EARLY ACCESS TO DOLUTEGRAVIR-BASED HIV TREATMENTS IN LOW- AND MIDDLE-INCOME COUNTRIES

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Issues

Despite progress in scaling up antiretroviral therapy (ART) worldwide, approximately 38% of adults and 46% of children living with HIV still lack access to ART. Among people on ART, many are still on suboptimal treatment, often for lack of access to affordable versions of optimised treatments. Access-oriented licences on patented medicines facilitate access to affordable, quality-assured generic medicines, benefitting millions of people in low- and middle-income countries (LMICs).

Description

The Medicines Patent Pool (MPP)'s public health-oriented licences allow the distribution of affordable versions of patented medicines in LMICs and the development of new treatments (e.g., paediatric formulations and fixed-dose combinations). Competition among multiple manufacturers brings prices down, supporting scale-up. In 2014, MPP and ViiV Healthcare entered into a licence agreement for dolutegravir (DTG), which has a low potential for drug-drug interactions, achieves rapid viral suppression, has a high genetic barrier to drug resistance, enables low cost production, is effective against both HIV-1 and HIV-2, and overall lowers the risk of discontinuing treatment. DTG is recommended as part of preferred first- and second-line HIV treatments for children and adults by the World Health Organization (WHO). The MPP-ViiV Healthcare licence, along with ViiV Healthcare's direct licence with one manufacturer, has enabled swift development of affordable, quality-assured generic versions of DTG and the fixed-dose combination TLD (tenofovir disoproxil fumarate/lamivudine/dolutegravir or TDF/3TC/DTG).

Lessons learned

The DTG licence nominally covers 94 countries; in addition to this territory, countries where DTG is not patented may also procure DTG-based products from MPP licensees. The non-exclusive nature of the DTG licence has promoted strong generic competition (with prices for TLD already below USD 70 per person per year). As of June 2019, six MPP licensees had received stringent regulatory approval (SRA) on DTG and/or TLD, and had made them available in 74 countries (including 34 in Africa). These licensing arrangements have facilitated an unprecedented acceleration in the availability of an important new medicine in LMICs, with nearly 5.9 million people living with HIV (PLHIV) in LMICs now having access to generic DTG-based products since DTG's initial U.S. Food and Drug Administration (USFDA) approval in 2013.

Next steps

Tenofovir alafenamide (TAF) + 3TC (or emtricitabine, FTC) + DTG is now recommended by WHO for adults in special circumstances, i.e. for people with established osteoporosis and/or impaired kidney function, as an alternative first-line regimen for children, and in some cases for second-line treatment. TAF may have safety advantages over TDF and enable further cost savings. The territory covered by both TAF and DTG licences is 87 countries. As of June 2019, one MPP licensee had received SRA approval for TAF/FTC/DTG. Early licensing of DTG has enabled prompt access to quality, affordable generic versions of TLD and other promising treatment options, setting new standards in promoting access to important new medicines. It is now important, in order to enable implementation of WHO guidelines, that countries update their national guidance and switch to DTG-based products, while ensuring that generic manufacturers register these products in all licensed countries.

TIMELINE

2013

August
USFDA approves DTG for HIV treatment

2014

April
MPP signs a licence with ViiV Healthcare, covering countries home to 94% of adults and 99%* of children living with HIV in LMICs*

2015

December
Four MPP licensees are developing products containing DTG

2016

June
WHO guidelines recommend DTG in first-line HIV treatment

2017

August
First MPP licensee receives USFDA approval for fixed-dose combination TLD

September
Multiple partners announce an annual price of USD 75 for TLD - a 83% price reduction from originator

