Lessons to be learned from HIV, TB and Malaria

Informal Consultation of Member States and relevant partners on the global development and stewardship framework to combat antimicrobial resistance
Stewardship of TB treatment to contain drug resistance

Dr Karin Weyer
Coordinator: Laboratories, Diagnostics & Drug Resistance
WHO Global TB Programme
Different mycobacterial populations require drugs in combination and prolonged drug exposure.
Long stewardship history in TB

- Vibrant & dynamic WHO policy landscape
- Widely acknowledged WHO standards of care
- Longstanding drug resistance surveillance programme
- Regulation and control of TB medicine use
- Global Drug Facility for procurement
- Global partnerships to ensure use of quality medicines
- Strong technical support networks (rGLCs)
- Strong WHO monitoring & evaluation system
30 High MDR-TB burden countries

TB
- Cambodia
- Sierra Leone

MDR-TB
- Azerbaijan
- Belarus
- Kazakhstan
- Kyrgyzstan
- Peru
- Republic of Moldova
- Somalia
- Tajikistan
- Ukraine
- Uzbekistan

TB/HIV
- Brazil
- Central African Republic
- Congo
- Lesotho
- Liberia
- Namibia
- UR Tanzania
- Zambia

Other countries
- Angola
- China
- DR Congo
- Ethiopia
- India
- Indonesia
- Kenya
- Mozambique
- Myanmar
- Nigeria
- Papua New Guinea
- South Africa
- Thailand
- Zimbabwe
WHO MDR-TB policy landscape
Global TB Drug Resistance Surveillance Programme

Global Project launched
SRL network launched


1st ed. DRS guidelines
2nd ed. DRS guidelines
3rd ed. DRS guidelines
4th ed. DRS guidelines
5th ed. DRS guidelines

1st global DRS report
2nd global DRS report
3rd global DRS report
4th global DRS report
M/XDR-TB report
Global TB reports

World Health Organization

END TB PROGRAMME
Anti-TB drugs

**First-Line**
- (H) Isoniazid
- (R) Rifampicin
- (Z) Pyrazinamide
- (E) Ethambutol
- (S) Streptomycin

- Standardised regimen 2HRZE/4HR, FDC-based

**Second-Line**
- Parenteral: kanamycin, amikacin, capreomycin
- Fluoroquinolones: ofloxacin, levofloxacin, moxifloxacin
- Oral, bacteriostatic: ethionamide, prothionamide, cycloserine, terizidone, p-aminosalicylic acid (PAS)
- Agents with unclear efficacy: clofazimine, linezolid, amoxicillin/clavulanate, thioacetazone, imipenem/cilastatin

- New agents: Bedaquiline, delamanid
<table>
<thead>
<tr>
<th>GROUP A</th>
<th>Fluoroquinolones</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Levofloxacin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moxifloxacin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gatifloxacin</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GROUP B</th>
<th>Second-line injectable agents</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Amikacin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Capreomycin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Kanamycin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Streptomycin)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GROUP C</th>
<th>Other Second-line Agents</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Ethionamide / Prothionamide</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cycloserine / Terizidone</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Linezolid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clofazimine</td>
<td></td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>GROUP D</th>
<th>Add-on agents</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>to the longer MDR-TB regimen</td>
<td></td>
</tr>
<tr>
<td></td>
<td>D1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pyrazinamide</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ethambutol</td>
<td></td>
</tr>
<tr>
<td></td>
<td>High-dose isoniazid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>D2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bedaquiline</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Delamanid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>D3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>p-aminosalicylic acid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Imipenem-Cilastatin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Meropenem</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Amoxicillin-Clavulanate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Thioacetazone)</td>
<td></td>
</tr>
</tbody>
</table>
Tuberculosis (TB)

New additions to the WHO Essential Medicines List related to TB treatment

The 20th WHO Expert Committee meeting on the selection and use of essential medicines has recommended the inclusion of five medicines (bedaquiline, delamanid, linezolid, rifapentine and terizidone) in the anti-tuberculosis (TB) medicines section of the WHO Model List of Essential Medicines (EML). Rifapentine is indicated for the treatment of latent TB infection (LTBI). The other four medicines are used as part of treatment regimens for multidrug and extensively drug-resistant TB (MDR-TB and XDR-TB respectively), two conditions with high lethality and poor treatment outcomes. Bedaquiline and delamanid are two new drugs which have recently been granted conditional approval by stringent regulatory authorities for use in the treatment of MDR-TB. Linezolid and terizidone are old drugs and their off-label use for severe forms of drug-resistant TB has now also been approved by the EML.

