ISSUE BRIEF

MÉDECINS SANS FRONTIÈRES ACCESS CAMPAIGN

UNTANGLING THE WEB: HIV MEDICINE PRICING & ACCESS ISSUES, 2020

INTRODUCTION

Over the past 20 years, the *Untangling the Web* report series[1] by the MSF Access Campaign has analysed and advocated for the availability of lifesaving antiretroviral (ARV) medicines for people living with HIV (PLHIV). Through these and other analyses, MSF monitors ARV accessibility, especially the critical issues of pricing and patent barriers, and promotes the need for policy changes to ensure access to affordable, quality-assured HIV treatment.

In 2019, 690,000 people died of HIV-related causes. While this is the lowest figure since 1993,[2] it is still too high, and mortality is decreasing too slowly to reach the global target of less than 500,000 deaths by 2020. ARV treatment (ART) coverage remains too low. By the end of 2019, 25 million people had access to ART, but this represents just 67% of the 38 million PLHIV, leaving a deadly gap of more than 12 million people in need of treatment. Of note, only 53% of the 1.8 million children living with HIV (0-14 years old) had access to ART in 2019.[3]

This issue brief analyses new developments in the access challenges to current and future ARVs and other critical medicines for the treatment of HIV and opportunistic infections that are responsible for the majority of HIV-related deaths. Numerous policies responsible for blocking access are presented including pricing, patents, registration, production, and supply. Specific updated ARV pricing and supplier information are also provided.

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Austin (right) and his wife Patuma at their home in Malawi, 2019. Austin was admitted to Nsanje District Hospital where he was diagnosed with advanced HIV.

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ACCESS CHALLENGES FOR CURRENT CRITICAL HIV DRUGS

DOLUTEGRAVIR (DTG)

Dolutegravir (DTG), an integrase inhibitor produced by ViiV (a joint venture by Pfizer, GlaxoSmithKline and Shionogi), is the backbone for first-line ARV treatment recommended by the World Health Organization (WHO) for infants, children, adolescents and adults living with HIV. DTG 50mg tablets can be used for treating adults and children 20 kg and greater.[4] Generic formulations of these tablets are filed for national registration in 21 countries, approved in 44 countries and supplied in 100 countries using waivers in lieu of registration.

DTG 5mg dispersible tablets are approved for children weighing 3 kg or greater, or aged 4 weeks or older.[4] However, the only formulation currently available commercially for these children under 20 kg is Viiv's dispersible tablet priced at $33-50[a] per bottle of 60 tablets.[5] This equates to $806-1,226 per year for a child weighing 10 kg, a price far out of reach for low- and middle-income countries (LMICs). ViiV has started developing a syrup formulation for children weighing less than 3 kg, or younger than 4 weeks of age.[6] Seven years after DTG was first approved by the US Food and Drug Administration (FDA) for adults,[7] most children still do not have access to this drug recommended for first-line treatment by WHO since 2018.

Generic DTG 10mg dispersible tablets have been developed by Mylan and Macleods, also for children less than 20 kg. Mylan's product was approved by the FDA in November 2020,[8] while Macleods' approval is expected by the end of 2020. The price for these generic formulations is expected to cost a fraction of the price of ViiV's products. Importantly, adult DTG 50mg tablets can be used in children 20 kg and up, but they are film coated and not bioequivalent to the paediatric 5mg and 10mg dispersible tablets, and are therefore not interchangeable in cases of shortages or stockouts.

Patent Barriers, and Licensing and Procurement Challenges

Some key manufacturing countries have granted and/or have pending patent claims on the DTG compound, which, if granted, only start expiring in 2026. The Medicines Patent Pool (MPP) signed a licensing agreement with ViiV in 2014 for the paediatric and adult formulations of DTG and further revised the agreement in 2016 for the adult formulation to include all lower middle-income countries.[9]

The ViiV-MPP license on DTG contains a term allowing generic sales in countries outside the "territory" if they do not infringe on a blocking patent. As a result, countries like Argentina, Costa Rica, Ecuador, Iran, and Thailand, where no patents have been granted, can procure generic DTG, even though they are not explicitly covered under the listed territories of the license.[10]

In 2017, MSF published a table to explain the direct and indirect territorial coverage of the ViiV-MPP voluntary license (VL) for DTG.[11] The agreement was revised in 2018 and 2020 to include Tunisia, Mongolia and Algeria. As of the time of this writing, the VL signed by ViiV and MPP for paediatric DTG includes 121 countries versus 95 for adult DTG.[9] While the license has been signed by multiple Indian and Chinese generics manufacturers, China itself is not included in the license territory. Companies in China can therefore export to other countries (directly or indirectly covered by the license), but people in China are left without access to generic versions of these lifesaving HIV medicines that are being manufactured domestically until at least 2026, unless China were to issue a compulsory license. Until generic DTG becomes available, the price from ViiV in the Chinese market is $1,825 per person per year,[12] almost 30 times more than the price of generics. This licensing practice raises ethical questions about harnessing the capacity of LMICs to develop, produce and supply quality medicines, while at the same time prohibiting generic companies from responding to considerable unmet medical needs domestically.[13] MSF recommends that ViiV and MPP include China at a minimum in the list of royalty-bearing countries.

The license also applies different terms for formulations that can be prescribed to both adults and children. For example, a 50mg dose of DTG may be prescribed to children over 20 kg, yet the ViiV-MPP license includes some countries like Azerbaijan, Colombia and Malaysia for paediatric formulations, but not the adult formulations. This means adult PLHIVs in these countries are left without affordable access to this first-line treatment. It also leaves procurers like MSF faced with unnecessary complexities in procurement. Generic suppliers request that purchase orders explicitly indicate the destination country and if supply will be used only for paediatric patients. However, MSF and other procurement agencies often maintain stock to support medical projects efficiently and requesting such data is not required from a regulatory or medical standpoint and will lead to unnecessary delays.[13]

Under the ViiV-MPP license, 12 countries are included as royalty-bearing countries, which are further categorised into different tiers with differential rates of royalties. For these countries, the license also differentiates the "public market," including treatment programmes provided by governments, UN agencies, or non-governmental and humanitarian organisations, from the "private market," where people are likely to pay much higher prices out of pocket.

[a] Price varies based on multiple variables including order volume, currency fluctuations, etc.

