Guide for the Healthcare Provider on Prescribing and Teaching the Caregiver to Administer RALTEGRAVIR (RAL) Granules as Suspension to an Infant

These training materials were developed with technical and financial assistance from EGPAF
RALTEGRAVIR (RAL) is a medicine to treat HIV infection. Correct dosing and administration of RAL along with other HIV medications is essential to achieve a good treatment outcome and to prevent the development of resistance!

**What is RAL?**
- RAL is an antiretroviral medicine that belongs to the same class of medications called integrase inhibitors as DOLUTEGRAVIR (DTG).
- **RAL granules are always administered in combination with two other HIV medications.**
  - The two other HIV medications most frequently prescribed to neonates and infants are either liquid or dispersable tablet formulations of ZIDOVUDINE (AZT) or ABACAVIR (ABC) plus LAMIVUDINE (3TC) (Table 1).
  
- The dosing of all HIV medications depends on the weight band of the neonate/infant (Table 2).
- Access to **clean drinking water** is essential for preparing RAL suspension from granules and needs to be addressed with the caregiver.

**Who is eligible to get RAL?**
- RAL is prescribed to neonates/infants with confirmed HIV infection.
- RAL granules are appropriate for neonates (0 to 4 weeks of age) who:
  - Weigh >2 kgs at birth **AND** have a gestational age of >37 weeks

**IMPORTANT:** A neonate/infant diagnosed with HIV after 2 weeks of age should be started on Lopinavir/Ritonavir (LPV/r) granule based regimen and this regimen can be used immediately without starting treatment with RAL. Seek specialist advice for HIV infected infants who do not meet eligibility criteria

**RAL dosing**
- When started within the first week of life, RAL is dosed once daily according to the weight band.
  
- The neonate’s capacity to break down RAL rapidly changes after birth, therefore it is necessary to increase RAL dose on **day 8 of life: the dose increases two fold and it also changes from once to twice daily.**
  
- The maximum dose of oral RAL suspension is 10 mL (RAL 100 mg) twice daily.
- RAL can be given before or after the neonate/infant feeds!
Table 1: Current recommended Zimbabwe pediatric optimal first line ART regimens

<table>
<thead>
<tr>
<th></th>
<th>Neonates (0≤ 4 weeks of age)</th>
<th>Infants/Children (4 weeks of age or older)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preferred</strong></td>
<td>AZT + 3TC + RAL</td>
<td>ABC + 3TC + DTG*</td>
</tr>
<tr>
<td><strong>Alternative</strong></td>
<td>AZT + 3TC + NVP</td>
<td>ABC + 3TC + LPV/r</td>
</tr>
</tbody>
</table>
| **Special circumstances** | AZT + 3TC + LPV/r**   | ABC + 3TC + LPV/r  
|                    |                             | AZT + 3TC + LPV/r  |

* Applies to children for whom approved DTG dosing is available

** For neonates ≥ or older than 2 weeks of age
Table 2: Dosing of Zidovudine (AZT), Lamivudine (3TC) suspensions or combination tablet and Raltegravir (RAL) suspension for infants <4 weeks of age by weight band

<table>
<thead>
<tr>
<th>Drug</th>
<th>Strength of oral liquid or tablet</th>
<th>2-3 kg</th>
<th>3-4 kg</th>
<th>4-5 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>AM</td>
<td>PM</td>
<td>AM</td>
</tr>
<tr>
<td>AZT</td>
<td>10 mg/mL</td>
<td>1 mL</td>
<td>1 mL</td>
<td>1.5 mL</td>
</tr>
<tr>
<td>3TC</td>
<td>10 mg/mL</td>
<td>0.5 mL</td>
<td>0.5 mL</td>
<td>0.8 mL</td>
</tr>
<tr>
<td>AZT/3TC</td>
<td>60/30 mg tablet (dispersible)</td>
<td>-</td>
<td>-</td>
<td>1 tablet</td>
</tr>
<tr>
<td>RAL &lt;1 week of age*</td>
<td>10 mg/mL (Oral granules for suspension: 100 mg/sachet)</td>
<td>0.4 mL once daily</td>
<td>0.5 mL once daily</td>
<td>0.7 mL once daily</td>
</tr>
<tr>
<td>RAL &gt;1 week of age*</td>
<td>10 mg/mL (Oral granules for suspension: 100 mg/sachet)</td>
<td>0.8 mL</td>
<td>0.8 mL</td>
<td>1 mL</td>
</tr>
</tbody>
</table>

*RAL granules for oral suspension should be used in neonates of at least 2 kg and be administered in once a day during the first week of life and twice a day starting at day 8 of life.
Handling RAL granules

- RAL granules come as a kit that includes mixing cups, oral dosing syringes, and 60 foil packets.
- Each foil packet is single-use and contains 100 mg of RAL, which will need to be mixed in 10 mL of water for a final concentration of RAL 10 mg/mL.
- One foil packet is also the maximal dose of RAL.
- RAL granules should always be stored unopened in the original container at room temperature, in a cool dry place away from direct sunlight.