Bedaquiline  
Delamanid  
Linezolid  
Terizidone  
Rifapentine
rGLCs for technical assistance

- Technical expertise
  - Regional coordination mechanism
  - Expertise on the management of MDR-TB
  - Technical assistance through networks of partners
- Technical assistance
  - Peer support and knowledge sharing
  - Independent external monitoring and evaluation
- Monitoring and evaluation
  - High-quality drugs to treat MDR-TB at considerably lower than market prices
- Access to drugs at low cost
Global partnerships

- GLI & GDI secretariats hosted by WHO/GTB
- Broad stakeholder membership
- Donor alignment on use and procurement of TB diagnostics and TB medicines
- Dedicated Task Forces to address specific technical issues and monitor progress in MDR-TB response (eg. policy uptake, access to diagnostics and medicines)
### The global TB situation

<table>
<thead>
<tr>
<th>Category</th>
<th>Estimated incidence, 2016</th>
<th>Estimated number of deaths, 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>All forms of TB</td>
<td>10.4 million (8.8–12.2 million)</td>
<td>1.3 million* (1.2–1.4 million)</td>
</tr>
<tr>
<td>HIV-associated TB</td>
<td>1.0 million (0.9–1.2 million)</td>
<td>374,000 (325,000–427,000)</td>
</tr>
<tr>
<td>Multidrug-/rifampicin-resistant TB (MDR/RR-TB)</td>
<td>600,000 (540,000–660,000)</td>
<td>240,000 (140,000–340,000)</td>
</tr>
</tbody>
</table>

* Excluding deaths attributed to HIV/TB

**Source:** WHO Global Tuberculosis Report 2017
MDR/RR-TB and financing (4)

Estimated cost per patient treated for MDR-TB, 2016*

* Limited to 80 countries with at least 20 patients on MDR-TB treatment in 2016
Stewardship framework: Lessons learned from malaria

Dr Pascal Ringwald
Drug Efficacy and Response Unit

Global Malaria Programme

World Health Organization
Key WHO recommendations on ACTs

- The WHO Guidelines for the Treatment of Malaria (MTGs),
  - provide comprehensible, global and evidence-based guidelines for the formulation of policies and protocols for the treatment of malaria.

**Treating uncomplicated *P. falciparum* malaria**

*Treatment of uncomplicated *P. falciparum* malaria*

Treat children and adults with uncomplicated *P. falciparum* malaria (except pregnant women in their first trimester) with one of the following recommended artemisinin-based combination therapies (ACT):

- artemether + lumefantrine
- artesunate + amodiaquine
- artesunate + mefloquine
- dihydroartemisinin + piperaquine
- artesunate + sulfadoxine–pyrimethamine (SP)

*Strong recommendation, high-quality evidence*

**Duration of ACT treatment**

ACT regimens should provide 3 days' treatment with an artemisinin derivative.

*Strong recommendation, high-quality evidence*
New medicines/indications in WHO MTG

Scope of prequalification
- Limited to priority medicines as published in Invitations for Expression of Interest (EOIs) on PQT-m website
- Medicines eligible for prequalification as determined by WHO disease-oriented programmes ("perceived medical need")
- From products in WHO Model List of Essential medicines and/or WHO treatment guidelines
- Mostly generics
Recommendations on malaria diagnostics

Quality assured RDT and microscopy are the primary diagnostic tools for the confirmation and management of suspected clinical malaria in all epidemiological situations, including areas of low transmission, due to their high diagnostic performance in detecting clinical malaria, their wide availability and relatively low cost. Similarly, RDT and microscopy are appropriate tools for routine malaria surveillance (of clinical cases) in the majority of malaria-endemic settings.
Managing threats
"It is critical that artemisinins be used correctly," said Dr LEE Jong-wook, WHO's Director-General. "We request pharmaceutical companies to immediately stop marketing single-drug artemisinin tablets and instead market artesunate tablets only. The new treatment guidelines are helping many malaria countries with clear and evidence-based direction on the best treatment options for malaria."

