



UNTANGLING THE WEB OF
**ANTIRETROVIRAL
PRICE REDUCTIONS**

18th Edition – July 2016

www.msfacecess.org



PREFACE

In this report, we provide an update on the key facets of HIV treatment access. It includes the latest HIV treatment guidelines from World Health Organization (WHO), an overview on pricing for first-line, second-line, and salvage regimens, and a summary of the opportunities for – and threats to – expanding access to affordable antiretroviral therapy (ART). There is a table with information on ARVs, including quality assurance, manufacturers and pricing on pages 19 to 21.

Detailed information on key antiretroviral drugs and fixed-dose combinations is available at:

 www.msfaccess.org/utw2016

THE MSF ACCESS CAMPAIGN

In 1999, on the heels of Médecins Sans Frontières (MSF) being awarded the Nobel Peace Prize – and largely in response to the inequalities surrounding access to HIV/AIDS treatment between rich and poor countries – MSF launched the Campaign for Access to Essential Medicines. Its sole purpose has been to push for access to, and the development of, life-saving and life-prolonging medicines, diagnostics and vaccines for patients in MSF programmes and beyond.

 www.msfaccess.org

MSF AND HIV

Médecins Sans Frontières (MSF) began providing antiretroviral therapy to a small number of people living with HIV/AIDS in 2000 in projects in Thailand, South Africa and Cameroon. At the time, treatment for one person for one year cost more than US\$10,000. With increased availability of low-cost, quality antiretroviral drugs (ARVs), MSF provides antiretroviral treatment to 247,000 people in 18 countries, implements treatment strategies to reach more people earlier in their disease progression, and places people living with HIV at the centre of their care.

Over the past 16 years, the MSF Access Campaign has been monitoring the barriers to availability and affordability of life-saving ARVs and appropriate formulations, including patent monopolies, prices and lack of generic competition through *Untangling the Web* and pushing for the uptake of policies that promote access to affordable quality medicines. Due primarily to generic competition, the price of ARVs has dropped by more than 99% over the last 15 years, but the price of the newest drugs, already needed by some people in MSF projects, is prohibitive and a source of great concern both for MSF and national treatment programmes.

PATENT OPPOSITION DATABASE

The Patent Opposition Database was launched by the MSF Access Campaign in October 2012 as an online space where civil society can share the resources and tools needed to oppose patents on medicines. The database gathers contributions from around the world. It allows documents to be shared, arguments to be replicated, and new alliances to be forged, with the aim of successfully opposing patents and ultimately improving access to medicines in developing countries. To find out more about patents that block access to essential medicines and what you can do to challenge them, or to contribute by sharing resources, visit:

 www.patentoppositions.org



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STATE OF HIV TREATMENT ACCESS

In 2000, when the International AIDS Conference was last held in Durban, South Africa, a basic antiretroviral (ARV) regimen cost over US\$10,000 per person per year (pppy), multilateral programmes funding the fight against HIV, TB, and malaria did not exist, and many donors – such as the US government – had yet to provide a single dollar for antiretroviral treatment in resource-limited countries.

Now, in 2016, 17 million HIV-positive people are receiving lifesaving antiretroviral therapy (ART),¹ and the lowest price for a generic, World Health Organization (WHO)-recommended first-line regimen is \$100 pppy.

In 2015, the number of people starting HIV treatment surpassed the number of new infections in Africa for the first time. Since 2010, the number of people receiving ART has more than doubled.^{1,2} The push to continue ARV scale-up has gained momentum around the UNAIDS global targets

for 2020, referred to as '90-90-90'.³ To meet these targets, the number of people on treatment will need to more than double again, since nearly 20 million HIV-positive people are newly eligible for ART under the new 'treat-all' recommendation.¹

At the UN High Level Meeting on HIV in June 2016, governments agreed on a global target: reaching 30 million people with treatment by 2020. Reaching this goal will require increased and sustained support from donors.

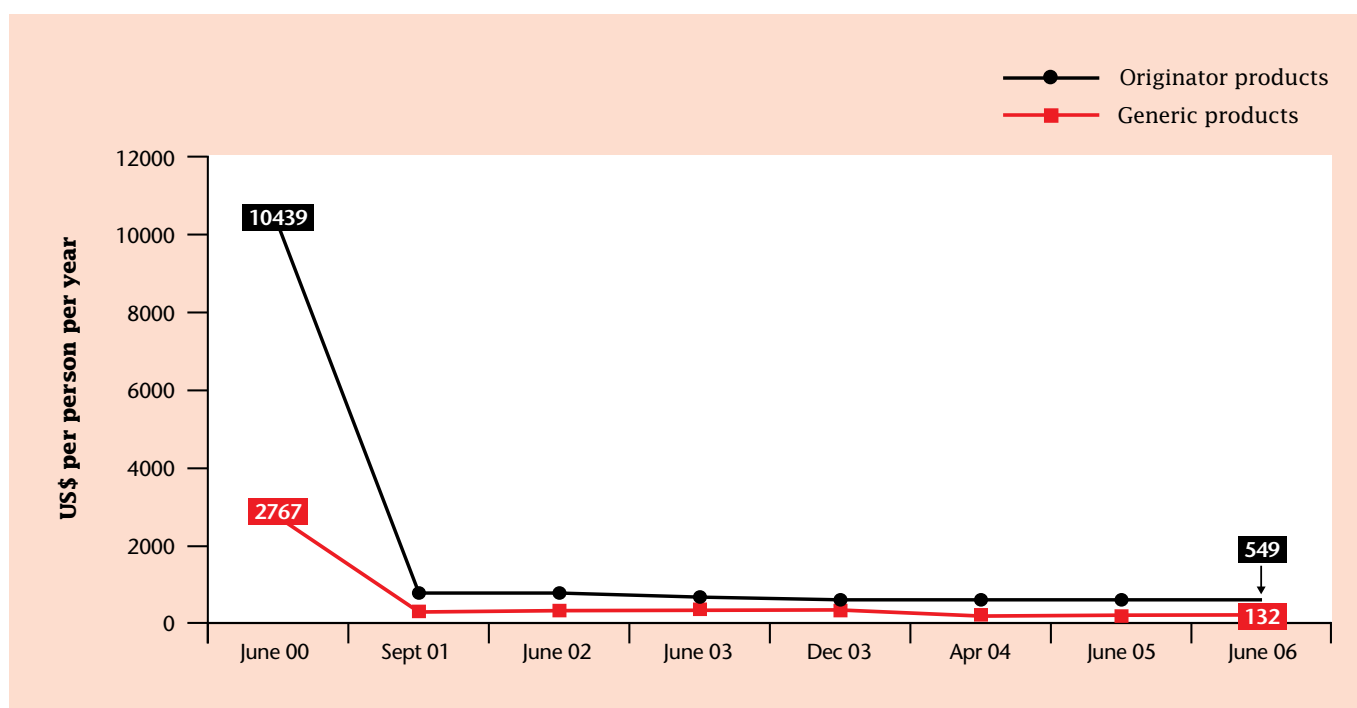
THE 2020 UNAIDS TARGET: 90-90-90

By 2020, 90% of all HIV-positive people will be aware of their status; 90% of all people diagnosed with HIV will have access to sustained ART; and 90% of people on ART – or 73% of all HIV-positive people – will achieve viral suppression.³



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Tsandia receives her antiretroviral medicines at the HIV department of the Arua Regional hospital in Uganda.

GRAPH 1: GENERIC COMPETITION AS A CATALYST FOR PRICE REDUCTION FOR A FIRST-LINE REGIMEN

Since 2000, MSF has been providing HIV care and treatment to people in developing countries. Today, MSF provides HIV treatment for nearly 250,000 people.

SPEED UP TREATMENT SCALE-UP IN WESTERN AND CENTRAL AFRICA

Although HIV prevalence is lower in Western and Central Africa than in Southern Africa, over a quarter of all AIDS-related deaths occur in the region, including 40% of all deaths among children.⁴

In Central African Republic, HIV prevalence is 5%, but HIV accounts for 84% of hospital-based deaths where MSF works. In Democratic Republic of the Congo, three out of four HIV-positive people who present to the hospital where MSF works are too sick to save.

In 2015, only 1.8 million people (28%) of the region's 6.5 million HIV-positive people were accessing ART.¹ Political instability, inadequate funding and weak healthcare systems - some

worsened by the Ebola outbreak - add to barriers that include limited access to diagnostic and monitoring

tests, drug stockouts, out-of-pocket fees for healthcare, and lack of decentralised treatment.⁴



Mohamed (left) is tested for HIV at an MSF mobile clinic in Conakry, Guinea.

© Sam Phelps

OPTIMISING HIV TREATMENT

COUNTRIES SHOULD IMPLEMENT WHO GUIDELINES

Immediate treatment and a steady supply of affordable medicines are essential to curbing the HIV epidemic. ART lowers the risk of serious illness and death, reduces the risk of developing tuberculosis (TB) by 65%, and reduces HIV transmission by 96%.^{5,6,7,8}

In light of the individual and community benefits of HIV treatment,

WHO has recommended immediate and lifelong ART for everyone with HIV: all infants, children, adolescents, and adults, including pregnant and breastfeeding women, regardless of CD4 cell count or disease stage.⁹

In June 2016, WHO issued new HIV treatment guidelines, including recommendations for new ARV regimens and differentiated models

of care that put the patient at the centre of their treatment.¹⁰

Countries should implement the WHO recommendations, including 'test and start', routine viral load monitoring [see below], better drugs (new ARVs and once-daily, fixed-dose combinations), adherence support, and differentiated models of care to facilitate rapid scale-up and quality patient care.¹⁰

ROUTINE VIRAL LOAD MONITORING

Access to viral load testing – the gold standard for HIV treatment monitoring – is essential to achieving the 90-90-90 targets. For infants, an early diagnosis can be life-saving – and requires viral load testing. In 2016, WHO recommended point-of-care viral load testing for HIV-exposed infants.¹⁰

Since 2013, WHO has recommended routine viral load monitoring for diagnosing HIV treatment failure; the 2015 guidelines recommend viral load monitoring – now with dried blood spot testing – at six and 12 months after starting ART. For stable patients, viral load monitoring is recommended once every year thereafter instead of CD4 cell count monitoring.^{9,10}

As tests have become more affordable and rollout less complex, more countries have adopted routine viral load as part of national policy. However, implementation still lags far behind; a 2014 WHO study of 122 low- and middle-income countries found that only 22% of people on ART received viral load monitoring.¹¹

MSF began implementing viral load testing in 2012. In Lesotho, Malawi, Mozambique, Swaziland, Uganda, and Zimbabwe, risk factors for having a detectable viral load have been identified, leading to interventions including a child-friendly clinic, community ART groups, and enhanced adherence counselling. Routine viral load testing has triggered a switch to second-line treatment and enhanced adherence counselling in 10% to 68% of patients.¹²



© Isabel Cortier

People wait to have their blood tested to measure their viral load at the HIV department of Arua Regional Hospital in Uganda.

