THIRD LINE REGIMENS
(ADULTS AND CHILDREN)

Access to third line ART will be managed centrally by the National Department of Health.

There is no empiric third line regimen. Consideration of the appropriate regimen will be determined by genotypic resistance tests. However, resistance tests are expensive and studies show that most patients failing ritonavir-boosted protease inhibitors (PIs) do not have PI resistance mutations. Therefore resistance tests will only be offered to patients with good adherence assessed objectively.

Adherence

Treatment failure while on a second line PI regimen is often due to non-adherence. The primary care site often has the best grasp of the circumstances around the patient's adherence, and is usually best placed to intervene. Doctors and nurses should participate directly in these adherence assessments, and not delegate the assessment to the adherence counsellor alone.

The following can be used to improve adherence:

- daily schedules with respect to medication administration,
- assessment of tolerance to medication and whether refusal, spitting out or vomiting of medications is experienced and incorporation of strategies to improve tolerance (e.g. sequencing of medication, coating mouth with sweet food, etc),
- return of leftover medication at clinic visits and pill counts, where possible, to assess adherence.
- medication ingestion is directly observed by a treatment partner or the responsible caregiver in the case of children.

Where possible, institute an objective evaluation of adherence (e.g. MEMS cap).

If the VL is detectable subsequently on a PI regimen, and all adherence interventions have failed, refer patient to a designated specialist site while still taking the regimen.

Treatment failure

Treatment failure is indicated by virological non-suppression with or without immunologic and/or clinical deterioration.

<u>Children</u>

- NNRTI regimen: Two consecutive viral load measurements >1 000 copies/mL (log 3) usually 8–12 weeks apart.
- PI regimen: Two consecutive viral load measurements 30 000 copies/mL (log 3.7) usually 8–12 weeks apart.
- Previous unboosted PI regimen (e.g. full-dose ritonavir): Two consecutive viral load measurements >1 000 copies/mL (log 3) usually 8–12 weeks apart.

<u>Adult</u>

- Two consecutive viral load measurements > 1 000 copies/mL (log 3) usually 3 months apart.
- First viral load measurement done at least 6 months after switching to PI.
- Repeat VL test after 3 months of good adherence.

Genotype resistance testing
Resistance testing is recommended if good adherence has been verified objectively (see below) **and** the patient has been on PIs for at least a year. In the case of children on NNRTIs, resistance testing can be done after confirmed failure.

The genotype result cannot meaningfully be interpreted in isolation from the past medicine exposure history.

Clinicians should maintain their patients on their current antiretroviral therapy as resistance testing must be performed whilst the patient is taking the antiretroviral therapy regimen they are failing (otherwise the virus reverts to wild type in the absence of the selection pressure of antiretroviral drugs and resistant mutations may not be detected).

Indications for resistance testing

- Good adherence (80% or more of doses correctly taken) for at least 3 months has been measured OBJECTIVELY with one of the following tests:
    - Electronic medication monitoring devices
    - Pharmacy refills
    - Hair PI concentrations
- All newly diagnosed infants whose mothers failed ART during pregnancy or breastfeeding.
- All patients with documented virologic failure on a PI regimen who have previously been treated with an unboosted PI like nelfinavir or full dose ritonavir.
- All patients failing a LPV/r regimen who received TB treatment while on LPV/r without appropriate dose adjustment having been done (double dose LPV/r for adults and “super-boosted” LPV/r plus ritonavir in children).
- All adult patients failing 2nd line regimens for more than 12 months

Motivation form
All third line drugs should be appropriately motivated by a senior consultant with antiretroviral expertise.

Clinicians comprehensively complete the standard motivation form. (Request for Third Line ART).

Medicine exposure history: The genotype result cannot meaningfully be interpreted in isolation from the past medicine exposure history. It is vital that clinicians accurately complete this section in order to optimise the recommendations of the committees.

Submit completed forms to:

The Secretariat: Third Line ARV Peer Review Committee (PRC)
jamalk@health.gov.za