



FORUM

Approaches to tenofovir and abacavir drug shortages in South Africa: A guide for clinicians

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Shortages of the nucleoside reverse transcriptase inhibitors (NRTI) abacavir and tenofovir have been reported recently at health facilities across South Africa. The Society issued the following clinical advice to healthcare providers experiencing shortages on 29 March 2012. These recommendations are intended only as a guide to clinical therapy, based on expert consensus and best available evidence. Treatment decisions for patients should be made by their responsible clinicians, with due consideration for individual circumstances.

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Tenofovir

If rationing of tenofovir (TDF) is required at a 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 who have experienced severe side-effects from d4T or AZT previously.
- If the patient developed symptomatic hyperlactataemia previously, d4T should not be used as this may result in life-threatening lactic acidosis.

In the event of TDF shortages, and if a patient on TDF is **virologically controlled**:

- The patient can in the short term be safely switched to d4T 30 mg bd or AZT 300 mg bd.
- d4T is well tolerated in the short term, but prolonged use (>6 months) results in high rates of mitochondrial toxicity, causing peripheral neuropathy, lipoatrophy and hyperlactataemia. In any patient on d4T >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 neutropaenia. This drug

should not be started in patients with haemoglobin <8 g/dl. Even if the patient has had AZT previously, Hb should be monitored after 4, 8 and 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.
- We recommend continuing TDF for 3 months – with step-up adherence counselling – and repeat the viral load after 3 months. If the patient becomes virally suppressed, and TDF stocks are still limited, switch TDF as described above. However, if the viral load remains detectable, switch to regimen 2.

In ART-naïve patients, do not delay ART initiation. Instead of TDF, use d4T 30 mg bd or AZT 300 mg 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 might have resulted in the emergence of drug-resistance.

Abacavir

Older children and adults on abacavir (ABC) have faced disruption owing 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 owing 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 described for TDF above should be followed.

If rationing of ABC is required at a facility, children with previous lactic acidosis or peripheral neuropathy owing to d4T or AZT should be prioritised to receive remaining ABC stocks.

In the event of ABC shortages, and if a patient on ABC is **virologically controlled**:

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

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

- Changing a single drug in these patients may fuel development of resistance. We recommend continue ABC for 3 months –

with step-up adherence counselling – and repeat the viral load after 3 months. If the patient becomes virally suppressed, and ABC stocks are still limited, switch ABC as described above. However, if the viral load remains detectable, switch to regimen 2.

- 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 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?

In ART-naïve patients, do not delay ART initiation. Instead of ABC, use d4T 1 mg/kg twice daily or AZT 240 mg/m² twice daily, with counselling on side-effects.

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