IMPROVING FIRST-LINE TREATMENT



An MSF outreach worker measures out antiretroviral medication during a home visit in Dawei, in southeastern Myanmar.

The 2015 WHO HIV treatment guidelines added recommendations for two alternative first-line ARVs: dolutegravir (DTG), a well-tolerated integrase inhibitor that rapidly lowers HIV viral load and is robust, with very few documented cases of resistance,¹³ and a lower, equally effective dose of efavirenz (EFV; 400mg vs. 600mg)⁹ that is better tolerated than the higher dose.¹⁴ Before these ARVs become part of a preferred first-line regimen, additional clinical data on their safety and efficacy during TB treatment, pregnancy, and breast-feeding are needed;^{9,15} these studies are planned or underway.

BETTER SECOND-LINE TREATMENT

As access to viral load monitoring increases, more people in need of second-line treatment will be identified. The WHO treatment guidelines have added two alternative recommendations for second-line ART: a heat-stable, fixed-dose combination (FDC) of darunavir/ritonavir (DRV/r) and a two-drug regimen of raltegravir (RAL; an integrase inhibitor) with lopinavir/ritonavir (LPV/r).¹⁰

DRV is a boosted protease inhibitor (PI) with fewer side effects than the other second-line protease inhibitors (although it cannot be used during rifampicin-based TB treatment).^{16,17,18} But access to DRV/r is limited; there is no quality-assured heat-stable FDC on the market, and the current price of generic DRV alone is at least three times more than other protease inhibitors, making it costly for wide-spread use.



Loved Mupandanana is HIV positive, and her first-line treatment for HIV seems to be failing. At Gombe clinic, in Manicaland Province in Zimbabwe, she is receiving counselling about the need to move on to second-line treatment.

In 2015, MSF provided second-line HIV treatment for 10,200 people.

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THE ARV PIPELINE FOR ADULTS

The ARV pipeline includes new drug formulations and classes. Tenofovir alafenamide (TAF), a new prodrug of tenofovir disoproxil fumarate (TDF), is equally effective as the currently available version, at one-tenth of the dose. TAF is likely to be safer, and should be significantly less expensive to produce than TDF,¹⁹ but data on drug interactions between TAF and TB treatment are needed.

The United States Food and Drug Administration (USFDA) has approved

three TAF-based FDCs (in November 2015, March 2016 and April 2016). Stand-alone TAF has been approved in Europe (and filed in the US) for hepatitis B treatment only. If Gilead, the company marketing TAF, does not register the drug as a single ARV for use in HIV, generic manufacturers may face complications and long delays in registering TAF-containing FDCs in other countries.

Long-acting, injectable ARVs with monthly or bi-monthly dosing could

improve adherence and significantly reduce the cost of HIV treatment; interim results from a trial of a long-acting injectable combination (rilpivirine and cabotegravir) are promising, although an interaction between cabotegravir and rifampicin requires further study.^{20,21,22,23}

New ARV classes include attachment and maturation inhibitors; there are also new versions of integrase inhibitors and non-nucleoside reverse transcriptase inhibitors (NNRTI) in development.

THE ARV PIPELINE FOR CHILDREN

Only 49% of the world's HIV-positive children had access to treatment in 2015.²⁴ Without treatment, over half of all HIV-positive children die before their second birthday;²⁵ treating infants when they are less than 12 weeks old lowers mortality by 75%.²⁶

Research and development of paediatric ARVs and FDCs has lagged far behind adult treatment, which has severely limited treatment options for HIV-positive infants and children.

There is a new pellet formulation of LPV/r, which is part of the WHO-recommended first-line regimen for children under three years old.¹⁰ In May 2015, the USFDA granted tentative approval for LPV/r pellets for children who weigh >5 kg and are over 14 days old.^{27,28} This formulation of LPV/r is available to a limited group of low- and middle-income countries through a Medicines Patent Pool (MPP) voluntary licence (VL), although one year after stringent regulatory authority (SRA) approval, it has not yet been made commercially available.

Pellets could replace LPV/r syrup, which contains 40% alcohol and propylene glycol, requires refrigeration, and has been described as tasting "horrible"²⁹ – all of which have made treating young

children difficult. The price of the pellets needs to be reduced so it is at least on par with the syrup, to encourage countries to adopt them.

The Drugs for Neglected Diseases *initiative* (DNDi) LIVING study is looking at the safety, effectiveness and acceptability of LPV/r pellet-based therapy in infants (>four weeks old) and children, with enrolment having begun in Kenya.³⁰

In 2015, MSF supported treatment for 6,800 HIV-positive pregnant women, and post-exposure treatment for 4,400 babies.



Jennipher Mwamvera is a mother of four and a patient in the prevention-of-mother-to-child transmission of HIV (PMTCT) program in Thyolo, Malawi.

PRICING

Affordable generic ARVs have made HIV treatment scale-up possible in countries that can access them. Robust competition between multiple generics producers has dramatically lowered the price of first-line antiretroviral therapy over the last decade-and-a-half.

FIRST-LINE REGIMENS

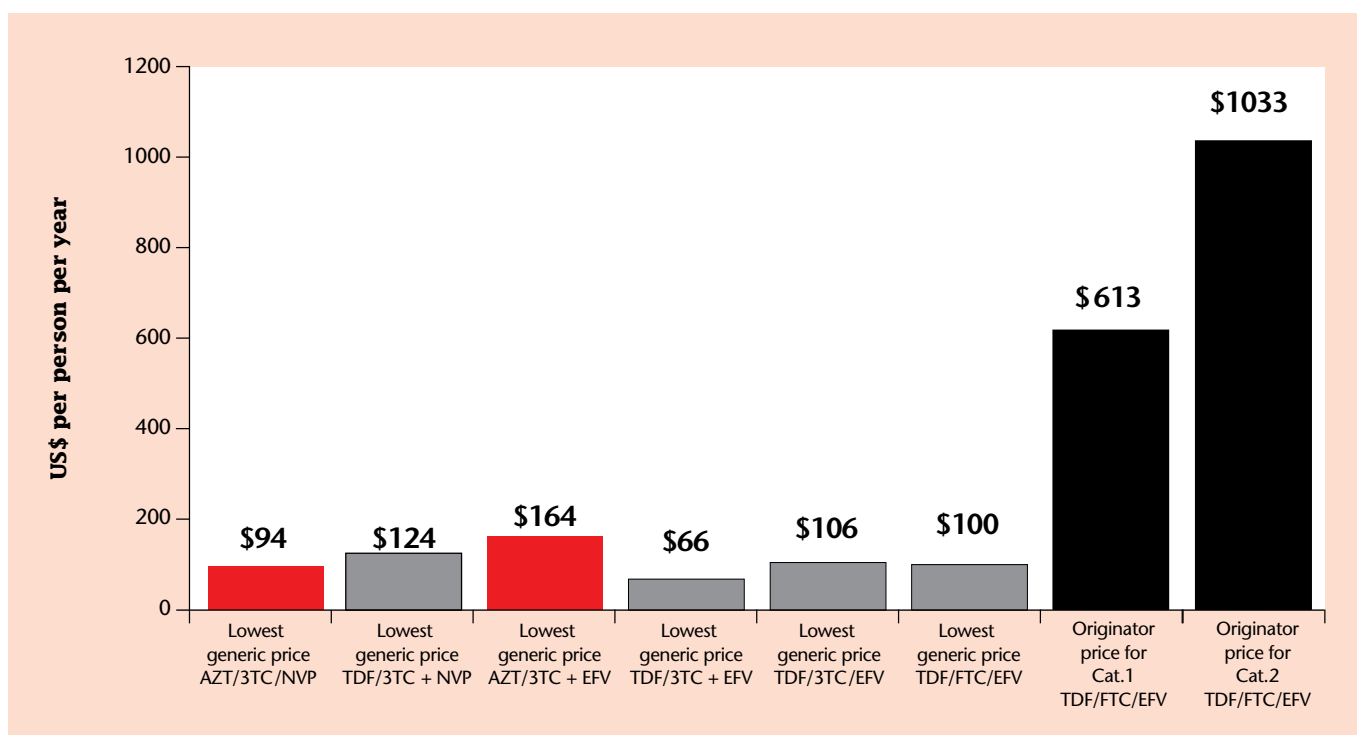
Since 2014, there has been a 30% reduction in the price for generic first-line treatment.* If countries are able to import and use generics, the price for the fixed-dose of the WHO-recommended combination of tenofovir/emtricitabine/efavirenz

(TDF/FTC/EFV) can be as low as \$100 pppy, down from \$143 pppy in 2014. Prices for first-line treatment are unlikely to decrease further, since they are now close to the minimum sustainable production price, according to experts.³¹