The ViiV-MPP license allows generic companies to supply both public and private health sectors in the royalty-free countries, but only in the public sector in the 12 royalty-bearing countries, with distinguishable packaging stating the restricted supply destination. While this approach may have been presented as expanding the overall number of countries included in the license territory, segmenting the market presents additional challenges.[13]

In some countries, government treatment programmes defined as the "public market" may face delays in updating national treatment guidelines to include new medicines, even if they have access to generic versions under a license. People who develop drug resistance and need urgent access to newer medicines have no choice but to seek treatment with these medicines in the private health sector, where they will pay higher prices for the branded DTG product in the absence of less expensive generic options.[14]

Another issue with the VL is the complex system of royalty payments. Under this license, sublicensed generic suppliers are required to pay ViiV 5% in royalties for DTG sold in India, Philippines, Moldova and Vietnam; 7.5% in Armenia, Egypt, Indonesia, Mongolia, Morocco, Tunisia and Ukraine; and 10% in Turkmenistan if there is a patent granted and in force. In MSF's experience, generic manufacturers transfer the burden of paying higher royalties on to procurers and people in need of treatment, by adding the royalty rate to the prices of the product supplied. MSF has also received requests to provide country-of-destination information to generic manufacturers that supply DTG and DTG-based fixed-dosed combinations in order to calculate royalties and final prices, which complicates and delays the process of procurement.[13]

Finally, one of the most challenging aspects of the license is the exclusion of upper middle-income countries such as Russia, China, Kazakhstan, Colombia, Belarus and Brazil from benefiting from the VL if there is a patent on the DTG compound granted and in force.[11] Prices in these countries remain high due to the patent monopoly and exclusion from the VL, with Brazil and Belarus paying up to $350[15] and $2,317[16] per person per year, respectively, for DTG 50mg from ViiV. They are also excluded from the paediatric license.

DARUNAVIR/RITONAVIR (DRV/r)

Darunavir (DRV) is a protease inhibitor from Janssen, given in combination with ritonavir (RTV) from Abbvie as a booster. Fixed-dose combinations (FDCs) of DRV/r 400/50mg and 800/100mg tablets for adults have been in development since 2015,[17] and recently the Clinton Health Access Initiative (CHAI) and Unitaid announced funding to develop a formulation of this combination for children.[18] Two generic producers for the 400/50mg tablets, and one for 800/100mg tablets, have filed for assessment by the WHO Prequalification (PQ) Programme.[19] However, these tablets lend themselves to once-daily dosing for people who are ARV-naive (800/100mg daily), which although approved in some high-income countries (HICs) is not aligned with WHO guidance (in which DRV is currently included at 600/100mg twice daily for those who are treatment-experienced).

Another key barrier to the availability of the adult FDCs of DRV/r are the individual patent claims filed by Abbott (now AbbVie) on the polymorphic and solid pharmaceutical dosage (tablet) formulation of RTV, which had been granted widely except in countries like India and Brazil, where civil society were successful in filing pre-grant oppositions.[20] However recent developments (discussed in the LPV/r section) have led to AbbVie relinquishing enforcement of its RTV patents globally, thereby freeing generic manufacturers to develop and supply the drug individually or in combination with protease inhibitors like DRV.

LOPINAVIR/RITONAVIR (LPV/r)

Lopinavir (LPV)/r is a protease inhibitor from AbbVie used widely as second-line HIV treatment in adults and first line in children. The global supply of LPV/r for HIV treatment has been plagued by shortages and stockouts for several years. This has impaired the transition and scale-up to pellets and granules for children,[21] and has forced countries that used LPV/r as preferred second-line treatment to switch to atazanavir/RTV (ATV/r).[22]

The combination (first patented in the early 1990s) is one of the most widely patented globally, with evergreening patents used to extend market exclusivity until 2024 and beyond.[23] For years, the patent holder AbbVie had enforced its monopoly and charged high prices in several middle-income countries, such as Brazil and Malaysia.[24]

AbbVie's VL with MPP left a significant gap for children over 3 years of age, as well as adults in need of suitable generic formulations of LPV/r in the countries not covered by the territory and prohibiting generic supply for people in all countries outside of Africa where its patents were in force.[25]

In March 2020, the Ministry of Health of Israel issued a compulsory license on LPV/r to enable generic supply to be potentially repurposed for use in treating COVID-19. Likely in order to avert a precedent set by the compulsory license, that same day, AbbVie notified the MPP that it would not enforce its patents over LPV/r for any purpose anywhere in the world (a "non-assert declaration").[26]

After years of restricted access to LPV/r around the world, the action of a single government towards implementing the WTO-sanctioned Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) public-health safeguard in the context of the COVID-19 pandemic led to AbbVie's relinquishing of enforcement of its patents globally. This freed all countries to produce, procure and use generics as needed. While LPV/r turned out not to be useful for COVID-19 treatment, PLHIV in middle- and high-income countries left out of AbbVie's VLs can now benefit from availability of less expensive generic LPV/r. Middle-income countries (MICs) were paying at least $740 per person per year for adult LPV/r tablets from AbbVie, whereas generic versions are available for as low as $227 per person per year (see Annex).

Drawings of ARVs in an HIV support group for children at Epworth Clinic, Harare, Zimbabwe, 2016. Children and young people come together to give each other support, and learn about living with HIV through games and education.

INFANT TREATMENT AND PROPHYLAXIS: ZIDOVUDINE (AZT) AND NEVIRAPINE (NVP) ORAL SOLUTIONS

Zidovudine (AZT) and nevirapine (NVP) oral solutions are available for use in prevention and treatment of HIV in neonates. However, as NVP has been phased out among adults and is actively being phased out for children, and AZT use is limited in adults, there is concern about the sustainability of supply of the active pharmaceutical ingredient (API) and finished pharmaceutical product (FPP) for such a small population. Already, longer lead times for ordering and supply difficulties have been seen.

Ideally, neonates should be treated with raltegravir (RAL) from Merck, as the backbone of the first-line preferred regimen, instead of NVP. However, the powder for suspension formulation of RAL for infants is more than 7 times the price of NVP; is more complicated to administer; and is not readily available in most of sub-Saharan Africa, where caregivers are still dependant on NVP oral solution.

As ART coverage for prevention of mother-to-child transmission (PMTCT) of HIV improves, alignment of neonatal treatment and prevention regimens is an important strategy for optimisation of treatment and sustainability of supply of paediatric ARVs. Studies assessing the use of the ABC-3TC-LPV/r 4-in-1 formulation for prophylaxis have recently started enrollment, and similar studies utilising DTG are needed.[27,28]

TREATMENTS FOR CRYPTOCOCCAL MENINGITIS

Cryptococcal meningitis remains a major killer of PLHIV, second only to TB. While effective treatments exist, persistent problems with supply and prices keep treatment out of reach.

