Update on the IATT Paediatric Formulary

WHO/UNAIDS Consultation with manufacturers

March 2015, Geneva, Switzerland

Summary

- The Challenge
- Rationale for Paediatric ARV Formulary Optimization
- 2015 Revised Optimal and Limited-use Paediatric ARV formularies
- Next Steps

The challenge: simply put there are too many paediatric ARVs for a relatively small patient population

NRTI's		
ABC	Tablet (disp,scored) as sulfate	60 mg
ABC	Tablet (scored) as sulfate	60 mg
ABC	Oral liquid as sulfate	100 mg/5ml
AZT	Tablet (disp, scored)	60 mg
AZT	Oral liquid	50 mg/5ml
AZT	Tablet (scored)	60 mg
AZT	Capsule	100 mg
AZT	Tablet	100 mg
3TC	Oral liquid	50 mg/5ml
3TC	Tablet (disp)	30 mg
3TC	Tablet	30 mg
D4T	Capsule	15 mg
D4T	Capsule	20 mg
D4T	Powder for oral solution	5 mg/5ml
DDI	Capsule (unbuffered, enteric coated)	125 mg
DDI	Capsule (unbuffered, enteric coated)	200 mg
DDI	Tablet (buffered, chewable, disp)	25mg
DDI	Tablet (buffered, chewable, disp)	50 mg
DDI	Tablet (buffered, chewable, disp)	100 mg
DDI	Powder for oral liquid (Buffered)	2g, 4g bottle
FTC	Oral liquid	10 mg/ml
TDF	Oral powder	40mg/scoop
TDF	Tablet (unscored)	150 mg
TDF	Tablet (unscored)	200mg

NNRTI's		
EFV	Tablet (scored)	200 mg
EFV	Tablet	50 mg
EFV	Tablet (unscored)	200 mg
EFV	Tablet (disp, scored)	100 mg
EFV	Tablet	100 mg
EFV	Capsule	50 mg
EFV	Capsule	100 mg
EFV	Capsule	200 mg
EFV	Oral liquid	150 mg/5ml
NVP	Tablet (disp, scored)	50 mg
NVP	Oral liquid	50 mg/5ml
NVP	Tablet (disp)	100 mg
ETV	Tablet	25 mg
ETV	Tablet	100 mg

PI's		
LPV/r	Tablet (HS)	100 mg/25mg
LPV/r	Oral liquid	80/20 mg/ml
RTV	Oral liquid	400 mg/5ml
DRV	Tablet	75 mg
DRV	Tablet	150 mg
DRV	Oral liquid	500 mg/5ml
ATV	Solid oral dosage form	100 mg
ATV	Solid oral dosage form	150 mg
ATV	Solid oral dosage form	200 mg
TPV	Oral liquid	500 mg/5mL
FPV	Oral liquid	250 mg/5mL

FDC's		
AZT/3TC	Tablet (disp, scored)	60/30 mg
AZT/3TC	Tablet (scored)	60/30 mg
AZT/3TC/NVP	Tablet (disp, scored)	60/30/50 mg
D4T/3TC/NVP	Tablet (disp, scored)	6/30/50 mg
D4T/3TC/NVP	Tablet (disp, scored)	12/60/100 mg
D4T/3TC	Tablet (disp, scored)	6/30 mg
D4T/3TC	Tablet (disp, scored)	12/30 mg
ABC/3TC	Tablet (disp, scored)	60/30 mg
ABC/3TC	Tablet (scored)	60/30 mg
ABC/3TC/AZT	Tablet (**non** disp, scored)	60/30/60 mg

Integrase Inhibitors		
RAL	Chewable tablet (scored)	100 mg
RAL	Chewable tablet	25 mg

The Market Risks

Market risks include…

Inability to procure low volume formulations
•Highly fragmented low volume products may not be supplied (e.g. non-essential IATT list)

Limited registration coverage
•Suppliers have lower incentives to register products in low volume markets

Limited new product options
•Creates further challenges to suppliers realizing a return on investment for new products

