The responsible use of a critical and threatened health resource we depend on to prevent and treat infectious disease.

Why is it needed?
Rising resistance rates
Limited manufacturing pipeline of new agents
Morbidity burden and large costs associated with improperly treated disease

Conserve what we have
ANTIMICROBIAL STEWARDSHIP

Implies:
• appropriate clinical decision-making for individual patients

• a population perspective that maximises overall benefits, minimises adverse events and costs

Delays the onset of widespread resistance to commonly used agents.
• Specialist intervention
• Formulary restriction
• Pre-authorisation
• Guidelines (indication, dose, duration)
THIRD LINE PROGRAMME

Third line ARV peer review committee (PRC)

Protocol

Motivation form

Recommendation

Standard operating procedures

First public sector third line ART access programme in the world.
Clinicians with expertise in resistance
- Adult group
- Paediatric group

**Terms of reference includes:**
- The development of a standard protocol for third line ART for adults and paediatrics.
- Make recommendations pertaining to placing of individual patients on third line regimens based on specific criteria in the standard protocol, i.e. resistance testing, adherence, etc.

**Screening**
- Administrative, assign a number
- Sent to Committee for consideration

**Decision making**
- Consensus after the evidence is considered and other relevant issues are taken into account.
**Adherence**
Treatment failure while on a second line PI regimen often due to non-adherence.

80% or more of doses correctly taken for at least 3 months has been measured **objectively**.

**Adherence improvement**
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**.
PROTOCOL

Genotype resistance test

• Expensive
• Recommended if good adherence has been verified objectively and the patient has been on PIs for at least a year.
• Children on NNRTIs - resistance testing done after confirmed failure.

Maintain patient on current antiretroviral therapy - resistance testing must be performed whilst the patient is taking the antiretroviral therapy regimen they are failing
Indications for resistance testing

• 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.

• All patients failing a LPV/r regimen who received TB treatment while on LPV/r without appropriate dose adjustment
  • (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

## REQUEST FOR THIRD-LINE ANTIRETROVIRAL THERAPY

### PATIENT DETAILS

<table>
<thead>
<tr>
<th>Patient First Name</th>
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<tbody>
<tr>
<td>Patient Surname</td>
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<tr>
<td>Date of Birth</td>
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<tr>
<td>[Day/Month/Year]</td>
<td></td>
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<tr>
<td>Identity Number</td>
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<td>Patient Number</td>
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<td>Gender</td>
<td>M/F</td>
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<tr>
<td>Weight</td>
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<tr>
<td>BMI (kg/m²)</td>
<td></td>
</tr>
<tr>
<td>Height (child)</td>
<td></td>
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</tbody>
</table>

### FACILITY DETAILS

| Facility Name |  |
| Doctor in Charge of Patient |  |
| Authorised Prescriber |  |
| Doctor’s Contact Number |  |
| Doctor’s Email Address |  |
| Signature of Authorised Prescriber |  |
| Date |  |

### Past Medication History

<table>
<thead>
<tr>
<th>Date Started</th>
<th>Regimen</th>
<th>Reason for Discontinuation</th>
<th>Concurrent TB Therapy</th>
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<tbody>
<tr>
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[Logo of Health Department: Republic of South Africa]
REGIMEN

No empiric third line regimen

Determined by genotypic resistance tests

If PI resistance mutations present
• darunavir-ritonavir

and depending on resistance profile
• raltegravir and etravirine
Recommendation sent to:

- Doctor in charge of patient
- Heads of Pharmaceutical Services
- Provincial HAST Manager / Medicine monitor
- Depot Manager
# STANDARD OPERATING PROCEDURE

<table>
<thead>
<tr>
<th>SOP Number</th>
<th>Revision NO:</th>
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<tbody>
<tr>
<td><strong>SOP Title</strong></td>
<td><strong>3rd Line Therapy Orders</strong></td>
</tr>
<tr>
<td>Institution</td>
<td>National Department of Health</td>
</tr>
<tr>
<td>Issue Date</td>
<td>February 2014</td>
</tr>
<tr>
<td>Effective date</td>
<td>February 2014</td>
</tr>
<tr>
<td>Number of pages including cover</td>
<td></td>
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<tr>
<td>Original author of the SOP</td>
<td>Central Procurement Unit</td>
</tr>
<tr>
<td>Issued by</td>
<td>NDoH: Affordable Medicines Directorate</td>
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Process Flow:

3rd Line ARV Treatment

Facility

Submit request on motivation forms

Inform

Provincial Office/Depot

Submit

Not Approved

Depot

ODV Order

Not Approved

NDoH: AMD

PRC reviews

Approved

Release Authorization

3rd Line Register

Supplier

Copy of Auth

Dispense

Issue Data
CHALLENGES

- Incomplete forms
- Scanned forms too large
- Resistance test – Stanford
- Resistance test done while patient was not on treatment
- Timelines
- Protocol not adhered to
- Supply issues
SUCCESSES

• Patients appropriately placed on treatment
  o Children
  o Adults

• Research (patient characteristics, resistance patterns, regimens used and response to therapy)

• Educational opportunities, dialogue

• Guideline development
Acknowledgements

• Prof Mendelson
• Third Line ARV Peer Review Committee
Questions?