

List of Optimal Paediatric Formulations

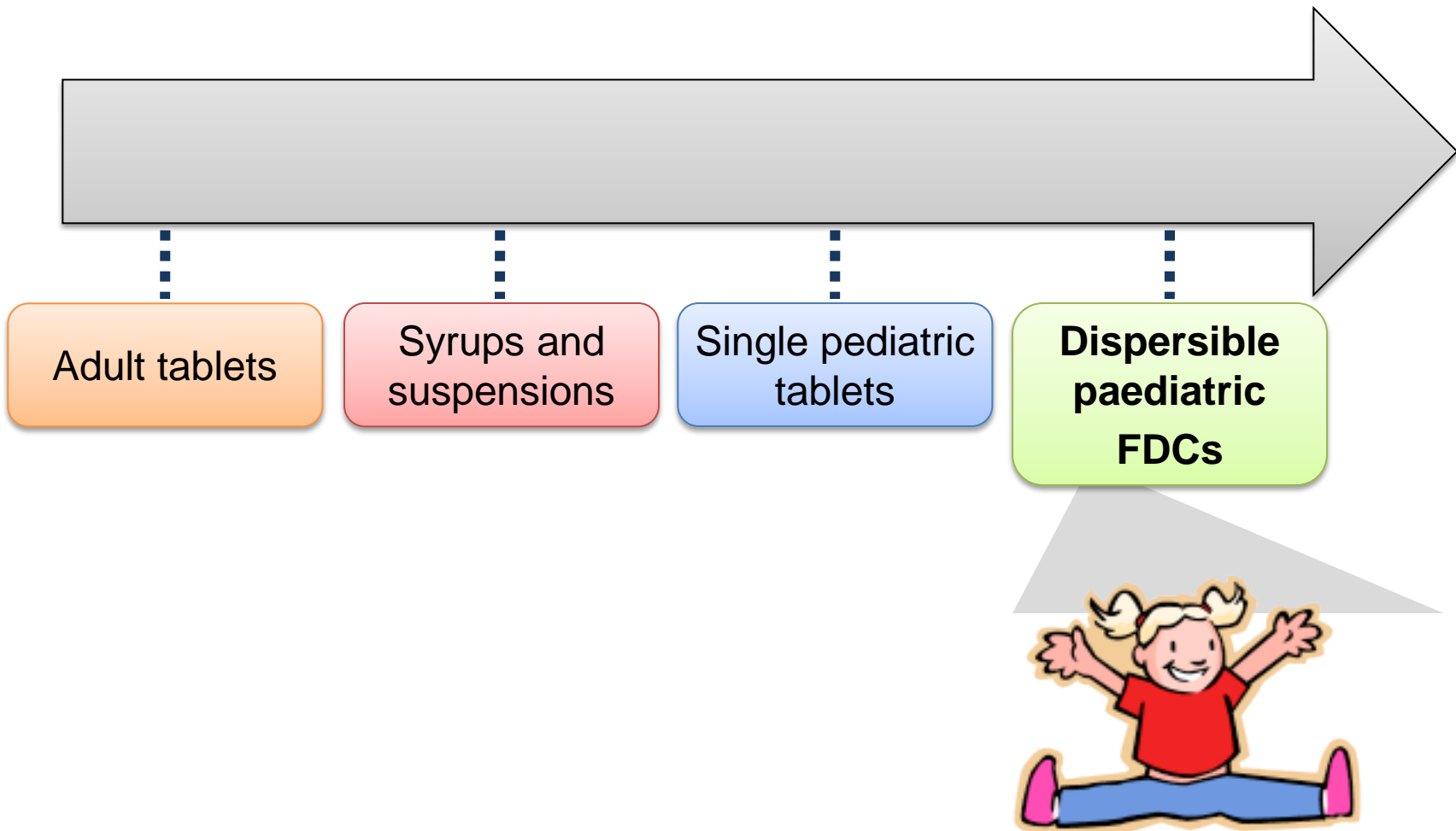
Marianne Gauval (CHAI)

