ARV Market Report:

The State of the Antiretroviral Drug Market in Low- and Middle-Income Countries, 2014-2019

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KEY DEVELOPMENTS TOWARDS UNIVERSAL ACCESS

UNAIDS target of 15 million people on ART by 2015 has been achieved but work remains

With an estimated 15.4 million people living with HIV/AIDS (PLWHA) on antiretroviral therapy (ART) worldwide as of March 2015, the target of 15 million people on ART by 2015, set in the United Nations 2011 Political Declaration on HIV/AIDS, has already been achieved.[i] This achievement is significant not only because the scale of effort required, but because it is one of the first major community goals to be met. However, the global community has not rested on its laurels for long, already advancing plans on the UNAIDS/WHO fast-track 90-90-90 treatment targets, which aim for 90 percent of people infected with HIV to know their status, 90 percent of those diagnosed with HIV to receive effective treatment, and 90 percent of those treated to be virally suppressed by 2020. The targets aim to mobilize governments and partners to end the AIDS epidemic as a public health threat by 2030.

Focusing on low- and middle-income countries (LMICs), 13.5 million people in LMICs were on ART by the end of 2014.[i] ART coverage has grown from 15 percent in 2009 to 40 percent in 2014 (of all PLWHA irrespective of CD4 count).[1] Specifically, in 2014 there was a 29 percent coverage rate among infected children and 41 percent coverage rate among adults.[1] The pace of patient scale-up in 2014 – i.e. 1.8 million additional patients from 2013 – was in line with the scale-up of 2 million patients observed from 2012 to 2013. Several countries are projected to approach universal coverage beginning in 2018, including Rwanda, Uganda, and Swaziland for adults, and Vietnam for children.

WHO guideline changes likely to significantly increase overall ARV market size

The WHO announced significant changes in its upcoming guidelines at IAS 2015[ii] and early release guidelines on when to start ART and pre-exposure prophylaxis (PrEP) were issued in September 2015.[iii]

Key changes include:

- *Adoption of test and treat approaches:* All 36.9 million PLWHA will be eligible for ART, regardless of CD4 count, across all ages. Several recent studies have demonstrated the benefits of test and treat approaches. Specifically, the TEMPRANO and START studies have demonstrated the positive impact of ART initiation at CD4>500 cells/mm^3 on severe HIV morbidity and disease progression, without increase in severe adverse events. Additionally, HPTN 052 showed a reduction of HIV transmission among HIV serodiscordant couples.
- *Oral PrEP (containing tenofovir) as "additional prevention choice for people at substantial risk of HIV infection as part of combination prevention approaches":* There is compelling efficacy evidence with oral PrEP particularly amongst men who have sex with men (MSM) and serodiscordant couples. Once implemented, PrEP will drive further demand for tenofovir.
- *New treatment initiation age band for adolescents (age 10-19)*
- *Option B+ the only standard for prevention of mother-to-child transmission (PMTCT): Option B will not be included going forward.*
- *Drug specific changes: INSTIs (DTG) and dose-reduced options will be included in first and second lines of therapy.*

Whereas the test and treat recommendation is a positive development, its immediate effect on ART scale-up over and above current rates is unclear, particularly without a concomitant increase in funding. Among LMICs, Brazil has been an early adopter of the test and treat policy, announcing its plans for adoption in back in 2013. Following that announcement, Brazil saw a 27 percent increase in patients on ART in 2014, with patient coverage growing from 39 percent to 48 percent by the end of 2014.

Exhibit 1.1: YEAR-ON-YEAR (Y-o-Y) ART PATIENT GROWTH AND COVERAGE RATES IN BRAZIL FOLLOWING ADOPTION OF TEST AND TREAT IN 2013[1]

	2012	2013	2014
Y-o-Y Growth	12%	3%	27%
Coverage	39%	39%	48%

Brazil's ability to primarily procure antiretrovirals (ARVs) from domestic manufacturers is an important distinction from most other LMICs. High levels of local ARV production and buyer concentration largely with the government may allow Brazil to scale up treatment faster than other countries. So far beyond Brazil, Malawi and Rwanda have publicly announced plans to adopt a test and treat policy; both countries already have relatively high coverage rates (i.e. >50 percent) even when defined by PLWHA.

As countries continue to expand eligibility criteria and adopt the WHO test and treat updates, approximately 23 million people are conservatively projected to be on ART in LMICs by 2019, comprising 95 percent adults and 5 percent pediatric patients.[2]

Funding outlook for 90-90-90: Commodity costs could be covered with resource optimization

Global ARV spending was approximately US$1.75 billion in 2014, up 18 percent from the estimated US$1.48 billion spent in 2013. At current LMIC per person per year (pppy) ARV costs, reaching global 90-90-90 targets in LMICs will require an estimated US$3.8 billion in ARV funding in 2020.[3] CHAI estimates that the total cost of treatment at "90-90-90", including lab commodities and service delivery costs, will increase funding needs to ~US$10 billion. In order to meet these goals, CHAI anticipates that countries will increase the allocation of HIV funding that goes towards treatment, and specifically ARVs.

International funding for HIV/AIDS has stagnated in recent years and is at risk of declining in the future unless renewed global advocacy efforts are successful. However, domestic resources for HIV/AIDS in LMICs have continued to increase over time, reaching 57 percent of global funding in 2014. UNAIDS reports that between 2009 and 2014, 46 of 121 LMICs

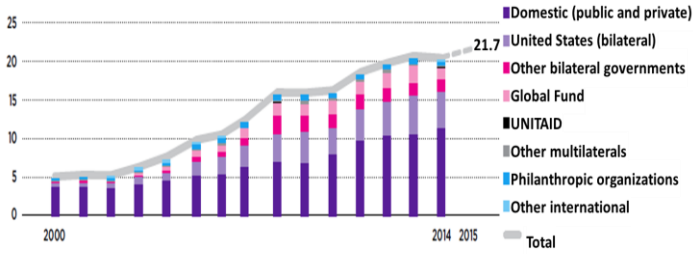
[1] *Coverage rate calculated using UNAIDS treatment and population data for adults and children living with HIV in UNAIDS AIDSInfo database. Classification of LMICs per World Bank.*

[2] *Conservative estimates were based on continued linear growth. For further detail, please see appendix D.*

[3] *Cost estimate uses average prices in CHAI procurement database for all LMIC countries except RSA for which actual procurement prices are used.*

increased domestic spending on HIV by 50 percent, with 35 countries increasing resources by more than 100 percent.[i] While this growth is promising, many countries were starting from a low base. In the face of stagnating international funding for HIV/AIDS, growth in domestic funding for ARVs will have to accelerate further. Upper middle-income countries (UMICs) will soon be expected to finance their programs almost entirely, which may prove challenging in countries where ARV prices remain high. South Africa, with the world's largest HIV burden, has been able to secure low ARV prices in recent years. Brazil and China, which make up 9 percent and 8 percent of total UMIC treatment costs respectively, benefit from strong national leadership and demonstrated commitment to scaling up care and treatment. The need for increased domestic funding will be particularly acute in countries such as Nigeria, where ability to pay is high in theory but political commitment has fallen short of expectations. Increased donor support will be especially required in low-income countries with high HIV burden such as Malawi and Uganda, where resource needs outstrip ability to pay.

EXHIBIT 1.2: GLOBAL RESOURCES FOR HIV/AIDS IN LMICS, 2000-2014 (IN US$, BILLION)[4]



Source: UNAIDS estimates June 2015, based on UNAIDS-KFF reports on financing the response to AIDS in low- and middle-income countries till 2014; OECD CRD last accessed June 2015, GARPR/UNGASS reports; FCAA Report on Philanthropic funding Dec 2014

The global funding envelope in 2015 is estimated to be US$21.7 billion. This suggests that, with the right allocation across countries and priority areas, global treatment costs at 90-90-90 could be covered using existing resources, while still leaving a significant amount of funding for prevention, program management, and other critical components of the AIDS response.

Additional money may be required for other interventions that benefit people affected by HIV and for interventions that help to address some of the fundamental social and political issues that contribute to the epidemic, such as discrimination and sexual violence. UNAIDS estimates a total price tag of US$31.9 billion for 2020, which includes some of these broader interventions.

Testing will continue to be critical to achieving universal access to effective treatment

While access to HIV testing services (HTS) has expanded exponentially over the last decade thanks to the introduction and scale-up of rapid diagnostic tests (RDTs), less than 50 percent of all PLWHA know their status. This large gap in the "First 90" target severely limits the progress that can be made in order to meet the ultimate goal of ending the HIV epidemic. The vast majority of testing in the developing world is conducted in health care facilities, which are inaccessible and inconvenient for many patients, particularly those who live in remote or rural areas. The current RDT products on the market are generally designed for facility-based testing, and have several characteristics that require tests to be conducted by trained healthcare workers in relatively well-resourced facilities. These include complicated testing procedures, specific test reading times, difficulty in collecting appropriate sample type or sample volume, or difficulty in interpreting results.