Liposomal Amphotericin B (L-AMB)

Gilead Sciences is the only supplier of quality-assured liposomal amphotericin B (L-AMB), an essential medicine for treatment of fungal infections, including first-line treatment per WHO guidelines for cryptococcal meningitis in PLHIV. In September 2018, the company announced a so-called "access" price for 116 LMICs of $16.25 per vial of L-AMB.[29] However, despite being off patent for many years and the promise of the lower price, Gilead has exclusive agreements with distributors in many countries where L-AMB is to be sold for as high as $200 per vial, essentially making its two-year old "access" plan meaningless.[30] India and South Africa are countries eligible for Gilead's access price, but more than two years later, the price is more than 4-12 times the access price, at $69 and $205, respectively.[31] As of September 2020, Gilead has only provided L-AMB in 5 countries in sub-Saharan Africa.[32]

Despite approval by WHO PQ in June 2018, Gilead has not made efforts to increase L-AMB's registration footprint, which could be facilitated using the WHO PQ's Collaborative Registration Procedure (CRP) to fast-track registration in participating countries – many of which are sub-Saharan African countries with a high burden of HIV and cryptococcal meningitis. As of July 2020, Gilead had not used this mechanism to register L-AMB in any of the participating countries.[33]

Furthermore, limited manufacturing capacity at Gilead has restricted scale-up and rollout of this drug. At the end of 2019, Gilead finally received FDA approval for a new manufacturing site in California, and an end to the usual 4-6 months lead time was thus anticipated. But this new facility is also being used to produce remdesivir, a potential treatment for COVID-19, effectively displacing production of L-AMB and causing continued delays.

Flucytosine (5-FC)

Flucytosine is used as WHO-recommended first-line treatment of cryptococcal meningitis, in combination with L-AMB. Despite being an old drug and off patent for many years, there has been little interest by generic companies to produce flucytosine. A few quality-assured products have been available but at very high prices. As countries start to implement WHO's guidelines for advanced HIV disease (AHD) and treat more patients with cryptococcal meningitis, two new quality-assured generic sources have finally become available, reducing the price to $75 per bottle.[32] Despite some progress, it is estimated that of the 162,000 cases in sub-Saharan Africa in 2020, only 1,000-2,000 of these people received treatment with a flucytosine-containing regimen.[34] Generic companies should prioritise registration in high-burden countries, ideally using WHO PQ CRP to fast-track the process and ensure availability of quality-assured flucytosine for those who need it.

As flucytosine is dosed 4 times per day, development of a sustained-release formulation would serve to improve adherence and treatment for PLHIV. This is being pursued by the Drugs for Neglected Diseases *initiative* (DNDi).[35]

ACCESSING THE PIPELINE: OLD CHALLENGES FOR NEW DRUGS

LONG-ACTING CABOTEGRAVIR (CAB) AND RILPIVIRINE (RPV)

Cabotegravir (CAB) and rilpivirine (RPV) in long-acting injectable (LAI) formulations present a new opportunity to address the challenges of adherence and stigma related to taking daily oral ART. CAB is an integrase inhibitor from ViiV, and RPV is a second-generation non-nucleoside reverse transcriptase inhibitor (NNRTI) from Janssen. In a pair of major studies (ATLAS and FLAIR), treatment with monthly LAI CAB and RPV has been shown to be non-inferior to current oral regimens (65%, 26%, and 9% of patients were on an integrase, NNRTI, or protease inhibitor baseline regimen, respectively).[36] Injection-site reactions were common (83%), but acceptability of these reactions significantly improved from week 5 onwards. More than 97% of participants receiving LAIs preferred this treatment compared to their prior oral therapy. Currently, this combination LAI has only been initiated for PLHIV already virally suppressed on an oral regimen.[37] Further studies are required to assess its use in PLHIV not already virally suppressed on their current oral regimen, as well as in children, adolescents, and pregnant and breastfeeding women, in order to maximise the range of populations who could benefit from this treatment option.

Currently, injections are given monthly, but studies have provided evidence supporting a move to dosing every 2 months. However, many settings are now dispensing 6 months of oral ARVs at a time, allowing decongestion of health facilities as they enable scale-up in the era of "treat all" and relieving the financial and time burdens on PLHIV. Innovative service-delivery models to provide injectable regimens will be needed for PLHIV for whom accessing a facility remains a challenge due to distance or user-fee costs. Other service-delivery considerations will include RPV's cold-chain requirement, and the need to give each drug in the combination as a separate injection at each visit. Finally, because the half-life of these ARVs is long, people taking the LAI will need to consult with their healthcare provider if they want to stop taking this combination in order to avoid inadvertently being on monotherapy, which could risk the development of drug resistance, as the drugs can remain in the body for up to one year after the last injection.

The CAB+RPV combination LAI was approved by Health Canada in March 2020,[38] and received recommendation for approval by the European Medicines Agency (EMA) in October 2020 for the maintenance of HIV treatment in people who already have a suppressed viral load. It is still under review by the FDA after initially being rejected due to reasons related to the manufacturing process and not clinical safety or efficacy.

The availability and access considerations for this combination remain to be seen. Available only from ViiV and Janssen, the price has not yet been set for LMICs, and it is unknown if generic companies have started working on developing these drugs, or if ViiV and Janssen would consider voluntary licensing to the MPP to facilitate this development.

According to an MPP/Unitaid patent landscape report, patents on long-acting CAB, including its combination with RPV, have been filed and granted in several LMICs. These patents do not expire until 2031.[39] Multiple patents have also been filed and granted on RPV products, salt and polymorphic forms, solid oral composition, and other formulations, which would expire between 2021 to 2032.[39]

Long-Acting Injectable CAB as Pre-Exposure Prophylaxis (PrEP)

CAB LAI has also been studied for prevention of HIV with promising results. In the HPTN 083 study, injections every 2 months in gay and bisexual men and transgender women prevented 69% more HIV infections than standard pre-exposure prophylaxis (PrEP) using a daily dose of tenofovir and emtricitabine (TDF/FTC), despite the majority of users in the oral PrEP arm demonstrating high levels of adherence.[40] In the study, 81% of participants reported tenderness at the injection site, but only 2% stopped using the injection because of it. A further study, HPTN 084, comparing long-acting CAB to oral PrEP in women was stopped early in November 2020, as CAB LAI was shown to be significantly more effective at preventing HIV than oral TDF/FTC.[41]

While CAB LAI has received approval in Canada and a favourable recommendation by the EMA when used in combination with RPV LAI for the treatment of HIV, ViiV has not yet filed to register stand-alone CAB LAI for prevention of HIV. Nor has the company given any indication on pricing. While most of the challenges and concerns discussed above remain the same, it is important to note that CAB LAI does not require a cold chain, which would facilitate its use in low-resource settings.

DAPIVIRINE (DPV) VAGINAL RING

Dapivirine (DPV) is an NNRTI originally developed by Janssen. In 2004, Janssen licensed DPV to the International Partnership for Microbicides (IPM), which developed the DPV vaginal ring for prevention of HIV. IPM now holds the exclusive worldwide rights for DPV and is developing it also in combination with contraceptives for a multipurpose ring.[42] The DPV ring is a flexible silicone ring that women can insert and leave in the vagina for protection against HIV for one month.

The Ring and ASPIRE studies have demonstrated the DPV ring to be safe and to reduce women's risk of HIV-1 infection by approximately 30%,[43] although no reduction was seen in HIV acquisition in women younger than 21 years of age, likely related to decreased adherence to ring use in this younger

population. The REACH study is assessing use in women aged 16-21 in South Africa, Uganda and Zimbabwe, with results expected in late 2020.[44] Further studies are ongoing to assess the use of the DPV ring in pregnant and breastfeeding women.

