HIV DRUG RESISTANCE REGIMENS 2025

For the management of protease inhibitor (PI) and integrase strand transfer inhibitor (INSTI) resistance[∞]

Developed by the ARV Drug Resistance Committee (ADReC)
(*previously the TLART Committee*)

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[∞]refers to INSTI (e.g., dolutegravir) resistance over 0 on the Stanford score

Contents

1. Treatment algorithm

1. Patient:
- **is on DTG regimen**
- **has developed DTG resistance**
- **is PI naïve**

a) TE + DRV/r dosed once daily

i. If not eligible for TDF*:
- Replace TE with TAF/FTC[¥]

ii. If not eligible for TAF[¥]:
- Replace TE with AL

2. Patient:
- **is on PI regimen**
- **has developed PI resistance**
- **is INSTI naïve, and:**

2.1. - **DRV score <10**

a) TLD[¥]

i. If not eligible for TDF*:
- Replace TLD with TAFED[¥] or TAFLD[¥]

ii. If not eligible for TAF[¥]:
- Replace TLD with ALD / AL+DTG

2.2. - **DRV score 10-59**

a) TLD[¥] + DRV/r dosed twice daily

i. If not eligible for TDF*:
- Replace TLD with TAFED[¥] or TAFLD[¥]

ii. If not eligible for TAF[¥]:
- Replace TLD with ALD / AL+D

b) Discretion may be applied if there are adherence concerns ***and DRV/r score <30***: In these cases, the committee may consider using TLD alone or changing the twice daily DRV/r to once daily DRV/r. Both cases will require close VL monitoring. If VL rebound occurs, consult with ADReC.

2.3 - **DRV/r score ≥60**

a) Refer to ADReC for an individualised regimen based on genotype and clinical history.
b) Discretion may be applied. If there are adherence concerns, ADReC may consider using TLD alone.

3. Patient has:
- **PI and INSTI resistance, or**
- **a history of multiple ARV class resistance**

a) Refer to ADReC for an individualised regimen based on genotype and clinical history.

4. Patient has
- **DTG resistance**

	- **prior ATV/r or LPV/r exposure, but no resistance test was done at time of switch to DTG regimen**

a) TE + DRV/r dosed once daily

i. If not eligible for TDF*:
- Replace TE with TAF/FTC¥ or TAF/3TC¥

ii. If not eligible for TAF¥:
- Replace TE with AL

b) VL at 3 months': if not suppressed then repeat the genotyping.

2. Notes

*TDF eligible patients:

- Age: ≥ 10 years of age
- Weight: ≥ 30kg
- Renal function: Adequate renal function according to age/pregnancy status (*see 'Adequate renal function' below***)
- No prior TDF nephrotoxicity

**Adequate renal function:

- Age requirement:
  - 10 - <16 years of age:
    - eGFR >80 mL/min using Counahan Barrett formula [(height (cm) x 40) / creatinine (µmol/L)]
  - ≥ 16 years of age:
    - eGFR >50 mL/min using MDRD equation as provided by the laboratory or EGFR App
- If pregnant:
  - Absolute creatinine level <85 µmol/L

¥TAF eligible patients:

- Age: adults or children
- Weight: Children ≥ 25kg may be treated with TAF 25 mg
- Renal function: eGFR ≥ 30mL/min
- Consult with ADReC if eGFR <30L/min
- *TAF can be used together with boosted protease inhibitors without any dose adjustments*

Drug-drug interactions with darunavir[1]:

This is a list of the most common drug-drug interactions with darunavir. This is **not** an exhaustive list, always check the patient's concomitant medicines for potential drug-drug interactions.

Interacting drug	Recommendation
Atorvastatin	Avoid, use alternative statin
Carbamazepine	Avoid, use alternative antiepileptic
Phenobarbitone	Avoid, use alternative antiepileptic
Phenytoin	Avoid, use alternative antiepileptic
Rifampicin	Avoid, use rifabutin instead
Rosuvastatin	Avoid, use alternative statin
Rifapentine	Avoid, use rifabutin instead

[1] https://www.drugs.com/drug-interactions/darunavir-index.html

3. Drug Regimens- rationale

1. If DRV fully susceptible (i.e. Stanford <10): Tenofovir/lamivudine/dolutegravir
2. If DRV score 10-59: Tenofovir/lamivudine/dolutegravir + darunavir/r 600mg/100mg bd
3. If DRV score 60 or above: Individualised regimen

Rationale: In patients who experience virological failure on a second line LPV/r or ATV/r regimen a switch to TLD is recommended provided DRV is reported as fully susceptible and there has been no prior DTG failure. TLD will be an effective regimen in most patients even if TDF + 3TC resistance is present, based on evidence from the NADIA (Paton NI, 2021), VISEND (Mulenga, 2022), D2EFT (Matthews GV, 2024) and ARTIST (van Heerden J, 2025) trials. For the minority of patients who will go on to fail this third line TLD regimen and develop DTG resistance then TDF + 3TC + DRV/r would be an appropriate and effective subsequent "rescue" regimen provided DRV is still fully active (based on NADIA findings).