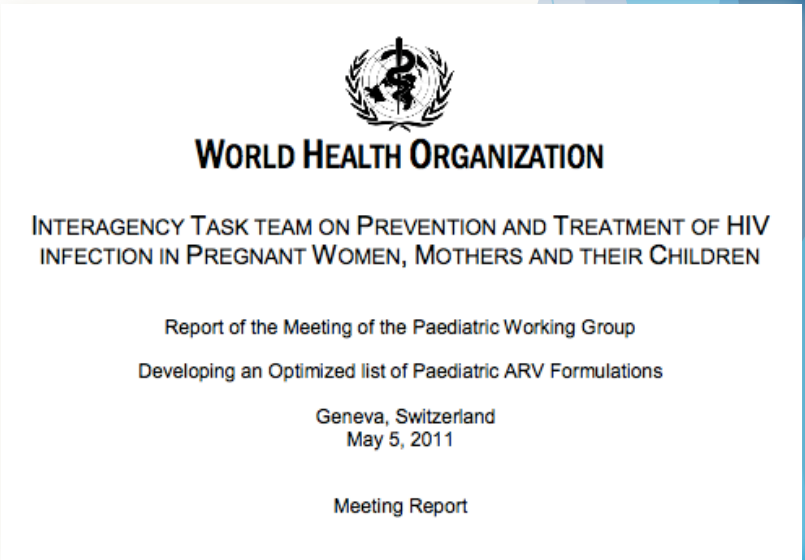
Who is at greatest risk…

- Low or medium volume countries
- Countries/programmes procuring a large number of formulations including multiple/redundant formulations for the same patient population
- Countries/programmes procuring formulations or drugs considered sub-optimal that most countries have transitioned away from (e.g. liquid formulations, ddI etc..)

2011: First IATT Optimal Paediatric ARV Formulary created by IATT

- **In mid-2011, the IATT began a selection process for optimal paediatric formulations given the following:**
- Proliferation of product choices and market fragmentation leading to instability in the paediatric marketplace
- Normative guidance was needed on the best options to deliver all required first- and second- line regimens for paediatric HIV patients
- An optimal formulary can serve as guidance for national programs, procurement agencies, manufacturers

To be updated and revised when the WHO updates regimen guidance
– or –
when new products and formulations become available in low-income settings



WORLD HEALTH ORGANIZATION

INTERAGENCY TASK TEAM ON PREVENTION AND TREATMENT OF HIV INFECTION IN PREGNANT WOMEN, MOTHERS AND THEIR CHILDREN

Report of the Meeting of the Paediatric Working Group

Developing an Optimized list of Paediatric ARV Formulations

Geneva, Switzerland
May 5, 2011

Meeting Report

WHO approach to recommending ARV Formulations

The principles that were followed in developing the WHO simplified tables include:

- Preference for age-appropriate Fixed Dose Combination for any regimen if available
- Oral liquid or syrup formulations should be avoided where possible
- Dispersible tablets are the preferred solid oral dosage forms
- Young children should be switched to available solid oral dosage forms as soon as possible
- Where children have to use adult formulations, care must be taken to avoid under-dosing. Adult tablets that are scored are more easily split.

Aim of the Optimal List: To address adherence and market challenges for Paediatric HIV Treatment

- Decrease pill burden and eases administration for caregiver and patient
- Promote adherence with simplified regimens, fewer bottles, fewer liquids, more temperature tolerance
- Improve availability by reducing complications in procurement, storage and distribution
- Simplify and clarify the market for suppliers
- Decrease costs over time

Evaluation criteria

Criteria	Description
Meets WHO requirements	Included in the latest WHO guidelines for paediatric treatment
Dosing flexibility	Allows for the widest range of dosing options
Approved by SRA/WHO PQ	≥ 1 quality assured product available
User friendly	Easy for HCWs to prescribe Easy for caregivers to administer Supports adherence in children
Optimizes supply chain	Easy to transport Easy to store Easy to distribute
Available in resource limited settings	In country registration Reliable supply
Comparative cost	Cost should NOT be the deciding factor in selection of a drug but comparative cost of similar drugs/drug formulations should be considered