Despite initial concerns about appearance and side effects, participants grew to like the method and adherence challenges were generally overcome with peer support, but this qualitative work highlights the need for investment in quality counselling when introducing this new long-acting woman-initiated HIV prevention option.[45] The fact that the ARV acts locally, therefore minimising systemic side effects, is seen as an advantage by both users and healthcare workers. Hence even though the ring has shown less impact on HIV transmission than other PrEP tools, it provides a woman-centred option to be offered within the prevention package. Use of the DPV ring is being considered in the review of prevention recommendations within the revised WHO guidelines due for publication in 2021.

IPM has worked with stakeholders and as part of the OPTIONS consortium[46] to prepare for introduction of the DPV ring. The DPV ring received a positive opinion by the EMA in July 2020 for use in women aged 18 years and older,[47] and plans are under way to file with the FDA and use the WHO PQ CRP for registration in multiple sub-Saharan African countries.[48] The DPV ring is expected to launch at a price of $6-8 per ring, or $72-96 per person per year.[49]

OTHER LONG-ACTING FORMULATIONS IN THE PIPELINE

A number of other long-acting formulations are in various stages of investigation. An oral nucleoside reverse transcriptase translocation inhibitor (NRTTI) developed by Merck, islatravir (MK-8591), has been shown to be effective and can be dosed once a week.[50] It is also under investigation for monthly dosing as PrEP and formulation for delivery via implant, which may further extend its duration of action.[51] An NNRTI from Merck (MK-8507) has shown potential for combination with islatravir as a weekly oral therapy.[52]

Lenacapavir (GS-6207) is a first-in-class capsid inhibitor from Gilead, active at several stages of the viral life cycle. A single subcutaneous injection is expected to provide treatment coverage for 6 months.[53]

The Unitaid and MPP Intellectual Property Report on Long-Acting Technologies is one of the first to provide an overview of the intellectual property status of long-acting products under development.[39] The report finds that, in general, long-acting products appear to have patents pending or granted in key manufacturing countries, preventing generic competition without licensing. This may lead to – in the absence of licensing – a delay in the development of more affordable generic versions and introduction of these in LMICs.[39]

Finda (left) collects her 6 months of ARVs and other HIV medicines at an MSF-supported pharmacy in Conakry, Guinea, 2018.

Broadly neutralising monoclonal antibodies (bNAbs) are another potentially long-acting therapeutic option. Ibalizumab from Theratechnologies and TaiMed Biologics was approved by the FDA in March 2018[54] and has been shown to suppress HIV for up to 48 weeks in people with highly resistant virus. It was also authorised by EMA in September 2019. Ibalizumab was the first biologic agent approved for HIV, requiring an intravenous loading dose, followed by an infusion of a maintenance dose every 2 weeks.[55] A small cohort of patients has now used ibalizumab for as long as 8-10 years, demonstrating continued viral suppression when used in combination with short-acting ARVs.[56] In the US, ibalizumab was introduced at a price of $118,000 per person per year in 2018.[57]

While multiple bNAbs are in clinical trials, with potential for dosing every 2 to 6 months, some drawbacks must be considered. They require sensitivity testing, to ensure they could work for a person's specific virus, and they must be used in combination to avoid developing drug resistance.[58] Expanding access to biologics, like bNAbs, in low-income countries is a challenge receiving heightened attention, given the increasing number of companies producing biosimilars of medicines for cancer and insulin for diabetes.[59]

CONCLUSION

The past two decades have seen immense progress in access to lifesaving HIV medicines – but challenges remain in reaching those people, from birth to adulthood, who still lack treatment. The UNAIDS 2020 Global AIDS Update Report showed that critical global targets will be missed, including the reduction of HIV-related deaths to fewer than 500,000 by the end of 2020.[2] The report also highlighted evidence from sub-Saharan Africa that people living with HIV are at higher risk of COVID-19-related death, and warned of disruptions in HIV services due to the pandemic.

To avoid backtracking on the decades of progress made against HIV, continued availability and scale-up of current ARVs, and affordable access to new key medicines in the pipeline, must be ensured. Access to the current WHO-recommended ARVs including dolutegravir, lopinavir, ritonavir, and darunavir face pricing, supply and intellectual property-related hurdles. Treatments for the youngest, infants and neonates, face production and supply issues for AZT and NVP. Similarly, high pricing and adequate production and supply issues are factors in the availability of drugs to treat HIV-associated cryptococcal meningitis (L-AMB and flucytosine).

Looking forward, the pipeline for new HIV treatments is promising, but old access challenges are poised to confront these new medicines as well. These include the new long-acting drugs cabotegravir and rilpivirine, and other new long-acting agents such as monoclonal-antibody biologics.

Remei Katadin (left) playing with her daughter at home, Manipur, India, 2019. Katadin is HIV-positive and says her children are her biggest motivation to fight the virus.

ANNEX: ANTIRETROVIRAL PRICES, 2020

Prices of ARVs in developing countries are presented here in US$ per person per year, as quoted by companies. The price in brackets corresponds to the price of one unit (tablet, capsule, ml, etc). Products included in the WHO list of Prequalified Medicines or approved by the FDA (as of November 2020) are in bold.

Each originator company applies its own eligibility criteria for discounting ARVs. Countries eligible for a discount from one company may not be eligible for discounts from other companies. Usually, companies create two groups of discount-eligible countries, often called 'Category 1' (countries that are eligible for the largest discounts) and 'Category 2' (countries that are offered a smaller discount).

Paediatric formulations are highlighted in pink. Prices for paediatric products are estimated, based on WHO-recommended dosing, for the 10-10.9 kg weight band. When it was not possible to calculate dosing for the 10-kg weight band, the unit price was used.

Global Fund prices are included as a comparison and additional reference. The prices indicated are the lowest reported for each item in the October 2020 update of the Global Fund's Pooled Procurement Mechanism (PPM) prices, which accounts for larger pack sizes and cartonless products where applicable.

Generic companies producing DTG or DTG-based FDCs provided price ranges, reflecting the royalties imposed for certain countries as per the ViiV/MPP voluntary license. Companies providing tiered pricing are marked with an asterisk (*) and the lowest price provided is indicated. Royalties paid for the generic product to ViiV vary by country but reflects as follows: 5% in India, Vietnam, Philippines and Moldova; 7.5% in Armenia, Egypt, Indonesia, Mongolia, Morocco, Tunisia and Ukraine; 10% in Turkmenistan.[60] At the time of publication, ViiV was reviewing their 2020 prices, and as such, those indicated with a plus (+) are the same as quoted in 2019.

Note that where multiple pack sizes are available (ie, 30, 90, 180 tablets), the lowest price is given.

NVP-based products for adults are no longer recommended and being phased out in most countries. Paediatric formulations are included as they are still required for prevention of HIV in neonates, and for treatment in certain exceptional situations.

