CLINTON HEALTH ACCESS INITIATIVE

Hepatitis B Market Report 2022

Highlighting the latest trends in HBV treatment and diagnostics

Photography by: Soksamphoas Im, Christine McNab

Disclaimer: The data sources primarily used for analysis in the report include the India Import Export data, CHAI country teams, Ministry of Health counterparts, and stakeholder (NGO and civil society partners) conversations. CHAI has taken precautions to verify the information shared on the report. However, the analysis in the report is not exhaustive, and the responsibility for the interpretation and use of the material lies with the reader. The mention of specific companies or supplier products does not imply that CHAI is endorsing or recommending them.

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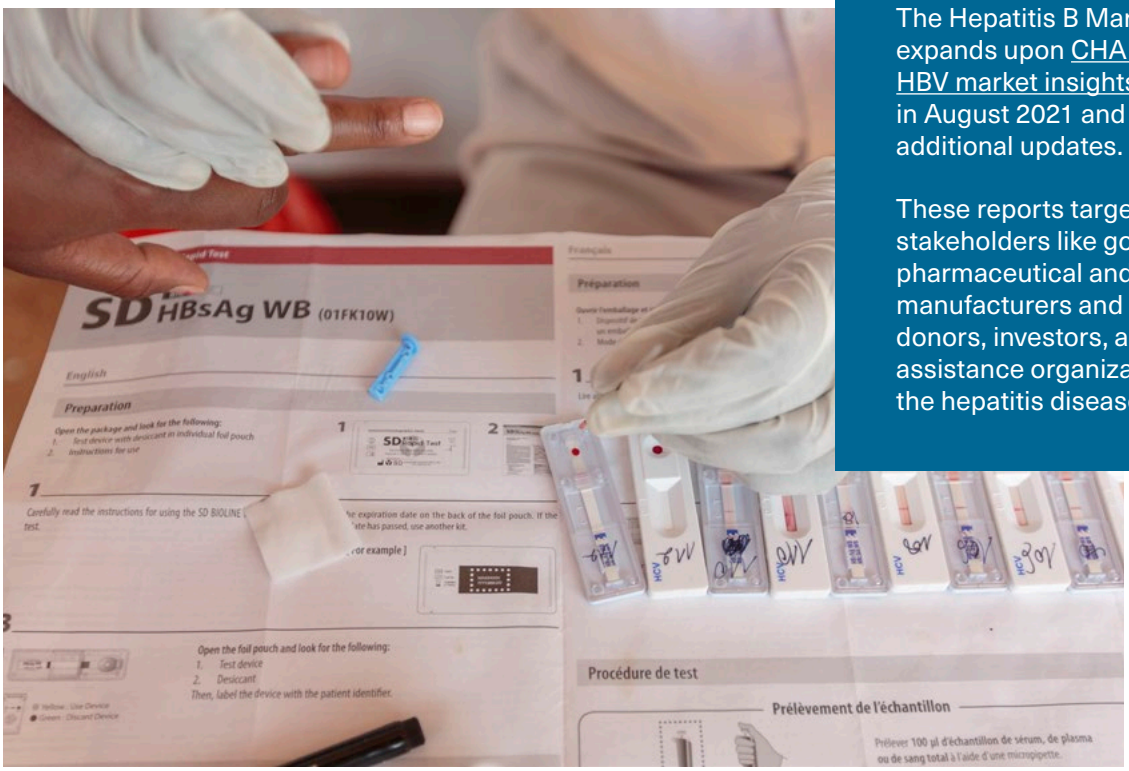

CHAI Hepatitis Market Reports

CHAI routinely collects and publishes market intelligence to highlight trends in the hepatitis C virus (HCV) and hepatitis B virus (HBV) markets.

These reports provide updates on diagnostic and treatment market trends, including supplier landscape, volume, and pricing trends, among others across low- and middle-income countries (LMICs).

In July 2022, CHAI published the Hepatitis C Market Memo, a brief covering the latest trends in the HCV diagnostics and treatment markets from January 2021 to April 2022. CHAI published its first and second editions of the HCV Market Intelligence Report in May 2020 and August 2021 covering market updates for 2019 and 2020, respectively.

The Hepatitis B Market Report 2022 expands upon CHAI's preliminary HBV market insights first published in August 2021 and provides additional updates.

These reports target a range of stakeholders like governments, pharmaceutical and diagnostic manufacturers and distributors, donors, investors, and technical assistance organizations working in the hepatitis disease area.

