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NEW FORMULATION: LOPINAVIR/ RITONAVIR (LOPIMUNE® 40/10 ORAL PELLETS) FOR USE IN CHILDREN ON ANTIRETROVIRAL TREATMENT

BACKGROUND

The lopinavir/ritonavir products on contract for paediatric use include Kaletra® 80mg/20mg/ml solution. The poor palatability of the solution affects adherence to treatment. Lopinavir/ ritonavir oral pellets are now available and recommended for children > 6 months of age who cannot tolerate the Kaletra® solution.

If a child is also on rifampicin, boosting with ritonavir is still required as per the *2019 Antiretroviral Drug Dosing Chart for Children*.

ACCESS

Lopinavir/ ritonavir oral pellets are available and must be ordered from CMD (ARV ledger).

ICN	Item Description	Cost
8706448	Lopinavir/ritonavir; 40mg/10mg capsule (oral pellets); 120's	R257.37

METHOD OF ADMINISTRATION

It is important to counsel the patient on the correct way to administer the new lopinavir/ritonavir oral pellets.

- Oral pellets come in capsules and there are 120 capsules per bottle. The pellets inside the capsule are white in colour.
- Capsules containing the oral pellets **should not be swallowed** whole, but should be administered with food as shown below.



Lopinavir/Ritonavir 40mg/10mg Oral Pellets Fact Sheet
Information for healthcare workers and caregivers



Introducing Lopinavir/ritonavir (LPV/r) Oral Pellets 40mg/10mg:
a product that is just as effective as the syrup and tablet, but in an alternative formulation

WHY ARE LPV/r ORAL PELLETS BEING INTRODUCED?:

For children on first line ARV regimens who cannot swallow tablets, the **LPV/r syrup** is the **only protease-inhibitor option**. Protease inhibitors, like lopinavir/ritonavir and atazanavir, combat HIV replication by blocking the HIV protease enzyme, thus preventing immature HIV cells from maturing and infecting CD4 cells. The **unpleasant taste** of the syrup leads to administration issues, and subsequent **pitfalls in retention in care and viral suppression**. The **improved tasting oral pellets** aim to address these issues.



INDICATIONS FOR LPV/r ORAL PELLETS:

In combination with other antiretrovirals, for the treatment of HIV in children **>6 months old** who are **not tolerating LPV/r oral solution**.

NB: Patients who can swallow tablets whole can take LPV/r (100/25mg or 200/50mg) tablets.

NOTE: LPV/r oral pellets can only be prescribed by a **doctor**.



Advantages of LPV/r oral pellets

LPV/r pellets were developed as an *alternative* for LPV/r syrups and tablets in young children because:



- ✓ The pellets are taste-masked to reduce the bitter taste
- ✓ The pellets do not require cold storage in the refrigerator. They can be stored at room temperature
- ✓ The pellets are easy to swallow
- ✓ The pellets do not contain any harmful additives

Eligibility for LPV/r oral pellets

It's important to assess the following criteria in children for *eligibility* for oral pellets:

- ✓ Is at least 6 months old
- ✓ Can swallow soft foods
- ✓ Cannot tolerate oral syrups
- ✓ Cannot swallow whole tablets

👍 If the child fulfils all the above criteria, then they are eligible for LPV/r oral pellets

👎 If the child does not fulfil all the above criteria, they will be eligible for the LPV/r oral syrup, or the LPV/r oral tablets

Demonstration on the use of LPV/r oral pellets

As this is a new product, it is **mandatory** that the healthcare workers carefully **explain** and **demonstrate** to caregivers how to open and administer oral pellets.