Antiretrovirals	**Daily Dose**	**Originator Company**		**Global Fund, 2020 PPM Prices**								
Abacavir (ABC)		ViiV		Global Fund	Cipla	Hetero	Micro Labs	Mylan	Strides			
20mg/ml oral solution	12ml	Cat 1	Cat 2	**132 (0.030)**		**136 (0.031)**						
		412+ (0.094)										
60mg dispersible tablet	4			**115 (0.079)**			**123 (0.084)**	**72 (0.049)**				
300mg tablet	2			**100 (0.138)**	**134 (0.183)**	**113 (0.154)**	**107 (0.147)**	**106 (0.146)**	**256 (0.350)**			
Atazanavir (ATV)		BMS		Global Fund	Emcure	Mylan						
		Cat 1	Cat 2									
150mg capsule	xx	**(0.564)**	**(0.564)**	**(0.283)**	**(0.283)**							
200mg capsule	1	**247 (0.677)**	**247 (0.677)**	**122 (0.333)**	**152 (0.417)**							
300mg capsule	1			**207 (0.567)**	**207 (0.567)**	**183 (0.500)**						
Atazanavir/ritonavir (ATV/r)		n/a		Global Fund	Emcure	Mylan						
300mg/100mg tablet	1			**164 (0.450)**	**183 (0.500)**	**176 (0.483)**						
Darunavir (DRV)		Janssen		Global Fund	Cipla	Hetero	Mylan					
75mg tablet	xx	**(0.084)**	Case by case									
150mg tablet	xx	**(0.169)**										
400mg tablet	2	**328 (0.449)**		**655 (0.897)**	**548 (0.750)**	**706 (0.967)**						
600mg tablet	2	**492 (0.674)**		**639 (0.875)**	**730 (1.000)**	**706 (0.967)**	**730 (1.000)**					
Dolutegravir (DTG)		ViiV		Global Fund	Aurobindo	Cipla	Emcure	Hetero	Laurus	Micro Labs	Mylan	Sun Pharma
		Cat 1	Cat 2									
50mg tablet	1	**181+ (0.497)**	**Case by case**	**32 (0.087)**	**39* (0.108)**	**43* (0.117)**	**40* (0.110)**	**44* (0.120)**	**32* (0.087)**	**38* (0.104)**	**43* (0.117)**	**40* (0.110)**
Efavirenz (EFV)		Merck		Global Fund	Aurobindo	Cipla	Hetero	Macleods	Micro Labs	Mylan	Strides	Sun Pharma
		Cat 1	Cat 2									
30mg/ml suspension	xx	**N/A**	**Case by case**									
50mg tablet	xx	**(0.114)**		**(0.054)**					**(0.075)**			
50mg capsule	xx								**(0.068)**			
200mg capsule	3								**52 (0.048)**			
200mg tablet (scored)	3	**394 (0.360)**	**Case by case**	**78 (0.071)**					**82 (0.075)**	**55 (0.05)**	**113 (0.103)**	
600mg tablet	1	**237 (0.650)**		**30 (0.083)**	**31 (0.085)**	**39 (0.106)**	**35 (0.095)**	**33 (0.092)**	**32 (0.088)**	**37 (0.100)**	**34 (0.093)**	**35 (0.097)**

Antiretrovirals	Daily Dose	Originator Company		Global Fund, 2020 PPM Prices						
Etravirine (ETV)		Janssen								
		Cat 1	Cat 2							
25mg tablet	xx	**(0.056)**	Case by case							
100mg tablet	4	**328 (0.225)**								
200mg tablet	2									
Lamivudine (3TC)		ViiV		Global Fund	Hetero	Macleods	Micro Labs	Mylan	Strides	
		Cat 1	Cat 2							
10mg/ml oral suspension	10ml	**221⁺ (0.060)**	Case by case	**46 (0.013)**	**34 (0.009)**	**61 (0.017)**				
150mg tablet	2	**144⁺ (0.197)**		**27 (0.037)**	**30 (0.042)**	**33 (0.046)**	**27 (0.037)**	**30 (0.042)**	**49 (0.067)**	
300mg tablet	1				**30 (0.083)**		**29 (0.078)**		**73 (0.200)**	
Lopinavir/ritonavir (LPV/r)		Abbvie		Global Fund	Aurobindo	Cipla	Hetero	Macleods	Mylan	
		Cat 1	Cat 2							
80/20mg/ml oral solution	4ml	**150 (0.103)**	**296 (0.203)**	**150 (0.103)**						
40/10mg pellets or granules	4	**N/A**		**444 (0.152)**		**467 (0.160)**			**444 (0.152)**	
100/25mg tablet	3	**108 (0.099)**	**278 (0.254)**	**119 (0.108)**	**128 (0.117)**		**201 (0.183)**	**173 (0.158)**	**131 (0.120)**	
200/50mg tablet	4	**241 (0.165)**	**740 (0.507)**	**227 (0.155)**	**304 (0.208)**	**292 (0.200)**	**365 (0.250)**	**414 (0.283)**	**238 (0.163)**	
Nevirapine (NVP)		Boehringer Ingelheim		Global Fund	Aurobindo	Cipla				
10mg/ml suspension	20ml			**106 (0.015)**	**146 (0.020)**	**91 (0.013)**				
50mg tablet for oral suspension	4			**35 (0.024)**		**35 (0.024)**				
Raltegravir (RAL)		Merck		Hetero						
		Cat 1	Cat 2							
100mg powder/sachet	2	**694 (0.95)**	**Case by case**							
25mg tablet	xx	**(0.300)**								
100mg tablet	xx	**(0.600)**								
400mg tablet	2	**675 (0.925)**		**791 (1.083)**						
Ritonavir (RTV)		Abbvie		Global Fund	Mylan	Hetero				
		Cat 1	Cat 2							
80mg/ml oral solution	xx	**(0.091)**	**Case by case**							
25mg tablet	xx	**N/A**								
50mg tablet	xx									
100mg tablet	1	**83 (0.114)**	**624 (0.855)**	**83 (0.114)**	**173 (0.237)**	**134 (0.183)**				
Tenofovir (TDF)		Gilead		Global Fund	Cipla	Hetero	Laurus	Macleods	Mylan	Strides
		Cat 1	Cat 2							
Oral powder 40mg/1g	2	**Case by case**	**Case by case**							
150mg tablet	xx	**329 (0.900)**								
200mg tablet	1	**329 (0.900)**								
250mg tablet	1	**365 (1.00)**								
300mg tablet	1	**183 (0.500)**		**29 (0.080)**	**37 (0.100)**	**32 (0.087)**	**29 (0.080)**	**30 (0.083)**	**40 (0.108)**	**49 (0.133)**
Zidovudine (AZT)		ViiV		Global Fund	Hetero	Macleods	Micro Labs	Mylan	Cipla	
		Cat 1	Cat 2							
10mg/ml oral solution	24ml	**442⁺ (0.050)**		**119 (0.014)**	**86 (0.010)**	**146 (0.017)**			**146 (0.017)**	
300mg tablet	2			**61 (0.083)**	**61 (0.083)**		**60 (0.082)**	**61 (0.083)**		
ABC/3TC		ViiV		Global Fund	Aurobindo	Cipla	Hetero	Mylan		
		Cat 1	Cat 2							
60/30mg tablet	4					**54 (0.073)**		**43 (0.058)**		
120/60mg dispersible tablet	2			**80 (0.110)**		**92 (0.127)**		**85 (0.117)**		
600/300mg tablet	1	**302⁺ (0.827)**		**112 (0.307)**	**183 (0.500)**	**152 (0.417)**	**122 (0.333)**	**116 (0.317)**		

