Supporting Sustained Supply through the Coordinated Procurement of ARVs

ARV Procurement Working Group Newsletter

January 2017

Introduction

It has been one year since the Paediatric ARV Procurement Working Group (PAPWG) broadened its mission with the inclusion of select adult ARVs through the establishment of the ARV Procurement Working Group (APWG). The expansion has allowed the working group to continue its support of at-risk paediatric ARVs while also enabling the same coordination and collaboration to be applied to adult products with challenging market conditions.

Through the quarterly order cycles and business calls, the APWG continued its support of the ARV market by coordinating procurement, strategically managing demand, and reducing fragmentation. In addition to these routine meetings, the APWG witnessed some notable ARV market developments in the second half of 2016, including:

- The release of the 2016 IATT Paediatric ARV Optimal Formulary and Limited-use List
- The first SRA approval of a generic dolutegravir (DTG) product
- An increasing number of planned orders for LPV/r oral pellets and ABC/3TC 120/60mg disp. tablets

The 2016 IATT Paediatric ARV Formulary and Limited-use List

The optimal and limited-use formulary list for the selection of optimal paediatric ARVs dosage forms has been revised by the Interagency Task Team on Prevention and Treatment of HIV Infection in Pregnant Women, Mothers and their Children (IATT) following recent updates to the WHO Guidelines.

The optimal list is designed to provide the minimum number of ARV formulations needed to provide all currently recommended WHO paediatric preferred 1st and 2nd line regimens across all paediatric weight bands. Provisions for drugs needed for WHO recommended paediatric alternative regimens are no longer provided on the optimal list but were considered for inclusion on the limited-use list. Additionally, the limited-use list includes dosage forms that may be needed during special circumstances such as paediatric 3rd line, alternative 2nd line, TB co-infection, and regimen transitions within programmes.

The 2016 Paediatric ARV Optimal Formulary and Limited-use List reflects currently available paediatric ARV dosage forms including newly approved paediatric products. The updated list includes lopinavir/ritonavir (LPV/r) 40mg/10mg oral pellets and raltegravir (RAL) 100mg chewable scored tablets (see full list below).

2016 IATT Optimal Formulary			
Drug Class	**Drug**	**Formulation**	**Dose**
NNRTI	EFV	Tablet (scored)	200mg
NNRTI	NVP	Tablet (disp. scored)	50mg
NNRTI	NVP	Oral liquid	50mg/ml, 100ml
PI	LPV/r	Tablet (heat stable)	100/25mg
PI	LPV/r	Oral liquid	80/20mg/ml
PI	LPV/r	Oral pellets	40/10mg

FDC	AZT/3TC	Tablet (disp. scored)	60/30mg
FDC	ABC/3TC	Tablet (disp. Scored)	60/30mg, 120/60mg
INSTI	RAL	Chewable tablet	100mg

AZT/3TC/NVP triple fixed-dose combination (FDC) scored dispersible tablets have been transitioned from the optimal formulary to the limited-use list to reflect increasing uptake of preferred first line regimens using LPV/r or efavirenz (EFV). The limited-use list has been updated with the inclusion of RAL 25mg chewable tablets for younger children, ritonavir (RTV) 25mg heat stable tablets for the boosting of noncoformulated PI's as well as the removal of TDF 200mg tablets, atazanavir (ATV) 150mg capsules and all etravirine (ETR) containing formulations (see full list below).

2016 IATT Limited-Use List				
Drug Class	**Drug**	**Formulation**	**Dose**	**Rationale For Use**
NRTI	AZT	Oral liquid	50mg/ml -100ml	Infant prophylaxis or as part of neonatal treatment regimen
NRTI	3TC	Oral liquid	50/5mg/ml – 240ml	Neonatal treatment regimen
NRTI	ABC	Tablet (disp. scored)	60mg	Children <3 years undergoing TB treatment requirement triple nucleoside regimen
NRTI	AZT	Tablet (disp. scored)	60mg	Children <3 years undergoing TB treatment requirement triple nucleoside regimen
PI	DRV	Tablet	75mg	Third line
PI	RTV	Tablet	25mg	Boosting of noncoformulated PIs (DRV and ATV)
PI	RTV	Oral liquid	400/5mg/ml -240ml	Super boosting of LPV/r during TB treatment
PI	ATV	Solid oral dosage form	100mg	Alternative second line
INSTI	RAL	Tablet (chewable, scored)	25mg	Second line after LPV/r –containing first-line failure
FDC	AZT/3TC/NVP	Tablet (disp. scored)	60/30/50mg	Alternative first-line

For more details on the revised IATT list, please see the published report on the EMTCT-IATT website or contact Martina Penazatto (penazzatom@who.int), Nandita Sugandhi (nsugandhi@clintonhealthaccess.org), or Wesley Kreft (wkreft@nl.pfscm.org).