Given these challenges, a number of countries are considering renewed investment in existing testing strategies, as well as the expansion of new approaches for out-of-facility testing and community-based testing. These include door-to-door testing, mobile clinic testing, public testing campaigns in settings such as sporting events or concerts, testing in workplaces and schools, targeted testing of key geographic areas with high prevalence, and targeted testing of key populations such as MSM, commercial sex workers (CSWs), and injecting drug users (IDUs). While these approaches have shown impressive results in terms of acceptability, testing uptake, testing yield, and uptake among at-risk individuals and those with relatively high CD4 counts, they have not yet been taken to scale. Some have also reported weak evidence in linkage of people from testing into care, resulting in losses to follow up and relatively poor yield of new diagnoses. Overall, more evidence needs to be collected in order to inform on the optimal strategies to adopt to achieve the "First 90" and better delineate the extent to which the market for initial diagnosis may grow.

In addition, HIV self-testing (HIVST) is a promising new tool with the potential to expand access beyond the reach of healthcare worker-based testing, and empower clients by addressing many of the stigma concerns that prevent some people from being tested. However, HIVST is currently not widely used in most developing countries because of lack of evidence to formalize it in the current care framework. This is also due to the lack of affordable and culturally-sensitive products, the lack of clear international and national normative guidance and policies on self-testing, as well as unclear regulatory pathways for such products. Despite challenges, efforts to introduce HIVST have the potential to improve the overall percent of PLWHA who know their status and, in turn, accelerate the uptake of treatment.

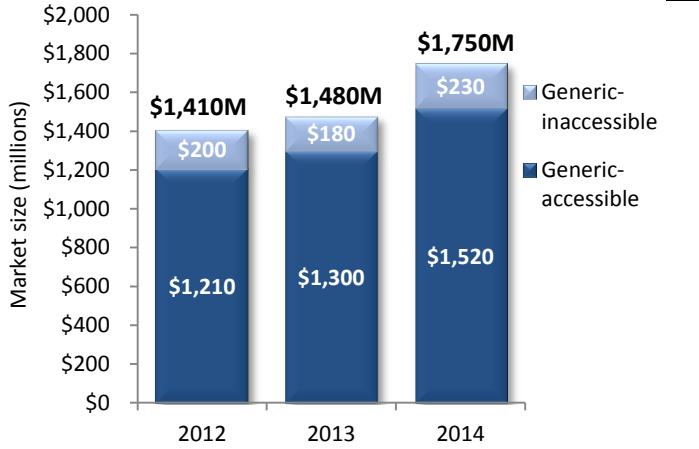
[4] *Exhibit from UNAIDS, "How AIDS changed everything, MDG 6: 15 years, 15 lessons of hope from the AIDS response".*

MARKET OVERVIEW[5]

ARV market in LMICs expanded to ~US$1.75 billion in 2014

The size of the LMIC market for ARVs expanded from US$1.48 billion in 2013 to US$1.75 billion in 2014. The 18 percent growth was driven by increased patient numbers, stabilized prices of ARVs as some well-established drugs approached the minimum prices at which they can be sustainably produced, and the transition of countries away from non-recommended and cheaper drugs like stavudine (d4T).

Exhibit 2.1: ARV MARKET SIZE (USD) IN GENERIC-ACCESSIBLE VS. GENERIC-INACCESSIBLE COUNTRIES

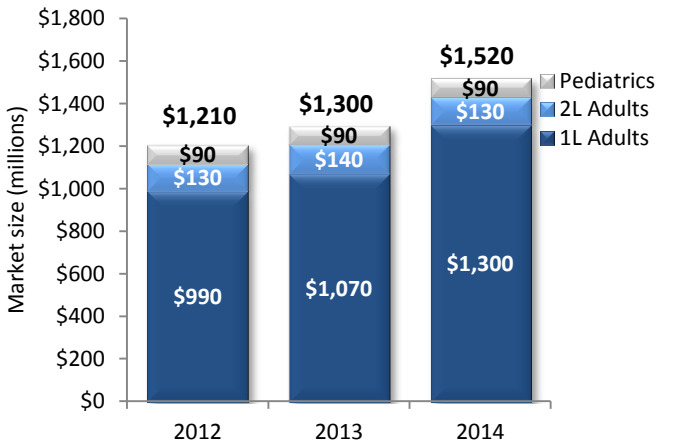


The generic-accessible (GA) ARV market, which represents 94 percent of patients in LMICs, increased from US$1.30 billion in 2013 to US$1.52 billion in 2014, a growth of 17 percent. Public data on ARV pricing in generic-inaccessible (GI) markets such as Brazil and China continues to be limited, beyond standardized cost of treatment provided in a 2013 report published by the Pan American Health Organization (PAHO).[iv] Using those figures, CHAI estimates the GI market in 2014 was US$230 million.

Within GA LMICs, 91 percent of patients on ART in 2014 were first line adults, 3 percent were second line-adults, and 6 percent were pediatric patients. Consequently, adult first-line ARVs accounted for ~86 percent of the total dollar value of the GA market, totaling US$1.3 billion. The adult first-line market value grew 21 percent from 2013, primarily due to patient scale-up, transition to more expensive regimens, and less dramatic ARV price decreases compared to the past.

As shown in Exhibit 2.2, the second-line adult and pediatric markets remained somewhat flat, due to relatively low growth in patient numbers (0.5 percent and 1.2 percent respectively), as well as moderate price decreases of ARVs over time. The potential impact of viral load testing on second-line patients is discussed in later sections. Conservatively, no major change in proportion of second-line patients is assumed for market sizing purposes. The pediatric market also experienced only moderate growth largely due to slow scale up of patients on ART, possible reasons for which will be discussed in later sections. As such, the GA market is expected to grow by over 30 percent to over US$2 billion by 2019.

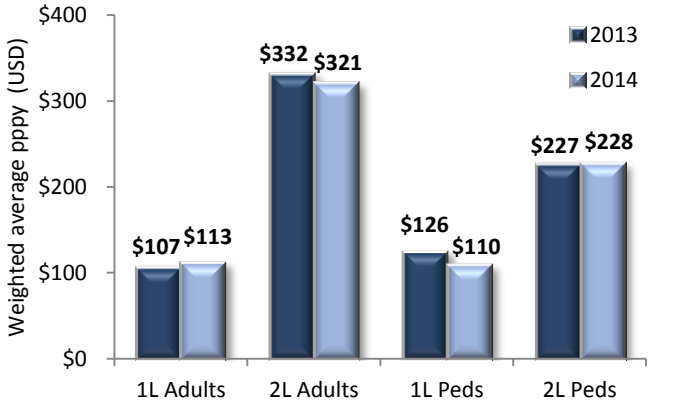
Exhibit 2.2: ARV MARKET SIZE (USD) IN GA COUNTRIES



ARV price decreases have slowed; the next major drop in treatment cost expected to be driven by pipeline products

Market prices for ARVs continued to decrease at a slower rate in 2014, particularly as some of the easier-to-tackle opportunities in terms of market inefficiencies have been addressed. The average market price in GA countries for adult first-line treatment, weighted by actual regimen and formulation use, increased slightly from US$107 pppy in 2013 to US$113 pppy in 2014. This increase is mainly driven by patients transitioning from non-optimal but cheaper d4T-based regimens to recommended but relatively more expensive tenofovir (TDF)-based regimens. In 2014, only 1 percent of first-line adult patients were on d4T-based regimens, compared to 6 percent in 2013.[v] Similarly, for NNRTIs, countries have increased utilization of WHO-recommended but higher-priced efavirenz (EFV) relative to nevirapine (NVP). Furthermore, there was increased use of the TDF triple fixed-dose combinations (FDCs), which can be somewhat more expensive than the combined cost of TDF/XTC dual plus EFV600 single.

Exhibit 2.3: WEIGHTED AVERAGE MARKET PRICE (USD) FOR REGIMENS IN GENERIC-ACCESSIBLE COUNTRIES[6]



The weighted average price for adult second-line regimens decreased slightly by 3 percent, from US$332 pppy to US$321 pppy. Notably, the average prices of both lopinavir/ritonavir (LPV/r) and atazanavir/ritonavir (ATV/r) decreased in 2014 relative to 2013 in GA countries, due to price competition between the two products driven by increased uptake of ATV/r.

[5] *Some 2013 figures in this section may not match those cited in the 2014 ARV Market Report due to a slight change in market sizing methodology.*

[6] *Pediatric pppy calculations exclude adult formulations that may be used in older children*

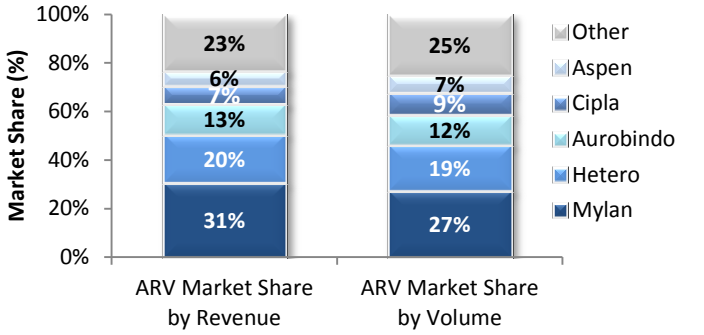
The recent South Africa tender reinforced this product competition as AbbVie offered LPV/r 200mg/50mg tablets at US$12.70 per pack[7], a price significantly lower than prevailing market prices for either LPV/r or ATV/r. For pediatric treatment, the weighted average price in 2014 was US$110 pppy for first-line which represented a 13 percent decrease from 2013, largely driven by the decreasing price of pediatric LPV/r. Pediatric second-line treatment costs remained largely steady at US$228 pppy.

