Due to increasing uptake of paediatric LPV/r formulations, the ARV Procurement Working Group (APWG) has developed the following memorandum to provide up-to-date information and guidance to country programmes planning to procure LPV/r oral pellets or LPV/r oral liquid.

I. INTRODUCTION OF LPV/r ORAL PELLETS

Ritonavir-boosted lopinavir (LPV/r)- based antiretroviral therapy (ART) has been recommended by the WHO as a preferred first-line for all children under 3 years of age since 2013. Despite this longstanding recommendation currently available formulations for LPV/r have prevented wide-scale implementation and the majority of infants and young children continue to be started and treated with inferior, NVP-containing regimens.

Heat-stable lopinavir/ritonavir oral pellets were approved by the US Food and Drug Administration (FDA) in May 2015 and became available for country procurement in mid-2016 as an alternative to LPV/r liquid for optimal first-line antiretroviral treatment for all children under 3 years of age. Early experiences have provided reassurance that LPV/r oral pellets offer a safe, effective and acceptable alternative to both liquid LPV/r and NVP-containing regimens for infants and young children. However as the current supplier scales-up production of this new formulation, the Antiretroviral Procurement Working Group (APWG) has developed this information brief to update programmes on available supply of LPV/r oral pellets and provide guidance on procurement and introduction to avoid both delays in implementation and mitigate risk of stock-out.

II. DEMAND FOR LPV/r ORAL PELLETS

Programmes interested in adopting pellets are encouraged to carefully define their eligible patient population to more accurately quantify the need for LPV/r oral pellets. Many children currently on treatment are stable on an NNRTI-based regimen, either NVP or EFV, or are able to take LPV/r 100mg/25mg heat-stable tablets which are approved for use in children weighing 10kgs or more and able to swallow tablets whole. Additionally, with the success of PMTCT fewer infants and young children are being newly diagnosed and require treatment.

Country programmes should closely investigate the number of paediatric patients who are eligible for this new formulation at the facilities where LPV/r oral pellets will first be introduced. It is critical for programmes to clearly define patient populations who need pellets in order to avoid inappropriate prescribing.

Suggestions include the following:

i. **Suggested patients to be prioritized for LPV/r oral pellets:**
   - Patients currently on or needing LPV/r- containing regimens (1st or 2nd line) who cannot tolerate LPV/r oral liquid and are not able to swallow LPV/r 100mg/25mg tablets whole.
• Patients <3 years newly initiating treatment

ii. Suggested patients for whom transition to LPV/r pellets may be delayed
• Patients currently stable on an NVP- or EFV containing 1st line regimen (i.e. viral suppression, or if viral load is not available, those who are clinically or immunologically stable)
• Patients tolerating LPV/r oral liquid if the program is able to maintain sufficient supply of oral liquid.

iii. Patients for whom LPV/r pellets should NOT be used
• Patients weighing 10kg more AND are able to swallow LPV/r 100mg/25mg tablets whole
• Patients <3 months (until further information is available about safety and tolerability in this group)
• Newly initiating patients 3 years or older who may be initiated on an EFV-containing regimen

iv. Additional recommendations for older children
• Programmes should consider procurement of the LPV/r 100mg/25g tablet for children 10kgs and above who are able to swallow tablets whole.
• If viral load monitoring is available, programmes may also consider adopting the recommendation to transition children 3 years or older who are on an LPV/r containing 1st line regimen and have maintained sustained viral suppression, to an EFV based regimen.
• Use of these two strategies serves to optimize pediatric ARV by offering older children simpler regimens and reserving LPV/r oral pellets for those with no other alternative.

III. SUPPLY OF LPV/r ORAL PELLETS
Since implementation began, efforts have been made to share early experiences with the oral pellets as well as develop useful guidance on administration and dispensing practices based on health care worker and caregiver feedback. Additionally, early guidance was developed in the form of a supply planning brief with considerations for country programmes choosing to introduce LPV/r oral pellets.

However there is concern that currently forecasted demand for LPV/r oral pellets may exceed the production capacity for the manufacturer though efforts are being made to increase capacity in the near future. Additionally, there is concern about reduced availability of LPV/r oral liquid due to the discontinuation of manufacturing by a supplier; as a result there is currently only a single supplier remaining for LPV/r oral liquid. The APWG is in communication with the current suppliers of both LPV/r oral pellets and LPV/r liquid to closely track levels of production in addition to monitoring the progress of a 2nd supplier currently developing a heat stable, child-friendly formulation of LPV/r granules. This product is expected to come to market in 2018. The development of a new 4-in-1 granule formulation (ABC/3TC/LPV/r) is also being closely watched with an anticipated approval date in early 2019. However, as with all drug development, timelines are subject to change. It is the aim of the APWG to provide transparency into available supply and communicate updates regularly so that programmes may plan appropriately and mitigate supply risks.
IV. GUIDANCE ON PROCUREMENT OF LPV/r ORAL PELLETS

- Lead times are currently estimated to be 6-8 months for orders of 1,000-10,000 packs of LPV/r oral pellets so programs should account for this time period and may consider utilizing remaining stocks of LPV/r liquid as appropriate.
- Programmes requiring larger quantities of LPV/r may consider receiving staggered shipments and should closely monitor consumption of LPV/r oral pellets and oral liquid. Should actual uptake be lower than anticipated, programmes may delay the next order and/or reduce the number of packs procured. This will avoid wastage while ensuring that stocks continue to be available for patients with immediate need.
- Countries are encouraged to share a 12-18-month procurement plan with the APWG for LPV/r pediatric formulations (both pellets and liquids) including quantities by age group and may reach out to the APWG with challenges procuring LPV/r oral pellets or if technical assistance is required.
- Partners are encouraged to support countries in accurate quantification, forecasting and procurement planning for pediatric formulations, especially during this transition phase.
- Countries which have yet to start transition to LPV/r pellets may choose to continue use of LPV/r liquid or may also consider maintaining some stocks of LPV/r oral liquid in addition to LPV/r oral pellets.

The APWG will continue to monitor manufacturing capacity, registration and pricing of LPV/r paediatric formulations in addition to tracking successes and challenges faced in the use of LPV/r oral pellets including issues related to procurement, stock management and support for programs, health-care workers and patients.

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References

i http://apps.who.int/iris/bitstream/10665/193543/1/FactsheetIATT_WHO_UNICEF_l
opinavir_eng.pdf?ua=1

VERSION-1-Sep-2015.pdf