ANNEX: ANTIRETROVIRAL PRICES, 2020

Antiretrovirals	Daily dose	Originator Company		Global Fund, 2020 PPM Prices									
ABC/3TC/DTG		ViiV		Global Fund	Laurus								
600/300/50mg tablet	1	**Not included. Case by case.**		**243 (0.667)**	256 (0.70)								
TDF/FTC		Gilead		Global Fund	Cipla	Hetero	Laurus	Macleods	Micro Labs	Mylan	Strides	Sun Pharma	
		Cat 1	Cat 2										
300/200mg tablet	1	**243 (0.667)**	**Case by case**	**55 (0.150)**	**61 (0.167)**	**58 (0.158)**	**50 (0.138)**	**58 (0.158)**	**60 (0.164)**	**64 (0.175)**	**58 (0.160)**	**55 (0.150)**	
TDF/FTC/EFV		Merck		Global Fund	Cipla	Hetero	Macleods	Mylan	Strides				
		Cat 1	Cat 2										
300/200/600mg tablet	1	**613 (1.680)**	**Case by case**	**75 (0.205)**	**90 (0.247)**	**79 (0.217)**	**79 (0.217)**	**76 (0.208)**	**83 (0.227)**				
TDF/3TC		N/A		Global Fund	Cipla	Emcure	Hetero	Macleods	Micro Labs	Mylan	Sun Pharma		
300/300mg tablet	1			**41 (0.113)**	**49 (0.133)**	**58 (0.158)**	**44 (0.120)**	**46 (0.125)**	**45 (0.124)**	**49 (0.133)**	**44 (0.120)**		
TDF/3TC/EFV		N/A		Global Fund	Aurobindo	Cipla	Hetero	Laurus	Macleods	Mylan			
300/300/400mg tablet	1			**66 (0.182)**				**67 (0.183)**	**73 (0.200)**	**70 (0.192)**			
300/300/600mg tablet	1			**68 (0.185)**	**76 (0.208)**	**70 (0.192)**	**67 (0.183)**	**71 (0.195)**	**73 (0.200)**	**73 (0.200)**			
TDF/3TC/DTG		N/A		Global Fund	Aurobindo	Cipla	Emcure	Hetero	Laurus	Macleods	Mylan	Strides	Sun Pharma
300/300/50mg	1			**63 (0.172)**	**64* (0.174)**	**70* (0.192)**	67* (0.183)	**70* (0.192)**	**62* (0.170)**	**66* (0.182)**	**70* (0.192)**	**65* (0.178)**	**71* (0.193)**
AZT/3TC		ViiV		Global Fund	Cipla	Hetero	Macleods	Micro Labs	Mylan	Strides	Sun Pharma		
		Cat 1	Cat 2										
60/30mg tablet	4			**46 (0.032)**	**45 (0.031)**				**79 (0.054)**				
300/150mg tablet	2	**190⁺ (0.260)**		**64 (0.088)**	**67 (0.092)**	**77 (0.105)**	**85 (0.117)**	**70 (0.096)**	**73 (0.100)**	**79 (0.108)**	**71 (0.097)**		
AZT/3TC/NVP		N/A		Global Fund	Mylan	Strides							
60/30/50mg tablet	4			**73 (0.050)**	**73 (0.050)**	**97 (0.067)**							
AZT/3TC + EFV (co-pack)		N/A		Strides									
300/150 + 600mg co-pack	1 kit/ 3tabs			**65 (0.178)**									

REFERENCES

[1] MSF. Untangling the Web. [Online]. [Cited 2020 Nov 9]. Available from: https://msfaccess.org/utw

[2] UNAIDS. 2020 Global AIDS Update - Seizing the moment - Tackling entrenched inequalities to end epidemics. [Online]. 2020 Jul 6 [Cited 2020 Nov 9]. Available from: https://www.unaids.org/en/resources/documents/2020/global-aids-report

[3] UNAIDS. Global HIV & AIDS statistics—2020 Fact Sheet. [Online]. 2020. [Cited 2020 Nov 9]. Available from: https://www.unaids.org/en/resources/fact-sheet

[4] WHO. WHO welcomes FDA approval of new formulation of dolutegravir for young children living with HIV. [Online]. 2020 June 18 [Cited 2020 Nov 9]. Available from: https://www.who.int/news/item/18-06-2020-who-welcomes-fda-approval-of-new-formulation-of-dolutegravir-for-young-children-living-with-hiv

[5] Personal communication, ViiV, 2020 Aug 5.

[6] NIH. Dolutegravir Pediatric Liquid Formulation Study. [Online]. 2020 July 31 [Cited 2020 Nov 9]. Available from: https://clinicaltrials.gov/ct2/show/NCT03921723

[7] US Food and Drug Administration. Drugs@FDA: FDA-Approved Drugs. New Drug Application (NDA): 204790. [Online]. 2020 [Cited 2020 Nov 9]. Available from: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=204790

[8] US Food and Drug Administration. Drugs@FDA: FDA-Approved Drugs. New Drug Application (NDA): 214521. [Online]. 2020 [Cited 2020 Nov 25]. Available from: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=214521

[9] Medicines Patent Pool. Dolutegravir—Adult (DTG). [Online]. 2014 April [Cited 2020 Nov 9]. Available from: https://medicinespatentpool.org/licence-post/dolutegravir-adult-dtg/

[10] Baker B. Beyond the obvious – direct and indirect territorial coverage of MPP/ViiV voluntary license for dolutegravir. [Online]. 2017 [Cited 2020 Sep 13]. Available from: https://www.ip-watch.org/2017/05/24/beyond-obvious-direct-indirect-territorial-coverage-mppviiv-voluntary-license-dolutegravir

[11] MSF. HIV & Opportunistic Infection Treatment: Spotlight on Access Gaps. [Online]. 2017 [Cited 2020 Nov 9]. Available from: https://msfaccess.org/sites/default/files/HIV_Brief_SpotlightOnAccessGaps_ENG_2017.pdf

[12] Jianke [Chinese]. Dolutegravir sodium tablets, 50mg. [Online]. [Cited 2020 Nov 9]. Available from: https://www.jianke.com/product/781538.html

[13] MSF. Voluntary Licenses and Access to Medicines. [Online]. 2020 October [Cited 2020 Nov 9]. Available from: https://msfaccess.org/sites/default/files/2020-10/IP_VoluntaryLicenses_full-brief_Oct2020_ENG.pdf

[14] MSF. Pharma company Viiv's attempt to secure patents for key HIV drugs dolutegravir and cabotegravir opposed in India. [Online]. 2016 [Cited 2020 Oct 10]. Available from: https://msfaccess.org/pharma-company-viivs-attempt-secure-patents-key-hiv-drugs-dolutegravir-and-cabotegravir-opposed

[15] Access to information request, Brazil, Demanda: 3479171, 2020.