According to the new WHO malaria treatment guidelines, uncomplicated falciparum malaria must be treated with ACTs and not by artemisinin alone or any other monotherapy.

Decision of Cambodia in March 2009

- Withdrawing marketing authorization of oral artemisinin-based antimalarial medicines;
- Widespread dissemination of new regulation (posters + leaflets);
- Empowerment of drug inspections (confiscation, fines, prosecution);
- Letters of appreciation + logos for approved outlets.
Antimalarial medicine pipeline: MMV-supported projects

**Data source:** https://www.mmv.org/research-development/mmv-supported-projects

MMV support to projects may include financial, in-kind, and advisory activities.

Footnotes: Included in MMV portfolio after product approval and/or development. DNDi and partners completed development and registration of ASMQ and ASAQ. WHO TDR completed Phase III trials of rectal artesunate. | Global Fund Expert Review Panel (ERP) reviewed product – permitted for time-limited procurement, while regulatory/WHO prequalification review is ongoing. | WHO Prequalified OR approved/positive opinion by regulatory bodies who are ICH members/observers. | Paediatric formulation. | For children 13 – 60 months; ** For infants 3 – 12 months.

Brand names 1: Coartem® Dispersible; 2: Artesun®; 3: Eurartesim®; 4: Pyramax® tablets or granules; 5: ASAQ Winthrop®; 6: SPAQ-COTM
Global malaria vaccine pipeline

**Data source:** http://www.who.int/vaccine_research/links/Rainbow/en/index.html
HIV Stewardship and response to HIVDR

Meg Doherty, MD, MPH, PhD
Coordinator Treatment and Care, HIV/Hep Department, WHO HQ

10 November 2017
# Current WHO ARV Treatment Recommendations

## Table 4.3. Summary of first-line ART regimens for adolescents

<table>
<thead>
<tr>
<th>Preferred regimens</th>
<th>TDF + 3TC (or FTC) + EFV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alternative regimens</td>
<td>TDF (or ABC) + 3TC (or FTC) + DTG</td>
</tr>
<tr>
<td></td>
<td>TDF (or ABC) + 3TC (or FTC) + EFV,ab</td>
</tr>
<tr>
<td></td>
<td>ABC + 3TC + EFV</td>
</tr>
<tr>
<td></td>
<td>ABC + 3TC + NVP</td>
</tr>
<tr>
<td></td>
<td>AZT + 3TC + EFV</td>
</tr>
<tr>
<td></td>
<td>AZT + 3TC + NVP</td>
</tr>
<tr>
<td></td>
<td>TDF + 3TC (or FTC) + NVP</td>
</tr>
</tbody>
</table>

Special circumstances:
- Regimens containing boosted PIs

---

## Table 4.19. Summary of sequencing options for first-, second- and third-line ART regimens in adults, adolescents, pregnant women and children

<table>
<thead>
<tr>
<th>Population</th>
<th>First-line regimens</th>
<th>Second-line regimens</th>
<th>Third-line regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults and adolescents (≥10 years)</td>
<td>2 NRTIs + EPV</td>
<td>2 NRTIs + ATV/r or LPV/rab</td>
<td>DRV/r + DTG (or RAL) ± 1–2 NRTIs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 NRTIs + DRV/rb</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 NRTIs + DTG</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 NRTIs + ATP or LPV/rb</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 NRTIs + NVP</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 NRTIs + DRV/r</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 NRTIs + EFV</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 NRTIs + ATV/r or LPV/rb</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 NRTIs + DRV/rb</td>
<td></td>
</tr>
<tr>
<td>Pregnant or breastfeeding women</td>
<td>2 NRTIs + EPV</td>
<td>2 NRTIs + ATV/r or LPV/rb</td>
<td>DRV/r + 2 NRTIs ± NNRTI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 NRTIs + NVP</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 NRTIs + DRV/r</td>
<td></td>
</tr>
<tr>
<td>Children (0–10 years)</td>
<td>2 NRTI + LPV/r</td>
<td>If less than 3 years:</td>
<td>RAL (or DTG)′ + 2 NRTIs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 NRTIs + RAL</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>If older than 3 years:</td>
<td>DRV/r + 2 NRTIs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 NRTIs + EFV</td>
<td>DRV/r + RAL (or DTG)′ + 1–2 NRTIs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 NRTIs + ATV/r or LPV/r</td>
<td></td>
</tr>
</tbody>
</table>

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* a To date, there is limited experience with the use of low-dose EFV and DTG in adolescents. While no age or weight restrictions apply to the use of EFV 400 mg/day, which can be used starting from a weight of 20 kg (Annex 11c), the use of DTG is approved only for adolescents who are older than 12 years and weigh more than 40 kg (311). In addition, safety and pharmacokinetic data on TB coinfection and pregnancy are still pending.