Acknowledgments

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Acronyms

Ag	Antigen
ALT	Alainaine aminotransferase
ARV	Antiretroviral
CDCP	Centre for Disease Control and Prevention
CE	Conformitè Europëenne
CHAI	Clinton Health Access Initiative
CPT	Carriage Paid To
CRP	Collaborative Registration Procedure
DAP	Delivered At Place
EPSS	Ethiopian Pharmaceutical Supply Service
ERP	Expert Review Panel
ETV	Entecavir
EXW	Ex-Works
FCA	Free Carrier
FDA	U.S. Food and Drug Administration
FOB	Freight on Board
GAP	Global Access Program
GFATM	The Global Fund to Fight AIDS, Tuberculosis and Malaria
GHTF	Global Harmonization Task Force
HBeAg	Hepatits B e-Antigen
HBsAg	Hepatits B Surface Antigen
HBV	Hepatitis B Virus
HCV	Hepatitis C virus
ICB	International Competitive Bid
LMIC	Low- and Middle-Income Countries
Mg	Milligram
MoH	Ministry of Health
NAT	Nucleic Acid Tests
NMS	National Medical Stores
NVHCP	National Viral Hepatitis Control Program
OOP	Out-of-pocket
PAHO	Pan American Health Organization
PEPFAR	U.S. President's Emergency Plan for AIDS
PLHIV	People living with HIV
PMTCT	Prevention of Mother-To-Child Transmission
PQ	Prequalification
PQ'd	Pre-qualified
RBC	Rwanda Biomedical Centre
RDF	Revolving Drug Fund
RDT	Rapid Diagnostic Test
SHI	Social Health Insurance
SRA	Stringent Regulatory Authority
TAF	Tenofovir Alafenamide
TDF	Tenofovir disoproxil fumarate
UNDP	United Nations Development Program
US$	United States Dollar
VL	Viral Load
WHO	World Health Organization

Introduction

HBV infection remains a major cause of liver disease globally, with an estimated 296 million people living with chronic HBV as of 2019.[1] In the same year, HBV resulted in an estimated 820,000 deaths, mostly from cirrhosis and hepatocellular carcinoma (primary liver cancer). This epidemic is fast growing with 1.5 million new infections per year mostly driven by vertical transmission from mother-to-child during birth and delivery. Blood-to-blood contact from unsafe injections, exposures to sharp instruments, and sex with an infected partner are other key contributors to the growing number of new infections. The World Health Organization (WHO) estimates that the burden of HBV infection is highest in the Western Pacific Region and in Africa, where 116 million and 81 million people, respectively, are chronically infected. Additionally, 60 million are chronically infected in the Eastern Mediterranean Region, 18 million in South-East Asia, 14 million in Europe, and 5 million in the Americas.

Chronic HBV infection is preventable by vaccines. For those chronically infected, with timely diagnosis and treatment, replication of the virus can be suppressed, and deaths can be prevented. Similar to antiretrovirals for HIV management, people who start HBV treatment generally continue it for life.

WHO guidance on testing and treatment of HBV[2] *(see Appendix 1 for summary)* is referenced across several guidelines that address prevention, care, and treatment, as well as screening and diagnosis for the general population.[3] It is also referenced in guidelines on the prevention of mother-to-child transmission of HBV, with a focus on specific interventions for mothers and infants.[4] Updated WHO consolidated guidelines for HBV are expected in 2023.

Based on estimates, 12 to 25 percent of people with chronic HBV infection (approximately 35 to 74 million people) are eligible for treatment because of either cirrhosis or the combination of raised alanine aminotransferase (ALT) and viral replication.[5] As of 2019, only 10.5 percent of all people estimated to be living with HBV were aware of their infection and only 2.2 percent (6.6 million) people were on treatment.[6] Despite these major gaps, few LMICs have public programs that provide HBV testing and treatment. Many factors contribute to this significant gap in access including limited awareness and lack of funding for a public program. In addition, a complex diagnostic algorithm makes it difficult to implement a public health approach to treatment.

The purpose of this report is to capture how HBV programs access tenofovir disoproxil fumarate (TDF) therapy for HBV treatment and provide key updates on diagnostics trends.

Key findings detailed in the report:

HBV Treatment:

- TDF is accessed by HBV programs at 1 to 12 times the price accessed by HIV programs.
- Several strategies are being used in countries to access TDF at an accessible price including pooled procurement, competitive bidding, and alternative financing mechanisms.

HBV Diagnostics:

- HBV rapid diagnostic tests (RDTs) prices remain consistent at around US$1 in most high-burden countries.
- The total cost paid by countries for HBV viral load (VL) tests varies across countries and often exceeds the global access prices which can range from US$8.90 to US$ 16.00.
- Although there is no WHO Prequalification (PQ) process for hepatitis B e antigen (HBeAg) tests, there are multiple products in the market, some of which have received Stringent Regulatory Authority (SRA) approvals.
- As countries introduce and scale triple elimination efforts for maternal and neonatal health across disease areas such as HIV, syphilis, and HBV, there is growing demand to improve service delivery through an integrated combination RDT

1 WHO Global Progress Report On HIV, Viral Hepatitis and Sexually Transmitted Infections (2021)
2 WHO guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection (March 2015)
3 WHO Guidelines on hepatitis B and C testing (February 2017)
4 WHO Prevention of mother-to-child transmission of hepatitis B virus: Guidelines on antiviral prophylaxis in pregnancy (July 2020)
5 Estimating the proportion of people with chronic hepatitis B virus infection eligible for hepatitis B antiviral treatment worldwide: a systematic review and meta-analysis, The Lancet Gastroenterology & Hepatology, Volume 6, Issue 2, 2021
6 WHO Global Progress Report On HIV, Viral Hepatitis and Sexually Transmitted Infections (2021)

HBV Treatment Market

Supplier Landscape

TDF, which has been a mainstay for HIV treatment, has the same dosage approved for HBV treatment (300 mg/day) and is broadly available from multiple generic manufacturers (see Exhibit 1). Alternatively, WHO also recommends the use of entecavir (ETV) for the treatment of chronic HBV infection. However, ETV is costlier than TDF, and TDF remains the preferred therapy across LMICs. A comparison of the export of drugs from Indian generics shows that volumes of ETV exported is three percent of TDF singles in 2021.