[16] Global Fund. Sourcing & Management of Health Products. Price & Quality Reporting. [Online]. [Cited 2020 Nov 9]. Available from: https://www.theglobalfund.org/en/sourcing-management/price-quality-reporting/

[17] Unitaid. Three new agreements announced with the potential to expand access to innovative HIV treatment in low- and middle-income countries. [Online]. 2015 Nov 30 [Cited 2020 Nov 9]. Available from: https://unitaid.org/news-blog/three-new-agreements-announced-potential-expand-access-innovative-hiv-treatment-low-middle-income-countries/#en

[18] Clinton Health Access Initiative. CHAI and Unitaid seek proposals to catalyze optimization of 2nd-line HIV treatment for children. [Online]. 2020 Sep 14 [Cited 2020 Nov 9]. Available from: https://www.clintonhealthaccess.org/rfp-for-2nd-line-hiv-treatment-for-children/

[19] WHO. FFPs Under Assessment. [Online]. 2020 [Cited 2020 Nov 9]. Available from: https://extranet.who.int/pqweb/content/dossier-status

[20] Medicines Patent Pool. The Medicines Patent and Licences Database. [Online]. 2020 [Cited 2020 Nov 9]. Available from: https://www.medspal.org/?product_standardized_name%5B%5D=Ritonavir+100+mg&page=1

[21] ARV Procurement Working Group. Memorandum on Paediatric LPV/r Formulations. [Online]. 2019 Jan 10 [Cited 2020 Nov 9]. Available from: https://www.arvprocurementworkinggroup.org/public/componenti/1395/files/APWGLPVrMemotoSuppliersandCountries_Jan2019.pdf

[22] ARV Procurement Working Group. HIV Stock Security Resources Amidst COVID-19. [Online]. 2020 Apr [Cited 2020 Nov 9]. Available from: https://www.arvprocurementworkinggroup.org/public/componenti/1439/files/APWGCOVID-19Newsflash_Apr2020_Final.pdf

[23] Amin T, Kesselheim A. Secondary patenting of branded pharmaceuticals: a case study of how patents on two HIV drugs could be extended for decades. [Online]. 2012 Oct [Cited 2020 Nov 9]. Available from: https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2012.0107

[24] Clayden P. High prices for antiretrovirals in middle-income countries outside Africa. [Online]. 2013 [Cited 2020 Jul 27]. Available from: https://i-base.info/htb/23851

[25] MSF. Untangling the Web, 18th Ed. [Online]. 2016 [Cited 2020 Aug 1]. Available from: https://msfaccess.org/untangling-web-antiretroviral-price-reductions-18th-edition

[26] Knowledge Ecology International. Israel issues compulsory license to allow the government to import generic versions of Kaletra. [Online]. 2020 Mar 23 [Cited 2020 Nov 9]. Available from: https://www.keionline.org/32503

[27] Desmond Tutu TB Centre. BENEFIT Kids. [Online]. 2020 [Cited 2020 Nov 9]. Available from: http://blogs.sun.ac.za/dttc/benefit-kids/

[28] Bekker A. Pharmacokinetic and safety of the 4-In-1 granules in neonates: PETITE Study. Trial ID: PACTR202007806554538. [Online] 2020 Nov 16 [Cited 2020 Nov 16]. Available from: http://www.pactr.org/

[29] Gilead Sciences. Gilead Sciences announces steep discounts for Ambisome to treat cryptococcal meningitis in low- and middle-income countries. [Online]. 2018 Sep 7 [Cited 2020 Nov 9]. Available from: https://www.gilead.com/news-and-press/company-statements/discount-for-ambisome

[30] MSF. Gilead Sciences fails on promise to expand access to lifesaving drug for people living with HIV. [Online]. 2019 Jul 27 [Cited 2020 Nov 9]. Available from: https://msfaccess.org/gilead-sciences-fails-promise-expand-access-lifesaving-drug-people-lmiving-hiv

[31] Medicine Prices. What should your medicines cost? [Online]. 2020 [Cited 2020 Nov 9]. Available from: https://medicineprices.org.za/#search:amphotericin

[32] Clinton Health Access Initiative. HIV Market Report, 11th Ed. [Online]. 2020 Sep [Cited 2020 Nov 9]. Available from: https://www.clintonhealthaccess.org/the-state-of-the-hiv-market-in-low-and-middle-income-countries-3/

[33] WHO. Accelerated Registration of Prequalified FPPs. [Online]. 2020 [Cited 2020 Nov 9]. Available from: https://extranet.who.int/pqweb/medicines/collaborative-registration-faster-registration

[34] Forthcoming publication, Lancet Infect Dis.

[35] Drugs for Neglected Diseases initiative. 5 FC (cryptococcal meningitis). [Online]. 2020 Apr 29 [Cited 2020 Nov 9]. Available from: https://dndi.org/research-development/portfolio/5fc-cryptococcal-meningitis/

[36] Rizzardini G, Overton ET, Orkin C, Swindells S, Arasteh K, Górgolas Hernández-Mora M, et al. Long-acting injectable cabotegravir + rilpivirine for HIV maintenance therapy: week 48 pooled analysis of phase 3 ATLAS and FLAIR trials. J Acquir Immune Defic Syndr 2020;85(4):498-506. [Cited 2020 Nov 9]. Available from: https://doi.org/10.1097/QAI.0000000000002466

Continued overleaf

References continued

[37] Murray M, Antela A, Mills A, Huang J, Jäger H, Bernal E, et al. Patient-reported outcomes in ATLAS and FLAIR participants on long-acting regimens of cabotegravir and rilpivirine over 48 weeks. AIDS Behav 2020;24:3533-44. [Cited 2020 Nov 9]. Available from: https://doi.org/10.1007/s10461-020-02929-8

[38] ViiV. ViiV Healthcare announces first global regulatory approval of CABENUVA; the first complete, long-acting, regimen for the treatment of HIV [Online]. 2020 Mar 20 [Cited 2020 Nov 9]. Available from: https://viivhealthcare.com/en-gb/media/press-releases/2020/march/viiv-healthcare-announces-first-global-regulatory-approval-of-ca/

[39] Medicines Patent Pool and Unitaid. Intellectual Property Report on Long-Acting Technologies. [Online] 2018 Nov [Cited 2020 Nov 9]. Available from: https://medicinespatentpool.org/news-publications-post/mpp-and-unitaid-intellectual-property-report-on-long-acting-technologies/