Evaluation criteria

Optimal

Minimum number of ARV formulations needed to provide all currently recommended preferred and alternative first- and second- line WHO recommended regimens for all paediatric weight bands

Limited-use

Formulations that may be needed during transition and /or for special clinical circumstances

Non-essential

All other formulations (not recommended for use)

Comparison of of 2011, 2013 and 2015 Optimal Formulary

2011

Optimal Formulations
ABC+3TC 30/60 disp scored FDC tab
AZT+3TC+NVP 60/30/50 disp scored FDC tab
AZT+3TC 60/30 disp scored FDC
d4T+3TC+NVP 6/30/50 disp scored FDC
d4T+3TC 6/30 disp scored FDC
ABC 60mg disp scored tab
ddI 125mg EC cap
ddI 200mg EC cap
ddI 25mg buffered chew tab
EFV 200mg scored tab
LPV/r 80/20 mg/mL oral liquid
LPV/r 100/25 tab
NVP 50mg disp scored tab
AZT 50MG/5ML oral liquid (for PMTCT only)
NVP 50mg/5mL oral liquid (for PMTCT only)

15 Products

2013

Drug Class	Drug	Formulation	Dose
NRTI	AZT	Oral liquid	50 mg/5mL
NNRTI	EFV	Tablet (scored)	200 mg
NNRTI	NVP	Tablet (disp, scored)	50 mg
NNRTI	NVP	Oral liquid	50 mg/5mL
PI	LPV/r	Tablet (heat stable)	100 mg/25mg
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

10 Products

2015

Drug Class	Drug	Formulation	Dose
NNRTI	EFV	Tablet (scored)	200 mg
NNRTI	NVP	Tablet (disp, scored)	50 mg
NNRTI	NVP	Oral liquid	50 mg/5mL, 100ml
PI	LPV/r	Tablet (heat stable)	100 mg/25mg
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, 120mg/60mg

9 Products

Comparison of 2013 and 2015 Optimal Formulary

2013

Drug Class	Drug	Formulation	Dose
~~NRTI~~	~~AZT~~	~~Oral liquid~~	~~50 mg/5mL~~
NNRTI	EFV	Tablet (scored)	200 mg
NNRTI	NVP	Tablet (disp, scored)	50 mg
NNRTI	NVP	Oral liquid	50 mg/5mL
PI	LPV/r	Tablet (heat stable)	100 mg/25mg
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

10 Products

2 Removed

1 Added

2015

Drug Class	Drug	Formulation	Dose
NNRTI	EFV	Tablet (scored)	200 mg
NNRTI	NVP	Tablet (disp, scored)	50 mg
NNRTI	NVP	Oral liquid	50 mg/5mL, 100ml
PI	LPV/r	Tablet (heat stable)	100 mg/25mg
		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,**120mg/60 mg**

9 Products

Need clean copy of new Optimal list

2015 Optimal Paediatric ARV Formulary

Drug Class	Drug	Dosage Form	Strength
NNRTI	**EFV**	Tablet (scored)	200 mg
NNRTI	**NVP**	Tablet (disp, scored)	50 mg
NNRTI	**NVP**	Oral liquid*	50 mg / 5mL, 100ml
PI	**LPV/r**	Tablet (heat stable)	100 mg / 25mg
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, 120mg / 60mg

** For infant prophylaxis during PMTCT*

Comparison of 2011, 2013 and 2015 Limited-use lists

2011

Drug	Formulation	Dose
ABC	Oral liquid	100mg/5ml
ATV	Solid oral dosage form	100mg, 150mg
DRV	Oral liquid	500mg/5ml
DRV	Tablet	75mg, 150mg
ddI	Powder for oral liquid*	2g, 4g bottle
3TC	Oral liquid	50mg/5ml
RTV	Oral liquid*	400mg/5ml
RTV	Tablet (heat stable)	100mg
d4T	Powder for oral liquid*	5mg/5ml