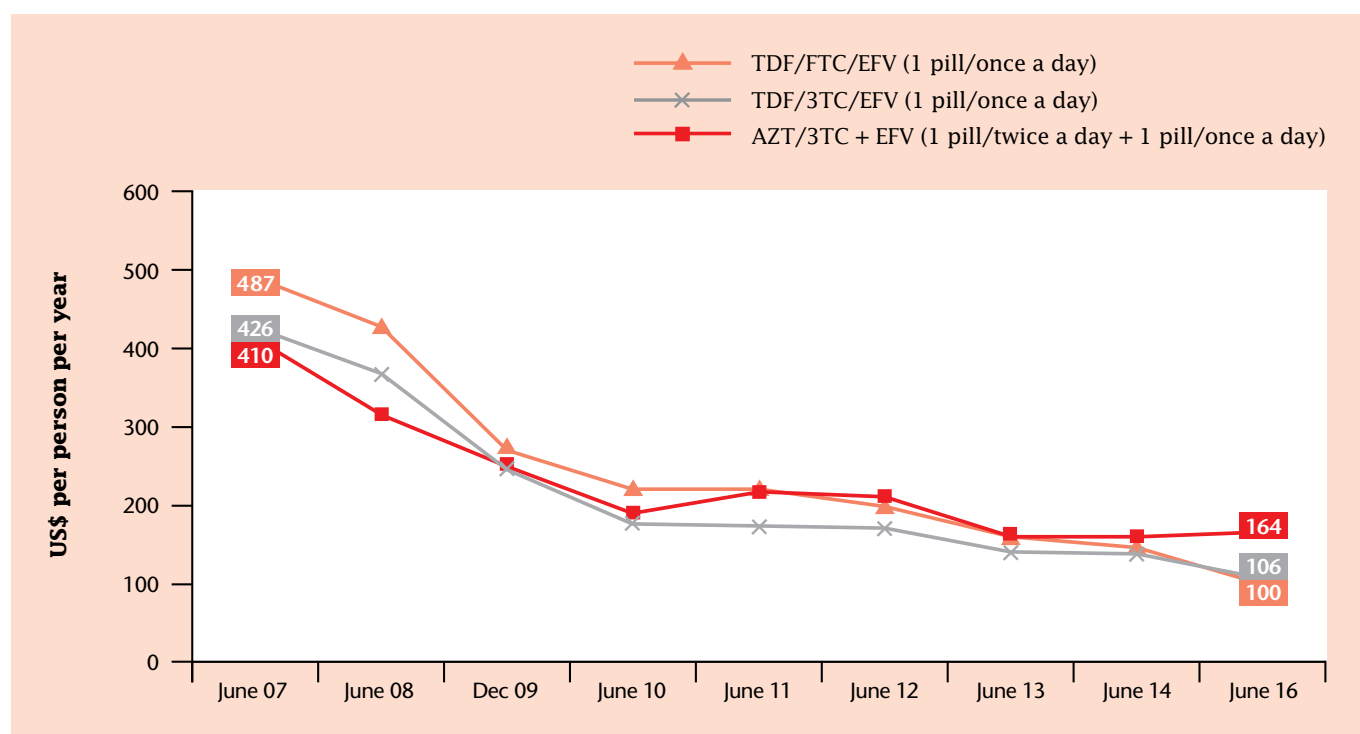
Aurobindo's generic version of dolutegravir will have a price of \$44 pppy,³² which is on par with the price of efavirenz 600mg. A fixed-dose combination of DTG with TDF/XTC should be available by the end of 2017.

Continued overleaf

GRAPH 2: THE PRICES OF DIFFERENT FIRST-LINE REGIMENS TODAY



* Price reductions may be due in part to currency fluctuations.

GRAPH 3: THE EVOLUTION IN PRICE OF DIFFERENT FIRST-LINE REGIMENS

HIGH ANTIRETROVIRAL PRICES IN MIDDLE- AND HIGH-INCOME COUNTRIES

According to UNAIDS, 70% of all HIV-positive people will be living in middle-income countries by 2020.³³

Several ARVs are still on patent in middle-income countries. Some lower- and upper-middle-income countries where patent barriers on key ARVs remain cannot produce or buy generic ARVs, because they are

not included in voluntary licensing agreements, and/or have not used TRIPS flexibilities such as compulsory licences.* Instead, they must pay high prices to originator companies for patented drugs on a case-by-case basis or under 'tiered pricing' schemes that are not based on a realistic concept of affordability.³⁴

High-income countries such as the US are struggling with spiralling costs of patented medicines, including ARVs. In the US, the combination of TDF/FTC/EFV (sold under the brand name Atripla) costs nearly \$30,000 ppy³⁵ versus \$100 ppy for Indian generic versions.

* The World Trade Organization's Trade-Related Aspects of Intellectual Property (TRIPS) Agreement can and should be interpreted in light of the goal "to promote access to medicines". Legal safeguards include (but are not limited to) enabling networks of people living with HIV/AIDS to challenge patent claims before and/or after they are granted; the right to examine patent claims strictly and reject new use and/or new forms of known medicines; the right to register generic versions of patented medicines; the right to issue compulsory licences (CLs; these allow countries to import or locally produce generic versions of patented medicines without the patent holder's consent); and the right to import and resell lower-priced medicines from other countries instead of paying higher prices for them – also without consent from the patent holder (called parallel importing).

SECOND-LINE REGIMENS

Boosted protease inhibitors are the backbone of second-line regimens. The lowest-priced generic second-line regimen, zidovudine/lamivudine (AZT/3TC) and atazanavir/r (ATV/r), is now priced at \$286 pppy. Since 2014, the price has dropped by 11%, from \$322 pppy.

Switching to second-line therapy nearly triples the price of treatment [see graph 5]. Currently, there are two WHO-preferred boosted protease inhibitors for second-line regimens, ATV/r and LPV/r; one alternative boosted protease inhibitor, darunavir+r (DRV+r); and an alternative, twice-daily two-ARV regimen, the integrase inhibitor raltegravir (RAL) plus LPV/r.¹⁰

A generic, fixed-dose, heat-stable formulation of ATV/r is available. It has fewer side effects than LPV/r, although it cannot be used during rifampicin-based TB treatment. Because of supply problems with LPV/r, an increase in demand for ATV/r is expected, hopefully leading to lower prices.

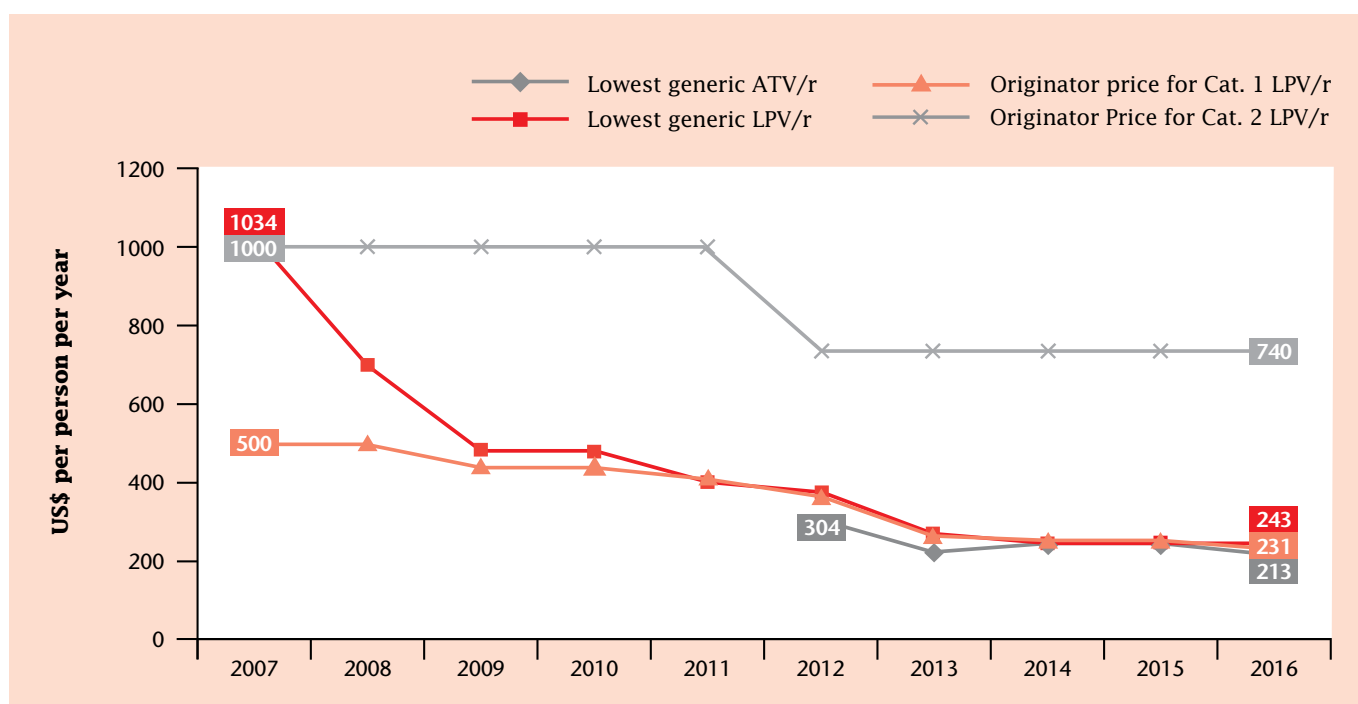
Although LPV/r must be taken twice a day, it can be dose-adjusted for use with rifampicin-based TB treatment. LPV/r is still more expensive than ATV/r, at \$243 pppy versus \$213 pppy [see graph 4]. The price of generic LPV/r is 5% higher than the originator product, because the originator company, AbbVie, has been consistently undercutting generic competition with slightly lower prices.

For several of the newer second-line options, current demand is low. The price of generic versions has not yet come down, and only a few producers have entered the market. DRV is much more expensive than ATV/r or LVP/r, and it is not available as a fixed-dose combination with ritonavir (RTV or r). Darunavir is available from the originator for \$663 pppy; generic versions are \$1217 pppy, since the current low demand prevents companies from being motivated to commercialise it in low- and middle-income countries.