Several new products are likely to be introduced in GA LMICs by 2019, resulting in a range of clinical and cost advantages to current products. Contingent on uptake, these pipeline ARVs, including tenofovir alafenamide fumarate (TAF), low dose EFV (EFV400), and dolutegravir (DTG), are expected to lower the cost of treatment significantly. On the one hand, these products will enable programs to put more patients on treatment with lower per capita spend, but at the same time their cheaper production costs will enable manufacturers to continue being profitable in a ARV market that also grows in overall value.

Indian generic manufacturers continue to dominate the ARV market

In 2014, four Indian generic manufacturers, Mylan, Hetero, Aurobindo, and Cipla supplied ~70 percent of the GA LMIC ARV market by revenue and by volume.[vi] Other Indian manufacturers accounted for a further ~6 percent of volume and revenue. Non-Indian generic manufacturers and distributors captured ~17 percent of the revenue and ~21 percent by volume, primarily driven by Aspen, leaving less than 7 percent of revenue and volume with innovators. Notably, AbbVie is among the top five innovators in terms of volume and revenue, primarily driven by South Africa's LPV/r 200mg/50mg procurements. This analysis should be interpreted with caution due to varying levels of reporting of procurement data from year to year, and because in the case of distributors most procurement data does not identify which manufacturers they ultimately source product from.

Exhibit 2.4: ARV MARKET SHARE IN GA LMICs BY TOP MANUFACTURERS[8]

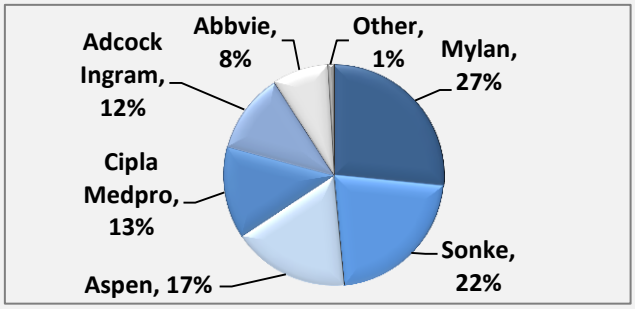


Mylan was among the top three manufacturers for each of the three most used formulations in LMICs – TDF/3TC/EFV, TDF/FTC/EFV, and AZT/3TC/NVP (all triple FDCs). For the critical TDF/3TC/EFV triple FDC Mylan and Hetero accounted for close to 75 percent market share between them. With approximately 7 million patients on either the TDF/3TC/EFV or TDF/FTC/EFV triple FDCs in GA LMICs in 2014, such high market concentration across these key products could pose potential supply security risk.

The recent South Africa and Global Fund Pooled Procurement Mechanism (PPM) tenders, which together represent over a third of all GA LMIC patients on ART, have shifted some of the dynamics in the market place since 2014.

RSA Tender (Q2 2015-Q1 2018): Volume Share by Packs

South Africa represents nearly a quarter of all patients on ART in GA LMICs and its tender awards can significantly impact generic companies. Below is an analysis of its most recent tender award.



Of note, 100% of LPV/r and 80% of TDF(300)/FTC(200) volumes were awarded to AbbVie and Mylan respectively.

Market Opportunity: Tender and Procurement Transparency

CHAI strongly believes that the ARV market would benefit from increased transparency around tendering and other procurement practices and outcomes. The table below provides validity periods of key tenders where information was public. It is hoped that more information from more tenders will be available for inclusion in next year's report.

Entity	Current Tender validity	2014 ART patients
South Africa	Q2 2015-Q1 2018	3.1 million
Global Fund (PPM)	2015-2017	>4 million[9]

[7] *From RSA tender award using exchange rate of 1 USD = 11.7 ZAR*

[8] *Analysis excludes procurements where manufacturer was not specified (~20% of overall procurement value and volume). The excluded volumes may or may not have the same supplier distribution as those included. Further, "Other" category also includes distributors who in turn procure from manufacturers that are not identified. Figures should therefore be interpreted with caution.*

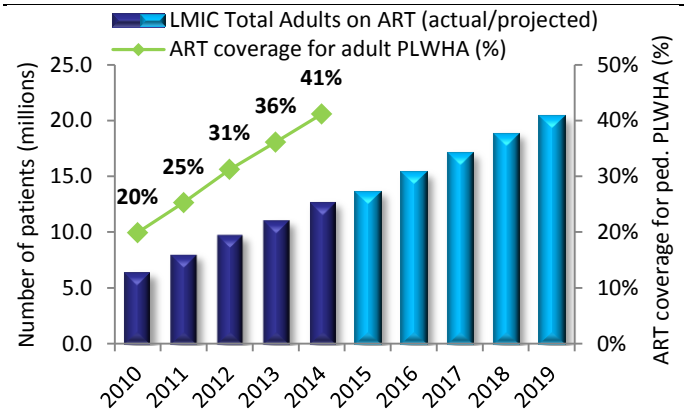
[9] *Per The Global Fund 2015 Results Report the number of people on ARV therapy in programs supported by the Global Fund has reached 8.1 million. PPM typically accounts for a little over half of all GF-funded ARV purchases*

ADULT MARKET TRENDS

Continued growth of adult patients on ART in 2014

There were 12 million adult patients on ART in GA LMICs at the end of 2014, a growth of 1.6 million patients from 2013.[vii] This incremental growth was similar to the 1.7 million patient increase seen between 2012 and 2013, and was driven, in part, by further adoption of treatment initiation at CD4 < 500 cells/mm^3, the use of Option B+ for pregnant women with HIV, and other specifications of the 2013 WHO Guidelines. As of August 2015, 15 of 22 Global Plan priority countries had adopted Option B+.[viii]

Exhibit 3.1 NUMBER OF ADULTS ON ART AND ADULT ART COVERAGE (BASED ON PLWHA) IN LMICs [10]



Treatment coverage for adults living with HIV/AIDS in LMICs increased from 36 percent at the end of 2013[ix] to 41 percent at the end of 2014.[vii] Exhibit 3.1 shows the number of adults on ART in GA LMICs through 2014, CHAI's patient projections, and the evolution of adult ART coverage in LMICs since 2009. CHAI's patient projections are relatively conservative, particularly compared to ambitious targets like the UNAIDS Fast-Track Targets.[x]

EFV400 and DTG expected to significantly impact current adult first-line NNRTI market

Concomitant with continued growth of TDF use among first-line adult patients, EFV use also increased, making up 69 percent of all first-line GA adult patients, or 8 million patients, by the end of 2014. As has been the case since EFV became the preferred NNRTI per the 2013 WHO Guidelines, the share of NVP is expected to continue to decrease, with only 7 percent market share projected in 2019.

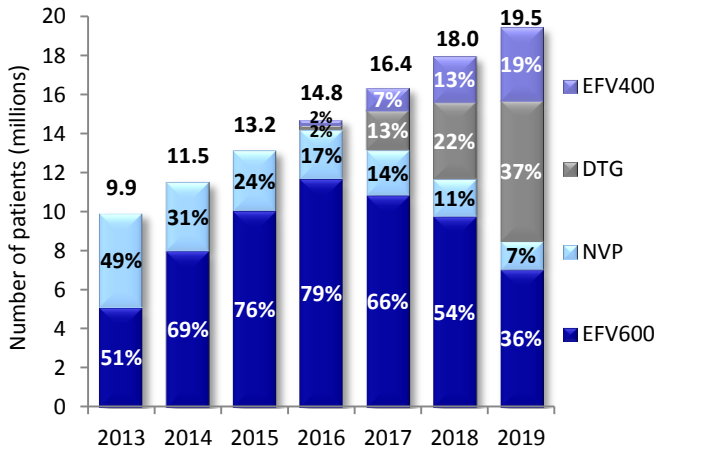
Lower-dose EFV will play an important role in adult first-line therapy. ENCORE1, a Phase III clinical study, showed that EFV 400mg was non-inferior to EFV 600mg, and suggested that adverse events and discontinuations would be reduced. The 96 week continuation of the ENCORE1 trial confirmed EFV400's non-inferiority to EFV600, when used in combination with TDF and FTC.[xi] Pharmacokinetic (PK) studies in pregnant women and TB co-infected patients are being planned; if the results show an insignificant change in EFV levels in these patients, the WHO should be able to suggest inclusion in guidelines without restrictions.

Several generic companies have initiated development of a fixed dose TDF/3TC/EFV400 and availability is expected in mid- to late-2016.

Dolutegravir (DTG) is an integrase inhibitor (INSTI) that was approved by the US FDA in 2013. It has shown non-inferiority or superiority, and better tolerability than EFV and PIs.[xii] DTG could be used in both first- and second-line therapy for LMICs. In May 2015, Aurobindo submitted an Abbreviated New Drug Application (ANDA) to the US FDA for DTG 50 mg.[xiii] Currently, DTG is only available through ViiV as a single tablet or as a FDC with ABC and 3TC.

WHO has indicated that both EFV400 and DTG may have a place in the upcoming 2015 guidelines. With projected generic availability of triple FDCs in 2017, EFV400 and DTG are expected to significantly impact the first-line adult NNTRI market by 2019. As shown in Exhibit 3.2, by 2019 DTG is projected to capture 37 percent, and EFV400 19 percent of the adult first-line NNRTI/INSTI market, or 7.2 million and 3.8 million patients, respectively. Generic DTG singles are expected to be available in mid-2016. Dependent on price competitiveness with EFV600 singles, DTG singles may have uptake in 2016 in first-line among patients who already take two pills a day (primarily those on AZT/3TC + EFV or TDF/3TC + NVP). CHAI estimates that there were ~2 million such patients in GA LMICs at the end of 2014.

