Expedited development and registration resulting in successful uptake of generic, pediatric dolutegravir products for low- and middle-income countries through an innovative public-private partnership

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1. Clinton Health Access Initiative (CHAI) 2. ViiV Healthcare UK Ltd , and 2a. Formerly ViiV Healthcare UK Ltd

Background

Children Living with HIV (CLHIV)[1]

- HIV remains a significant public health issue amongst children
- 1.7M CLHIV globally, predominantly in low- and middle-income countries
- 54% CLHIV are receiving antiretroviral therapy, compared with 74% of adults
- 40% CLHIV had suppressed viral loads, compared with 67% of adults
- Lack of accessible, effective, child-friendly formulations leads to low adherence, inadequate viral suppression and poor health outcomes
- A significant contributor is the delay between adult and pediatric formulation development, followed by generic product development

Dolutegravir (DTG)

- DTG is an integrase strand transfer inhibitor with once-daily dosing, high barrier to resistance and a favorable safety profile
- In 2013, FDA approved DTG 50mg film-coated tablets for adults and adolescents (≥12 years, ≥40 kg)
- In 2016:
  - FDA approved DTG 10 & 25mg film-coated tablets for children (>30kg)
  - EMA approved DTG 10 & 25mg film-coated tablets for ≥6 years
- In 2018:
  - WHO updated guidelines recommended DTG, in combination with NRTI backbone, as first-line treatment for adults, adolescents and children (where approved dosing is available)
  - ViiV Healthcare was developing a pediatric DTG dispersible tablet (≥ 4 weeks, ≥3 kg)
  - Generic development of a pediatric DTG dispersible tablet had not yet commenced

Public-Private Partnership - Objectives

- To **expedite** the development and registration of generic, pediatric DTG 10 mg scored, oral dispersible tablets for use in low- and middle-income countries included within ViiV's voluntary licensing territory[2]

Public-Private Partnership – Key Activities

- ViiV conducted Phase I-II and III clinical studies to demonstrate safety, tolerability and efficacy in children living with HIV[3,4]. ViiV provided a technical package, clinical supplies for BE studies and ongoing technical and regulatory support. Efficacy was based on achieving PK targets shown to be safe and effective in adults.
- CHAI (funded by Unitaid) provided a financial incentive for accelerated generic development, developed a novel regulatory strategy and provided ongoing technical support. CHAI also negotiated a global price of USD$4.50 per 90ct pack[5], which is a 75% cost reduction from the existing standard of care (LPV/r).
- Mylan (a Viatris company) and Macleods committed to an accelerated development and registration timeline of the pediatric DTG dispersible product and openly shared product data in a trilateral project team structure.

Lessons Learned

- Technical support throughout the generic development process was critical to reducing timelines
- Early engagement with US FDA prior to generic filing was key to gain alignment on the proposed regulatory strategy and timing of submissions

Results

The collaborative partnership **significantly reduced** the time between FDA approvals of innovator and generic products from several years to 5 months, compared with historical pediatric ARV products

- ✓ ViiV obtained U.S. FDA approval in June 2020
- ✓ Mylan (a Viatris company) obtained U.S. FDA tentative approval in November 2020 (5 months after ViiV's approval)
- ✓ Macleods obtained U.S. FDA tentative approval in March 2021 (9 months after ViiV's approval)

12X
Faster than average generic pediatric HIV treatment approval
SINCE PEPFAR
was established

25X
Faster than average generic pediatric HIV treatment approval
EVER

Conclusions/Next Steps

- The collaboration partnership between CHAI, ViiV, Mylan (a Viatris company) and Macleods **significantly accelerated** development and registration of generic, pediatric DTG dispersible products with the gap between FDA approval of innovator and generic products reduced from years to months
- Generic pediatric DTG was launched at an affordable and sustainable price and is enabling greater access for CLHIV in low- and middle-income countries
- Expanding country-level access to generic dispersible pediatric DTG formulations:
  - Mylan (a Viatris company) country registrations: Chad, Ghana, India, Malawi, Mozambique, Namibia, Republic of Congo, South Africa, Tanzania & Zimbabwe (as of 30th June 2022)
  - Macleods country registrations: Democratic Republic of Congo, Ghana, India, Mozambique, Namibia, South Africa & Tanzania, plus WHO Prequalification (as of 30th June 2022)
  - More than 40 countries have started product introduction
- This collaborative public-private partnership approach may be a viable model for future development of public-health prioritized pediatric medicines

2018: Initiation

- Formal public-private partnership was initiated
- ViiV clinical studies were ongoing
- Technical transfer from ViiV to Mylan (a Viatris company) & Macleods was initiated
- Generic product development commenced