IAS-ILF Round table

Geneva, Switzerland

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History of development of treatment options for children



<7% patients on ART are children

93 adult patients



All ages & weight bands



One pill, once-a-day



7 pediatric patients



Multiple weight bands



Multiple formulations



Current list of paediatric ARV formulations available

| 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 |

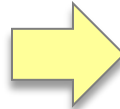
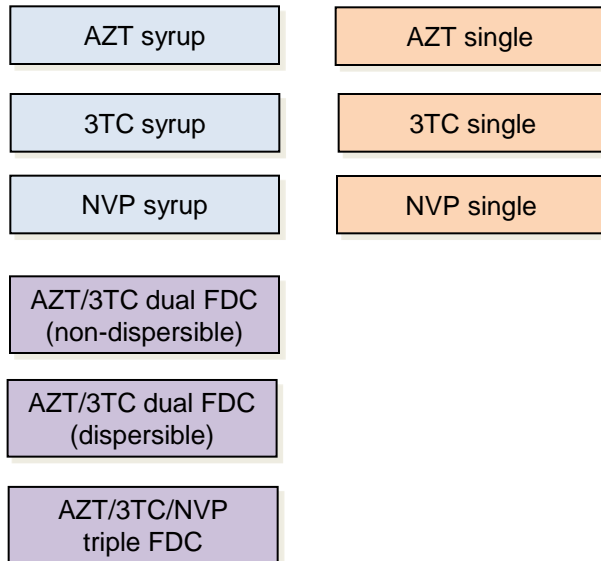
| Integrase Inhibitors | | |
|----------------------|--------------------------|--------|
| RAL | Chewable tablet (scored) | 100 mg |
| RAL | Chewable tablet | 25 mg |

Consolidation of demand around a subset of optimal paediatric ARV formulations is essential to ensure a sustainable supply

EXAMPLE: AZT+3TC+NVP regimen for 3 - 24.9 kg weight band

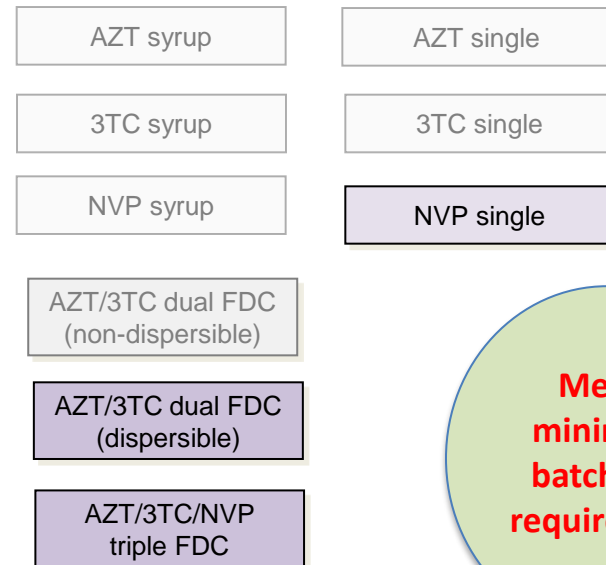
Product Fragmentation

- Multiple formulations procured for one regimen



Product Consolidation (to improved formulations)

- Improve patient outcomes
- Limit supply risks
- Decrease costs



WHO 1L and 2L Paediatric Regimens: 10 Options

Drug #1

- AZT (zidovudine)
- ABC (abacavir)
- TDF (tenofovir)

Drug #2

- 3TC (lamivudine)

Drug #3

- NVP (nevirapine)
- EFV (efavirenz)
- LPV//r
(lopinavir/ritonavir)

IATT Paediatric ART Formulary

Optimal

- Minimum number of ARV formulations needed to provide all currently recommended preferred and alternative 1st and 2nd line WHO recommended regimens for all paediatric weight bands

Limited-use

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

Non-essential

- Everything else (not needed)

Steps for revision of optimal list

STEP 1

- What does WHO recommend for preferred/alternative first and second-line regimens?