Exhibit 3.2 PATIENT GROWTH AND SHARE OF FIRST-LINE NNRTI/INSTI MARKET IN GA LMICs [11]



Significant changes to first-line adult NRTI landscape expected over next 5 years

In 2014, TDF comprised 72 percent of the first-line NRTI market in GA LMICs, increasing from 56 percent at the end of 2013. By the end of 2014, all 21 high ART patient volume countries in CHAI's forecast (representing 85 percent of all LMIC ART patients) had adopted TDF as the preferred NRTI for first-line adults. In total, 8.3 million first-line adult patients were on TDF-based regimens at the end of 2014. With increasing use of TDF in first-line, AZT continues to decline.

Tenofovir alafenamide fumarate (TAF), a potential alternative to TDF, is a tenofovir prodrug that offers high antiviral efficacy and an improved renal and bone safety profile at much lower doses than TDF.[xiv] As of October 2015, Gilead had filed three New Drug Applications (NDAs) with the US

[10] *ART coverage for adults calculated based on data available in UNAIDS AIDSinfo database as of August, 2015 (only includes countries with both ART and PLWHA numbers reported)*

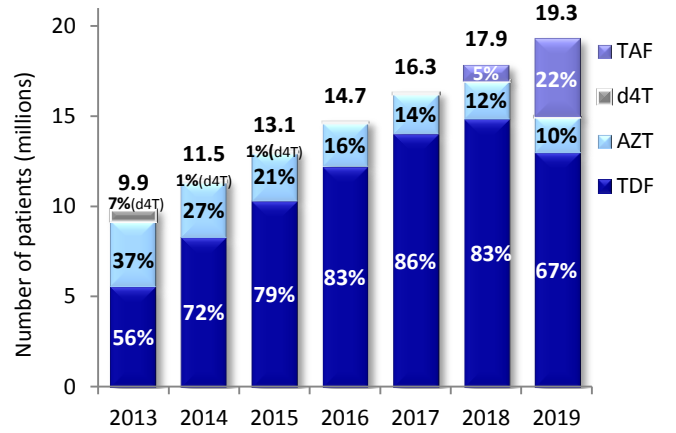
[11] *Shares may not sum exactly to 100 percent due to rounding*

FDA for FDCs containing TAF.[xv] The US FDA approved the "Quad" in November 2015, and set a target action date for TAF/FTC in April 2016.[12]

The first generically available TAF FDC is expected to launch as early as mid-2018. Assuming certain API production steps can be optimized by generic companies, it is expected that TAF will be significantly less expensive than TDF since the required dose is about 10-fold lower.

There will likely be some uptake in the latter half of 2018, and during its first full year of availability in 2019, TAF is projected to garner up to 22 percent of the first-line NRTI market in GA LMICs, or 4.3 million patients. TDF is expected to remain the dominant drug that year, maintaining 67 percent of the first-line market, or 13 million patients. However, in subsequent years, TDF is expected to be almost completely replaced by TAF due to its price and clinical advantages

Exhibit 3.3 PATIENT GROWTH AND SHARE OF FIRST-LINE NRTI MARKET IN GA LMICs[13]



Use of FTC limited outside South Africa

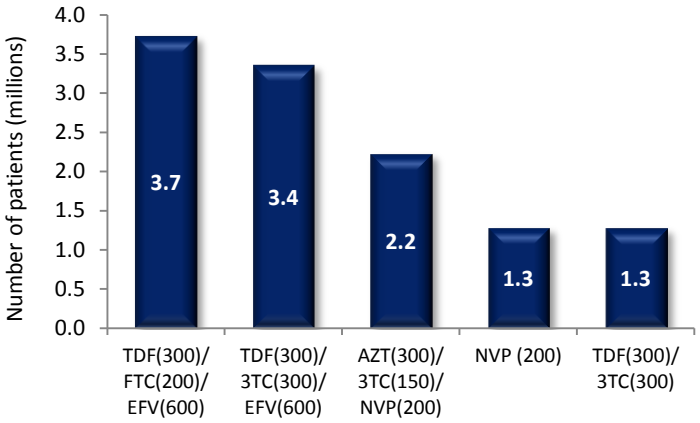
Use of FTC continues to be limited outside of South Africa. Although both 3TC and FTC were advertised In South Africa's current tender valid through March 2018, FTC was favored for the lucrative first-line TDF/XTC/EFV segment.[xvi] South Africa represented over two thirds of all GA LMIC adult patients on FTC at the end of 2014, with Zambia being the next largest market. However, with Zambia recently transitioning to 3TC, patients on FTC outside of South Africa are projected to represent less than 6 percent of all GA LMIC adults by the end of 2019. Although FTC production costs have hitherto been higher than for 3TC, it may be possible to reach price parity for FDCs containing 3TC and FTC at large volumes and with process improvements to the FTC API production process.

It is also important to note that all of Gilead's filings with the US FDA are for TAF FDCs rather than the single, and they all include FTC and not 3TC.[xvii] Whether or not TAF/3TC formulations are developed and approved, will significantly impact FTC usage after 2019, when TAF is expected to be generically available and used widely.

Use of triple FDCs in first-line continues to grow

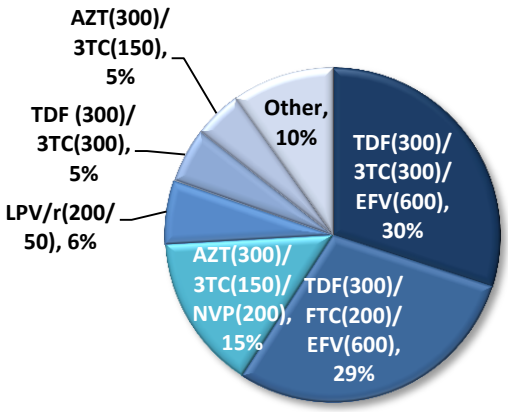
In 2014, the top five adult formulations by volume were the TDF/FTC/EFV triple FDC, the TDF/3TC/EFV triple FDC, the AZT/3TC/NVP triple FDC, the NVP(200) single, and the TDF/3TC dual FDC. Approximately 77 percent of all adults in GA LMICs were on at least one of these formulations at the end of 2014.

Exhibit 3.4 TOP FIVE ADULT FORMULATIONS BY PATIENT VOLUME IN GA LMICs, 2014



As shown in Exhibit 3.5, the TDF/3TC/EFV and TDF/FTC/EFV triple FDCs represented the largest share of the market by revenue, each representing ~30 percent. TDF/FTC/EFV use is largely driven by South Africa, which makes up 67 percent of patients on the regimen (similar to the use of FTC overall). The NVP 200mg single appears in the top five formulations by volume but not by revenue due to the fact that, as a single, is it less expensive than the FDCs. The LPV/r dual FDC, conversely, does not appear in the top five formulations by volume but does comprise 6 percent of the market by revenue due to its relatively high price of US$252 pppy (GA LMIC weighted average).

Exhibit 3.5 TOP ADULT FORMULATIONS BY REVENUE IN GA LMICs, 2014



TDF+3TC+EFV, TDF+FTC+EFV, and AZT+3TC+NVP are the three main adult regimens where a triple FDC is available for use in GA LMICs. In countries where CHAI has access to aggregate patient data at the formulation level, nearly 100 percent of patients on these regimens are on the triple FDC rather than dual + single or singles. Although the data is not inclusive of all usage in LMICs, this trend suggests continued country prioritization to reduce pill burden for patients.

[12] *The TAF "Quad" is an FDC of elvitegravir, cobicistat, FTC, and TAF (E/C/F/TAF)*

[13] *Shares may not sum exactly to 100 percent due to rounding*

ATV/r expected to continue growing vs. LPV/r; strong potential of DRV/r dependent on price

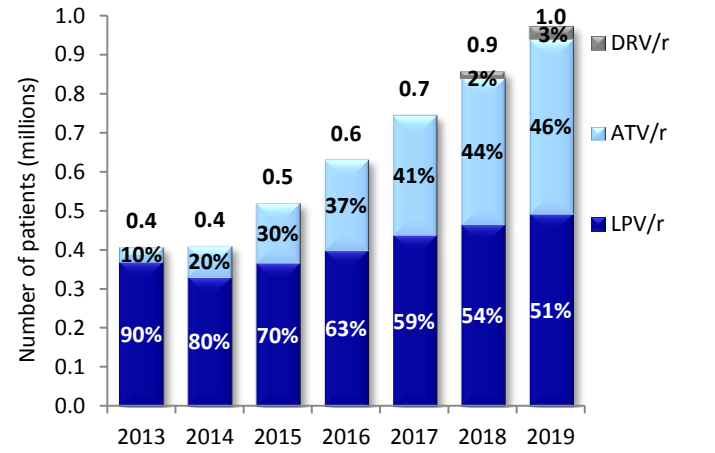
Although ATV/r has benefits over LPV/r on several fronts such as tolerability, pill burden, and (in most geographies) price, many countries continue to maintain LPV/r as the preferred PI for second-line patients. AbbVie offered a per pack price of US$12.70 in South Africa's recent tender which is significantly lower than average market prices,[xviii] and drove, in part, the decision to continue use of LPV/r as the preferred PI for second-line adult patients in this major market. It is worth noting that South Africa experienced recent struggles in mid-2015 in obtaining the necessary stock volumes for LPV/r, offering yet another cautionary tale to procurers who do not split tenders for key products, and instead rely on one manufacturer in favor of aggressive pricing. The ATV/r market also did encounter some supply constraints in 2014, which have since been resolved. The issues appeared to be largely due to mismatched timing of order placement and manufacturing plans. It will be important for procurers to share updated forecasts and order on a timely and regular basis to ensure manufacturer confidence in demand going forward, and in turn for manufacturers to be transparent about manufacturing capacity to give confidence to procurers about order fulfilment and lead times.