* b Special circumstances may include situations where preferred or alternative regimens may not be available or suitable because of significant toxicities, anticipated drug–drug interactions, drug procurement and supply management issues or for other reasons.

* c Using d4T as an option in first-line treatment should be discontinued.

3TC lamivudine, ABC abacavir, AZT zidovudine, DTG dolutegravir, EFV efavirenz, FTC emtricitabine, NVP nevirapine, PI protease inhibitor, TDF tenofovir.
ARV Drug Optimization: Key Principles

- Reduce toxicity
- Improve palatability/pill burden
- Increase resistance barrier
- Reduce drug interactions
- Safe use across different age groups and populations’ Harmonization
- Reduce cost

Gallant, 2002
National pretreatment HIVDR surveys, 2014-2016 and beyond
The Emerging Threat of HIV Drug Resistance

WHO’s Report on HIV drug resistance 2017

NNRTI (EFV/NVP) pretreatment drug resistance (national surveys, 2014-2016)

Prevalence of NNRTI pre-treatment resistance by calendar year (systematic review)
Pretreatment HIVDR in first-line ART initiators by drug (national surveys), 2014-2016
Acquired HIVDR surveys 2014-2016 and beyond

- Viet Nam (36+)
- Guatemala (12 and 48+)
- Cameroon (12 and 48+)
- Zambia (12)

Legend:
- Completed and results reported
- Completed
- Ongoing
- Planned
- Not applicable
Acquired HIVDR by drug and country (national surveys), 2014-2016
WHO recommended response to pretreatment HIV drug resistance: SUMMARY

Are nationally representative PDR data available?

YES
Implement viral load monitoring; prevent HIVDR emergence and transmission

NO
Implement nationally representative PDR survey

≥10% PDR to EFV/NVP
Is it feasible to introduce non-NNRTI first-line ART for ALL starters?

YES
Urgently consider using non-NNRTI first-line ART for ALL starters

NO
Consider introducing pre-treatment HIVDR testing

<10% PDR to EFV/NVP
Prioritize use of non-NNRTI containing first-line ART in people with prior exposure to ARV drugs

ART: Antiretroviral therapy
ARV: Antiretroviral
EFV/NVP: Efavirenz or nevirapine
HIVDR: HIV drug resistance
PDR: Pre-treatment drug resistance
# GLOBAL ACTION PLAN (GAP)

<table>
<thead>
<tr>
<th>#</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><strong>PREVENTION &amp; RESPONSE</strong>&lt;br&gt;Timely use of all available evidence to guide public health actions regarding HIVDR.</td>
</tr>
<tr>
<td>2</td>
<td><strong>MONITORING &amp; SURVEILLANCE</strong>&lt;br&gt;Obtain quality data on HIVDR &amp; HIVDR service delivery from periodic surveys, while expanding routine viral load &amp; HIVDR testing.</td>
</tr>
<tr>
<td>3</td>
<td><strong>RESEARCH &amp; INNOVATION</strong>&lt;br&gt;Encourage relevant &amp; innovative research which will have the greatest public health impact in minimizing HIVDR.</td>
</tr>
<tr>
<td>4</td>
<td><strong>LABORATORY CAPACITY</strong>&lt;br&gt;Support and expand use of viral load testing &amp; build capacity to monitor HIVDR in low and middle income countries.</td>
</tr>
<tr>
<td>5</td>
<td><strong>GOVERNANCE &amp; ENABLING MECHANISMS</strong>&lt;br&gt;Ensuring country ownership, coordinated action, awareness / advocacy &amp; sustainable funding are in place to support action on HIVDR.</td>
</tr>
</tbody>
</table>
Conclusions: GAP is a Framework for collective action

Each strategic objective has actionable items specific for each stakeholder

1. Prevention & Response
2. Monitoring & Surveillance
3. Research & Innovation
4. Laboratory Capacity
5. Governance & Enabling Mechanisms
How WHO support countries in transitioning to new ARV drugs?