Prices for boosted protease inhibitors are especially high in middle-income countries, since many of them have patent barriers and are excluded from voluntary licensing agreements. In its designated Category 2 countries,* AbbVie charges higher prices for LPV/r than in least-developed countries (LDCs): \$740 pppy (which has not changed since 2012), compared to \$231 pppy in LDCs [see graph 4]. In Malaysia, prices for LPV/r were quoted above \$3,500 pppy in 2014.³⁶ The originator price from Bristol-Myers Squibb (BMS) for atazanavir– which must be used with ritonavir (RTV) – is \$816 pppy; AbbVie’s originator price for RTV is set on a “case-by-case” basis.

The lowest originator price for RAL is \$675 pppy; the lowest-price generic version is \$973 pppy [see graph 6]. Currently, RAL is taken twice daily, however, Merck plans to submit data to the USFDA and the European Medicines Agency (EMA) to seek approval for once-daily RAL.³⁷ RAL can be dose-adjusted for use during rifampicin-based TB treatment.³⁸

GRAPH 4: THE EVOLUTION IN PRICE OF BOOSTED PROTEASE INHIBITORS FOR SECOND-LINE REGIMENS



* Albania, Armenia, Azerbaijan, Belarus, Bolivia, Bosnia and Herzegovina, China, Colombia, Dominican Republic, Ecuador, El Salvador, Fiji, Georgia, Guatemala, Guyana, Honduras, India, Indonesia, Jamaica, Jordan, Kazakhstan, Kyrgyzstan, Macedonia, Marshall Islands, Micronesia, Moldova, Mongolia, Montenegro, Nicaragua, Pakistan, Papua New Guinea, Paraguay, Peru, Philippines, Serbia, Sri Lanka, Suriname, Syria, Tajikistan, Thailand, Tonga, Turkmenistan, Ukraine, Uzbekistan, Viet Nam.

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SALVAGE REGIMENS

There is an urgent need for more affordable third-line, or salvage regimens for people that have acquired resistance to first- and second-line treatment. Low volume and high prices from both originator and generic companies keep these medicines out of reach.

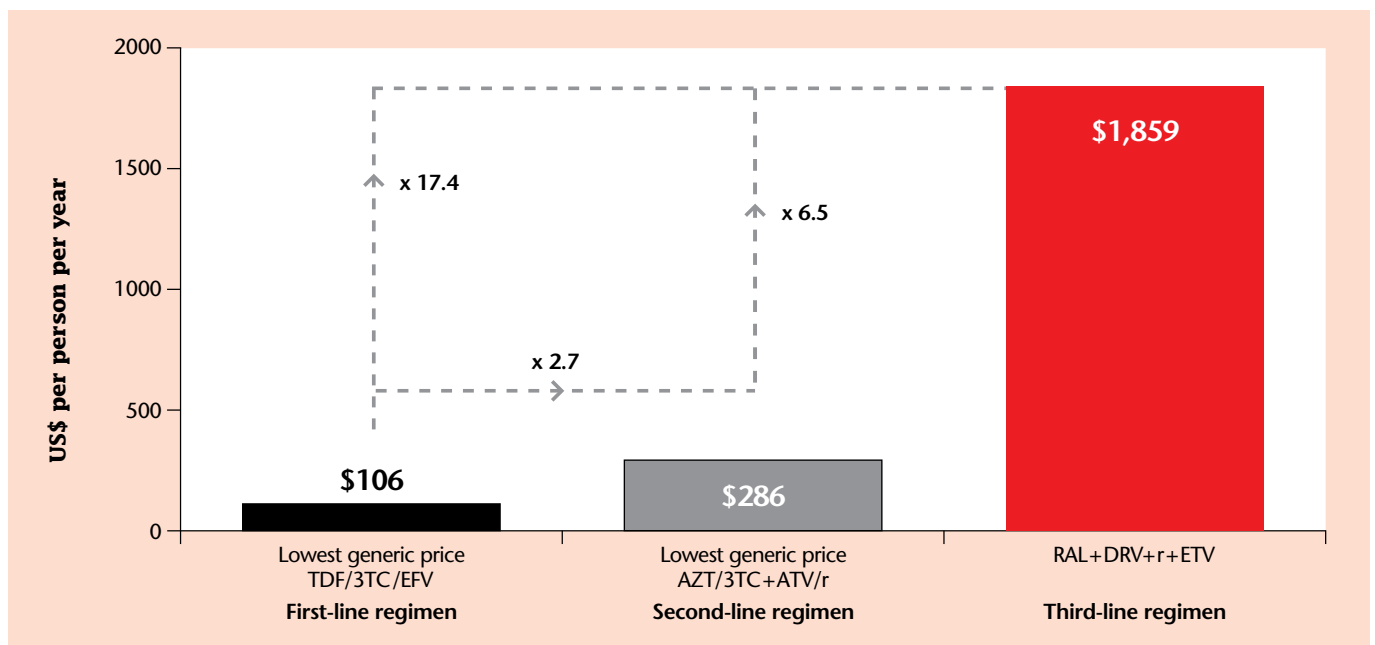
The lowest price for a salvage regimen today is \$1,859 pppy, for darunavir+r, raltegravir and etravirine (DRV+ r + RAL

+ ETV), in countries that fall into the select group eligible for access pricing from originators (but many countries are paying much more). This represents nearly an 18-fold increase over the lowest first-line prices, and nearly a seven-fold increase over the most affordable second-line regimen [see graph 5].

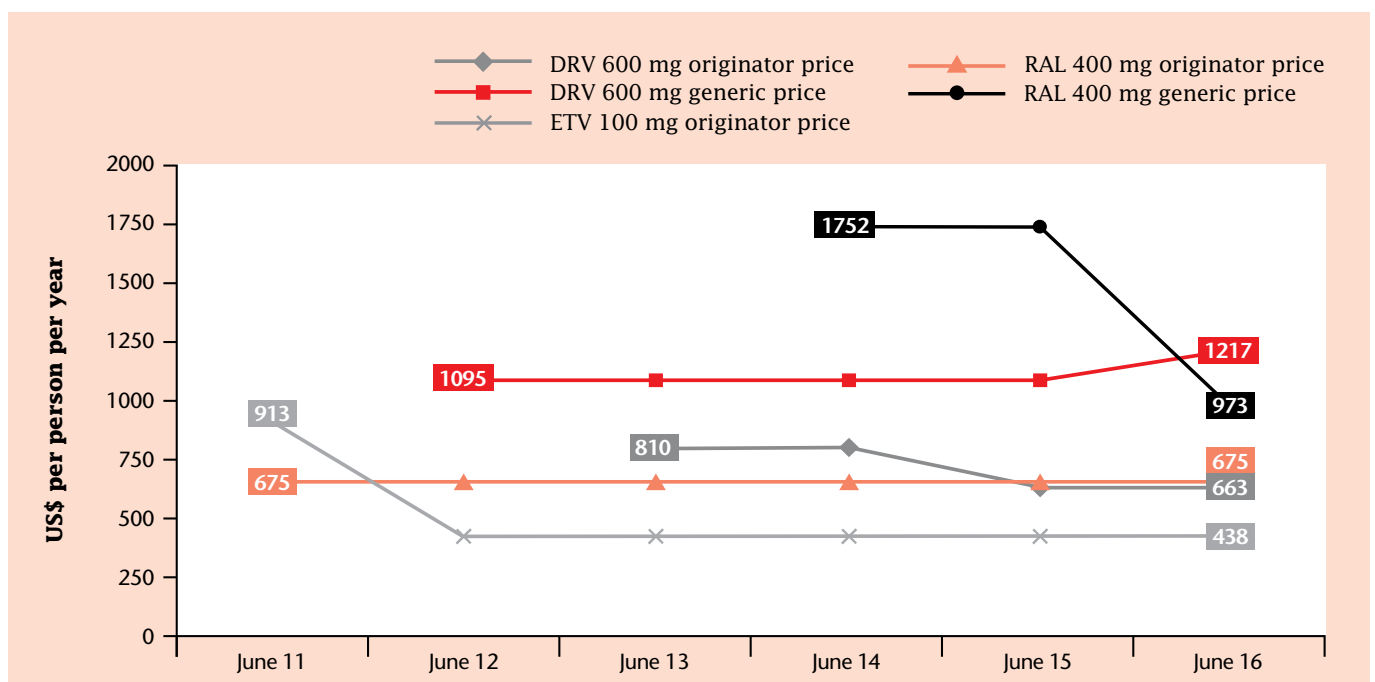
Since 2014, the price of generic DRV has increased by 10%, from \$1,095 to

\$1,217; this does not include the ritonavir it must be used with. At the same time, the access price from the originator has dropped by 17%, from \$810 to \$675. A quality-assured generic RAL is priced at \$973 pppy, but it is still more expensive than the originator version, which has stayed at \$675 since 2011. The originator price for ETV has stayed at \$438 since 2011 [see graph 6].

GRAPH 5: PRICE COMPARISONS OF FIRST-LINE, SECOND-LINE AND POSSIBLE THIRD-LINE TREATMENT REGIMENS



GRAPH 6: PRICES FOR THIRD-LINE ARVS



REGISTRATION

In many countries, marketing authorisation for promising new ARVs can take several years; this type of regulatory lag forces people living with HIV/AIDS to wait for life-saving medicines. National Drug Regulatory Authorities (NDRAs) do not always have the resources to ensure timely registration of more affordable generic versions of new ARVs, and/or fail to prioritise them.³⁹

Pharmaceutical companies don't often prioritise registration in low- and middle-income countries. Some originator companies shift the responsibility for filing registration dossiers in high-burden developing countries to generics companies that have signed voluntary licences.

In some countries, generics companies are able to register generic versions of medicines, but in others, when originators don't register their ARVs before generics companies do, it may cause significant delays, or become an absolute barrier to treatment access.

Countries have different regulatory pathways, priorities, rules, requirements, legal frameworks, capacities, and timelines, and some do not have NDRAs. There is no 'essential documentation package' to streamline the registration process across all NDRAs in developing countries, and country-level bureaucracy can delay registration.