2019: Development

- ViiV completes clinical studies & submits to US FDA
- Mylan (a Viatris company) and Macleods continue their product development

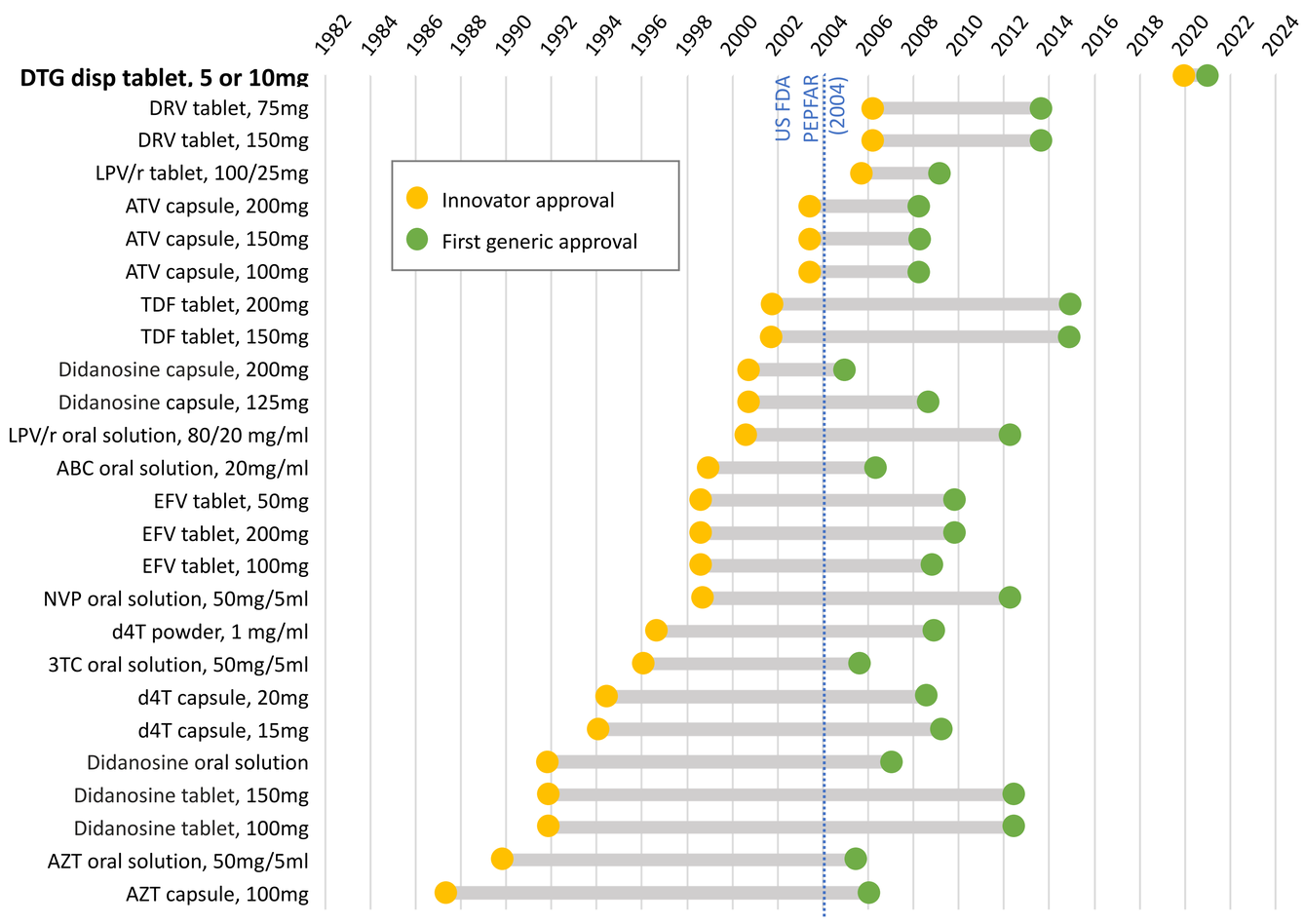
2020: Regulatory

- ViiV obtains US FDA approval (June 2020) & starts commercialization of their pediatric DTG product
- Mylan and Macleods complete their product development & bioequivalence studies and submit to US FDA
- Mylan (a Viatris company) obtains US FDA tentative approval under PEPFAR (November 2020)

2021: Commercialization

- Macleods obtains US FDA tentative approval under PEPFAR (March 2021)
- Mylan (a Viatris company) and Macleods complete their process validation & start commercialization of their generic DTG product

Time between FDA Approvals for Innovator and First Generic Pediatric ARV Products



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