Despite the aforementioned challenges, ATV/r use for second-line patients has continued to grow, with 20 percent of adult second-line patients on the drug at the end of 2014. This represents a doubling of market share in just one year, which may have been unexpected by suppliers and contributed to the supply challenges. Côte d'Ivoire, India, Tanzania, and Uganda had the largest growth in total ATV/r patients between the end of 2013 and the end of 2014 (all >50 percent growth). Countries with the highest individual market shares for ATV/r were India, Malawi, Rwanda, and Zimbabwe, all at more than 80 percent of their second-line adult patients on ARV/r at the end of 2014. Additionally, Kenya started procuring ATV/r in 2014 and is projected to have substantial ATV/r uptake especially amongst newly initiated second-line patients. Globally ATV/r is expected to continue to capture market share, reaching 46 percent market share by 2019, though this may increase even further should South Africa adopt ATV/r through its next tender or even earlier because of emerging LPV/r supply constraints.

Darunavir (DRV) is a PI that can be used in place of LPV or ATV. The combination of darunavir and ritonavir (DRV/r) was recommended in the 2013 WHO guidelines as an alternative second-line regimen, but it is currently not available as a heat-stable FDC. In terms of safety and efficacy, DRV/r has shown superiority or non-inferiority over other PIs in multiple clinical trials and has a favorable resistance profile.[xix]

Contingent on availability of an FDC at a competitive price, DRV/r has the potential to play an important role in second-line treatment. In particular, it could serve as a long-needed alternative to LPV/r for TB co-infected patients taking rifampicin (for whom ATV/r is contraindicated). A generic FDC of DRV/r is expected to be available in LMICs sometime in 2017 as a 400/50mg formulation (two pills for once daily dosing of 800/100mg), and DRV/r may be promoted from being a mere footnote mention in the 2015 WHO guidelines. CHAI is working with several partners to address the current high price of DRV/r relative to LPV/r from multiple angles. Pending further pricing clarity, CHAI is using conservative projections for DRV/r uptake as shown in Exhibit 3.6.

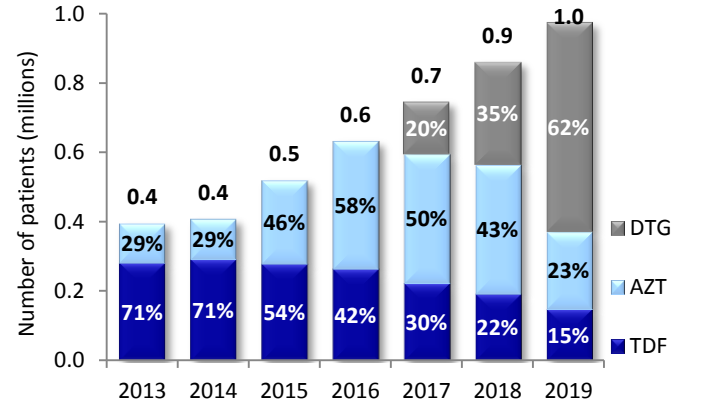
Exhibit 3.6 PATIENT GROWTH AND SHARE OF SECOND-LINE PI MARKET IN GA LMICs[14]



Introduction of DTG expected to significantly impact second-line adult market

In 2014, TDF comprised 71 percent of the second-line NRTI market, remaining unchanged from the end of 2013. As tenofovir-based backbones become predominant in first-line, the TDF share of second-line adult treatment is expected to decline in future years, with AZT's second-line share conversely increasing. This inversion of market shares is unlikely to happen concurrently given that patients may be on first-line treatment for several years before being switched to second-line, so TDF share may appear to be high across both lines for a few years yet.

Exhibit 3.7 PATIENT GROWTH AND SHARE OF SECOND-LINE NRTI/INSTI MARKET IN GA LMICs[14]



In addition to use in first-line, DTG is likely to also significantly impact the second-line adult market, replacing both the AZT+3TC and TDF+XTC backbones. Use of DTG in first-line (in place of NNRTIs) may not preclude use in second-line (in place of NRTI backbones), though more data is required to be sure. By 2019, DTG is expected to garner 62 percent of the second-line adult NRTI/INSTI market, totaling 600,000 patients. Exhibit 3.7 shows the evolution of that market through 2019.

[14] *Shares may not sum exactly to 100 percent due to rounding*

Viral load implementation may increase second-line patients; more data is needed

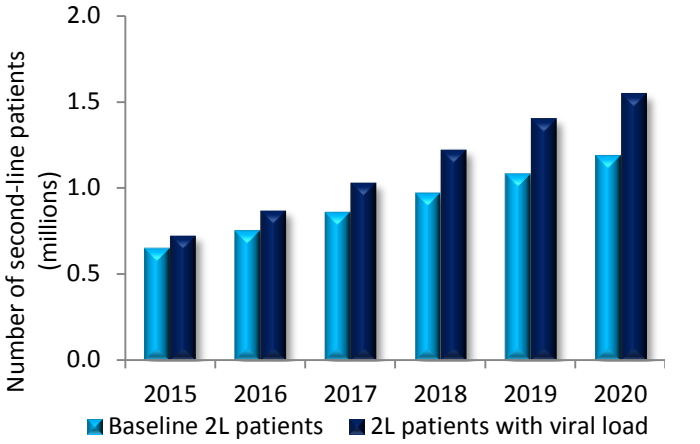
In the 2013 guidelines, the WHO made a strong recommendation in favor of using routine viral load testing to monitor the effectiveness of ART treatment in patients.[xx] Viral load testing measures the quantity of virus in a patient's blood, the results of which can be used by clinicians to evaluate the effectiveness of treatment in conjunction with the patient's adherence. In September 2014, Roche, South Africa, The Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund), PEPFAR, and CHAI announced a $9.40 Global Access Price for viral load reagents and proprietary consumables, which supported efforts to accelerate scale-up.[xxi] In mid-2015, the Global Fund published the results of its viral load tender, which quoted pricing from diverse suppliers such as Abbott, BioMérieux, Cepheid, Hologic, Roche, and Qiagen, yielding further price reductions and transparency around scale-up costs that can be accessed by countries.

Several countries in sub-Saharan Africa, including Botswana, Kenya, Namibia, Rwanda, and South Africa, already have public sector viral load programs with high patient coverage. More recently, Malawi and Uganda have begun scaling up national viral load testing programs. A number of others, including Ethiopia, Swaziland, and Zimbabwe, have begun pilot programs or are in the process of approving national guidelines and developing a scale-up plan. Outside of sub-Saharan Africa, India is expected to launch a major tender to support national scale-up in the next year, and Brazil already has a well-established viral load testing program.

Routine viral load monitoring should provide a means of detecting cases of treatment failure earlier and more accurately than clinical or immunological monitoring alone,[xxii] while providing opportunities to strengthen adherence to first-line regimens. Still, there are very few studies on the impact of viral load testing on the number of patients on second-line ART, particularly at a national program level. Countries such as Kenya have seen higher year-over-year increases in the relative proportion of patients on second-line since 2011, but there remain further opportunities to generate evidence to say with certainty what degree this has been impacted by the availability of viral load testing.

While studies from a number of groups suggest that most patients can achieve viral suppression with adherence counseling,[xxiii] viral loads may not be driven to suppression at the expected success rates early in program scale-up, given the variability in the availability and quality of adherence support interventions and percent of results delivered to patients. Consequently, the percent of patients that achieve suppression in a national program may be significantly lower than current studies anticipate, particularly in the initial years of implementation. Over time, however, the implementation of viral load testing should yield a net increase in the number of patients on second-line. Based on the limited data that does exist, Exhibit 3.8 shows a potential scenario where the appropriate use of viral load testing increases the proportion of patients on second-line.

Exhibit 3.8 POTENTIAL IMPACT ON SECOND-LINE BASED ON VIRAL LOAD IMPLEMENTATION IN GA LMICs[15]



The scenario in Exhibit 3.8 yields a net increase of 1.5 million patients on second-line through 2020, demonstrating the relatively modest impact of viral load testing on the uptake of second-line regimens in the near-term. Given the relative paucity of data that exists at a national program level, among other issues such as the availability and decentralization of second-line regimens and pattern of clinical decisions, the observed change in the number of patients on second line due to viral load scale-up will need to be continue to be monitored against expectations.