TDF has a robust supplier landscape with six WHO Prequalified (PQ'd) suppliers. ETV only has one WHO PQ'd supplier (see Exhibit 1).

Exhibit 1: Quality-approved generic supplier landscape of TDF and ETV

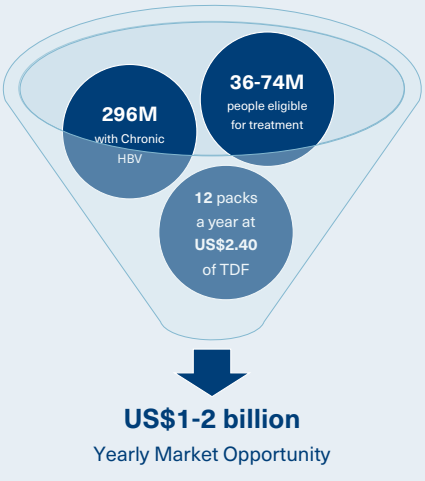
Drug	WHO PQ'd Suppliers
TDF	Aurobindo, Cipla, Viatris, Macleods, Strides, Laurus Labs
ETV	BrightGene Bio-Medical Technology

Volume Trends

Between January 2021 and December 2021, approximately three million packs of TDF singles were exported by Indian generics to LMICs, a 150 percent increase from the previous year *(an overview of the CHAI analyses and methodologies used in this section is provided in Appendix 2)*. Since people living with HIV (PLHIV) are mostly treated by fixed-dose combination (FDC) therapies of TDF, we can assume that a majority of TDF singles exports are for HBV treatment.

Only 2.2 percent of chronic HBV-infected patients are estimated to be on treatment, leaving more than 29 to 67 million patients worldwide eligible but not on treatment. This demonstrates a significant opportunity to scale-up HBV treatment across countries. Based on these volumes, the yearly market size of the untapped market for suppliers is estimated to be US$1-2 billion (see Exhibit 2). Approximately 60 percent of this market is across LMICs, accounting for the geographical distribution of HBV burden.[7]

