAL-based regimens are no longer recommended as a first line regimens
3) NNRTI- and DRV/r-based regimens can be considered as alternative first line regimens if INSTI-based regimens cannot be used

** To note: DTG and ABC/3TC/DTG are on the Standard Drug List; BIC is not.*
Cost considerations to be discussed with patients.

ABACAVIR-BASED REGIMENS

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NRTI backbone	3rd Drug		Singapore	DHHS 2021	IAS 2020	WHO 2021
ABC* + 3TC (HLA B*57:01 screening would only be cost-effective non-Chinese including late-stage Malay and Indian ethnicities)	INSTI	DTG	ABC/3TC/DTG is formulated as a single combination pill			
		RAL				
	PI	DRV/r				
	NNRTI	EFV 400mg OD	Only if: - HIV1 RNA <100,000 copies/ml			
		EFV 600mg OD	Only if: - HIV1 RNA <100,000 copies/ml			
		RPV	Only if: - CD4>200, HIV1 RNA <100,000 copies/ml			

ABC: Abacavir; 3TC: Lamivudine; NNRTI: Non-nucleoside reverse transcriptase inhibitor; PI: Protease inhibitor; INSTI: Integrase strand transfer inhibitor; EFV: Efavirenz; RPV: Rilpivirine; DRV/r: Darunavir/ritonavir; ATV/r: Atazanavir/ritonavir; LPV/r: Lopinavir/ritonavir; DTG: Dolutegravir; BIC: Bictegravir; RAL: Raltegravir

*To be avoided in patients with high cardiovascular risks and patients with HBV co-infection.

TENOFOVIR-BASED REGIMENS

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NRTI backbone	3rd Drug		Singapore	DHHS 2021	IAS 2020	WHO 2021
TFV (TDF or TAF) # PLUS FTC or 3TC	INSTI	DTG	Only if: 1) Hep B co-infected or 2) HLA B*57:01 +			TDF+3TC/FTC+ DTG
		BIC	BIC is combined with TAF and FTC as a single combination tablet			
		RAL				
	PI	DRV/r				
	NNTI	EFV 400mg OD				
		EFV 600mg OD				
		RPV				

TFV: Tenofovir; TDF: Tenofovir disoproxil fumurate; TAF: Tenofovir alafenamide; FTC: Emtricitabine; 3TC: Lamivudine; NNRTI: Non-nucleoside reverse transcriptase inhibitor; PI: Protease inhibitor; INSTI: Integrase strand transfer inhibitor; EFV: Efavirenz; RPV: Rilpivirine; DRV/r: Darunavir/ritonavir; ATV/r: Atazanavir/ritonavir; LPV/r: Lopinavir/ritonavir; DTG: Dolutegravir; BIC: Bictegravir; RAL: Raltegravir; Hep B: Hepatitis B virus; HLA B5701: Human leukocyte antigen B5701

#TDF to be avoided in patients with CrCl <60 mL/min. TAF to be avoided in patients with CrCl <30 mL/min

TWO-DRUG REGIMENS

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Regimen	Singapore	DHHS 2021	IAS 2020	WHO 2020
DTG/3TC	Except if HIV RNA > 500,000 copies/mL, HBV co-infection or ART initiated before GRT for NRTI or HBV testing is available			

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SWITCHING TO NRTI-SPARING/2 DRUG REGIMENS

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INITIAL DRUG	REASON TO SWITCH (EXAMPLES)	SWITCH TO	IF	WHEN TO SWITCH
Tenofovir-based regimens (TDF or TAF)	Nephrotoxicity Osteoporosis	DTG/3TC DTG/RPV DRV/r/3TC*	- No resistance to either drug component is present - If patient has HBV-CoI, additional HBV-active agent such as entecavir should be added *DRV/r/3TC should only be used if unable to use DTG-based two drug regimens	≥ 6 months stable
Abacavir-based regimen	Myocardial infarction Significant cardiac risk factors			

TDF: Tenofovir disoproxil fumurate; TAF: Tenofovir alafenamide; ABC: Abacavir; DTG: Dolutegravir; 3TC: Lamivudine; RPV: Rilpivirine; DRV: Darunavir

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MONITORING RECOMMENDATIONS

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- CMV IgG is no longer required as part of baseline serologies for all newly diagnosed patients with HIV infection.
- Toxoplasma antibody should be checked for all newly diagnosed patients with HIV infection. If cost is a concern, physicians may opt to check it only for individuals with CD4 cell count <100 cells/uL.
- Serum cryptococcal antigen should be checked for individuals with CD4 cell counts < 100 cells/uL.

ACKNOWLEDGEMENTS

National Centre for Infectious Diseases

- ART Recommendations Workgroup
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Thank you!