[40] Landovitz RJ, Donnell D, Clement M, Hanscom B, Cottle L, Coelho L, et al. HPTN083 interim results: Pre-exposure prophylaxis (PrEP) containing long-acting injectable cabotegravir (CAB-LA) is safe and highly effective for cisgender men and transgender women who have sex with men (MSM,TGW). Abstract number 10750. 23rd International HIV Conference (AIDS 2020: Virtual). [Online]. 2020 [Cited 2020 Nov 9] Available from: https://aids2020.org/wp-content/uploads/2020/07/HIV-Highlights-Press-Conference-Abstracts.pdf

[41] WHO. Trial results reveal that long-acting injectable cabotegravir as PrEP is highly effective in preventing HIV acquisition in women. [Online]. 2020 Nov 9 [Cited 2020 Nov 9]. Available from: https://www.who.int/news/item/09-11-2020-trial-results-reveal-that-long-acting-injectable-cabotegravir-as-prep-is-highly-effective-in-preventing-hiv-acquisition-in-women

[42] International Partnership for Microbicides. IPM receives license from Janssen to develop FDA-approved HIV-1 drug as microbicide for HIV prevention. [Online]. 2015 Dec 1 [Cited 2020 Nov 9]. Available from: https://www.ipmglobal.org/publications/ipm-receives-license-janssen-develop-fda-approved-hiv-1-drug-microbicide-hiv-prevention

[43] Nel A, van Niekerk N, Kapiga S, Bekker L-G, Gama C, Gill K, et al. Safety and efficacy of a dapivirine vaginal ring for HIV prevention in women. N Engl J Med 2016;375:2133-43. [Cited 2020 Nov 9]. Available from: https://doi.org/10.1056/NEJMoa1602046

[44] Microbicide Trials Network. MTN-034 - The REACH Study - Questions and Answers. [Online]. 2020 May [Cited 2020 Nov 9]. Available from: https://mtnstopshiv.org/news/mtn-034-reach-study-questions-and-answers

[45] Montgomery ET, van der Straten A, Chitukuta M, Reddy K, Woeber K, Atujuna M, et al. Acceptability and use of a dapivirine vaginal ring in a phase III trial. AIDS 2017;31(8):1159–67. [Cited 2020 Nov 9]. Available from: https://doi.org/10.1097/QAD.0000000000001452

[46] PrEP Watch. Common agenda for the dapivirine vaginal ring.[Online]. 2019 Dec 26 [Cited 2020 Nov 9]. Available from: https://www.prepwatch.org/resource/common-agenda-dapivirine-ring/

[47] European Medicines Agency. Dapivirine Vaginal Ring 25mg H-W-2168. [Online]. 2020 Jul [Cited 2020 Nov 9]. Available from: https://www.ema.europa.eu/en/dapivirine-vaginal-ring-25-mg-h-w-2168

[48] International Partnership for Microbicides. Dapivirine Ring. [Online]. 2020 [Cited 2020 Nov 9]. Available from: https://www.ipmglobal.org/our-work/our-products/dapivirine-ring

[49] Glaubius R, Ding Y, Penrose K, Hood G, Engquist E, Mellors J, et al. Dapivirine vaginal ring for HIV prevention: modelling health outcomes, drug resistance and cost-effectiveness. J Int AIDS Soc 2019;22(5):e25282. [Cited 2020 Nov 9]. Available from: https://doi.org/10.1002/jia2.25282

[50] Schürmann D, Rudd DJ, Zhang S, De Lepeleire I, Robberechts M, Friedman E, et al. Safety, pharmacokinetics, and antiretroviral activity of islatravir (ISL, MK-8591), a novel nucleoside reverse transcriptase translocation inhibitor, following single-dose administration to treatment-naive adults infected with HIV-1: an open-label, phase 1b, consecutive-panel trial. Lancet 2020;7(3):E164-E172. [Cited 2020 Nov 9]. Available from: https://doi.org/10.1016/S2352-3018(19)30372-8

[51] Matthews RP, Barrett SE, Patel M, Zhu W, Fillgrove KL, Haspeslagh L, et al. First-in-human trial of MK-8591-eluting implants demonstrates concentrations suitable for HIV prophylaxis for at least one year. Abstract TUAC0401LB. 10th International AIDS Society Conference on HIV Science, Mexico City, 2019 [Cited 2020 Nov 9]. Available from: http://programme.ias2019.org/Abstract/Abstract/4843

[52] Ankrom W, Schürmann D, et al. Single doses of MK-8507, a novel HIV-1 NNRTI, reduced HIV viral load for at least a week. Oral presentation O416. HIV Glasgow 2020. 2020 [Cited 2020 Nov 9].

[53] Daar E, McDonald C, Crofoot G, Ruane P, Sinclair G, DeJesus E, et al. Dose-response relationship of subcutaneous long-acting HIV capsid inhibitor GS-6207. Abstract number 469. CROI 2020. 2020 Mar 8-11 [Cited 2020 Nov 9]. Available from: https://www.croiconference.org/abstract/dose-response-relationship-of-subcutaneous-long-acting-hiv-capsid-inhibitor-gs-6207

[54] US Food and Drug Administration. Highlights of prescribing information for Trogarzo. [Online]. 2018 [Cited 2020 Nov 9]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761065lbl.pdf

[55] Beccari MV, Mogle BT, Sidman EF, Mastro KA, Asiago-Reddy E, Kufel WD. Ibalizumab, a novel monoclonal antibody for the management of multidrug-resistant HIV-1 infection. Antimicrob Agents Chemother 2019;63:e00110-19. [Cited 2020 Nov 9]. Available from: https://doi.org/10.1128/AAC.00110-19

[56] Towner W, et al. Long-term efficacy, safety, and durability of ibalizumab-based regimens in subgroup of TMB-202 participants. Abstract 1027. IDWeek. 2020 [Cited 2020 Nov 9].

[57] Formulary Watch. FDA approves breakthrough drug for HIV patients with dwindling options. [Online]. 2018 Mar [Cited 2020 Nov 9]. Available from: https://www.formularywatch.com/view/fda-approves-breakthrough-drug-hiv-patients-dwindling-options

[58] i-Base. Pipeline-HIV lite 2020. [Online]. 2020 Mar [Cited 2020 Nov 9]. Available from: https://i-base.info/htb/wp-content/uploads/2020/03/i-Base-HIV-pipeline-LITE-March-2020.pdf

[59] IAVI. Expanding access to monoclonal antibody-based products: A global call to action. [Online]. 2020 [Cited 2020 Nov 9]. Available from: https://www.iavi.org/phocadownload/expanding/Expanding%20access%20to%20monoclonal%20antibody-based%20products.pdf

[60] Medicines Patent Pool. Licence Agreement. Dolutegravir. [Online]. [Cited 2020 Nov 9]. Available from: https://medicinespatentpool.org/uploads/2014/04/Amended-and-Restated-Form-of-SUBLICENCE-DTG-Adults.pdf

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