Exhibit 2: Potential market size for HBV treatment market



7 CDA Foundation, Polaris Observatory HBV Data

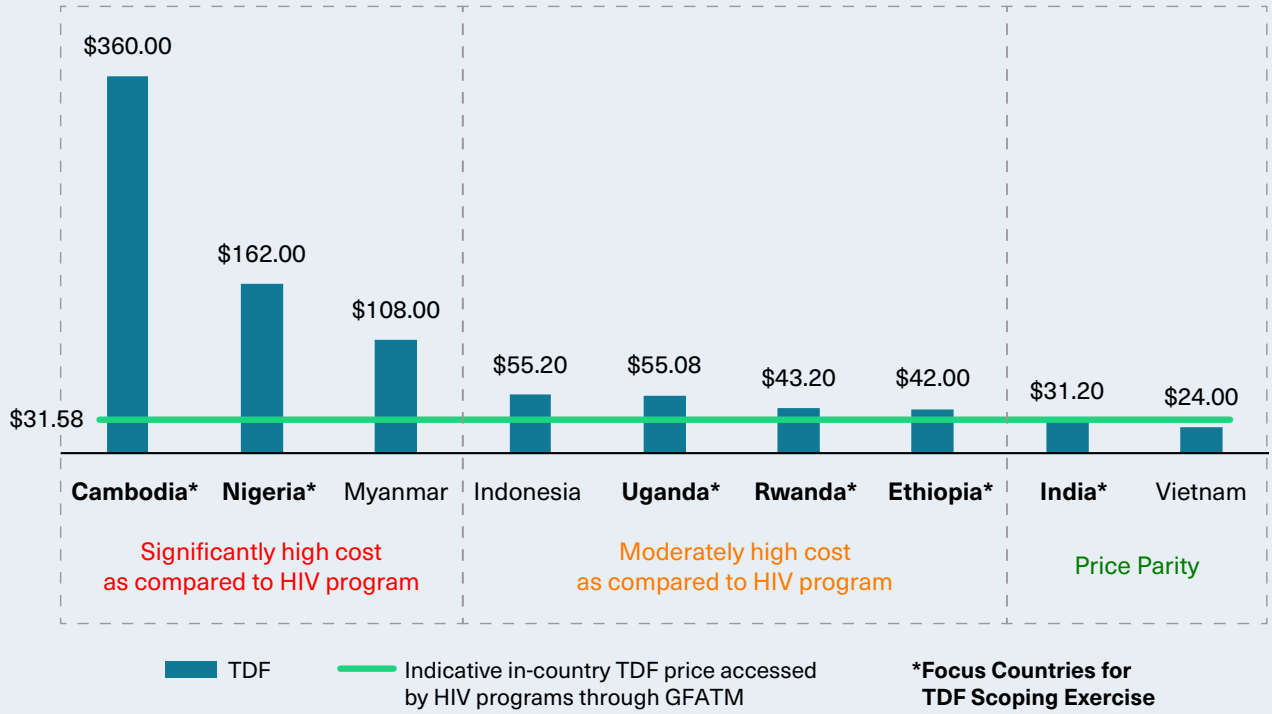
Pricing Trends

The price of TDF has been driven down over the past two decades due to its wide use in HIV treatment. The current price of TDF negotiated by The Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) is US$28.80 per year Ex-Works (EXW) and US$31.60 per year (indicative in-country price). **However, several programs/ hospitals report procuring TDF at significantly higher prices for HBV mono-infection and there is significant variability across LMICs.**

The graph below (see Exhibit 3) shows the variance in the price of a one-year HBV treatment course across nine countries. Patients in Cambodia pay the highest at approximately US$360 for a year of TDF treatment. In countries such as Nigeria and Myanmar, a one-year TDF course costs over US$100, while countries such as India procure TDF at prices similar to the HIV program.

There is limited information about the drivers of price variation of TDF between HBV and HIV programs. To better understand this price variation and recommend best practices and strategies for hepatitis programs to procure TDF at price parity with HIV programs, CHAI undertook a TDF scoping exercise in a subset of these countries based on the scope of resources. A diverse portfolio of countries was selected, ensuring that collected data points provided a robust analysis. CHAI aims to replicate this type of analysis in other countries to build on the recommendations to access TDF for HBV at price parity with HIV programs.

Exhibit 3: Price for one-year HBV treatment course in 2022 (US$)



Note:

1. *GFATM in-country pricing accessed by HIV programs has been taken as a benchmark for TDF prices as it is one of the lowest negotiated prices of the drug; this pricing is indicative; refer to Appendix 3 for more details.*
2. *GFATM-funded HIV programs use its online procurement platform, Wambo, to procure TDF-based therapy at this negotiated price.*
3. *Products procured through the GFATM mechanism are WHO PQ'd/ Expert Review Panel (ERP) reviewed, while products procured from government budgets across LMICs comply with country-specific procurement policies, which require products to be locally approved.*
4. *The TDF pricing for Ethiopia, India, Rwanda, and Uganda is the price at which the national program procures in these countries.*
5. *The TDF pricing for Nigeria was collected from Nasarawa State.*
6. *The TDF pricing for Cambodia is from the private sector.*
7. *The TDF pricing for Myanmar reflected in the graph above is the price-to-patient from the private sector. The official exchange rate has been used to estimate this price in US$.*
8. *The TDF pricing for Vietnam is the lowest price reported by MoH, Vietnam.*
9. *The TDF pricing for Indonesia is the price as reflected in the e-Katalog.*

TDF Scoping Exercise

Objectives, Methodology and Countries of Focus

The TDF scoping exercise was undertaken with three broad objectives:

1. Collect pricing for TDF for mono-infected HBV and HIV programs in focus countries to determine price differential.
2. Identify key factors that are driving the price differential by examining volumes, suppliers, and procurement and distribution mechanisms utilized by viral hepatitis and HIV programs.
3. Evaluate whether there is a potential market-shaping strategy to catalyze TDF price reductions for HBV programs.

CHAI undertook the exercise in two phases. The first phase involved secondary research to understand and review information available on hepatitis programs, drug prices, and program progress. In addition to this, CHAI also reviewed TDF procurement data from HIV programs across LMICs. The second phase of the exercise involved stakeholder discussions in focus countries. These interactions with key stakeholders included in-country procurement agencies, relevant government officials in HBV and HIV programs, in-country suppliers, and distributors to understand the current TDF procurement landscape, challenges, and best practices.

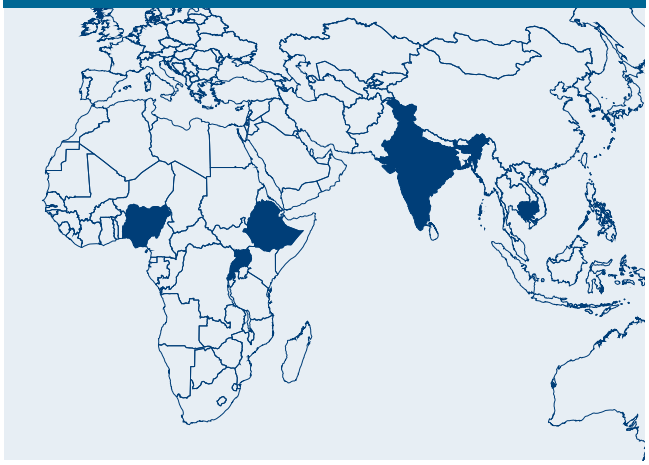
As part of the exercise, six countries across Southeast Asia and Sub-Saharan Africa were included, namely: Cambodia, Ethiopia, India, Nigeria, Rwanda, and Uganda. These countries are at different stages of the HBV treatment scale-up and have a cumulative HBV burden of over 65 million, providing a set of diverse data points and approaches to HBV care. In addition, these countries provided insights into strategies for enhanced HBV care and alternative methods of program financing.