Collaborative or regional registration processes have reduced the time to registration for some products in some participating countries. These collaborations should be considered by national regulatory authorities to reduce the considerable workload associated with reviewing registration dossiers. For example, in East Africa, a pilot of the African Medicines Registration Harmonisation Initiative has reduced the time to registration by 50% in Burundi, Kenya, Rwanda, Uganda, and Zanzibar.³⁹

India's lack of intellectual property (IP) barriers and historically efficient regulatory pathway made it possible for generics companies to produce and register more affordable medicines for developing countries. But availability of new quality-assured generic ARVs and FDCs from India is starting to be delayed. This is partly because India's criteria to waive phase III clinical trials are restrictive in certain cases. These criteria need to be expanded to include

new drugs for neglected diseases, ARVs for paediatrics, and salvage regimens. In addition, the Indian NDRA should prioritise new ARVs, FDCs, and child-friendly formulations, taking note of, and relying on WHO guidelines and/or Expression of Interest from the WHO prequalification programme.*

Another delay is the WHO prequalification programme, which has been essential for reviewing the quality, safety, and efficacy of generic ARVs that aren't always reviewed or approved by a stringent regulatory authority (SRA). In 2013, the median wait for WHO prequalification was 15.1 months.³⁹

97% of the medicines MSF uses to treat people with HIV are generics made in India.

BARRIERS TO UNIVERSAL ACCESS TO GENERIC DOLUTEGRAVIR FROM INDIA

The pharmaceutical company ViiV has granted voluntary licences (VLs) for the integrase inhibitor dolutegravir (DTG) to several Indian generic companies through the Medicines Patent Pool (MPP). The VLs will not result in universal access to the drug, since a number of high-burden countries are excluded from the territories that can import the generic version from India.

In India, generic DTG will only be available on the public market or to non-governmental providers, leaving a number of patients with drug resistance who need immediate access without any source from Indian pharmacies.

Although DTG has been registered in many other countries, ViiV, the originator company, has not filed

for registration in India. As a result, the responsibility for registration is now with Indian producers that have developed generic dolutegravir. They will need to do local clinical trials, as per the Indian NDRA requirements for new drugs, which will lead to a significant delay in the availability of affordable generics across the developing world. In the meantime, patients in India who have exhausted other treatment options are left without access to DTG, since ViiV has been dragging its feet to provide the medicine via compassionate use.

To ensure open generic competition in the future, a patent opposition for DTG has been filed in India, by and on behalf of people living with HIV, and supported by MSF.

* These include: dolutegravir (DTG) singles and FDCs, including tenofovir/lamivudine/dolutegravir; a low-dose (400mg) efavirenz FDC and heat-stable darunavir/ritonavir Priority pediatric formulations for HIV include: lopinavir/ritonavir pellets or sachets; abacavir/lamivudine/lopinavir/ritonavir (ABC/3TC/LPV/r) zidovudine/lamivudine/lopinavir/r (AZT/3TC/LPV/r) pellets or sachets for children over three years old and lamivudine/abacavir/efavirenz (3TC/ABC/EFV 75/150/150mg) dispersible tablets for children ages 3-10 years.

PATENT OPPOSITIONS AND PATENT LAW REFORM

INDIA, THE 'PHARMACY OF THE DEVELOPING WORLD', IS UNDER PRESSURE TO DROP ITS PUBLIC HEALTH SAFEGUARDS

Indian generics comprise 76% of the ARVs used in low- and middle-income countries and more than 97% of those used by MSF in its treatment programmes.^{31,44} India encouraged generic competition for decades, since it did not introduce patents for pharmaceuticals until 2005 (when it had to comply with international trade rules under the World Trade Organization [WTO] Agreement on Trade-related Aspects

of Intellectual Property Rights [TRIPS]). India's national patent laws include public health safeguards such as stringent patentability criteria, and the opportunity to file legal challenges to patents before and/or after they are granted (called pre-and post-grant patent oppositions).

India has fought off numerous challenges to its public health safeguards, but it has been under excessive external and domestic

pressure – led by the multinational pharmaceutical lobby – to change its national intellectual property laws and policies, or sign free trade agreements that will dismantle them. Over the last two years, pharmaceutical industry-led pressure from the US has been escalating. India must reject the demands to grant patents more easily, as well as TRIPS-plus rules that the United States is trying to force upon India's Ministry of Commerce.

PATENT OPPOSITIONS FOR HEPATITIS C

Patent oppositions have been used when patent claims do not meet national patentability criteria, and when a patent directly blocks or delays access to essential medicines.

Worldwide, an estimated 150 million people have chronic hepatitis C virus infection; without treatment, they are at risk of developing liver failure and liver cancer.⁴⁵

Hepatitis C can be cured with a few months' treatment using oral drugs, called direct-acting antivirals (DAAs). In 2013, the price of the first DAA on the market, sofosbuvir, sent shock waves throughout the world. Although it can be mass-produced for less than \$1 per pill,⁴⁶ sofosbuvir's launch price was \$1,000 per pill in the US.

Gilead's patent on sofosbuvir has been opposed – and rejected – in some countries. The patent on the pro-drug form of sofosbuvir was rejected in China and Ukraine. In Egypt, where the primary patent application for sofosbuvir was rejected, a company called Pharco

has applied for WHO prequalification for their generic version of the drug.

In India, one critical sofosbuvir patent has been recently granted, reversing its prior rejection in 2015. This decision is now under appeal. If upheld, the patent will block additional competition from the Indian generics companies that do not want to sign a voluntary licence with Gilead, leaving them unable to supply sofosbuvir to millions of people in India and other middle-income countries. In addition, this decision would allow Gilead to disrupt or stop exports of the raw materials from India that are used to make sofosbuvir's key active pharmaceutical ingredient (API). This will make it difficult for the generics companies in Egypt, Bangladesh, Pakistan and Latin America that are producing sofosbuvir without a patent in force – and without a licence agreement with Gilead – to continue production. More patent oppositions on sofosbuvir have been filed in Argentina, Brazil, Russia, Thailand, France and India.

PATENT LAW REFORM IN BRAZIL, SOUTH AFRICA AND ARGENTINA

South Africa and Brazil are in the process of reforming their patent laws, in part to more effectively manage prices for medicines, and to encourage competition (and local production). There is a lot at stake: South Africa has the largest number of people living with HIV in the world, and Brazil guarantees HIV treatment for all, with many people on salvage therapy, as well as first- and second-line treatment. But delays in patent law reform will undermine access to affordable medicines, including ARVs.

SOUTH AFRICA

In 2015, 3.1 million people living with HIV were accessing antiretroviral therapy through South Africa's public sector,⁴⁷ and the government recently announced a 'test and start' policy.⁴⁸ As more people are treated, the need for second-line and salvage regimens will increase. Many of these ARVs are patented and are too expensive for the government to procure for the public sector. But South Africa has not introduced or implemented key measures to safeguard public health, including fully adopting TRIPS flexibilities, and especially substantive examination of patent claims. In 2008 alone, South Africa granted 2,442 patents, while Brazil granted only 272 patents between 2003 and 2008.⁴⁹

In 2009, South Africa's Department of Trade and Industry (DTI) initiated a process to reform the country's IP law and policy. In 2011, TAC, Section 27 and MSF co-launched the 'Fix the Patent Laws' campaign, which now includes 18 other non-governmental organisations. The campaign highlights how pharmaceutical companies have used evergreening tactics to exploit South Africa's patent system. In September 2013, the DTI released a draft policy document for public comment. But the new policy is still not finalised, and is not expected until mid-2017.

The longer DTI delays, the longer it will take for South Africa to introduce short- and long-term reforms that can accelerate and promote generic competition, and to drive down prices for patented drugs. The delay also raises concern about undue political and commercial pressure from multinational

pharmaceutical companies involved in the 'Pharmagate' scandal (a covert, \$600,000 campaign funded by large pharmaceutical companies and medical device producers to delay - and influence - South African patent reforms). South African Health Minister Aaron Motsoaledi has accused the multinational pharmaceutical companies in South Africa of conspiring against the state and the people of South Africa, and called on all South Africans to fight back "...to the last drop of their blood."⁵⁰

BRAZIL

Brazil is consistently excluded from voluntary licensing programmes, and therefore forced into tiered pricing schemes from originator companies

that charge unaffordable prices. In order to overcome IP barriers to generic competition, a coalition of civil society groups has recently filed a patent opposition in Brazil on the main patent related to TAF. In addition, in November 2015, GTPI (Working Group on Intellectual Property), a civil society coalition, filed a patent opposition to deny a patent to BMS (for atazanavir; ATV) that could extend the patent holder's monopoly until 2024. Brazil currently pays \$496.40 pppy for the 300mg version of ATV; a Health Ministry-approved licence between BMS and the Brazilian government-linked pharmaceutical laboratory Farmanguinhos forbids production of atazanavir in newer formulations and combinations, such as ATV/r.⁵¹



MSF and the Treatment Action Campaign launched the 'Fix the Patent Laws' campaign to demand patient-focused reforms to South Africa's patent laws.

EVERGREENING

Many countries often do not examine patent claims strictly, leaving them vulnerable to 'evergreening', whereby pharmaceutical companies make minor changes to medicines that are already on the market to extend their patents. Several ARVs should now be free from patent barriers (including ABC, DRV, EFV and RTV) since their basic patents have

expired, but they are not because of evergreening.

In Ukraine, home to nearly 265,000 people living with HIV,⁴⁰ GSK extended its abacavir (ABC) patent monopoly by eight years with its secondary patent on the hemisulfate salt.⁴¹ Ukraine's price for originator ABC is \$277.40 pppy⁴² versus \$123.42 pppy for the generic version.⁴³

Continued overleaf ❖

❖ Patent oppositions and patent law reform continued

At the same time, multinational drug companies are using lawsuits to challenge measures that promote generic competition in Brazil, including the country's patent examination process. Since 2001, ANVISA, Brazil's national drug regulatory agency, has participated in analysing pharmaceutical patent applications, instead of leaving this task exclusively to patent office examiners, and ANVISA has rejected more than 400 of them. ANVISA's role in pharmaceutical patent examination has been considered an important safeguard to public health and access to medicines.⁵² Multinational companies have frequently contested ANVISA's rejections in court. In 2011, the Attorney General's Office (AGU) issued a legal opinion strengthening the position of pharmaceutical companies – although it proved unenforceable, the AGU has not formally withdrawn its legal opinion.