The success of HIV treatment of the baby taking RAL depends on how well we teach the caregiver to prepare and give the RAL!

Preparing to teach the caregiver to administer RAL

- Take time to review instructions in detail and practice during the training by yourself or with the assistance of an experienced colleague.
- Even if you feel that you are an experienced provider, consider practicing at least a couple of times before providing instructions and hands on training to others.
- When teaching the caregiver about RAL granule administration, secure protected time and identify a reliable caregiver to teach. If there are more caregivers involved, help the family select the one who is going to be primarily responsible and focus your effort on this caregiver.
- Check the expiration date on the box before dispensing it to the caregiver.
Teaching the caregiver to administer RAL

• Make sure the caregiver understands the importance of using clean drinking water for mixing RAL for the infant in care. Give clear instructions to the caregiver on how to boil and cool water before mixing it with RAL.

• Review the instructions with the caregiver before the RAL kit is dispensed. Make sure to explain in a simple clear manner. Make sure you answer all the caregiver’s questions and address all concerns.

• Ideally, you should observe the caregiver repeat each step using dummy drug when available, or package of sugar for training, or one actual drug packet.

• Make sure to use the actual mixing cup and syringe the caregiver will be given to use at home. An additional set of mixing cups and syringes will be contained in the kit.

• It might take the caregiver more than one attempt to perform all steps correctly!

• You should also observe the caregiver administering the first dose of the drug to the child.

• Praise the caregiver for each step completed correctly. Provide corrective feedback if mistakes are made.

• Once the caregiver has performed all steps in drug mixing and preparations from instructions, confirm his/her willingness and comfort repeating it at home every day first once a day then twice daily after the age of one week.

• Emphasize the need for a dose increase on **day 8 of life** and make plans for follow up of dose adjustment at day 7 postnatal visit.

• Where possible, caregivers will also be supported by a home visit by a community health worker or mentor mother on day 8 of life. Dosing of RAL will be reviewed by a health worker during the opportunistic infection (OI) clinic review on day 14 of life when the child’s weight will be checked.

• Provide the caregiver with a telephone contact to reach out to in case of any problems with the medicine or the infant on treatment.

• Make sure the caregiver has two other HIV medicines (AZT and 3TC) and separate dosing syringes as needed for them if given as liquids to take home.

• It is important to help caregiver to develop realistic daily schedule that fits the lifestyle. Discuss with the caregiver the time windows during which the doses will be administered to the baby. For example, you might agree with caregiver that morning (am) dose will be given between 6 and 8 am each day and evening (pm) dose will be given between 6 and 8 pm window each evening.
Kit contents

- Prescription (on box)
- 60x packets of ISENTRESS
- 2x Mixing Cups
- 2 blue (10mL) syringes
- 2 green (3mL) syringes
- 2 white (1mL) syringes

Steps to administer RAL

1. Fill the blue syringe with 10mL clean water and eliminate any air bubbles.
2. Fill the mixing cup with 10 mL of clean water.
3. Add the whole content of the RAL packet and swirl for approx. 45 sec, do not shake.
4. Choose the syringe you need in light of the child dosage and measure the correct quantity. **Blue** (10 mL) for 3.5 mL to 10 mL. **Green** (3 mL) for 1.5 mL to 3 mL. **White** (1 mL) for 1 mL or less.
5. Give RAL to your baby.

Photos: Steven Chikosi/EGPAF, 2020
Following up with the caregiver on dosing and administering RAL

- When infant is started on RAL within first week of life, the dosing of RAL must be increased and switched to twice daily at **day 8 of life**.

- During Day 7 postnatal review remind the caregiver about the dose change and demonstrate dispensing the new dose in the syringe. When feasible, observe the caregiver prepare and administer the dose to the child. Do not forget to emphasize the change from once daily to twice-daily administration of RAL.