These six countries can be categorized into two broad groups:

1. **Countries with coordinated public HBV programs providing free care**

   Three out of six countries in this exercise, namely **India**, **Rwanda**, and **Uganda**, fall under this bucket of publicly coordinated HBV programs. These countries have centralized financing with services being delivered free of charge to patients. Commodities in these countries are centrally procured and distributed to facilities, which has resulted in low prices of TDF between US$2.60 – 4.60 per pack.

Six countries included in TDF Scoping Exercise: Cambodia, Ethiopia, India, Nigeria, Rwanda, and Uganda



2. **Countries with no publicly funded services**

   Three out of six of the focus countries, **Cambodia**, **Nigeria**, and **Ethiopia** have not initiated a publicly funded viral hepatitis program; however, services are available in some public health facilities but are not provided free of charge or under a publicly coordinated effort.

   In Cambodia and Nigeria, this has led to either fragmented procurement by public hospitals or outsourcing of treatment to the private sector. In either case, patients pay high out-of-pocket (OOP). It is to be noted that in Cambodia, some public services are set to be rolled out under the prevention of mother-to-child transmission program.

   In the case of Ethiopia, the country has a unique publicly coordinated program. The public healthcare system pools demand and leverages volumes at a central level using a revolving drug fund. While the patients pay OOP, Ethiopia with its alternative financing mechanism procures TDF at the lowest Freight on Board (FOB) price of US$2.50 per pack. It is to be noted that HBV RDT for screening of pregnant women is available for free at antenatal care clinics in Ethiopia.

The HBV programs and procurement mechanisms in the six focus countries are detailed in the next section.

Major Takeaways from CHAI's TDF Scoping Exercise in Six Countries

CHAI performed a detailed country-wise analysis of HBV programs including the scale of the public programs, procurement trends and mechanisms, drug pricing across HBV and HIV programs, and patient OOP expenses. We used quantitative and qualitative data points collected via stakeholder interviews across the six countries. The findings from this exercise are summarized below:

Across the selected countries, the mechanisms for procuring antiretroviral (ARV) drugs for HIV programs depend on the funding mechanism. Commodities funded by government budget funds are procured by national procurement bodies following state-specific procurement guidance. Commodities funded by non-government entities are done outside the national procurement system. The GFATM procurements are done through its online procurement system (Wambo.org), and the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) procurements through PEPFAR's procurement service agent that delivers to the in-county central warehouses. Some countries leverage multiple funding mechanisms for HIV drug procurement.

Cambodia

Cambodia has a high burden of HBV, with a 4.39 percent seroprevalence among pregnant women.[8] Cambodia is on the path to addressing this burden by integrating HBV testing into its existing elimination of vertical transmission program, which already includes screening for HIV and syphilis.

For the general population seeking HBV service, no publicly coordinated program exists. Service delivery in certain operational districts is expected to kick off in 2023 after domestic financing is secured for commodity procurement. Currently, some referral hospitals provide hepatitis B surface antigen (HBsAg) testing and refer eligible patients to a private lab for diagnostics, and/or write a drug prescription. TDF is available to patients from private hospitals/ pharmacies at US$30 per pack.

Services for pregnant women include HBV screening, further diagnosis in women who screen positive, TDF therapy when needed, and HBV birth dose for all infants. The program prioritizes access, offering services at health centers, maternity wards, and hospital HBV units. Procurement for the program is in process currently for the pilot screening and treatment of pregnant women in the capital Phnom Penh.

Ethiopia

Ethiopia has an estimated 11 million people living with HBV (prevalence of ~9.4 percent). Ethiopia is committed to halting transmission by providing access to safe, affordable, and effective care to those living with HBV. The Ethiopian government has scaled-up its HBV program by increasing the number of health facilities providing treatment services from 13 to 90.

The Ethiopian National Viral Hepatitis Treatment Guidelines recommend TDF and ETV therapies for chronic HBV, with TDF being the most widely used. A revolving drug fund (RDF) is used to aggregate demand and procure centrally to leverage volume-based pricing. The Ethiopian Pharmaceutical Supply Service (EPSS) is the procurement agency tasked with procuring healthcare commodities in the country and it purchases TDF through International Competitive Bidding (ICB). Ethiopia procured around 197,000 packs of TDF at US$2.20–2.50 FOB price in 2021-22 for the HBV program.

Under RDF, demand from hospitals is aggregated to forecast need and leverage volume-based pricing; hospitals are then able to procure TDF from EPSS between US$3.50-4.00 (FOB product price plus service fee and logistics cost). This revenue is typically used by EPSS to replenish commodities.