2018

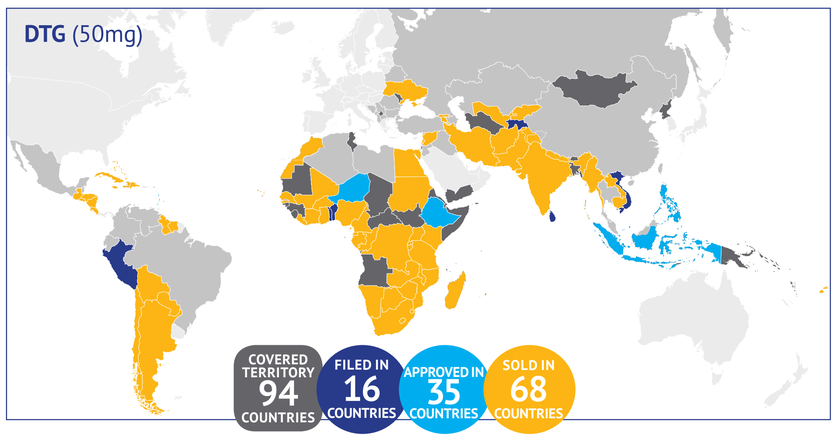
June
Six quality-assured generic manufacturers are ready to supply TLD to PLHIV in LMICs

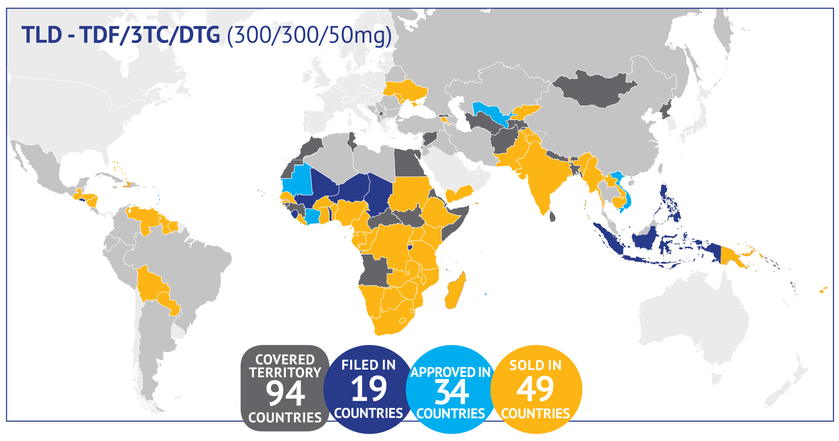
2019

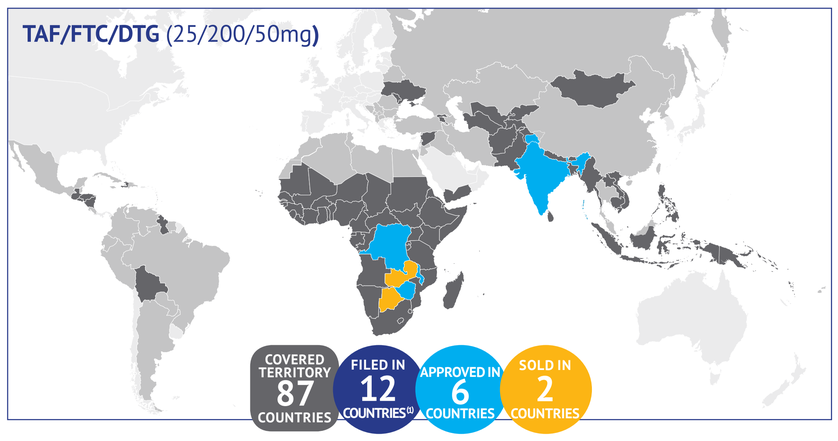
June
DTG 50mg is commercialised in 68 countries and TLD in 49 countries, with six MPP manufacturing partners ready to supply

** At time of announcement*

RECOMMENDED DTG PRODUCTS DEVELOPED BY MPP LICENSEES WORLDWIDE







High-income countries Low- and middle-income countries

(1) For confidentiality purposes, the list of filed countries for TAF/FTC/DTG will be disclosed when approval from a SRA for this product will have been granted to more than one licensee.