11 Products

2013

Drug Class	Drug	Formulation	Dose	Rationale
NRTI	3TC	Tablet (disp)	30 mg	For use with TDF single
NRTI	TDF	Oral powder	40 mg/ scoop	Until FDC available
NRTI	TDF	Tablet (unscored)	150 mg	Until FDC available
NRTI	TDF	Tablet (unscored)	200 mg	Until FDC available
NNRTI	ETV	Tablet	25 mg	Special circumstances
NNRTI	ETV	Tablet	100 mg	Special circumstances
PI	DRV	Tablet	75 mg	Special circumstances
PI	RTV	Oral liquid	400 mg/ 5mL	For boosting non-co-formulated PI's
PI	ATV	Solid oral dosage form	100 mg	Alternative 2nd line
PI	ATV	Solid oral dosage form	150 mg	Alternative 2nd line
Int Inh	RAL	Chew tab (scored)	100 mg	Special circumstances
FDC	d4T/3TC/ NVP	Tablet (disp, scored)	6 mg/30 mg/ 50 mg	To be phased out
FDC	d4T/3TC	Tablet (disp, scored)	6 mg/30 mg	To be phased out

13 Products

2015

Drug Class	Drug	Formulation	Dose	Rationale for use
NRTI	AZT	Oral liquid	50 mg/5mL-100ml	Infant prophylaxis during PMTCT for replacement fed infants
NRTI	ABC	Tablet (dispersible, scored)	60mg	For children <3 years undergoing TB treatment requiring triple nucleoside regimen
NRTI	AZT	Tablet (dispersible, scored)	60mg	For children <3 years undergoing TB treatment requiring triple nucleoside regimen
NRTI	TDF	Tablet (unscored)	200 mg	Older children <35 kg until FDC available
NNRTI	ETV	Tablet	25 mg	Special circumstances
NNRTI	ETV	Tablet	100 mg	Special circumstances
PI	DRV	Tablet	75 mg	Special circumstances
PI	RTV	Oral liquid	400 mg/5mL	For boosting non-co-formulated PI's
PI	ATV	Solid oral dosage form	100 mg	Alternative 2nd line
PI	ATV	Solid oral dosage form	150 mg	Alternative 2nd line
Int Inh	RAL	Chew tab (scored)	100 mg	Special circumstances

11 Products

Comparison of 2013 and 2015 Limited-use Formulary

2013

Drug Class	Drug	Formulation	Dose	Rationale
~~NRTI~~	~~3TC~~	~~Tablet (disp)~~	~~30 mg~~	~~For use with TDF~~ single
~~NRTI~~	~~TDF~~	~~Oral powder~~	~~40 mg/scoop~~	~~Until FDC available~~
~~NRTI~~	~~TDF~~	~~Tablet (unscored)~~	~~150 mg~~	~~Until FDC available~~
NRTI	TDF	Tablet (unscored)	200 mg	Until FDC available
NNRTI	ETV	Tablet	25 mg	Special circumstances
NNRTI	ETV	Tablet	100 mg	Special circ
PI	DRV	Tablet	75 mg	circ
PI	RTV	Oral liquid	400 mg/5mL	For b co-formulated PI's
PI	ATV	Solid oral dosage form	100 mg	Alternative 2nd line
PI	ATV	Solid oral dosage form	150 mg	Alternative 2nd line
Int Inh	RAL	Chew tab (scored)	100 mg	Special circumstances
FDC	d4T/3TC/ NVP	Tablet (disp, scored)	6 mg/30 mg/ 50 mg	To be phased out
FDC	d4T/3TC	Tablet (disp, scored)	6 mg/30 mg	To be phased out