[15] *This analysis considers the potential implications of viral load scale-up on the number of patients on second-line. Projections account for anticipated viral load testing access within 21 high-ART patient burden countries and other LMICs, further reduced by the percent of patients expected to receive results and be switched to a new drug regimen. The percent of results returned and clinical decisions made is based on research from the implementation of conventional EID testing in Mozambique and Malawi. Projected viral load testing volumes from the CHAI viral load forecast.*

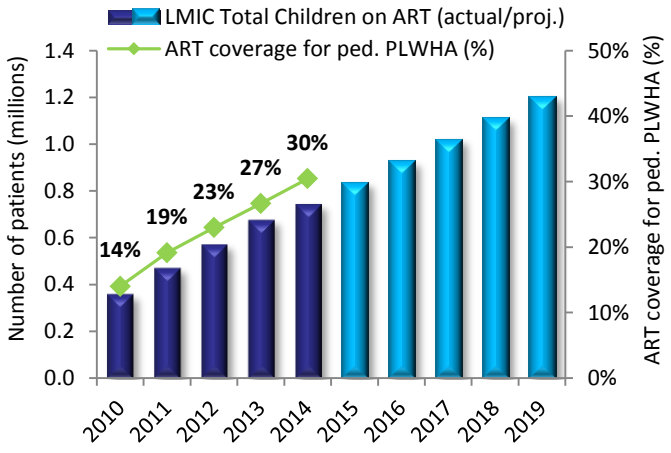
PEDIATRIC MARKET TRENDS

Small increase in pediatric patients on ART in 2014 compared to previous years

UNAIDS reported 823,000 children globally on ART at the end of 2014, up from 750,000 in 2013.[i] These 73,000 additional children on treatment represent a 10 percent annual growth, which is less than observed in previous years. In contrast, 2013 saw an incremental gain of 115,000 patients on treatment compared to 2012. This trend appears despite the 2013 WHO guidelines recommending universal coverage for children under the age of 5. Most of the countries represented in CHAI's forecast have already adopted this guideline, but the actual impact on patient scale-up appears to be minimal. This slowdown in patient growth can partially be attributed to decreasing rates of new infections in children due to successful PMTCT efforts, "ageing out" of older children to the adult population, and the continued high barrier of identifying children outside of PMTCT programs. Consequently, pediatric coverage rates remain low especially compared to adults. Globally, the 2014 ART coverage rate for children was only 32% (30% in LMICs).[vii]

As shown in Exhibit 4.1, CHAI conservatively expects 1.2 million pediatric patients on treatment in all LMIC by 2019, although this may be further increased by potential market-shaping events such as the Accelerating Children's HIV/AIDS Treatment (ACT) initiative and the recommendation of test and treat in the 2015 WHO guidelines. ACT is a partnership between PEPFAR and Children's Investment Fund Foundation (CIFF), which aims to double the total number of children receiving ART across 10 priority African countries over the next two years. It is expected to provide US$200 million in additional funding and enable 300,000 more children living with HIV to receive treatment. The first commodity orders through this program are expected in late 2015 for delivery in 2016.

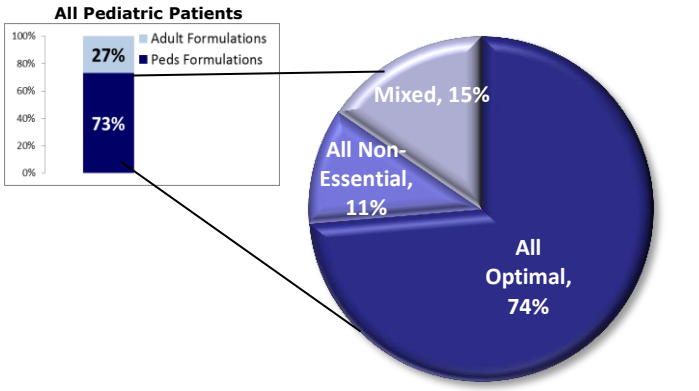
EXHIBIT 4.1: NUMBER OF PEDIATRIC PATIENTS ON ART IN LMICs, ACTUALS AND CHAI PROJECTIONS[16]



Updated 2015 IATT formulary published

The Interagency Task Team on Prevention and Treatment of HIV Infection in Pregnant Women, Mothers and their Children (IATT) developed a list of preferred pediatric formulations in an effort to improve pediatric ARV supply security by consolidating the market around a limited number of key products that offer the highest standard of care for children of all weight bands and ages on first- and second-line treatment. A revised list was released in 2015 with several key changes. d4T dual and triple formulations are now considered non-essential, along with the ABC/3TC/AZT triple FDC. Two pediatric TDF formulations (TDF 40mg scoop and TDF 150mg) were moved from limited-use to non-essential, leaving only one pediatric TDF formulation (TDF 200mg) on the limited-use list. The new ABC/3TC 120/60mg dual FDC formulation was added to the optimal list.

EXHIBIT 4.2: FORMULATION BREAKDOWN OF PEDIATRIC REGIMENS IN GA LMICs BY IATT STANCE, 2014



Using the IATT classifications, CHAI estimated the proportion of pediatric patients who are on regimens comprised of all optimal or other formulations. The analysis only includes children who are on IATT-reviewed formulations and is shown in Exhibit 4.2. In 2014, 74 percent of included children were on all optimal formulations (83 percent outside of South Africa). These figures are encouragingly high, and although similar to 2013, it would be expected that a small proportion of patients would continue to (appropriately) use non-optimal formulations.

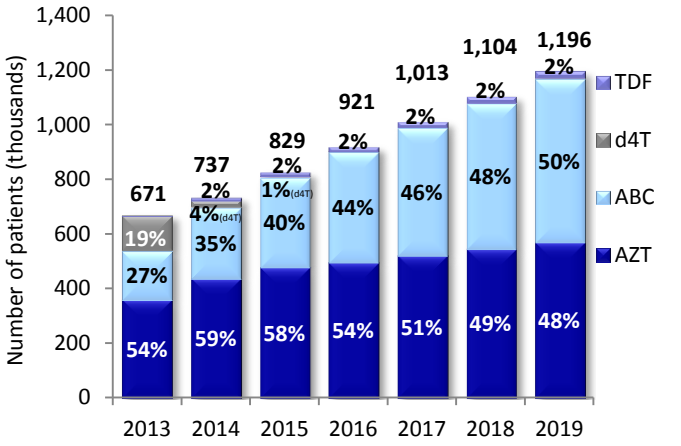
AZT and ABC will continue to dominate the pediatric NRTI market

AZT and ABC remain the most common NRTIs for pediatric patients, especially since d4T has largely been phased out. In 2014, there were only 4 percent of pediatric patients on d4T regimens in GA LMICs compared to 19 percent in 2013, and d4t use is expected to be completely discontinued by 2016.

CHAI estimates that 59 percent of pediatric patients were on AZT in 2014, up from 54 percent in 2013. Most of the increase was driven by patients who have been switched from d4T regimens. Many GA countries have continued to keep AZT as their preferred first-line pediatric NRTI, most likely due to availability of an AZT/3TC/NVP triple FDC dispersible tablet as well as a lower price compared to ABC. These countries include Malawi, Mozambique, and Nigeria, where AZT+3TC+NVP remains recommended in national treatment guidelines as the preferred first-line regimen for children 10 and under.

[16] *ART coverage calculated based on UNAIDS AIDSinfo database as of August, 2015 (only includes countries with both ART and PLWHA numbers reported)*

Exhibit 4.3: PEDIATRIC NRTI MARKET IN GA LMICs[17]



ABC had an estimated NRTI market share of 35 percent in 2014, up from 27 percent in 2013. By 2019, ABC share is expected to increase to 50 percent of patients. This increase is driven by several high-volume countries such as India and Swaziland having adopted ABC in their national guidelines in 2014, along with others who are continuing the transition made in earlier years. In particular, Kenya, Rwanda, South Africa, Uganda, and Zambia are all expected to have over 60 percent of pediatric patients on ABC regimens by 2019.

New pediatric ARV formulations available

***LPV/r oral pellets**: Cipla received tentative US FDA approval in mid-2015 for this long-awaited alternative to LPV/r syrup which has had limited adoption despite of the WHO recommendations primarily due to cold chain challenges. Although the approval is for use in children > 5 kg, the safety of dosing in infants 3-4.9 kg has been demonstrated in a small number of infants in the CHAPAS-2 trial. Production is expected to start in late 2015 and availability may accelerate adoption of LPV/r.*

***ABC/3TC formulations**: Mylan received tentative US FDA approval in late 2014 for ABC/3TC 60/30mg and ABC/3TC 120/60 mg dual FDCs, both of which are dispersible and scored. Both are important as they provide additional available supply for the preferred first-line regimen for patients ≤10 years of age and assure better treatment options for children. The ABC/3TC 120/60mg dual will also reduce pill burden in children down to 3 kg, and is a direct result of an innovative public-private partnership between ViiV, Mylan, and CHAI (supported by DFID).*

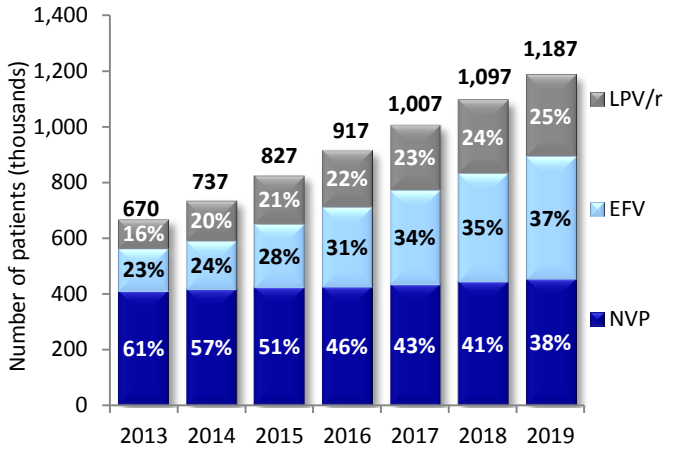
TDF use amongst children remains minimal, with most countries opting to recommend use only in those aged 10 and above and weighing over 35 kg. Zambia is one exception, where TDF was adopted as the recommended regimen for children age 5 and above. Zambia also began procurement of pediatric TDF singles from Gilead in late 2015. Pediatric formulations of TDF are still only available from the innovator and FDCs are yet to be developed.