In November 2014, a multinational group of pharmaceutical companies (INTERFAMA, the Pharmaceutical Research Industry Association) filed a Collective Action against ANVISA, questioning the legitimacy of ANVISA's participation in the patent granting process. Local civil society groups have strongly reacted to these setbacks.

Patent law reform that would improve affordability of new medicines has been delayed for more than two years. In 2013, a 'package' of bills to amend Brazil's patent law was introduced. If approved, it will ensure that Brazil has clearer criteria for patent examination, and introduce important flexibilities into its national laws.⁵³

ARGENTINA

Argentina has taken steps to improve its patent laws. In 2012,

Argentina adopted new patentability examination guidelines for the pharmaceutical sector to prevent the granting of numerous patents that do not meet specific criteria such as novelty, inventive step, and industrial application. Since Argentina's new guidelines were enacted, 95% of ARV patent applications have been rejected, an increase from the 51% rejection rate in 2012.⁵⁴

In 2015, CAEME – the association of multinational pharmaceutical companies in Argentina – filed a court case questioning the validity of the patent guidelines. In response, civil society groups from Brazil and Argentina launched the 'Big Pharma Drop the Case' campaign at the 31st session of the UN Human Rights Council, to push CAEME and INTERFARMA to abandon their actions.

TRADE AGREEMENTS

Governments, civil society and generics producers should use TRIPS flexibilities to improve affordability of, and access to, needed medicines. But TRIPS flexibilities are endangered by free trade agreements (FTAs) that pose serious threats to access to affordable medicines. These FTAs include intellectual property provisions – so-called 'TRIPS-plus' provisions – that exceed countries' obligations under World Trade Organization (WTO) trade rules.

EU-INDIA FTA

Negotiations on the EU-India FTA began in 2007. They have been stalled since 2012, in part due to public pressure, but may resume this year. The EU-India FTA could jeopardise access to India's affordable generic medicines for millions of people, by limiting production, sale and export of medicines in the future.

In the past, the EU has demanded a range of intellectual property provisions that exceed India's obligations under TRIPS, including measures that would allow companies to prevent legitimate export of medicines to developing countries or bring legal action against people who buy or distribute generics.⁵⁵

TRANS PACIFIC PARTNERSHIP AGREEMENT (TPP)

The TPP is a far-reaching trade agreement across the Asia-Pacific region. If ratified, the TPP will be the worst-ever trade agreement for access to medicines: it will lengthen, deepen and expand intellectual property and patent monopolies, and prevent or delay access to affordable, life-saving generic medicines for millions of people.⁵⁶ While the TPP agreement has been signed by governments, it has yet to be ratified by any country.

REGIONAL COMPREHENSIVE ECONOMIC PARTNERSHIP (RCEP)

The RCEP trade negotiations among 16 Asia-Pacific countries could threaten

access to generic medicines due to the proposed inclusion of TPP-like intellectual property rules by Japan and South Korea.

Countries that did not join the TPP – particularly India and key members of the Association of Southeast Asian Nations – will be pushed to adopt similar standards in the RCEP negotiations, which would represent a rollback of protections against extended patent terms and data exclusivity that are part of past agreements.

The RCEP negotiations will have serious repercussions globally, since both India, the 'pharmacy of the developing world', and China, the world's largest producer of the active pharmaceutical ingredients (API) used to make medicines, are among the 16 countries included in the negotiations.

COLOMBIA: COMPULSORY LICENCE THREAT INVITES US PRESSURE

In April 2016, a leaked letter from the Colombian Embassy described how the US Senate Finance Committee and the United States Trade Representative were pressuring the Colombian government not to issue a compulsory licence* for the anti-cancer drug imatinib.⁵⁸

A number of countries have also faced similar pressure (Brazil,

Thailand, Ecuador), which has discouraged other governments from issuing compulsory licences to ensure affordable medicines.

As WHO states in its letter to Colombia's Minister of Health, "unaffordable high prices of essential medicines, including for non-communicable diseases, are a legitimate reason for issuing a compulsory licence".⁵⁹

As of mid-June 2016, the Colombian Minister of Health announced that they had issued a 'public interest declaration' regarding imatinib, without public information about whether the government will issue a compulsory licence to allow manufacturing and import of price-lowering generic versions of the drug, or simply reduce the price of the Novartis product.⁶⁰

LDC EXEMPTION FROM PHARMACEUTICAL IP EXTENDED

Least-developed countries (LDCs) have been granted an exemption from certain obligations under TRIPS, in recognition of their economic, financial and administrative constraints and their need to make or procure low cost generic medicines. Under this transition period, LDCs do not have to apply or enforce TRIPS provisions concerning patents (TRIPS section 5) or test data protection (TRIPS

section 7) for pharmaceutical products until 1 January 2033.⁵⁷ But the free-trade agreements that are being negotiated in many countries across the Asia-Pacific region, in particular RCEP [see **Trade Agreements, page 14**], could undermine the LDC transition period, unless UN agencies and civil society provide technical and political support to negotiating countries, particularly LDCs, to

protect their TRIPS flexibilities in complex FTA negotiations.

LDCs in Asia, including Laos, Bangladesh, Cambodia and Myanmar, as well as countries in sub-Saharan Africa, should continue to use the waiver to the fullest extent possible to improve access to medicines and should resist any pressure to prematurely introduce intellectual property rules that would undermine access to generic medicines.



Regular check-up session for HIV positive patients at Muse clinic in Myanmar.

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* A compulsory licence (CL) is an effective option for increasing access to ARVs and other medicines in countries where they are patented. It is a legal mechanism to allow producers other than the originator company to make the drug or to import generic versions into a given country.

STOCKOUTS

For years, many countries have faced shortages and stockouts of essential medicines. Stockouts can be caused by logistical and administrative challenges in procurement, supply chain management, or 'last mile delivery', and by medicines having only a single source (which may lead to shortages: these are generally those under patent, without compulsory or voluntary licences that allow generic manufacturers to supply them).

Because of stockouts, people may receive smaller amounts of the medicine they need, which means extra time-consuming trips to the clinic. They may also be switched to different, less-optimal doses or regimens, or be told to buy the medicines they need from the private market with the promise of reimbursement (which is usually not fulfilled), or go without medicine altogether - which can lead to drug resistance and illness.

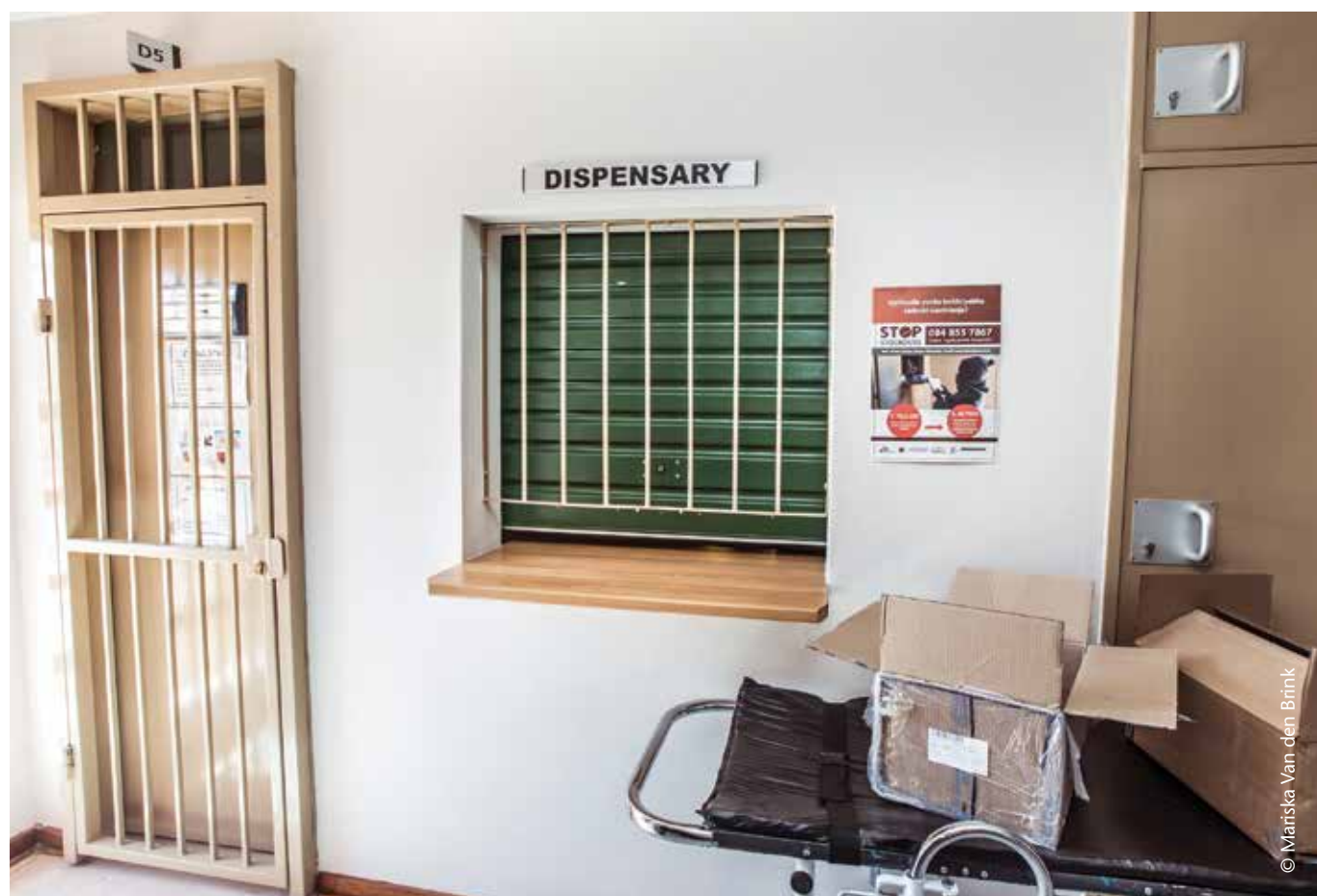
As countries upgrade their protocols to reflect WHO's new ARV guidelines,

governments should make plans for treatment transitions, ensure appropriate buffer stocks and give clear clinical guidance on making switches correctly.