STEP 2

- Which formulations are needed to make up these regimens across all weight bands <35kg?

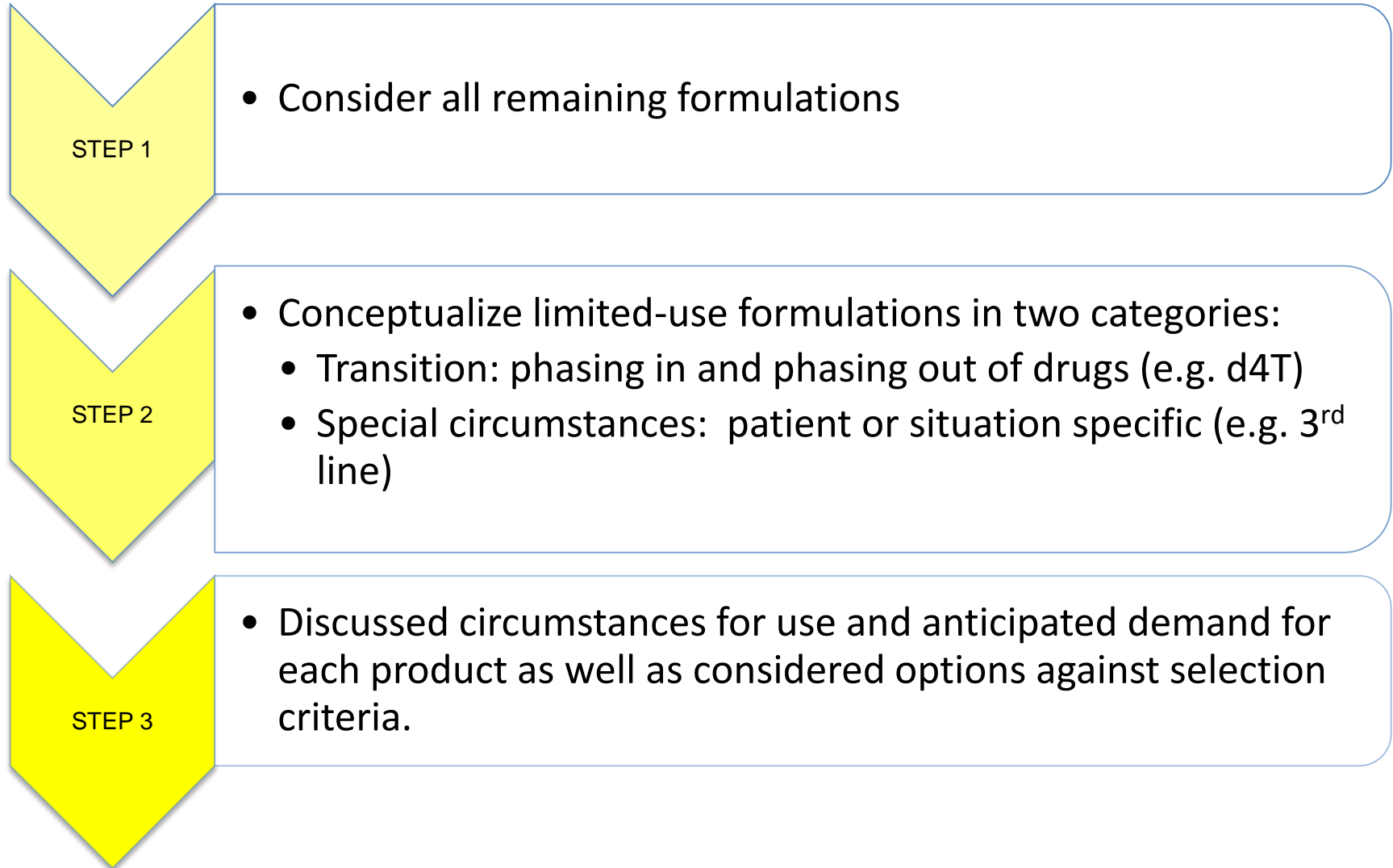
STEP 3

- Does each formulation meet the selection criteria defined by the group?