India

India has an estimated 33 million people living with HBV (HBV prevalence at around 0.95 percent). The Indian government has established the National Viral Hepatitis Control Program (NVHCP) which offers free diagnostics for the management of patients with hepatitis B or C. The viral hepatitis program is scaling, with 868 facilities nationwide (across most district hospitals and some sub-district hospitals) providing hepatitis treatment. It is 100 percent domestically funded by the Government of India, and all services are offered free of cost to patients.

NVHCP recommends TDF, ETV, and tenofovir alafenamide (TAF) therapies for HBV treatment. However, most patients are treated with TDF and ETV therapies. India uses a central procurement mechanism under which the Central Medical Services Society (National Procurement Agency for

8 Ork V, Woodring J, ShafiqulHossain M, Wasley A, Nagashima S, Yamamoto C, et al. Hepatitis B surface antigen seroprevalence among pre- and post-vaccine cohorts in Cambodia, 2017. Vaccine. 2019 14;37(35):5059–66

medical commodities) pools demand at a central level and procures drugs via tenders or rate contracts. Procured drugs are then supplied to the state health departments via a robust supply chain.

India procured 20,000 patient courses (around 240,000 packs) of TDF for approximately US$2.60 in 2021 for the HBV program. The latest tender was awarded to two companies that supply 70 percent and 30 percent of the requirement, respectively. This is in line with procurement guidelines laid out by the Ministry of Finance, India. The guidance says that "in case of critical/vital/safety/security nature of the item, large quantity under procurement, urgent delivery requirements and inadequate vendor capacity it may be advantageous to decide in advance to have more than one source of supply."[9]

India is now decentralizing the hepatitis commodities' procurement process from a national level to a state level, where the state procurement agencies will be tasked with procuring TDF. Future assessments will need to be done to evaluate how this shift will impact price.

Nigeria

With over 16 million estimated chronic HBV infections, Nigeria faces a significant public health challenge in scaling up access to testing and treatment. HBV screening is available at all facilities, while treatment is available at secondary and tertiary care hospitals. In the absence of financing support, patients must pay OOP for both diagnostic and treatment.

Hospital pharmacies are responsible for procuring TDF, the recommended treatment for HBV in Nigeria, through a facility-based revolving drug fund mechanism. However, procurement at a hospital level leads to fragmented and low-volume orders making it difficult to access volume-based pricing.

For example, in Nasarawa state in Nigeria, due to such low and fragmented procurement, hospitals opt to purchase from a single source supplier in an open market, resulting in a higher price of TDF of over US$12 per pack. An additional 10 percent service charge is levied by hospitals, adding to the cost to patients.

The high price of TDF is a contributing factor to high OOP expense and poses a challenge to initiating patients on HBV treatment. While Nigeria achieved price parity with the HIV program back in 2019, challenges around centralized procurement coordination and fluctuating currency exchange rates have posed major obstacles to maintaining these prices.

There is an opportunity to scale up HBV care in Nigeria by reducing TDF prices through market-shaping efforts such as pooling demand across facilities to leverage volume-based pricing, improving demand forecast to better plan for procurement, and fostering competition by exploring purchasing options such as tenders.

Rwanda

Rwanda has an estimated HBV burden of 399,000 (HBV prevalence of ~0.82 percent) infections. The country's Viral Hepatitis program sits within the wider HIV program at Rwanda Biomedical Centre (RBC). The program is in a scaling stage, and HBV diagnosis and treatment services are available at all health facilities across the country, entirely free to the patients. HBV screening is mandatory for pregnant women through antenatal care. Free screening services are available for the general population. The country's treatment guidelines on HBV recommend TDF and ETV therapies. However, TDF therapy is preferred. The program's commodity budget is funded by GFATM and the Centre for Disease Control and Prevention (CDCP) for service delivery activities.

The Rwanda Medical Supply (RMS) Ltd is responsible for procuring diagnostic and treatment commodities in the country and an annual quantification exercise is conducted to inform national procurement. RMS pools the drug requirement at the program level and procures via an open tender which is awarded for one year with the possibility of renewal twice.

Rwanda procured TDF at US$3.60 for June 2022-July 2023.

Uganda

In Uganda, there are more than 800,000 people estimated to be infected with chronic HBV *(estimate based on 4.1 percent seroprevalence of HBsAg among persons aged 15-64 years, established through a Population-based HIV impact assessment - UPHIA 2016)*.

Since the program's inception in 2015 until April 2022, nearly 433,000 patients have been enrolled in treatment. TDF, which is recommended for adolescents above 12 years and adults weighing at least 35 kilograms (kg), is available at no cost at the level of a health center IV and above (district

9 Government of India, Manual for Procurement of Good 2017

hospital, regional and national referral hospitals). The National Medical Stores (NMS), the government entity responsible for procuring health-related items, procures TDF for the HBV program.

