



GUIDANCE TO CLINICIANS EXPERIENCING TENOFOVIR AND ABACAVIR DRUG SHORTAGES

The Southern African HIV Clinicians Society has been notified by concerned clinicians and patient advocacy groups of drug stock outs of tenofovir (TDF) and abacavir (ABC) across the country. The Southern African HIV Clinicians Society would like to ensure that no HIV infected South African currently on this treatment suffers because of these stock outs.

Antiretroviral (ARV) treatment interruptions and suboptimal ARV therapy are associated with treatment failure and the development of viral resistance to available ARVs. Treatment interruptions are also associated with a number of health complications. Changing a patient back to stavudine (D4T), with its known side effects, could lead to increased rates of non-adherence and consequent treatment failure if not accompanied by careful counselling.

Tenofovir

If rationing of TDF is required at your facility, the following patients should be prioritised to receive remaining TDF stocks:

- Patients with chronic hepatitis B, as indicated by positive Hep B surface antigen. Interrupting TDF can cause life-threatening rebound hepatitis in these patients.
- Patients having previously experienced severe side-effects from d4T or AZT
- If the patient previously developed symptomatic hyperlactitaemia then d4T should not be used as this may result in life-threatening lactic acidosis.

If a patient on TDF is **virologically controlled** and there is a TDF shortage:

- The patient can be safely, in the short term, switched to d4T 30mg bd or AZT 300 mg bd
- d4T is well tolerated in the short term but prolonged use (for more than 6 months) results in high rates of mitochondrial toxicity, causing peripheral neuropathy, lipoatrophy and hyperlactataemia. In any patient on d4T for longer than 4 months who complains of nausea, vomiting and/or weight loss the diagnosis of symptomatic hyperlactataemia should be excluded with a measure of blood lactate. Peripheral neuropathy can be caused by d4T so avoid in patients with pre-existing peripheral neuropathy.
- Short term side effects of AZT include nausea, vomiting, headache, dizziness, fatigue, weakness and muscle pain. In addition, AZT can cause bone marrow suppression and may result in severe anaemia or neutropenia. This drug should not be started in patients with haemoglobin below 8 g/dl and, even if the patient has had AZT previously, Hb should be monitored after 4, 8 & 12 weeks after switching to AZT.
- It is very important to explain to the patient that both d4T and AZT are given twice daily, not once daily as with TDF.

If a patient is currently on TDF, and **NOT virologically controlled**

- Changing a single drug in these patients may fuel development of resistance. Continue TDF for 3 months - with step-up adherence counselling - and repeat the viral load after 3 months. If virally re-suppressed, and stocks still short, switch as described below. If detectable viral load start regimen 2.

In ART-naïve patients:

- Do not delay ART initiation. Instead of TDF, use d4T 30mg bd or AZT 300mg bd. counselling as to side effects should be provided and monitoring performed as per guidelines.

When TDF stocks are adequate, patients can transition immediately back to TDF from d4T or AZT if they are virologically controlled and have normal creatinine levels. Poor adherence during this disrupted period may have resulted in the emergence of drug-resistance.

Abacavir

Older children and adults on Abacavir have faced disruption due to stock-outs of the tablet formulation. The response in this situation is to dispense the paediatric syrup to replace the tablets. However, the syrup is not very palatable, particularly in the large quantities required for older children and adults. Many of these patients cannot tolerate the syrup as it causes vomiting due to its taste. As this threatens adherence, it may be preferable to switch these patients to an alternative NRTI for the short term and reserve the syrup for the younger children who require smaller, more manageable volumes.

The same principles as for TDF above should be followed:

- Patients with detectable viral load. Changing a single drug in these patients may fuel development of resistance. Continue ABC for 3 months - with step-up adherence counselling - and repeat the viral load after 3 months. In adults, be alert as to why the patient is on ABC. Is it due to previous severe side-effects such that the patient should not be re-challenged with certain other NRTIs?

Where rationing of ABC is required, the following patients should be prioritised to receive ABC:

- Children with previous lactic acidosis or peripheral neuropathy due to d4T or AZT

If a patient is currently on ABC, and **virologically controlled**, and there is an ABC shortage:

- The patient can be safely, in the short term, switched to d4T 1mg/kg bd (with close counselling as to side effects).
- Patients with current or previous lipodystrophy due to d4T may benefit from switching to AZT 240mg/m² (with close counselling as to side effects)

If a patient is currently on ABC, and **NOT virologically controlled** on more than one VL measure

- Children on an NNRTI based regimen should switch to a second line PI based regimen as per guidelines.
- Children on a PI based regimen should be discussed with an expert before switching to a second line regimen.

In ART-naïve patients:

- Do not delay ART initiation. Instead of ABC, use d4T 1mg/kg bd or AZT 240mg/m² bd. Counselling as to side effects should be provided ,

When ABC stocks are adequate, patients can transition immediately back to ABC from d4T or AZT if they are virologically controlled.