Data as of June 2019

DTG & TLD UPTAKE IN AFRICA, INCLUDING ILLUSTRATIVE COUNTRY SNAPSHOTS

AFRICA - Overall data

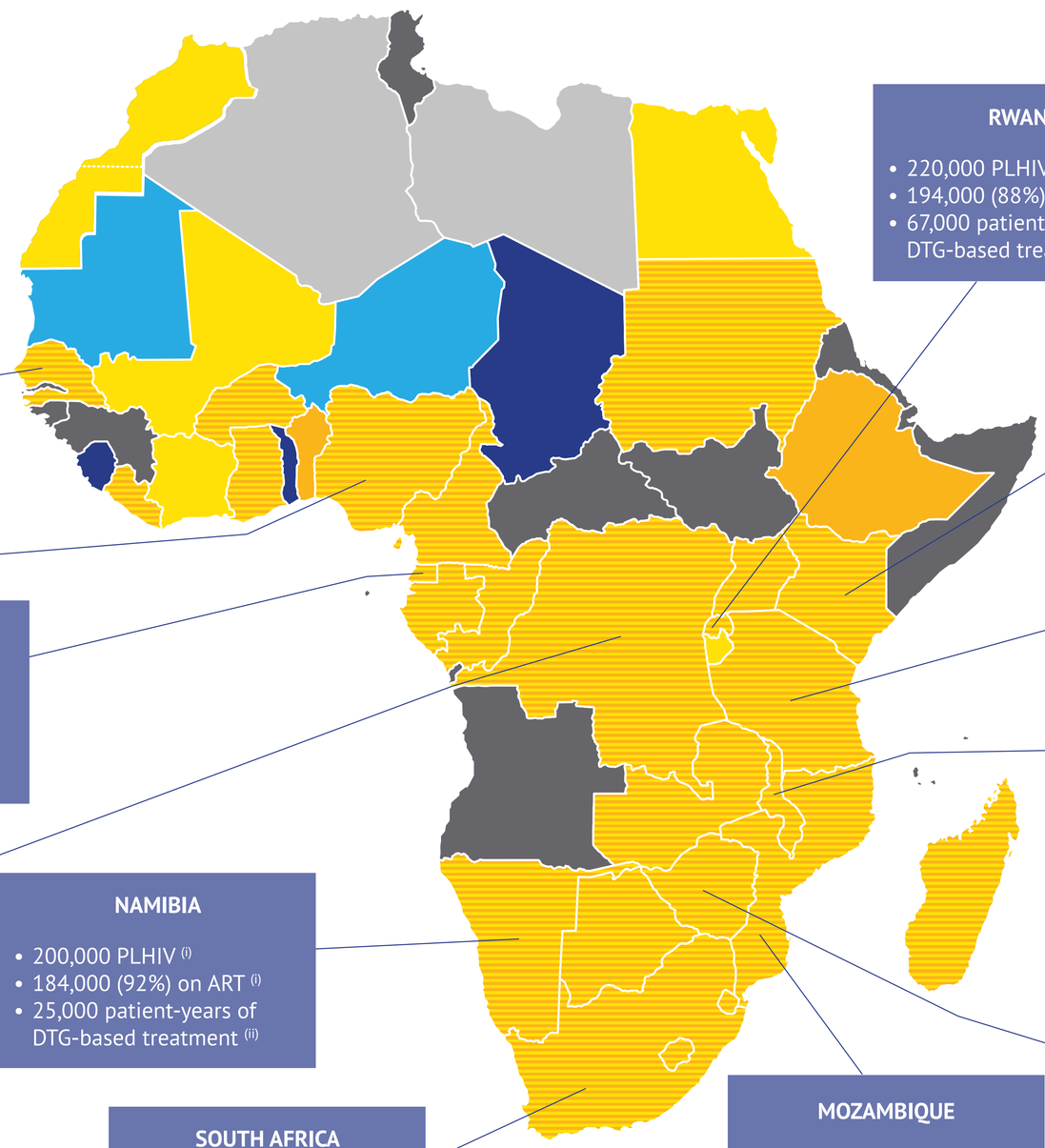
- **25,900,000** PLHIV (i)
- **16,500,000** (64%) on ART (i)
- **4,550,000** patient-years of DTG-based treatment (ii)

(i) Epidemiology and treatment coverage data for 2018 as per UNAIDS
(ii) Patient-years of DTG-based treatment having been procured from MPP licensees (Cipla, Emcure, Hetero, Laurus Labs, Macleods, and Mylan) and from Aurobindo, a direct licensee of ViiV Healthcare, between January 2017 and June 2019. This number refers to the number of people that could have been treated over a period of one full year using the total amount of product procured over this period of 2.5 years. This number does not take into account the time between product procurement and delivery to patients, and other supply chain and programmatic considerations.

