SOUTHERN AFRICAN HIV CLINICIANS SOCIETY

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Recommended management during lopinavir/ritonavir (Aluvia) stockout

If your facility is experiencing a lopinavir/ritonavir stock out then please follow this guidance.

NB: Report stockouts to the Stop Stockouts Project on 084 855 7867 (SMS, Please Call Me, WhatsApp) or report@stockouts.co.za. This can be done anonymously and is critical for both developing an understanding of the scale of the problem and resolving it.

ALTERNATIVE DRUG REGIMENS

Review patient file to **clarify reason patient is on lopinavir/ritonavir:**

1. If patient was on first-line ART, and was switched to lopinavir/ritonavir due to NNRTI side effect and has NOT experienced previous virological failure on first line, then consider an alternative first-line regimen. It is preferable not to re-challenge the drug that caused the previous side effect, but it may be the case that an alternative drug has been added to guidelines and can be used - this will depend on the reason for switching. (An example: efavirenz was avoided previously because female patients had reproductive intentions; patient developed nevirapine rash and was switched to lopinavir/ritonavir; it has subsequently been established that efavirenz can be used in women with reproductive intentions).

Remember: virological failure = at least 2 viral loads, at least 2 months apart, of more than 1000 copies/mL

2. If patient is on lopinavir/ritonavir due to confirmed VIROLOGICAL FAILURE on first-line ART previously:
    a. Switch to an alternative boosted PI: atazanavir/ritonavir or darunavir/ritonavir (if available). This is preferable, however these drugs cannot be used with rifampicin.
    b. If the above is not available, provide them with a TRIPLE NRTI REGIMEN (if available) e.g. ABC/AZT/3TC or d4T/3TC/TDF or AZT/TDF/3TC. Ensure that a triple NRTI regimen is used for as short a time as possible. Try to access a boosted-PI regimen for the patients as soon as possible.
    c. While there is little to no evidence to support this, if the above is not available, 3TC monotherapy can act as a “holding” regimen. The M184V mutation which is associated with 3TC resistance cripples, or weakens, the virus so that its replicative ability is reduced. However, this option must be used with great caution and seen as a last resort if no other medicines are available; and only until the shortage is resolved. Then lopinavir/ritonavir and the second NRTI can be restarted together once the stock out is resolved.

Rationale for this approach:

- Patients who have failed first-line therapy very likely already have existing NRTI resistance.
- Providing these patients with dual NRTI therapy, without boosted PI cover or returning them to first-line therapy, will likely result in further accumulation of NRTI resistance mutations.
- A triple NRTI regimen, for a short period of time, might remain effective and maintain viral suppression. However, when making a choice of regimen, try to avoid creating more stockouts for other patients (e.g. of abacavir). Keep the duration of this regimen as short as possible as it may also result in further NRTI mutations accumulating.

Monitoring affected patients

- In patients who are switched to an alternative first-line regimen because they have no prior history of virological failure:
    - Check viral load THREE MONTHS after switch
    - If virally suppressed, continue with new first-line regimen (e.g. FDC of TDF/FTC/EFV) and repeat viral load at 1 year on new regimen
- In patients who are switched to an alternative boosted PI:
    - Monitor bloods as per guidelines for the new PI
    - Check viral load after 3 months
- In patients who are placed on a triple NRTI regimen
    - Monitor as per guidelines for the new NRTI which is introduced
    - Monitor viral load after 3 months if still on triple NRTI
    - Monitor viral load 3 months after Lopinavir/Ritonavir based regimen re-established

Restarting lopinavir/ritonavir and second NRTI once stock out is resolved

- Re-introducing lopinavir/ritonavir after the interruption should not be problematic
- Some patients may experience a recurrence of side effects, including diarrhoea and nausea
- If necessary, provide with symptomatic relief e.g. loperamide
- Counsel and reassure patient that, with good adherence, side effects should settle relatively quickly
- For those on triple NRTI regimen, switch back to lopinavir/ritonavir and 2 NRTIs, as per previous second-line regimen, once stock is available

Adherence and prevention messaging during stock out

- Please take time to explain the situation to the patient
- Reassure them that the optimal approach is being taken to manage them during the stockout
- Explain that maintaining high level adherence to their new regimen is crucially important
- Because their viral load may not remain undetectable, emphasise the importance of consistent condom use with any sexual partner(s)
- If possible, depending on number of patients affected at the facility, keep a register of those who are awaiting lopinavir/ritonavir availability so they can be contacted as soon as stock returns to the facility to be re-established on optimum treatment

- A register of affected patients may also help to ensure that these patients receive the requisite viral load monitoring to assess emergence of second-line drug resistance by flagging them for additional viral load 3 months after being re-established on lopinavir/ritonavir and 2 NRTIs

NRTIs (Nucleoside Reverse Transcriptase Inhibitors)

- Lamivudine (3TC)
- Tenofovir (TDF)
- Stavudine (D4T)
- Zidovudine (AZT)
- Abacavir (ABC)
- Emtricitabine (FTC)