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TRANSITIONING TO NEW HIV/AIDS TREATMENT REGIMENS –

Recommendations to address phase-out of d4T and ddI procurement challenges in the paediatric ARV market. August 2014

This update has been prepared by the Inter-agency Task Team on the Prevention and Treatment of HIV infection in Pregnant Women, Mothers and Children (IATT) and the WHO to provide further guidance to implementers and buyers on the current state of the market for the supply of paediatric ARVs. The advice in this update is drawn from the recent experience of the Paediatric ARV Procurement Working Group, suppliers and IATT sub-committee responsible for the Optimal List of Paediatric ARVs.

Background

WHO's 2013 Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection[1] provide clear guidance on regimen selection (see Table 1), but not on product selection. Compared with the market for adult ARV's, drugs for paediatric patients are challenged by the relatively small size of the market and the fragmented nature of demand across multiple products. To address these challenges, and to provide more specific guidance on paediatric product selection, two mechanisms have been established:

1. An updated version of the optimal list of paediatric ARV formulations was published in March 2014 by the Inter-agency Task Team on the Prevention and Treatment of HIV infection in Pregnant Women, Mothers and Children (IATT) to guide program procurement of products that enable provision of WHO recommended first- and second- line regimens for all pediatric ages and weight bands.[2]

2. The Paediatric ARV Procurement Working Group (PAPWG) is a group of funders and procurers of paediatric ARVs[3] established to support improved access to paediatric ARVs. The PAPWG can assist country programs to align demand and procurement activities through its Procurement Consortium in order to place viable order quantities to the manufacturers on a quarterly basis.

Current situation – August 2014

Stavudine

Since 2010, WHO has encouraged programs to phase-out the use of stavudine (d4T). In the 2013 Consolidated Guidelines and in the March 2014 supplement, WHO strengthened this position across adult and paediatric populations, recommending that programs stop initiation of new patients on d4T containing regimens and plan phased transitions of existing patients to alternatives such as abacavir (ABC), zidovudine (AZT), or tenofovir (TDF).[4] Use of d4T in paediatric patients is only recommended for specific circumstances where other NRTIs may be contraindicated, not tolerated or unavailable. Acting on this advice many countries are transitioning all paediatric patients to ABC, AZT or TDF- containing regimens. Some programs continue to use remaining stocks of d4T for existing patients with plans to transfer to alternative regimens in the near future. However a limited number of programs continue to request pediatric d4T products with no apparent transition plan in place.

[1] http://www.who.int/hiv/pub/guidelines/arv2013/en/

[2] http://www.emtct-iatt.org/wp-content/uploads/2014/04/IATT-Sept-2013-Updated-Paediatric-ART-Formulary-Report1.pdf, http://apps.who.int/iris/bitstream/10665/104264/1/9789241506830_eng.pdf

[3] Working Group Members currently include: Clinton Health Access Initiative (CHAI); The Global Fund to Fight AIDS, TB and Malaria; Médecins Sans Frontières (MSF) [observer]; Organization of Eastern Caribbean States (OECS); Partnership for Supply Chain Management- Pooled Procurement Mechanism (PFSCM); Supply Chain Management Systems (SCMS/PEPFAR); UNICEF; UNITAID; World Health Organization (WHO).

[4] http://www.who.int/hiv/pub/guidelines/arv2013/arvs2013upplement_march2014/en/

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The market is currently experiencing a scale down in production of pediatric d4T products due to the decline in demand. It is important that remaining programs using d4T establish transition plans to support manufacturers in establishing a clear and transparent exit strategy from these products.

Didanosine

The WHO 2013 Consolidated Guidelines also no longer recommend didanosine (ddI) for use. Similar to d4T, ddI has been in only limited use in recent years, resulting in very low demand and extreme difficulty in sourcing the product. It is important that countries continuing to use ddI introduce transition plans at the earliest opportunity to facilitate a managed exit strategy that is clear for all concerned.

Through coordination activities the PAPWG is monitoring availability and stocks of d4T and ddI, and is able to provide procurement assistance to programs still in the transition phase by consolidating demand and working with manufacturers to schedule production.

Recommendations

1. Implementers still requiring new stocks of d4T-containing fixed dose combinations or ddI formulations are strongly recommended to contact the PAPWG to discuss procurement options via the focal points listed at the end of this note.

2. Implementers still using d4T or ddI are recommended to establish plans to transition to use of other products in the WHO Consolidated Guidelines in order to end the use of these drugs in 2014 or at latest early 2015. If implementers require new stocks to facilitate such a transition they should contact the PAPWG.

3. Uptake of products on the optimal pediatric ARV formulary is trending strongly upwards, but the paediatric market remains inherently fragile, due to low overall volumes and the range of products necessary to serve paediatric patients. Implementers are advised to plan in advance for all low volume products (including 2nd line ARVs). Planning allows for global coordination of procurement and avoids treatment interruptions resulting from stock-outs.

Table 1: Preferred and alternative first-line regimens for children, adapted from the 2013 WHO Consolidated ARV Guidelines

Age Group	Preferred first-line regimens	Alternative first-line regimens
Children < 3 years	ABC or AZT + 3TC + LPV/r	ABC + 3TC + NVP AZT + 3TC + NVP
Children 3 years to less than 10 years and adolescents <35kg	ABC + 3TC + EFV	ABC + 3TC + NVP AZT + 3TC + EFV AZT + 3TC + NVP TDF + 3TC (or FTC) + EFV TDF + 3TC (or FTC) + NVP
Adolescents (10-19 years) ≥ 35 kg	TDF + 3TC (or FTC) + EFV	AZT + 3TC + EFV AZT + 3TC + NVP TDF + 3TC (or FTC) + NVP ABC + 3TC + EFV (or NVP)

http://www.who.int/hiv/pub/guidelines/arv2013/en/index.html)

Table 2: Optimal Formulary List

Drug Class	Drug	Formulation	Dose
NRTI	AZT	Oral liquid	50 mg/5 mL
NNRTI	EFV	Tablet (scored)	200 mg
NNRTI	NVP	Tablet (disp, scored)	50 mg
NNRTI	NVP	Oral liquid	50 mg/5 mL
PI	LPV/r	Tablet (heat stable)	100 mg/25 mg
PI	LPV/r	Oral liquid	80 mg/20 mg/mL
FDC	AZT/3TC	Tablet (disp, scored)	60 mg/30 mg
FDC	AZT/3TC/NVP	Tablet (disp, scored)	60 mg/30 mg/50 mg
FDC	ABC/3TC	Tablet (disp, scored)	60 mg/30 mg
FDC	ABC/AZT/3TC	Tablet (non disp, scored)	60 mg/60 mg/30 mg

http://www.emtct-iatt.org/wp-content/uploads/2014/04/IATT-Sept-2013-Updated-Paediatric-ART-Formulary-Report1.pdf, http://apps.who.int/iris/bitstream/10665/104264/1/9789241506830_eng.pdf

The PAPWG was created to serve as a global facilitating group supporting the procurement of paediatric ARVs, while technical assistance for clinical and programmatic transition planning can be facilitated through the IATT on an as needed basis.

For further information or assistance please contact:

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