Adequate instructions must be provided to the caregiver to ensure:

- ✓ the correct number of capsules is given
- ✓ the entire dose is administered as required

Infants should be carefully observed by caregivers for **signs of aspiration** which may include:

- Coughing
- Choking
- Gagging
- Eye reddening

NOTE: Healthcare workers must **ask the caregiver about how they give the pellets** when they come back for follow up visits to ensure that administration is as per the guidelines, and to ensure that the child is getting the correct, therapeutic dose of the pellets

How to open LPV/r oral pellets

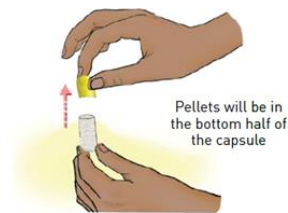
Oral pellets come in capsules and there are 120 capsules per bottle. The pellets inside the capsule are white in colour.

Step 1: Twist



Hold the capsule with the yellow side up and twist until it is loose

Step 2: Lift



Lift the yellow half of the capsule

Step 3: Pour



Pour all pellets into a teaspoon

NOTE: the capsule must **never be swallowed whole**. Throw the capsule casing away after the pellets have been emptied from it

How to administer LPV/r oral pellets with soft food

Oral pellets **CANNOT** be stirred, dissolved or crushed in soft foods prior to administration. The pellets must not be chewed as they will develop a bad taste.

Step 1: Prepare food to give with pellets

1. Pour pellets onto a **teaspoon**, then pour food over pellets



Pour food over the pellets

2. Pour food onto a **teaspoon**, then sprinkle pellets over food



OR

Do **not stir** the pellets with the food, make sure you can still see them

Step 2: Feed the mixture to the child



Feed the mixture immediately to the child. Do not let the pellets dissolve in the food. The pellets must not be chewed



Feed the rest of the food to the child or give him/her water to make sure the pellets have all been swallowed

TIP: give pellets with **food that the child prefers to take** & will swallow without chewing (e.g. porridge, yoghurt, mashed potato)

TIP: The child must try to finish all the pellets. If the child cannot finish the food with the pellets, **do not store it for later use**

How often to administer LPV/r oral pellets

Oral pellets must be given **twice a day**, once in the morning and once at night.

Pellets should be given **twice a day** (approximately every 12 hours)



For example: At 7 o'clock in the morning...

...and again at 7 o'clock at night

Decide two times that you will give the pellets to your child. There should be approximately 12 hours in between the two times



Make sure that the child takes **all** the pellets



TIP: keep **reminders** for when to give oral pellets to your child. Use a calendar or an alarm on your phone

TIP: give **1 or 2 capsules of pellets at a time** otherwise the amount of pellets may be too much for child to swallow at once

How many LPV/r oral pellets to give the child according to their weight

The nurse or doctor at the clinic will always tell you how many capsules of pellets to give your child
 The number of capsules of pellets that the child takes will increase as the child grows and gains weight

CHILD'S WEIGHT IN KG	NUMBER OF CAPSULES OF ORAL PELLETS TO GIVE		NUMBER OF 100/25MG PAEDS TABS TO GIVE	
	MORNING	EVENING	MORNING	EVENING
3 – 3.9kg	2	2	use syrup: 1 ml bd	use syrup: 1 ml bd
4 – 4.9kg	2	2	use syrup: 1 ml bd	use syrup: 1 ml bd
5 – 5.9kg	2	2	use syrup: 1.5 ml bd	use syrup: 1.5 ml bd
6 – 6.9kg	3	3	use syrup: 1.5 ml bd	use syrup: 1.5 ml bd
7 – 7.9kg	3	3	use syrup: 1.5 ml bd	use syrup: 1.5 ml bd
8 – 8.9kg	3	3	use syrup: 1.5 ml bd	use syrup: 1.5 ml bd
9 – 9.9kg	3	3	use syrup: 1.5 ml bd	use syrup: 1.5 ml bd
10 – 10.9kg	4	4	2	1
11 – 13.9kg	4	4	2	1
14 – 14.9kg	5	5	2	2
15 – 16.9kg	5	5	2	2
17 – 19.9kg	5	5	2	2

TIP: The more the child grows, the more pellets they need to take.
Fewer 100/25mg tablets need to be taken than oral pellets.
 As soon as a child is **developmentally able to swallow** the 100/25mg tablets, they should do so as this will ease the pill burden, but the **tablets need to be swallowed whole** without crushing, chewing or biting the tablets

Note: If a patient who weighs more than 20kg is unable to tolerate LPV/r oral solution and unable to swallow whole tablets, LPV/r pellets may be considered with expert guidance on the dosing. Consult with a clinician experienced in paediatric ARV formulations.