Dolutegravir Receives First Generic SRA Approval

In September of 2016, Aurobindo received tentative approval of dolutegravir (DTG) 50mg from the US Food & Drug Administration (USFDA). Dolutegravir, an integrase strand transfer inhibitor (INSTI), has been shown to be non-inferior, or superior, and more tolerable than EFV and PIs. Some advantages of the drug include a short time to viral suppression, a higher genetic resistance barrier, long half-life, low-cost, and low dosing requirements.

Various countries have already begun to make provisions for DTG in their guidelines. Earlier in 2016, Botswana adopted TDF/FTC + DTG as the preferred first line regimen for adults and adolescents. In addition, countries like Cambodia, Kenya, Nigeria, Tanzania, and Zimbabwe are at various stages of considering DTG for their national treatment guidelines. Procurement plans have been initiated in many countries including Cameroon, Cote d'Ivoire, DR Congo, Kenya, Mozambique, Nigeria, Uganda, and Zimbabwe.

LPV/r Oral Pellets and ABC/3TC 120/60mg Disp. Tablets See Adoption

LPV/r (40/10mg) oral pellets have gained interest in several countries seeking an alternative LPV/r formulation to the existing oral solution and (100/25mg) non-crushable, non-dispersible, paediatric tablets. Cipla is scaling-up their capacity for production in 2017 while more than a dozen countries have already procured or are planning to procure LPV/r oral pellets.

ABC/3TC (120/60mg) dispersible tablets, which can significantly decrease pill burden in children by at least 50% compared to existing formulations of ABC, particularly when used as a once daily regimen, have also seen adoption. The reduced pill burden may improve patient adherence, prevent sub-optimal dosing, and simplify the supply chain at no additional cost to national HIV programs. Countries like Kenya, Tanzania, Uganda, Vietnam, and Zimbabwe have already procured or are planning to procure ABC/3TC 120/60mg dispersible tablets.

Phasing-out Non-optimal ARVs

A number of countries are still procuring ARVs or formulations that have largely been phased out of treatment guidelines and are often no longer recommended by WHO. These include several non-essential paediatric formulations (e.g. non-dispersible tablets) or extremely low volume products such as oral solutions for abacavir, efavirenz, and lamivudine (where dispersible fixed dose combinations are preferred). A thorough deep dive of non-optimal products procured in 2016 was conducted during Peds Week in Geneva during December 2016. Procurement agents are tasked to follow-up with member organizations to continue to encourage product optimization and scale-out of non-optimal ARVs.

Programs are reminded that such products or formulation may not only be sub-optimal for patients, but are also increasingly difficult to procure as they are not regularly produced and long lead times could be expected. There is also a risk of discontinuation of some of these products. Programs are urged to proactively consider moving to more optimal formulations where supply can be assured.

Quarterly Order Cycle Coordination

The APWG Procurement Consortium consolidates the submissions of ARVs around fixed quarterly order cycle dates. These dates have been agreed upon by the AWPG and shared with suppliers and other stakeholders.

The aggregation of orders for at-risk ARVs around this schedule allows manufacturers to plan production accordingly. Furthermore, consolidated product orders are more likely to meet the required minimum batch size and thus potentially avoid extended lead times associated with sub-batch orders.

Countries procuring ARVs independently or through non-APWG procurement agents are encouraged to use the quarterly order dates below to ensure a reliable supply of paediatric ARVs.

Deadline for Orders to be placed with Suppliers*	
Q1 2017	**31 March 2017**
Q2 2017	**30 June 2017**
Q3 2017	**29 September 2017**
Q4 2017	**29 December 2017**
*Orders should be submitted to procurement agents at least 6 weeks before these dates	

Scheduled ordering four times a year is especially recommended for low volume paediatric and adult ARVs, a list of these prioritised products is provided:

Prioritised Paediatric ARVs (2016 IATT status)	
Optimal	ABC/3TC (120/60mg) dispersible
	LPV/r (80/20mg/ml) solution
	LPV/r (40/10mg) oral pellets
	NVP (50mg) dispersible
	RAL (100mg)
Limited-Use	3TC (50mg/5ml) solution (100ml)
	ABC (60mg) dispersible
	ATV (100mg)
	AZT (60mg) dispersible
	RTV (25mg) tablets
Non-Essential	AZT (50mg/5ml) solution (240ml)
	ATV 150mg

Prioritised Adult ARVS
ABC 300mg
ATV 300mg
AZT 300mg
DRV 400mg
DTG 50mg and FDCs*
EFV 400mg FDCs*
RAL 400mg
RTV 100mg
TDF 300mg
3TC 150mg
**when generics are SRA-approved*

New Product Availability

Some new products have received SRA approval since the last newsletter:

- *Aurobindo:* As mentioned above, DTG (50mg) tablets have received tentative US FDA approval, the first SRA approval for a dolutegravir generic.
- *Cipla:* AZT (50/5mg/ml) Oral Solution has received US FDA tentative approval for another manufacturing site.
- *Cipla:* ABC/3TC (120/60mg) dispersible tablets have received WHO PQ approval. This is the second supplier of the product, after Mylan, to receive SRA approval.
- *Hetero:* LPV/r (100/25mg) tablets have received US FDA tentative approval for 60- and 120-count packs.

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