DTG AND/OR TLD

COVERED TERRITORY 52 COUNTRIES | FILED IN 14 COUNTRIES | APPROVED IN 24 COUNTRIES | DTG SOLD IN 32 COUNTRIES | TLD SOLD IN 27 COUNTRIES | DTG&TLD SOLD IN 25 COUNTRIES

Stakeholders interested in expanding access to DTG-based products in countries where these medicines have not yet been registered or supplied are invited to reach out to the MPP team.



SENEGAL
- 42,000 PLHIV (i)
- 26,600 (63%) on ART (i)
- 1,270 patient-years of DTG-based treatment (ii)

NIGERIA
- 1,900,000 PLHIV (i)
- 1,020,000 (54%) on ART (i)
- 222,000 patient-years of DTG-based treatment (ii)

EQUATORIAL GUINEA
- 62,000 PLHIV (i)
- 21,400 (35%) on ART (i)
- 5,700 patient-years of DTG-based treatment (ii)

DEMOCRATIC REPUBLIC OF THE CONGO
- 450,000 PLHIV (i)
- 256,000 (57%) on ART (i)
- 208,000 patient-years of DTG-based treatment (ii)

NAMIBIA
- 200,000 PLHIV (i)
- 184,000 (92%) on ART (i)
- 25,000 patient-years of DTG-based treatment (ii)

SOUTH AFRICA
- 7,700,000 PLHIV (i)
- 4,790,000 (62%) on ART (i)
- 609,000 patient-years of DTG-based treatment (ii)

RWANDA
- 220,000 PLHIV (i)
- 194,000 (88%) on ART (i)
- 67,000 patient-years of DTG-based treatment (ii)

KENYA
- 1,600,000 PLHIV (i)
- 1,070,000 (67%) on ART (i)
- 512,000 patient-years of DTG-based treatment (ii)

TANZANIA
- 1,600,000 PLHIV (i)
- 1,110,000 (69%) on ART (i)
- 537,000 patient-years of DTG-based treatment (ii)

MALAWI
- 1,000,000 PLHIV (i)
- 814,000 (81%) on ART (i)
- 948,000 patient-years of DTG-based treatment (ii)

ZIMBABWE
- 1,300,000 PLHIV (i)
- 1,150,000 (88%) on ART (i)
- 165,000 patient-years of DTG-based treatment (ii)

MOZAMBIQUE
- 2,200,000 PLHIV (i)
- 1,210,000 (55%) on ART (i)
- 47,000 patient-years of DTG-based treatment (ii)

REFERENCES

MPP - Licence for Dolutegravir (DTG): https://bit.ly/37rm8eP
MPP - Licence for Tenofovir Alafenamide (TAF): https://bit.ly/2DbPboN
MPP - MedsPaL: www.medspal.org
MPP - Update on Progress of MPP Sublicensees: https://bit.ly/2NDyINd
MPP - Website: www.medicinespatentpool.org
UNAIDS AIDSinfo: www.aidsinfo.unaids.org/
UNAIDS Fact Sheet: www.unaids.org/en/resources/fact-sheet
World Health Organization, Key Facts: www.who.int/news-room/fact-sheets/detail/hiv-aids

Information on patents and licences for DTG-based products and other patented essential medicines, in more than 130 LMICs, is available in the MPP open access and free database **MedsPaL** *at www.medspal.org.*

We would like to thank our founder Unitaid which serves as sole funder for MPP's activities in HIV, hepatitis C and tuberculosis.

We also thank our partners and important contributors to expanding access to optimal HIV medicines in LMICs: civil society (including community networks representing people living with and affected by HIV), governments, international organisations, funders and implementing partners, industry and other stakeholders.