- During the Day 7 postnatal visit ask the caregiver about any issues they have encountered during preparation and administration of RAL to the child.

- Praise caregiver for the job well done and do not hesitate repeating instructions at each encounter! When errors are discovered, address the challenges and repeat the training!

- If in-home follow up is available (e.g. home visit by a community health worker or mentor mother), utilize it to verify the correct handling and dosing of RAL and other HIV medications at home.

Special circumstances

- It is very important to prepare the caregiver to handle the special circumstances when administering RAL and other drugs to child.

- Instruct caregiver how to handle the dosing if child vomits the dose, misses the dose or has adverse events. (See caregiver instructions).

Changing to Lopinavir/ritonavir (Lpv/r) granules

- At 4 weeks of age, make sure the caregiver and infant returns to the clinic.

- At this time, explain to the caregiver that you will be switching the treatment for the child from the RAL granules to the Lopinavir/ritonavir (Lpv/r) granules.

- Ask caregiver to return any remaining RAL granules to the health facility at the 4 week review visit.

- Please see separate guidance on the administration of LPV/r granules for more information.
## Appendix

**Dosing on Antiretroviral Drugs**

Dosing of Zidovudine (AZT), Abacavir (ABC), Lamivudine (3TC) suspensions or tablets, Lopinavir/Ritovari (LPV/r) granules and Raltegravir (RAL) suspension for infants ≥4 weeks of age by weight band

| Drug       | Strength of tablets, granules or oral suspension | Number of tablets or milliliters by weight-band morning (AM) and evening (PM) | 3–5.9 kg | 6–9.9 kg | 10–13.9 kg | 14–19.9 kg | 20–24.9 kg |
|------------|---------------------------------------------------|--------------------------------------------------------------------------------|---------|---------|---------|---------|---------|---------|
|            |                                                   |                                                                                  | AM      | PM      | AM      | PM      | AM      | PM      | AM      | PM      |
| **Oral suspension/granules** |                                                   |                                                                                  |         |         |         |         |         |         |         |         |
| AZT        | 10 mg/ml                                          |                                                                                  | 6 ml    | 6 ml    | 9 ml    | 9 ml    | 12 ml   | 12 ml   | -       | -       |
| ABC        | 20 mg/ml                                          |                                                                                  | 3 mL    | 3 mL    | 4 mL    | 4 mL    | 6 mL    | 6 mL    | -       | -       |
| 3TC        | 10 mg/ml                                          |                                                                                  | 3 mL    | 3 mL    | 4 mL    | 4 mL    | 6 mL    | 6 mL    | -       | -       |
| LPV/r      | Granules sachet 40/10                             |                                                                                  | 2       | 2       | 3       | 3       | 4       | 4       | 5       | 5       |
| RAL        | 10 mg/mL Oral granules for suspension 100 mg/sachet|                                                                                  | 3 mL    | 3 mL    | 5 mL    | 5 mL    | 8 mL    | 8 mL    | 10 mL   | 10 mL   |
| **Tablet** |                                                   |                                                                                  |         |         |         |         |         |         |         |         |
| AZT        | Tablet (dispersible) 60 mg                         |                                                                                  | 1       | 1       | 1.5     | 1.5     | 2       | 2       | 2.5     | 2.5     |
| ABC        | Tablet (dispersible) 60 mg                         |                                                                                  | 1       | 1       | 1.5     | 1.5     | 2       | 2       | 2.5     | 2.5     |
| AZT/3TC    | Tablet (dispersible) 60/30 mg                      |                                                                                  | 1       | 1       | 1.5     | 1.5     | 2       | 2       | 2.5     | 2.5     |
| ABC/3TC    | Tablet (dispersible) 60/30 mg                      |                                                                                  | 1       | 1       | 1.5     | 1.5     | 2       | 2       | 2.5     | 2.5     |
| ABC/3TC    | Tablet (dispersible) 120/60 mg                     |                                                                                  | 0.5     | 0.5     | 0.5     | 1       | 1       | 1       | 1       | 1.5     |
| LPV/r      | Tablet (coated) 100/25 mg                          |                                                                                  | -       | -       | -       | -       | 2       | 1       | 2       | 2       |
| DTG        | Tablet (coated) 50 mg                              |                                                                                  | -       | -       | -       | -       | -       | -       | -       | -       |

Notes: AM = morning, PM = evening, once daily.
Guide for the Healthcare Provider on Prescribing and Teaching the Caregiver to Administer Raltegravir (RAL) Granules as Suspension to an Infant