13 Products

5 Removed

2015

Drug Class	Drug	Formulation	Dose	Rationale for use
NRTI	AZT	Oral liquid	50 mg/5mL-100ml	Infant prophylaxis during PMTCT for replacement fed infants
NRTI	AZT	Tablet (dispersible, scored)	60mg	For children <3 years undergoing TB treatment requiring triple nucleoside regimen
NRTI	AZT	Tablet (dispersible, scored)	60 mg	For children <3 years undergoing TB treatment requiring triple nucleoside regimen
	TDF	Tablet (unscored)	200 mg	Older children <35 kg until FDC available
	ETV	Tablet	25 mg	Special circumstances
NNRTI	ETV	Tablet	100 mg	Special circumstances
PI	DRV	Tablet	75 mg	Special circumstances
PI	RTV	Oral liquid	400 mg/5mL	For boosting non-co-formulated PI's
PI	ATV	Solid oral dosage form	100 mg	Alternative 2nd line
PI	ATV	Solid oral dosage form	150 mg	Alternative 2nd line
Int Inh	RAL	Chew tab (scored)	100 mg	Special circumstances

3 Added

11 Products

2015 Limited-use Paediatric ARV Formulary

Drug Class	Drug	Dosage Form	Strength	Rationale for Use
NRTI	**AZT**	Oral liquid*	50 mg / 5mL-100ml	Infant prophylaxis during PMTCT for replacement fed infants
NRTI	**ABC**	Tablet (dispersible, scored) as sulfate	60mg	For children undergoing TB treatment requiring triple nucleoside regimen
NRTI	**AZT**	Tablet (dispersible, scored)	60mg	For children undergoing TB treatment requiring triple nucleoside regimen
NRTI	**TDF**	Tablet (unscored)	200 mg	Older children <35 kg until FDC available
NNRTI	**ETV**	Tablet	25 mg	Special circumstances
NNRTI	**ETV**	Tablet	100 mg	Special circumstances
PI	**DRV**	Tablet	75 mg	Special circumstances
PI	**RTV**	Oral liquid	400 mg / 5mL-90ml	For boosting non-co-formulated PIs and super-boosting of LPV during TB treatment
PI	**ATV**	Solid oral dosage form	100 mg	Alternative 2nd line
PI	**ATV**	Solid oral dosage form	150 mg	Alternative 2nd line
Int Inh	**RAL**	Chewable tablet (scored)	100 mg	Special circumstances

** For infant prophylaxis during PMTCT*

The lists are living documenst and we are watching out for new formulations including

- TDF 200mg
- ATV 100mg and 150mg
- ETV dosage formulations (25mg, 100mg)
- LPV/r pellets- acceptability and effectiveness
- ABC 60mg and AZT 60mg (use of triple nuc regimen)

The List is now used by multiple stakeholders

Paediatric ARV Procurement Working Group (PAPWG) which now coordinates across:

- Major agencies funding paediatric ARVs
- Major buyers of paediatric ARVs
- Ministries of Health, national drug regulatory agencies, national HIV/AIDS programmes and procurement offices
- Manufacturers of paediatric ARVs

Other stakeholders involved:

- Civil society stakeholders in paediatric HIV
- Community organization of people living with HIV

Key Points

- The IATT Optimal Formulary is designed to guide selection and procurement of paediatric ARV's around a subset of optimal products
- Consolidation of demand stabilizes supplies of paediatric ARVs
- Success requires global consensus, cooperation with the manufacturers, regional collaboration and country implementation to ensure paediatric ARV's will continue to be available to children in need
- Country process for optimization should include:
  - Regimen selection
  - Product selection
  - Coordinated procurement
- PAPWG is the global body created to support and coordinate procurement of paediatric ARV's

Next Steps by the IATT

- Publicize the new lists
- Prepare additional communications for countries
  - Implementation brief
  - Formulations for infant prophylaxis brief
- Work with manufacturers on supply challenges
- Coordinate with Paediatric ARV Procurement WG and other stakeholders to address outlier countries and opportunities

Feedback and questions

- The 2015 list is available from:
  - *Insert web link here*
- For additional information or technical assistance please contact:
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Thank you

Presented by:

David Jamieson, from the Partnership for Supply Chain Management on behalf of the IATT