2013 IATT Optimal Paediatric ARV Formulary

| 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 |

Steps for revision of limited-use list



2013 IATT Limited-use Paediatric ARV formulary

| 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 2 nd line |
| PI | ATV | Solid oral dosage form | 150 mg | Alternative 2 nd 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 Special circumstances |

Current list of paediatric ARV formulations available

| 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 |

Dissemination of the IATT formulary

- Relevant stakeholders for this formulary at the global and country level include:
 - Paediatric ARV Procurement Working Group (PAPWG) of the Global Fund
 - All major agencies funding procurement of paediatric ARVs
 - All major buyers of paediatric ARVs
 - WHO Prequalification and USFDA tentative approval programme
 - Ministries of Health, including National Drug Regulatory authorities, National HIV management programmes and, where applicable, procurement offices more specifically
 - Civil society stakeholders involved in the paediatric HIV treatment response but not represented in IATT
 - Organizations of People Living with HIV (PLHIV) and other Community Based Organizations (CBOs)
 - Manufacturers of paediatric ARVs

More information needed for future updates

- Availability and usage
 - ABC/AZT/3TC or ABC 60mg
- Phase-out timeline
 - d4T dual and triple FDC's
- Demand
 - TDF for children
 - AZT syrup for PMTCT
 - “Adult” formulations e.g.. ABC/3TC 600/300mg scored tab
- Patient population
 - DRV

Questions to initiate review (or every 6 months) for consideration of revisions to the list

- Are there new WHO recommendations for paediatric ART?
- Are there new paediatric ARV products available? Have there been any new paediatric drug/formulation approvals?
- Have there been any shortages in supply due to supplier exit or changes in availability of products, or are any such shortages anticipated?
- Have there been any significant shifts in HIV paediatric treatment practices?
- Any notable ordering trends /use of list within last 6 months? (e.g., d4T-based formulations; ABC/AZT/3TC; AZT syrup; DRV)

Thank you
on behalf of the Child Survival Working Group and
Supply Chain Management Working Group

Evaluation Criteria

| Criteria | Description |
|---|--|
| WHO recommended | Safety and efficacy established |
| Available in resource limited settings | In country registration Reliable supply |
| SRA/WHO PQ approved | ≥ 1 quality assured product available |
| User friendly | Easy for HCW's to prescribe Easy for caregivers to administer Supports adherence in children |
| Optimizes supply chain | Easy to transport Easy to store Easy to distribute |
| Dosing flexibility | Allows for the widest range of dosing options |
| 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 |

Comparison of 2011 and 2013 lists

2011

5 formulations removed

2013

| 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) |



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

15 products

10 products

Non-essential Paediatric ARV formulations

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 | Tablet (scored) | 60 mg |
| AZT | Capsule | 100 mg |
| AZT | Tablet | 100 mg |
| 3TC | Tablet | 30 mg |
| D4T | Capsule | 15 mg |
| D4T | Capsule | 20 mg |
| D4T | Powder for oral solution | 5 mg/5 ml |
| 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 |

Integrase Inhibitors

| | | |
|-----|-----------------|-------|
| RAL | Chewable tablet | 25 mg |
|-----|-----------------|-------|

NNRTI's

| | | |
|-----|-----------------------|------------|
| EFV | Tablet | 50mg |
| 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) | 100 mg |

FDC's

| | | |
|-------------|-----------------------|--------------|
| AZT/3TC | Tablet (scored) | 60/30 mg |
| D4T/3TC/NVP | Tablet (disp, scored) | 12/60/100 mg |
| D4T/3TC | Tablet (disp, scored) | 12/30 mg |
| ABC/3TC | Tablet (scored) | 60/30 mg |

PI's

| | | |
|-----|------------------------|------------|
| DRV | Tablet | 150 mg |
| DRV | Oral liquid | 500 mg/5ml |
| ATV | Solid oral dosage form | 200 mg |
| TPV | Oral liquid | 500 mg/5ml |
| FPV | Oral liquid | 250 mg/5ml |