Photo: Eric Bond/EGPAF, 2018

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

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Fighting for an AIDS-free generation

The Faith-Based Action for Scaling Up Testing and Treatment for Epidemic Response project, or FASTER, aims to mobilize government, civil society and faith-based organizations to achieve targets for finding, linking and retaining children and adolescents in HIV care. Through the U.S. President's Emergency Plan for AIDS Relief, or PEPFAR, the Centers for Disease Control and Prevention is funding Catholic Relief Services with the Elizabeth Glaser Pediatric AIDS Foundation to catalyze the HIV response for children and youth in Zimbabwe.

RALTEGRAVIR (RAL) is a medicine used 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 dispersible tablet formulations of ZIDOVUDINE (AZT) **or** ABACAVIR (ABC) **plus** LAMIVUDINE (3TC) (Table 1).
- The dosing of all RAL medications depends on the weight AND age of the 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 on RAL should be transition to pediatric DTG (pDTG) when they have reached 4 weeks of age. Infants diagnosed with HIV at 4 weeks of age or after should be started directly on pDTG (not RAL).

RAL dosing

- When started within the first week of life, RAL is dosed once daily according to the infant's weight band.
- The neonate's capacity to break down RAL rapidly changes after birth; therefore, it is necessary to increase the RAL dose on **Day 8 of life**, at which time the dose **doubles** and is increased from once daily 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

	Neonates (0-≤ 4 weeks of age)	Infants/Children (4 weeks of age or older)
Preferred	AZT + 3TC + RAL	ABC + 3TC + pDTG*
Alternative	AZT + 3TC + NVP	ABC + 3TC + LPV/r
Special circumstances	AZT + 3TC + LPV/r**	ABC + 3TC + EFV AZT + 3TC + LPV/r

* pDTG 10mg dispersible tablets available for infants ≥ 4 weeks of age and ≥ 3kg

** For neonates ≥ 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

Drug	Strength of oral liquid or tablet	2-3 kg		3-4 kg		4-5 kg	
		AM	PM	AM	PM	AM	PM
AZT	10 mg/mL	1 mL	1 mL	1.5 mL	1.5 mL	2 mL	2 mL
3TC	10 mg/mL	0.5 mL	0.5 mL	0.8 mL	0.8 mL	1 mL	1 mL
AZT/3TC	60/30 mg tablet (dispersible)	-	-	1 tablet	1 tablet	1 tablet	1 tablet
RAL <1 week of age*	10 mg/mL (Oral granules for suspension: 100 mg/sachet)[C]	0.4 mL once daily		0.5 mL once daily		0.7 mL once daily	
RAL >1 week of age*	10 mg/mL (Oral granules for suspension: 100 mg/sachet)[C]	0.8 mL	0.8 mL	1 mL	1 mL	1.5 mL	1.5 mL

*RAL granules for oral suspension should be used in neonates of at least 2 kg and be administered once daily during the first week of life and twice daily 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 clean 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 for 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

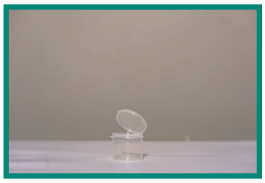
- Take time to review instructions in detail and practice during the training by yourself or with the assistance of an experienced colleague.
- Even if you feel that you are an experienced provider, consider practicing at least a couple of times before providing instructions and hands-on training to others.
- When teaching the caregiver about RAL granule preparation and 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. Do not mix RAL with breastmilk. Give clear instructions to the caregiver on how to boil and cool water before mixing it with RAL granules. If available, the caregiver can use bottled water.
- Review the instructions with the caregiver before the RAL kit is dispensed. Be sure to explain in a simple, clear manner and address all of the caregiver's questions and concerns.
- Ideally, you should observe the caregiver repeat each step using dummy drug when available, package of sugar for training, or one of the actual medicine packets.
- Make sure to use the actual mixing cup and syringes the caregiver will be given to use at home. The HCW can mark the dose on the syringe for the caregiver. 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 medicine to the infant.
- Praise the caregiver for each step completed correctly. Provide corrective feedback if mistakes are made.
- Once the caregiver has performed all of the steps in drug mixing and preparations from the instructions, confirm their willingness and comfort repeating it at home every day--first once a day, and then twice daily starting on day 8 of life.
- Emphasize the need for a dose increase on day eight of life and make plans to follow up on dose adjustment at the day seven postnatal visit
- When possible, caregivers will also be supported by a home visit by a community health worker or mentor mother on day eight 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 use 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 the caregiver develop a realistic daily schedule that fits their lifestyle; therefore, discuss the time windows in which the doses will be administered to the baby. For example, you might agree with the caregiver that the morning (a.m.) dose will be given between 6:00 a.m. and 8:00 a.m. each day, and the evening (p.m.) dose will be given between a 6:00 p.m. and 8:00 p.m. window each evening.

Kit contents

Prescription (on box)



2x Mixing Cups

60x packets of ISENTRESS

2 **blue** (10mL) syringes

2 **green** (3mL) syringes

2 **white** (1mL) syringes

Steps to administer RAL

Fill the **blue** syringe with 10mL clean water and eliminate any air bubbles

Fill the mixing cup with 10 mL of clean water

Add the whole content of the RAL packet and swirl for approx. 45 sec, do not shake.

Choose the syringe you need per the child's 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.

Give RAL to your baby.

Photos: Steven Chikosi/EGPAF, 2020

Following up with the caregiver on dosing and administering RAL

- When the infant is started on RAL within first week of life, the dosing of RAL must be increased and switched to twice daily at **day eight of life.**
- During day seven 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 seven postnatal visit, ask the caregiver about any issues they have encountered during preparation and administration of RAL to the child.
- Praise the caregiver for a 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 dosing if the child vomites the dose, misses the dose, or has adverse events when administering RAL and/or other medicines to the child (see caregiver instructions.)

Changing to pediatric dolutegravir (pDTG)

- At four weeks of age (on Day 28 of life), make sure the caregiver and infant return to the clinic.
- At this time, explain to the caregiver that you will be switching the treatment for the baby from the RAL granules to pediatric dolutegravir 10 mg (pDTG) dispersible tablets.
- The backbone ART medicine will also change from zidovudine/lamivudine (AZT/3TC) to abacavir/lamivudine (ABC/3TC).
- Ask caregiver to return any remaining RAL granules to the health facility at the four week review visit.
- Please see separate guidance on the administration of pDTG granules for more information.

Appendix: Dosing of Antiretroviral Drugs

Dosing of Zidovudine (AZT), Abacavir (ABC), Lamivudine (3TC) suspensions or tablets, Lopinavir/Ritonavir (LPV/r) granules, dolutegravir (DTG) dispersible tablets, and Raltegravir (RAL) suspension for infants ≥4 weeks old 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	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	3	3
ABC	Tablet (dispersible) 60 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3
AZT/3TC	Tablet (dispersible) 60/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3
ABC/3TC	Tablet (dispersible) 60/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	6 (once daily)	
ABC/3TC	Tablet (dispersible) 120/60 mg	0.5	0.5	0.5	1	1	1	1	1.5	3 (once daily)	
LPV/r	Tablet (coated) 100/25 mg	-	-	-	-	2	1	2	2	2	2
pDTG	Tablet (dispersible) 10 mg	.5 (once daily)		1.5 (once daily)		2.0 (once daily)		2.5 (once daily)		Switch to adut formulation	
DTG	Tablet (coated) 50 mg	-	-	-	-	-	-	-	-	1 (once daily)	