- evaluating efficacy and safety data in **clinical studies** with new drugs
- providing **guidance and tools** for monitoring drug toxicity and HIVDR
- providing advice on **how to phase in** new drugs
- sharing **country experiences**

Summary of optimization profiles of new ARVs recommended in 2016 WHO ARV guidelines - comparative analysis

<table>
<thead>
<tr>
<th>Optimization criteria</th>
<th>DTG</th>
<th>EFV400</th>
<th>DRV/r</th>
<th>RAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Efficacy and safety</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High virologic potency</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Low toxicity</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>High genetic barrier to resistance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Simplification</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Available as generic FDC</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Low pill burden</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Harmonization</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use in pregnant women</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Use in children</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Use in HIV-associated TB</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Few drug interactions</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low price</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
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</tbody>
</table>
Estimated timelines for completion of new clinical trials of DTG and EFV 400

<table>
<thead>
<tr>
<th>ARV</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Q3-Q4</td>
<td>Q1-Q2</td>
<td>Q3-Q4</td>
<td>Q1-Q2</td>
</tr>
<tr>
<td>DTG</td>
<td>RADIO DAWNING ADVANZ-4</td>
<td>IMPAACT 1093</td>
<td>DOLPHIN 1 NAMSAL</td>
<td>DOLPHIN 2 D2EFT</td>
</tr>
<tr>
<td>EFV400</td>
<td>SSAT 062</td>
<td>SSAT 063</td>
<td>NAMSAL</td>
<td></td>
</tr>
</tbody>
</table>

- Pregnant women
- Children
- TB
- Adults

Adapted from Vitoria et al, Current Opinion HIV/AIDS, 12: 369-76 2017
Some programmatic factors that can influence the transition to DTG in 1st Line ART

- DTG introducing policy (eligibility criteria/priority populations)
- Regulatory issues: availability of low cost generic formulations (FDCs)
- Supply chain management (procurement preparedness, current stocks of EFV containing regimens)
- Pre-treatment levels of HIVDR to NNRTIs
- Programme monitoring for toxicity and pregnancy safety (pharmacovigilance)
- “Bandwidth” capacity to develop multiple implementation polices (training, logistic management, monitoring capacity, quality)
Licensing and pricing of DTG in LMICs

<table>
<thead>
<tr>
<th>Country</th>
<th>DTG U$ price (pppy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LMICs (generic)</td>
<td>48 - 60</td>
</tr>
<tr>
<td>LMICs (originator)</td>
<td>396 - 1740</td>
</tr>
<tr>
<td>Botswana</td>
<td>272</td>
</tr>
<tr>
<td>Brazil</td>
<td>547</td>
</tr>
<tr>
<td>Mexico</td>
<td>2200</td>
</tr>
<tr>
<td>Belarus</td>
<td>2300</td>
</tr>
<tr>
<td>Ukraine</td>
<td>72</td>
</tr>
</tbody>
</table>

Sources: MSF, GFTAM, CHAI, MoH Brazil, Botswana, Mexico & Ukraine

Tentative SRA Approval Timeline for DTG, TDF/3TC/DTG, and TDF/3TC/EFV400 formulations

(2016-2019)

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*Assumes SRA approval received 12 months after filing date

*Expected SRA approval of product by generic suppliers

TDF/3TC/DTG in 92 LMICs = 75 U$ pppy (Sep/2017)
WHO support to DTG routine toxicity monitoring in 2017

- Malawi - full time consultant
- Technical support to Zimbabwe, Tanzania, South Africa, RDC in partnership with University of Cape Town (Collaborating Center)
- Evaluation and technical assistance missions in Brazil, Botswana, Kenya, Mozambique
- Dissemination workshops – Harare May 2017, Senegal February 2018 for francophone AFRO countries

WHO priorities for 2018:
- Phase 1: 10 early adopter fast track countries
- Phase 2: any adopter country with patient and toxicity monitoring
Conclusions: GAP is a Framework for collective action

Each strategic objective has actionable items specific for each stakeholder

1. Prevention & Response
2. Monitoring & Surveillance
3. Research & Innovation
4. Laboratory Capacity
5. Governance & Enabling Mechanisms