[17] *Shares may not sum exactly to 100 percent due to rounding*

Pediatric market shares of EFV and LPV/r expected to increase in the next five years; NVP likely to remain dominant

Although no longer recommended by the WHO as part of a preferred regimen, NVP use remains high due to the availability of the AZT/3TC/NVP triple dispersible FDC which provides significant advantages in terms of price and adherence. Fifty-seven percent of patients were on NVP based regimens in 2014, compared to 24 percent on EFV and 20 percent on LPV/r. NVP use is decreasing however, and by 2019, CHAI expects 38 percent of patients on NVP, 37 percent on EFV, and 25 percent on LPV/r. LPV/r uptake for children has been limited because cold-chain capacity is required for storage and transport of the syrup. Several high volume countries are ramping up LPV/r use, including South Africa, Swaziland, and Zambia, which are all projected to have over 30 percent of patients on LPV/r by 2019.

EXHIBIT 4.4: PEDIATRIC NNRTI/PI MARKET IN GA LMICs[18]



Improving access to EID testing and strengthening linkage to care will greatly aid pediatric scale-up

Despite a substantial increase in access to Early Infant Diagnosis (EID) testing in recent years, it is estimated that only 45 percent of the tests needed for HIV-exposed infants born in developing countries were met in 2014.[19] Even for those infants who receive EID testing, turnaround time for results can take up to several months. During this time, only 22-38 percent of HIV-positive infants are initiated on treatment.[xxiv] Evidence suggests that in some settings, loss-to-follow up of infants can be as high as 33.9 percent at 3 months and 78 percent by the first year in a population whose mortality for in-utero infections peaks at 2-3 months of age.[xxv]

Countries and partners are considering a number of strategies to improve access to EID, including deploying new testing technologies and expanding testing algorithms. The WHO currently recommends an EID test for all HIV-exposed infants at 4-6 weeks, and subsequently at 9-18 months to identify transmission during breastfeeding.[xxvi] However, growing evidence that suggests many infants who are infected in utero or intra-partum do not get diagnosed at the recommended 4-6 weeks and the early peak in mortality at 2-3 months of age has led to increased interest in EID at birth.[xxvii] If this change were incorporated into testing algorithms as expected beginning in

[18] *Shares may not sum exactly to 100 percent due to rounding*

[19] *Need is estimated based on number of patients enrolled in HIV care and treatment, and assuming national guidelines for both pre-ART staging and ART monitoring*

2016, the EID market size could increase significantly to account for one additional test per HIV-exposed infant.

In addition, it is expected that the WHO will make a recommendation around the use of point-of-care (POC) EID testing in the upcoming 2015 ART Guidelines, which will fuel the demand for POC EID technologies to further decentralize EID testing, and to accelerate ART initiation for infected infants. Initiatives by partners such as the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF), PEPFAR, and CIFF are likely to support efforts to strengthen sample transportation, improve results delivery, and decentralize access to testing through the deployment of POC technologies. It is estimated that between 2014 and 2019, the number of HIV-exposed infants will stay relatively constant, but due to the potential expansion of EID testing at birth beginning in 2016 to improve case finding in infants, total EID testing can be expected to increase to 1.7 million tests by 2019, potentially driving a modest uptake in pediatric ART patients.

The PAPWG continues to improve pediatric ARV market dynamics

In 2015, the Pediatric ARV Procurement Working Group (PAPWG) continued to engage with manufacturers of pediatric ARVs and global partners, including the Child Survival Working Group of the IATT with closer collaboration on optimal formularies and drug optimization. This group plays a key role in directing approximately 65 percent of the pediatric ARV volumes. For more information about the group or its members interested parties are encouraged to visit the PAPWG web page[xxviii] which includes current and future activities.

Appendix A: Projected API demand in GA LMICs

The graphs below show the estimated generic-accessible patient demand and API volume forecast for key adult ARVs. Patient years represent the effective number of patients on treatment for a full year and used to calculate yearly API demand. Patient years calculated by assuming newly-initiated patients are on treatment for 6 months on average in the year of initiation; 15 percent attrition rate assumed to estimate yearly new initiations. Note that all figures are based on demand for adults only.

Exhibit A.1: TDF

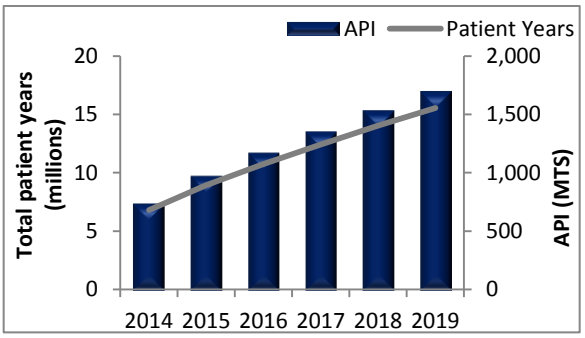


Exhibit A.2: AZT

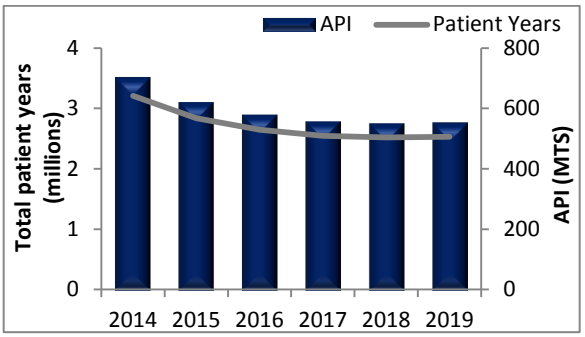


Exhibit A.3: 3TC

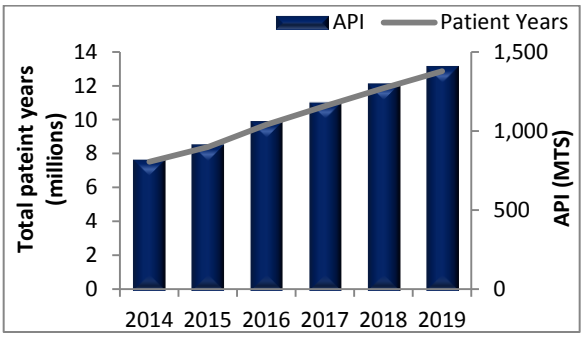


Exhibit A.4: EFV

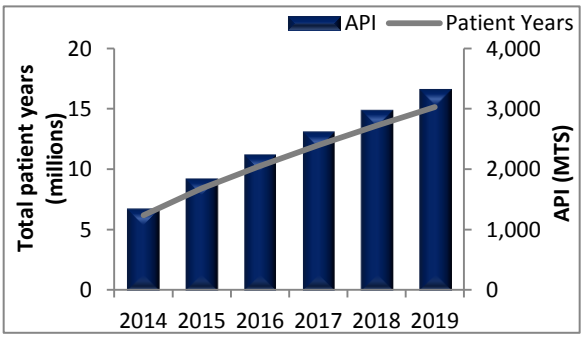


Exhibit A.5: NVP

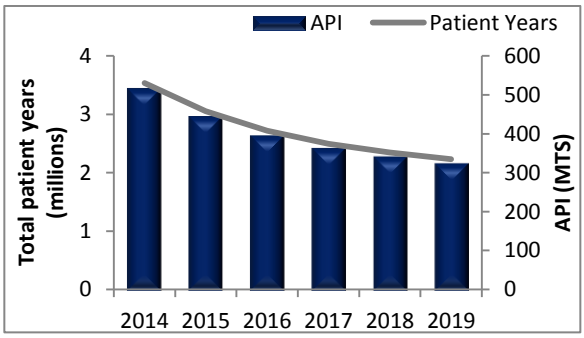


Exhibit A.6: LPV

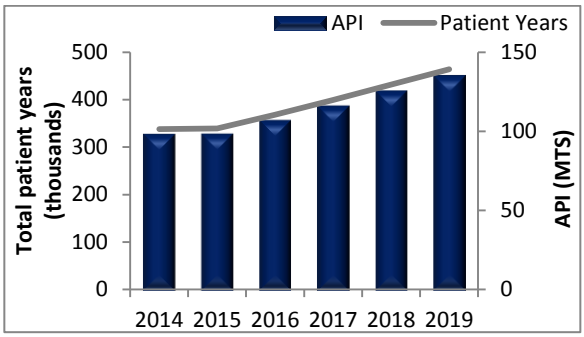


Exhibit A.7: ATV

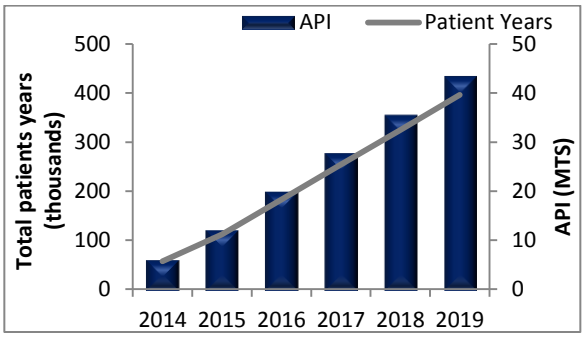
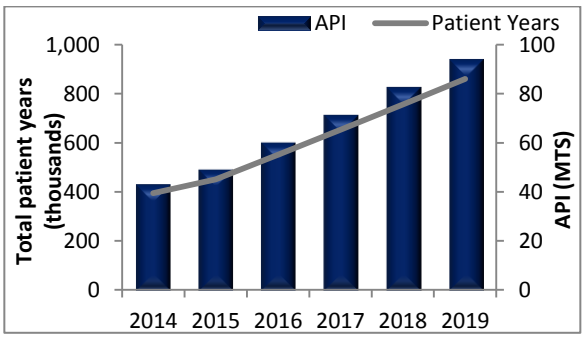


Exhibit A.8: RTV



Appendix B: Reference Price List

The reference price list below provides per pack or bottle prices for key adult and pediatric ARVs included in CHAI's most recent Reference Price List. Prices are EXW unless otherwise noted.