NMS has established a framework contract through a national competitive bidding process that allows only in-country manufacturers to bid. A similar three-year framework arrangement is running for ARVs, including TDF with CIPLA quality chemicals industries until 2025. The decision to allow in-country manufacturers to bid exclusively is due to the Buy Uganda Build Uganda (BUBU) policy. The current price of the TDF singles for HBV from the local supplier to the central warehouse at NMS is US$4.59 per pack. This price was negotiated referencing the GFATM pricing for ARVs used for both HIV and HBV programs.

Recommended Strategies for HBV Programs to Procure TDF At Price Parity with HIV Programs

1. **Pool demand and procure centrally at a national or state level to leverage volume-based pricing**

   Hepatitis programs should consider procuring TDF centrally at a national or state level by aggregating demands to leverage volume-based pricing. Countries that have implemented centralized procurement have been able to access TDF for HBV at par with the HIV program pricing by leveraging higher volumes. For instance, countries such as Ethiopia and Uganda leverage centralized procurement to get competitive rates from suppliers. Between April 2021 and March 2022, EPSS, the procurement agency tasked with procuring healthcare commodities in Ethiopia, procured more than 190,000 packs of TDF at US$2.20 –2.50 FOB, which is at par with the price to the HIV program. EPSS further distributes these drugs to hospitals as per need.

2. **Implement tendering mechanisms to get competitive quotes**

   While various purchasing options exist for countries, from open tender to competitive negotiation to direct purchase, these purchasing options come with an inverse relationship between cost and complexities such as lead time. Open tenders usually require more time commitments for tender preparation, bid management, and selection of qualified bidders, but also yield significant benefits by fostering an environment favorable to lower prices. For instance, India procures through a competitive tendering process that enables the government to buy TDF at competitive and affordable prices. In the last tender where India procured 20,000 patient courses (approximately 240,000 packs) of TDF at around US$2.60 in 2021, more than 15 suppliers participated in the tender. Two companies were awarded the tender to supply 70 percent and 30 percent of the volumes, respectively.

3. **Leverage pricing negotiated by international procurement mechanisms as a benchmark**

   Often governments are not able to use domestic budgets to directly purchase commodities through the procurement mechanisms of organizations such as the GFATM, United Nations Development Program (UNDP), and Pan American Health Organization (PAHO), due to their country's procurement policies. However, the prices negotiated by these international organizations can be used by countries as benchmarks for local tenders or negotiating price deals directly with suppliers. Uganda's NMS regularly uses GFATM-negotiated ARV prices to inform its negotiations for tenders through the government budget.

4. **Implement alternative financing mechanisms such as revolving drug funds for programs where patients pay OOP**

   Countries, where patients pay for HBV treatment OOP, can look to establish financing mechanisms such as revolving drug funds to pool demand and facilitate centralized procurement. Hospitals can then procure from central procurement departments at lower rates than in the open market where they don't have leverage in price negotiation due to fragmented, low-volume orders. Such alternative mechanisms tailored to a country's healthcare needs often promote access to volume-based pricing without significant central expenditure. However, implementing such financing mechanisms requires strong political will, multiple stakeholders' buy-in, coordination, and seed-funding by the government, and continued investment in demand-generating activities such as clinical training and monitoring, and evaluation. For instance, Nigeria uses RDF at the hospital level. Another focus country, Ethiopia leverages a revolving drug fund to pool volumes at a national level and has used aggregated demand to negotiate an affordable price for TDF. In Ethiopia, forecasting is done by aggregating demands from hospitals at a central level, and the national procurement division (EPSS) then sources TDF. Hospitals are then able to procure TDF from EPSS while revenue earned by EPSS from this purchase is typically used to replenish the commodity.

   In addition to the above recommendations, it is important to emphasize the role of a large in-country supplier base in accessing TDF at affordable prices. While TDF is registered by many suppliers across LMICs due to its wide use in HIV treatment, countries with a limited supplier

base should ensure expedition of the registration of generic TDF by allowing the use of WHO's Collaborative Registration Procedure (CRP). [10] This enables national medicines regulatory authorities to use WHO PQ evaluations and inspections to reduce work duplication and shorten the time for product registration. The time frame for registration of products via the CRP is ninety days once filed in the country. A broad supplier base in the country will ensure competition and is conducive to price reduction for commodities.

For details on purchasing options for TDF, please refer to Appendix 4.

Conclusion

TDF drug is widely available with six WHO PQ'd suppliers in the market. However, accessing TDF at the benchmark in-country pricing of US$31.60 (12 months course) remains a challenge for HBV programs.

Out of the six analyzed countries, only India was able to access TDF at a price parity with HIV programs. Ethiopia, Uganda, and Rwanda were able to access TDF at a higher albeit relatively affordable price. Cambodia and Nigeria accessed TDF at the highest prices in the group of countries analyzed. The factors contributing to the lack of price parity between HIV and HBV programs need to be explored further. Furthermore, the reasons for this disparity vary, depending on country-specific context and require extensive country scoping to understand and address the challenges.

It is imperative to increase investments toward HBV programs in low and middle-income countries. Domestic and/or external financing for HBV programs can support optimal market strategies like centralized procurement and pooling demand that in turn enable greater accessibility and affordability of the drug.