Adverse effects of LPV/r oral pellets

LPV/r oral pellets are safe, but mild adverse events / side-effects can occur after administering the treatment. It's important to observe infants and young children periodically for any adverse events, and to report them to your healthcare facility



POSSIBLE ADVERSE REACTIONS:

- Nausea
- Vomiting
- Diarrhea
- Abdominal pain
- Yellowing of the eyes and skin
- Dark coloured urine
- Light coloured bowel movements
- Loss of appetite
- Itchy skin
- Sensation of abnormal heart beats

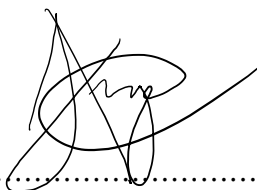


Report any of these symptoms to your nearest health facility



Dosing of LPV/r by formulation & dose modification (RTV super-boosting/double-dose LPV/r) for children receiving rifampicin-containing TB treatment

	Lopinavir/ritonavir (LPV/r)	Lopinavir/ritonavir when on Rifampicin (& for 2 weeks after stopping Rifampicin) Choose only one option
Target dose	300/75 mg/m ² /dose LPV/r TWICE daily	Double-dose LPV/r tabs ONLY if able to swallow whole LPV/r tabs TWICE daily
Available formulations	Solution 80/20 mg/ml Adult tabs 200/50 mg Paed tabs 100/25 mg TABLETS MUST BE SWALLOWED WHOLE Pellets 40/10 mg per capsule ONLY FOR USE IF NOT TOLERATING LPV/r SOLUTION CAPSULES ARE NOT RECOMMENDED <6 MONTHS OF AGE CAPSULES MUST NOT BE SWALLOWED WHOLE	Adult tabs 200/50 mg Paed tabs 100/25 mg
Weight (kg)	Choose only one option	
3-4.9	1 ml bd OR 2 capsules bd	
5-5.9	1.5 ml bd OR 2 capsules bd	
6-9.9	1.5 ml bd OR 3 capsules bd	
10-13.9	2 ml bd OR 4 capsules bd OR 2 x 100/25 mg paed tabs am + 1 x 100/25 mg paed tab pm	Do not use double-dose LPV/r tabs
14-19.9	2.5 ml bd OR 5 capsules bd OR 2 x 100/25 mg paed tabs bd OR 1 x 200/50 mg adult tab bd	3 x 100/25 mg paed tabs bd
20-24.9	3 ml bd OR 6 capsules bd OR 2 x 100/25 mg paed tabs bd OR 1 x 200/50 mg adult tab bd	4 x 100/25 mg paed tabs bd OR 2 x 200/50 mg adult tabs bd
25-29.9	3.5 ml bd OR 7 capsules bd OR 3 x 100/25 mg paed tabs bd OR 1 x 200/50 mg adult tab bd + 1 x 100/25 mg paed tab bd	6 x 100/25 mg paed tabs bd OR 3 x 200/50 mg adult tabs bd
30-34.9	5 ml bd OR 8 capsules bd OR 4 x 100/25 mg paed tabs bd OR 2 x 200/50 mg adult tabs bd	8 x 100/25 mg paed tabs bd OR 4 x 200/50 mg adult tabs bd
≥35	5 ml bd OR 10 capsules bd OR 4 x 100/25 mg paed tabs bd OR 2 x 200/50 mg adult tabs bd	8 x 100/25 mg paed tabs bd OR 4 x 200/50 mg adult tabs bd



Mr James Kruger
Director: HIV/AIDS, STI & TB
Date: **22 June 2020**