Generic manufacturers must work quickly to avoid shortages and stockouts, using information about current and pipeline ARVs, dose optimisation, changes in treatment guidelines and eligibility, national and global targets for treatment scale-up, and HIV epidemiology to anticipate the quantity of API and final product

needed to ensure sufficient availability, while achieving economies of scale.

In South Africa, the Stop Stockouts Project has empowered patients and pushed for accountability in the supply of medicines. The Project receives and publishes daily reports about drug stockouts from people living with HIV and health care workers, conducts comprehensive national surveys to monitor the locations and extent of stockouts, and works with National and Provincial Departments of Health to identify and implement solutions.⁶¹



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In South Africa, the Stop Stockouts Project – a consortium bringing together six civil society organisations – is pushing for more accountability on stockouts of medicines that impact people's access to regular treatment.

MARKET SHAPING INSTITUTIONS – WHAT NEEDS TO HAPPEN

The Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), UNITAID and the Medicines Patent Pool have played a central role in the provision of affordable ARVs around the world, including use of quality-assured generic drugs by the GFATM, PEPFAR and other funders.

The GFATM's market-shaping actions go beyond its ability to provide treatment for millions of people, and have an important impact on worldwide ARV access.

After years of contributing towards collective efforts to reduce medicine prices, the scope and remit of the GFATM is increasingly less ambitious and potentially counter-productive. Progress has stalled, especially for middle-income countries, where pharmaceutical companies seek to charge high prices. Some of these countries have a high disease burden, limited ability to pay for ARVs, and decreasing support from

the GFATM and other donors. The GFATM may not be able to guarantee that these countries will be able to access the lowest prices for new medicines, including those under patent, and it may even facilitate problematic tiered pricing strategies used by drug companies in lieu of promoting robust generic competition.

There are clear warning signs that the GFATM is unwilling or unable to defend generic competition for the countries it supports. The GFATM did not signal support for the LDC extension, and has been silent about the Trans-Pacific Partnership trade agreement. It has not explicitly supported the use of TRIPS flexibilities, although this principle has been endorsed since the GFATM started. Instead, the GFATM has been championing an 'e-marketplace' (currently known as wambo.org) to make procurement more efficient. But the e-marketplace is not expected

to overcome any access barriers to affordable medicines.

Recent GFATM correspondence indicates that it may seek to optimise tiered pricing policies from drug companies, instead of overcoming commercial pricing strategies. The e-marketplace has been recently criticised by the GFATM's Office of the Inspector General for failing to implement competitive bidding processes for the first products offered over the website.⁶²

At best, if the e-marketplace can overcome the challenges it is facing, it could provide minimal technical fixes as to how governments purchase medicines, without dealing with the underlying barriers that make them unaffordable in the first place. At worst, prices offered under the e-marketplace will be insulated from the demands of government and civil society if such products remain unaffordable.

UPDATE ON THE MEDICINES PATENT POOL'S NEW LICENCES

The MPP voluntary licences (VLs) offer some countries the opportunity to gain access to affordable generic versions of new ARVs, although many middle-income and upper-middle-income countries, such as China and Brazil, continue to be left out of these VLs and are therefore prevented from buying the generic drugs produced through manufacturers based in their countries.

On one hand, the MPP has added new VLs, and increased the geographic scope or added new formulations to other licences. In 2014, the MPP announced a new agreement with AbbVie, for two specific paediatric formulations of LPV/r covering 102 low- and middle-income countries.⁶³

In late 2015, a separate agreement was signed between MPP and AbbVie on the adult formulation of LPV/r which only covers African countries.⁶⁴

The VL for tenofovir now includes tenofovir alafenamide (TAF) and has an expanded geographic scope that allows generic producers from South Africa and China to join. The VL for elvitegravir (EVT) was amended to include production in China and South Africa, provided that products are made from Gilead-licensed producers of active pharmaceutical ingredients (API).

In March 2016, GlaxoSmithKline (with ViiV) announced that it would increase the geographic scope of its voluntary licensing agreements to include all lower-middle-income countries. The MPP's VL for DTG has been expanded to include Ukraine, Morocco, Moldova, Armenia and 14 other low- and middle-income countries. Although this is a welcome first step, excluded upper-middle-income countries will still be forced into tiered pricing schemes, and price-lowering competition will be prevented.

Some MPP licences have been disappointing. AbbVie's new MPP adult licence for LPV/r has a limited geographic scope and may force specific generics companies that sign the licence agreement to forego the right to supply specific countries that they currently have the right to supply. Furthermore, a new MPP licence with Bristol-Myers Squibb for daclatasvir, a hepatitis C medicine, introduces a worrying precedent: it allows BMS to sign sub-licence agreements with generics companies together with the MPP (the normal practice is to not allow branded companies to be involved in signing a sub-licence agreement). MSF is concerned that such a practice could allow branded companies to influence the practices of generics companies, including for unrelated products, and undermine the neutrality of the MPP in managing the sub-licence agreements.

CONCLUSION

The global response to HIV/AIDS has reached a turning point. Ensuring sustainable access to affordable generic ARVs will save millions of lives. Scaling up to 90-90-90 is projected to save over 1.1 million lives and prevent 873,000 new HIV infections in the next five years; keeping up the pace for 10 years will save more than 2.4 million lives (including the mothers of 1.7 million children), and prevent over 2 million new infections.⁶⁵

To accomplish this, governments must commit to scaling-up, optimising, and maintaining access to affordable generic ARVs in the long run, as HIV is a disease that requires people to have constant access to a range of treatment options. This will require governments to use TRIPS flexibilities, reform patent laws, and reject harmful TRIPS-plus provisions proposed in various FTA negotiations.

Market-shaping institutions must keep their focus on securing and ensuring a sustainable supply of diagnostics and adult and paediatric ARVs in low- and middle-income countries, and the pharmaceutical industry should commit to registering ARVs in all countries, and expanding the scope of their voluntary licensing agreements to include all low- and middle-income countries.

All governments and donors must do their part to accelerate the global HIV response and meet the challenge of the 90-90-90 goals, including fully implementing the latest WHO guidelines, putting in place effective policies at the national level, and ensuring all people living with HIV have access to the most effective drugs, diagnostics, and models of care.



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ANNEX: SUMMARY TABLE OF ALL PRICES

Developing country prices in US\$ per patient per year, as quoted by companies.

This table contains comprehensive information about ARV pricing in developing countries. It includes adult and paediatric formulations and doses, suppliers and WHO pre-qualification status/ US FDA SRA approval. The prices for developing countries are in US \$, per person, per year, based on WHO dosing recommendations, as quoted by companies. Currency conversions were made when the pricing information was received, using the currency converter from www.oanda.com.

Each originator company applies its own eligibility criteria for discounting ARVs. Countries that are 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 deepest discounts) and 'Category 2' (countries that are offered a lesser discount).

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

The ARVs that are included in the WHO list of Prequalified Medicinal Products or that have tentative or full US FDA approval (as of May 2016) are in **bold**.

ARVs in alphabetical order	Daily dose	Originator company		Generic companies												
Abacavir (ABC)		ViiV		Aspen	Aurobindo	Cipla	Hetero									
20mg/ml oral solution	12ml	289 (0.066)		249 (0.057)	228 (0.052)		123 (0.028)									
60mg tablet	4					97 (0.067)										
Atazanavir (ATV)		BMS		Aspen	Cipla	Emcure										
		Category 1 countries	Category 2 countries													
100mg capsule	xx					(0.267)										
150mg capsule	2	412 (0.564)	412 (0.564)	380 (0.520)		207 (0.283)										
200mg capsule	xx	(0.677)	(0.677)	(0.670)		(0.433)										
300mg capsule	1				170 (0.467)	219 (0.600)										
Atazanavir/ritonavir (ATV/r)				Cipla	Emcure	Hetero										
300/100mg tablet	1			213 (0.583)	213 (0.583)	219 (0.600)										
Darunavir (DRV)		Janssen		Aspen	Hetero											
75mg tablet	xx	(0.114)														
150mg tablet	xx	(0.227)														
400mg tablet	2	438 (0.600)				973 (1.333)										
600mg tablet	2	663 (0.908)		658 (0.901)	1,217 (1.667)											
Efavirenz (EFV)		Merck		Aspen	Aurobindo	Cipla	Emcure	Hetero	Macleods	Microlabs	Quality Chemicals	Strides	Sun Pharma			
		Category 1 countries	Category 2 countries													
30mg/ml suspension	xx	(0.094)	Case-by-case													
50mg capsule	xx				(0.058)					(0.057)						
50mg tablet	xx	(0.114)	Case-by-case													
200mg capsule	3				81 (0.074)					57 (0.052)						
200mg tablet	3	394 (0.360)	Case-by-case											113 (0.103)		
600mg tablet	1	237 (0.650)	Case-by-case	84 (0.231)	37 (0.100)	20 (0.055)	47 (0.129)	45 (0.123)	38 (0.105)	35 (0.095)	70 (0.192)	38 (0.105)	38 (0.103)			