Therefore, avoid switching to TLD alone after second-line ATV/r or LPV/r regimen failure if there is DRV cross-resistance reported on the resistance test. If DRV is reported as potential low level, low level or intermediate on this resistance test (i.e. Stanford score 10-59), switch to TLD plus DRV/r 600/100mg twice daily to provide a more robust regimen, because there is no fully active regimen with DRV available if the third-line regimen fails. Due to the higher pill burden with this DRV-based regimen, it is important to monitor adherence closely and address problems early.

The overarching rationale is that if there is not full susceptibility to DRV then DRV cannot be relied upon to ensure a "rescue" regimen for the minority of treatment-experienced patients who develop DTG resistance on TLD and therefore it should rather be used earlier in a regimen with TLD to provide a more robust regimen and prevent DTG resistance.

If patients in this scenario cannot take TDF (renal impairment or prior TDF nephrotoxicity) the regimen needs to be individualised.

4. Darunavir/ritonavir dosing chart

DRV/r is not recommended in children <3 years of age OR <10 kg.

Formulations available:

Darunavir (DRV):

1. 75 mg, 150 mg, 600 mg tablets (if not able to swallow whole, may be crushed or chewed).
2. FDC DRV/r 400/50 mg tablet must be swallowed whole.

Ritonavir (RTV):

1. Oral powder: 100 mg/packet (each 100 mg packet of RTV powder should be mixed with a small amount of water if administering the whole packet (100 mg), or 10 ml water if not administering the whole packet and administer the appropriate dose as per Table below or soft food and immediately ingested).
2. Tablets: 100 mg (must be swallowed whole, not crushed, or divided or chewed).

Weight band (kg)	Dose of DRV / RTV once daily with food	Dose of DRV / RTV twice daily with food	Weight band (kg)
14-29.9	1 x 600 mg DRV tab (OR 4 x 150 mg DRV tabs) + RTV 100 mg (1 x 100 mg oral powder (1 packet) OR 1 x 100 mg tab if able to swallow whole tab)	3 x 150 mg DRV tabs + RTV 100 mg (1 x 100 mg oral powder (1 packet) OR 1 x 100 mg tab if able to swallow whole tab)	14-29.9
≥30	2 x 400/50 mg DRV/RTV tabs (must swallow whole tab)	1 x 600 mg DRV tab + RTV 100 mg (1 x 100 mg oral powder (1 packet) OR 1 x 100 mg tab if able to swallow whole tab)	≥30

5. Acronyms

3TC	Lamivudine
ABC	Abacavir
ADReC	ARV Drug Resistance Committee (*previously TLART Committee*)
AL	*Combination tablet:* abacavir, lamivudine
ALD	*Combination tablet*: abacavir, lamivudine, dolutegravir
ARV	Antiretroviral
ATV	Atorvastatin
DR	Drug resistance
DRV	Darunavir
DTG	Dolutegravir
eGFR	Estimated glomerular filtration rate
FTAF or TAF/FTC	*Combination tablet*: emtricitabine, tenofovir alafenamide
INSTI	Integrase strand transfer inhibitor
LPV	Lopinavir
PI	Protease inhibitor
RTV or r	Ritonavir
TAF	Tenofovir alafenamide
TAFED	*Combination tablet*: tenofovir alafenamide, emtricitabine and dolutegravir
TAFLD	*Combination tablet*: tenofovir alafenamide, lamivudine, dolutegravir
TDF	Tenofovir disoproxil fumarate
TE	*Combination tablet*: Tenofovir disoproxil fumarate, emtricitabine
TLART	Third line antiretroviral therapy
TLD	*Combination tablet:* Tenofovir disoproxil fumarate, lamivudine, dolutegravir
VL	Viral load

6. References

Matthews GV, o. b. (2024). D2EFT: A randomised trial to compare dolutegravir plus boosted darunavir versus recommended standard of care antiretroviral regimens in people living with HIV-1 whose recommended first-line non-nucleoside reverse transcriptase inhibitor therapy has failed. *Lancet HIV*, 11(7): e436-e448.

Mulenga, L. F. (2022). Dolutegravir with recycled nRTIs is noninferior to PI-based ART: VISEND trial. *Conference on Retroviruses and Opportunistic Infections*, (pp. 12-16). Virtual.

Paton NI, M. J. (2021). Dolutegravir or darunavir in combination with zidovudine or tenofovir to treat HIV. *The New England Journal of Medicine*, 385: 330-41.

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