Product	Packaging	CHAI Reference Price, 2015 (USD)	SCMS E-Catalog Price (USD)[xxix]	MSF, July 2014 (USD)[xxx]	2014-2015 GPRM Weighted Average Price (USD)[xxxi]	2015-2018 RSA Tender Weighted Average Price (USD)[xxxii]	GF Pricing, October 2015 (USD)[xxxiii]	Kenya Tender Prices, awarded 2014 (USD)[xxxiv]
Adult Products								
3TC(150)	HDPE bottle 60 tablets[1]	$2.40	$2.25	$1.98	$2.05	$1.66	$2.25	$2.12
ABC(300)	HDPE bottle 60 tablets[1]	$11.50	$11.21	n/a	$12.99	$10.20	$11.70	$11.14
AZT(300)	HDPE bottle 60 tablets[1]	$6.25	$5.33	$5.64	$5.74	$5.63	$5.60	n/a
AZT(300) + 3TC(150)	HDPE bottle 60 tablets[1]	$6.60	$6.52	$6.48	$6.65	$7.04	$6.54	$6.65
AZT(300) + 3TC(150) + NVP(200)	HDPE bottle 60 tablets	$8.20	$8.11	$8.22	$8.32	n/a	$8.30	$8.24
EFV(600)	HDPE bottle 30 tablets[2]	$3.80	$3.19	$3.09	$3.33	$3.37	$3.20	$3.25
LPV/r(200/50)	HDPE bottle 120 tablets[3]	$21.00	$19.36	$20.04	$22.63	$12.70	$18.41	$18.73
NVP(200)	HDPE bottle 60 tablets[1]	$2.50	$2.17	$2.16	$2.22	$2.35	$2.20	$2.21
RTV(100) heat-stable	HDPE bottle 30 tablets	$7.50	n/a	$7.29	$7.28	n/a	$7.30	n/a
TDF(300)	HDPE bottle 30 tablets[2]	$4.00	$3.77	$2.13	$4.36	$2.45	$3.60	n/a
TDF(300) + 3TC(300)	HDPE bottle 30 tablets	$4.75	$4.32	$4.65	$4.78	n/a	$4.62	$4.49
TDF(300) + FTC(200)	HDPE bottle 30 tablets[2]	$5.60	$5.74	$5.79	$6.93	$5.32	$5.37	n/a
TDF(300) + 3TC(300) + EFV(600)	HDPE bottle 30 tablets	$9.00*	$9.10	$11.16	$10.48	n/a	$8.99	$10.50
TDF(300) + FTC(200) + EFV(600)	HDPE bottle 30 tablets[2]	$9.50	$10.51	$11.76	$11.10	$8.91	$8.99	n/a
ATV/r(300/100)	HDPE bottle 30 tablets	$16.50**	$20.00	$20.01	$19.51	n/a	$16.50	$18.50
Pediatric Products								
ABC(60mg)	HDPE bottle 60 tablets[1]	$5.20	$5.50	$4.98	$5.11	$5.13	$4.00	n/a
ABC(60) + 3TC(30) disp	HDPE bottle 60 tablets	$3.50	$5.00	$6.00	$5.61	n/a	$3.50	$3.16
AZT(60) + 3TC(30) disp	HDPE bottle 60 tablets	$2.00	$1.92	$1.98	$2.61	n/a	$1.90	$2.03[4]
AZT(60) + 3TC(30) + NVP(50) disp	HDPE bottle 60 tablets	$3.50	$3.50	$3.60	$3.63	n/a	$3.60	$3.60
EFV(200) scored tablets	HDPE bottle 90 tablets	n/a	$9.30	$9.27	$9.30	n/a	$9.30	n/a
LPV/r(80+20 mg/ml)	HDPE bottle 5 x 60mL (300mL)	n/a	$30.82	n/a	$31.33	$19.70[5]	$30.82	$32.15
LPV/r(100/25mg)	HDPE bottle 120 tablets	n/a	n/a	$11.88	n/a	n/a	$10.00	n/a

**Price offered for higher volume orders **Lower prices may be offered for higher volume orders. Please contact Carolyn Amole at camole@clintonhealthaccess.org for more details.*

[1] RSA is 56 tablet bottle
[2] RSA is 28 tablet bottle
[3] RSA is 112 tablet bottle
[4] Assumes dispersible was procured based on indicated supplier, though not explicitly stated in tender document
[5] RSA price provided for 60mL bottle. Multiplied by 5 to get 300mL estimate for comparability purposes

Appendix C: IATT List of Optimal Pediatric Products (2015)

Product	Dosage	Formulation	Stance
ABC + 3TC	60/30mg	Tablet (dispersible, scored)	Optimal
ABC + 3TC	120/60mg	Tablet (dispersible, scored)	Optimal
AZT + 3TC	60/30mg	Tablet (dispersible, scored)	Optimal
AZT + 3TC + NVP	60/30/50mg	Tablet (dispersible, scored)	Optimal
EFV	200mg	Tablet (scored)	Optimal
LPV/r	100 mg/25mg	Tablet (heat stable)	Optimal
LPV/r	80/20mg/ml	Oral liquid	Optimal
NVP	50mg	Tablet (dispersible, scored)	Optimal
NVP**	50/5mg/ml (100ml)	Oral liquid	Optimal

** For infant prophylaxis as part of PMTCT.

Appendix D: Notes on Methodology

There are several CHAI analyses from which the majority of figures in this report are derived:

- *ART patient forecast*: Each year, CHAI develops a five-year forecast for the total number of patients on ART in LMICs. CHAI compiles historic data on the number of patients on ART in 21 high ART patient burden countries (Botswana, Brazil, Cameroon, China, Côte d'Ivoire, Ethiopia, India, Kenya, Lesotho, Malawi, Mozambique, Myanmar, Nigeria, Rwanda, South Africa, Swaziland, Tanzania, Uganda, Vietnam, Zambia, and Zimbabwe) from progress reports issued and annual data published by the WHO, UNICEF and UNAIDS. For each country CHAI assumes that the number of people receiving treatment will increase linearly at the same rate as the linear trend observed in the last four years and will plateau as universal access is approached, and then extrapolates to the rest of the world. CHAI made three notable changes to this forecast in 2015. First, the team changed the linear extrapolation to be based on the past four years instead of three years in order to capture a broader view of scale-up in the included countries. Second, CHAI adjusted the definition of universal access (for the growth plateau) to be defined by PLWHA rather than CD4 count <500, to reflect WHO Guideline changes and subsequent anticipated ART scale-up. Finally, due to data availability, Myanmar and Vietnam were included in this year's analysis in place of Namibia and Thailand. The portion of ART patient burden in LMICs represented by the included countries remained unchanged at 85 percent.

- *ARV demand forecast*: CHAI collects aggregate country data on patient regimens, formulations used, national guidelines, and anticipated future trends from CHAI's country teams and published literature each year. CHAI uses the data, an internally developed forecasting model, and the ART patient forecast (above) to project ARV demand in LMICs over the next five years.

- *ARV procurement database*: CHAI aggregates procurement data from several sources, including Supply Chain Management System (SCMS), The Global Fund, UNITAID, IDA, and national governments. The data is evaluated on an annual basis to understand pricing and volume trends by country, region, and globally.

- *Market sizing analysis*: Each year, CHAI combines the ARV demand forecast with pricing data from the ARV procurement database to calculate the current size of the ARV market in dollar terms, to estimate the market size over the next five years, and to calculate the average cost of treatment for first- and second-line adult and pediatric patients. A slight modification in approach was made in 2015 to be more be more inclusive of less common regimens; this did not result in significant changes to overall market size.

- *Pipeline forecast*: Shared publicly for the first time in 2015, CHAI combines the global ARV demand forecast (above) with new product uptake assumption to form a pipeline forecast based on three main factors: 1) anticipated price differential between new and current products, 2) relative clinical improvement of new product relative to current, and 3) anticipated launch year. These three factors inform an uptake curve choice for new products relative to current products, separately amongst existing and newly initiating patients, to estimate the total number of patients in a given year.

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