ARVs in alphabetical order	Daily dose	Originator companies		Generic companies																			
Etravirine (ETV)		Janssen		Aspen																			
25mg tablet	xx	(0.075)																					
100mg tablet	4	438 (0.300)		438 (0.300)																			
Lamivudine (3TC)		Viiv		Aspen	Aurobindo	Cipla	Hetero	Macleods	Microlabs	Strides	Sun Pharma												
10mg/ml oral suspension	10ml	216 (0.059)			23 (0.006)	46 (0.013)	32 (0.009)	26 (0.007)															
150mg tablet	2	75 (0.102)		55 (0.075)	27 (0.037)	28 (0.038)	29 (0.040)	23 (0.031)	23 (0.031)	27 (0.037)	26 (0.035)												
300mg tablet	1	75 (0.204)				33 (0.092)	32 (0.087)	23 (0.063)	18 (0.049)	67 (0.183)													
Lopinavir/ritonavir (LPV/r)		Abbvie		Aurobindo	Cipla	Hetero	Macleods																
		Category 1 countries	Category 2 countries																				
80/20mg/ml oral solution	4ml	150 (0.103)		296 (0.203)																			
40mg/10mg capsule heat-stable pellets	8				467 (0.160)																		
100/25mg heat-stable tablet	3	108 (0.099)		278 (0.254)	151 (0.138)	155 (0.142)		143 (0.131)															
200/50mg heat-stable tablet	4	231 (0.158)		740 (0.507)	243 (0.167)	268 (0.183)	280 (0.192)	293 (0.201)															
Nevirapine (NVP)				Aspen	Aurobindo	Cipla	Emcure	Hetero	Macleods	Microlabs	Quality Chemicals	Strides	Sun Pharma										
10mg/ml suspension	20ml					61 (0.008)	91 (0.013)																
50mg tablet for oral suspension	4					73 (0.050)	30 (0.021)																
200mg capsule	2																						
200mg tablet	2			63 (0.087)	28 (0.038)	28 (0.038)	28 (0.038)	29 (0.040)	27 (0.037)	24 (0.033)	37 (0.051)	27 (0.037)	26 (0.035)										
Raltegravir (RAL)		Merck		Hetero																			
		Category 1 countries	Category 2 countries																				
25mg chewable tablet	xx	(0.300)		Case-by-case																			
100mg chewable tablet	xx	(0.600)		Case-by-case																			
400mg tablet	2	675 (0.925)		Case-by-case	973 (1.333)																		
Ritonavir (RTV)		Abbvie																					
		Category 1 countries	Category 2 countries																				
80mg/ml oral solution	xx	(0.091)		Case-by-case																			
100mg heat-stable tablet	2	83 (0.114)		Case-by-case																			
Tenofovir (TDF)		Gilead		Aurobindo	Cipla	Hetero	Macleods	Quality Chemicals	Strides	Sun Pharma													
		Category 1 countries	Category 2 countries																				
300mg tablet	1	207 (0.567)		365 (1.000)	57 (0.155)	46 (0.127)	39 (0.107)	40 (0.110)	67 (0.183)	45 (0.123)	43 (0.117)												

ARVs in alphabetical order	Daily dose	Originator companies		Generic companies								
Zidovudine (AZT)		ViiV		Aurobindo	Cipla	Hetero	Macleods	Microlabs	Sun Pharma			
10mg/ml oral solution	24ml	450 (0.051)		73 (0.008)	110 (0.013)		91 (0.010)					
60mg tablet	4							40 (0.027)				
100mg capsule	xx	(0.093)		(0.055)								
250mg capsule	xx	(0.187)										
300mg tablet	2			69 (0.094)	67 (0.092)	75 (0.103)		63 (0.086)	50 (0.068)			
ABC/3TC		ViiV		Aurobindo	Cipla	Hetero						
60/30mg tablet	4			110 (0.075)	110 (0.075)							
600/300mg tablet	1	225 (0.617)		220 (0.602)	164 (0.450)	161 (0.442)						
TDF/FTC		Gilead		Aurobindo	Cipla	Hetero	Macleods	Strides				
		Category 1 countries	Category 2 countries									
300/200mg tablet	1	319 (0.875)	548 (1.500)	72 (0.197)	70 (0.192)	64 (0.175)	77 (0.210)	67 (0.183)				
TDF/FTC/EFV		Merck		Aspen	Aurobindo	Cipla	Hetero	Macleods	Strides	Sun Pharma		
		Category 1 countries	Category 2 countries									
300/200/600mg tablet	1	613 (1.680)	1033 (2.830)	251 (0.689)	112 (0.307)	122 (0.333)	110 (0.300)	120 (0.328)	103 (0.283)	100 (0.273)		
TDF/3TC				Aurobindo	Cipla	Hetero	Macleods	Microlabs	Quality Chemicals	Sun Pharma		
300/300mg tablet	1			57 (0.155)	58 (0.158)	46 (0.125)	50 (0.138)	47 (0.130)	84 (0.230)	52 (0.143)		
TDF/3TC/EFV				Aurobindo	Cipla	Hetero	Macleods	Quality Chemicals				
300/300/400mg tablet	1					97 (0.265)						
300/300/600mg tablet	1			110 (0.300)	110 (0.300)	106 (0.292)	106 (0.292)	161 (0.440)				
TDF/3TC + NVP (co-pack)				Hetero								
300/300 + 200mg co-pack	1 kit (3 tabs)			124 (0.340)								
AZT/3TC		ViiV		Aurobindo	Cipla	Emcure	Hetero	Macleods	Microlabs	Quality Chemicals	Strides	Sun Pharma
60/30mg tablet	4			54 (0.037)	46 (0.032)				46 (0.032)			
300/150mg tablet	2	161 (0.221)		82 (0.113)	82 (0.113)	127 (0.173)	84 (0.115)	84 (0.113)	73 (0.100)	116 (0.159)	76 (0.104)	74 (0.102)
AZT/3TC/ABC				Sun Pharma								
60/30/50mg tablet	3			420 (0.383)								
AZT/3TC/NVP				Aurobindo	Cipla	Hetero	Macleods	Quality Chemicals	Strides	Sun Pharma		
60/30/60mg tablet	4				88 (0.060)				80 (0.055)			
300/150/200mg tablet	2			97 (0.133)	96 (0.132)	95 (0.130)	102 (0.139)	126 (0.173)	94 (0.129)	96 (0.131)		
AZT/3TC + EFV (co-pack)				Aurobindo	Strides							
300/150 + 600mg tablets (co-packs)	1 kit (3 tabs)			164 (0.450)	170 (0.467)							



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GLOSSARY AND ABBREVIATIONS

3TC: Lamivudine, a nucleoside analogue reverse transcriptase inhibitor.

ABC: Abacavir, a nucleoside analogue reverse transcriptase inhibitor.

AIDS: Acquired Immune Deficiency Syndrome.

ANVISA: Brazil's national health surveillance agency, responsible for approval and oversight of pharmaceutical products, medical devices, health services, food, cosmetics, and tobacco.

ARV: Antiretroviral; medicines that treat HIV/AIDS.

ART: Antiretroviral therapy; a combination of ARVs used to treat HIV/AIDS.

ATV, ATV/r: Atazanavir, an HIV protease inhibitor; atazanavir/ritonavir, a boosted HIV protease inhibitor.

AZT: Zidovudine, a nucleoside analogue reverse transcriptase inhibitor.

BMS: Bristol Myers-Squibb.

CAEME: Association of multinational pharmaceutical companies in Argentina.

Category 1: In this document, 'Category 1' refers to the countries that are eligible to receive the deepest discount on a company's ARV price.

Category 2: In this document, 'Category 2' refers to countries that are not eligible for a company's deepest discount on ARV pricing, but are nevertheless offered a lesser discount.

DAAs: Direct-acting antivirals, oral drugs used to treat hepatitis C virus.

DRV, DRV/r: Darunavir, an HIV protease inhibitor; darunavir/ritonavir, a boosted HIV protease inhibitor.

DTG: Dolutegravir, an HIV integrase inhibitor.

DTI: Department of Trade and Industry.

EFV: Efavirenz, an HIV non-nucleoside reverse transcriptase inhibitor.

EMA: European Medicines Agency.

ETV: Etravirine, an HIV non-nucleoside reverse transcriptase inhibitor.

EU: European Union.

Evergreening: Making minor changes to medicines that are already on the market, to extend patents.

FTAs: Free trade agreements.

FTC: Emtricitabine; a nucleoside analogue reverse transcriptase inhibitor.

Generic drug: According to WHO, a generic drug is a pharmaceutical product that is usually intended to be interchangeable with the originator product.

GFATM: The Global Fund to Fight AIDS, Tuberculosis and Malaria.

GSK: GlaxoSmithKline.

HCV: Hepatitis C virus.

HIV: Human Immunodeficiency Virus.

INTERFARMA: The Pharmaceutical Research Industry Association; a multinational group of pharmaceutical companies located in Brazil.

IP: Intellectual property.

LDCs: Least-developed countries.

LPV/r: Lopinavir/ritonavir, a boosted HIV protease inhibitor.

MPP: Medicines Patent Pool.

MSF: Médecins Sans Frontières; Doctors Without Borders.

NDRA: National Drug Regulatory Authority.

PEPFAR: The President's Emergency Plan for AIDS Relief.

PI: Protease inhibitor.

PPPY: Per person, per year.

RAL: Raltegravir, an HIV integrase inhibitor.

RCEP: Regional Comprehensive Economic Partnership.

RTV or /r: Ritonavir, an HIV protease inhibitor used only at a low dose to boost levels of other HIV protease inhibitors.

SRA: Stringent regulatory authority.

TAF: Tenofovir alafenamide, a pro-drug of tenofovir.

TB: Tuberculosis.

TDF: Tenofovir; a nucleotide analogue reverse transcriptase inhibitor.

TPP: Trans-Pacific Partnership.

TRIPS: Trade-Related Aspects of Intellectual Property Rights.

UNAIDS: Joint United Nations Programme on HIV/AIDS.

UNITAID: a market-shaping institution that facilitates and accelerates availability of medicines and diagnostics for HIV/AIDS, tuberculosis, malaria and hepatitis C.

US: United States.

US FDA: United States Food and Drug Administration.

VL: Voluntary licence.

WHO: World Health Organization.

WTO: World Trade Organization.

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