Key learnings:

1. Across the focus countries, TDF emerged as the preferred treatment for chronic HBV and public programs/ hospitals use different mechanisms to procure the drug.
2. A centrally financed program responsible for procurement or other appropriate mechanisms to facilitate pooled procurement across health facilities could enable countries to procure TDF at low and affordable prices, at parity with HIV programs.
3. HIV programs mostly procure fixed-dose combination HIV treatment products which include 300 mg TDF and other antiretrovirals. These fixed-dose therapies, including small volumes of TDF singles, are often procured through the international procurement mechanisms of GFATM and PEPFAR.
4. In Nigeria and Cambodia, there is no publicly funded HBV program and hospitals still grapple with high TDF prices due to fragmented demand and low order quantities.
5. Procurement mechanisms that utilize volume-based pricing via pooled procurement and competitive bidding can optimize prices, as in the case of countries like India, Uganda, Rwanda, and Ethiopia.
6. Alternative financing mechanisms such as revolving drug funds also emerged as potential methods to combat high OOP expenses in countries with no publicly funded HBV care.

10 WHO Collaborative Procedure for Accelerated Registration of PQ'd Finished Pharmaceutical Products

HBV Diagnostic Market

Supplier Landscape

WHO Prequalified Hepatitis B Surface Antigen (HBsAg) Products

As per WHO guidance, conducting an HBsAg RDT or laboratory-based immunoassay is the primary step to diagnose individuals for HBV. There remain several HBV diagnostic products that have retained WHO prequalification status, for both rapid diagnostic tests (RDTs) and laboratory-based immunoassays (IAs) (see Exhibit 4). Since the last update in 2021, BioMerieux SA HBsAg RDT is no longer WHO PQ'd.

Exhibit 4: WHO Prequalified HBV Surface Antigen (HBsAg) Tests

	Product Name	Manufacturer	Sample Type
Rapid Diagnostic Tests	Bioline HBsAg WB	Abbott	plasma, serum, venous whole blood
	Determine HBsAg 2	Abbott	plasma, serum, venous and capillary whole blood
Lab-based Immunoassay	Murex HBsAg Version 3	DiaSorin	plasma, serum
	DS-EIA-HBsAg-0.01	RPC Diagnostics Systems	plasma, serum

Source: WHO Public Reports for In Vitro Diagnostics (Hepatitis B Assays)

Additional Quality-Assured HBsAg Products

There are several other products on the market with notable approvals from SRAs (see Exhibit 5). For example, based on GFATM's Quality Assurance Policy,[11] grant funds can be used to procure diagnostic products that meet base global quality standards. These criteria include (1) products that have been WHO PQ'd (2) diagnostic products that have been authorized by regulatory authorities of the founding members of the Global Harmonization Task Force (GHTF) [12] (such as CE-mark, FDA, etc.), or (3) products that have been determined acceptable for procurement by GFATM based on the advice of the WHO ERP.

Exhibit 5: Other Quality-Assured HBsAg Tests

	Product Name	Manufacturer	Sample Type	Approvals
Rapid Diagnostic Tests	First Response HBsAg Card Test	Premier Medical Corporation	plasma, serum, whole blood	CE-Mark
	STANDARD Q HBsAg Test	SD Biosensor	plasma, serum, whole blood	ERPD
Lab-based Immunoassay	Monolisa HBsAg ULTRA Assay	Bio-Rad Laboratories	serum, plasma	CE-Mark
	Elecsys HBsAg II	Roche Diagnostics	serum, plasma	CE-Mark

Source: Global Fund List of HIV (and Hepatitis) Diagnostic Products (Updated July 2022)
As a note, the above list is a non-exhaustive list of quality-assured products.

11 Global Fund Quality Assurance Policy for Diagnostics
12 The GHTF evolved into what is now known as the International Medical Device Regulators Forum a voluntary group of medical device regulators from around the world

Quality-Assured HBV VL Products

There are currently several HBV VL products with notable regulatory approvals (see Exhibit 6). Although there has been no prequalification certification, the WHO has developed a protocol outlining the technical specifications needed for HBV nucleic acid tests (NAT) or viral load (VL) tests to meet prequalification requirements.[13] The document is scheduled to be released by the end of the year. Once released, manufacturers will be invited to submit applications for the PQ process.

Prioritizing quality, accessible HBV VL products can facilitate market expansion in high-burden countries. From a supply side, this presents an opportunity for manufacturers to accelerate the development and introduction of new HBV molecular products. Furthermore, from a demand side, this would enable countries to access high-quality products, allowing them to scale existing HBV programs and reduce the rate of individuals who are lost to follow-up throughout the cascade of care.

Exhibit 6: Quality-Assured HBV VL Products

Product	Manufacturer	Sample Type	Platform	Regulatory Status	Price (US$)	Incoterm
High Throughput						
Alinity m HBV	Abbott	plasma, serum	Alinity m System	CE-Mark	NA	
RealTime HBV Viral Load Assay		plasma, serum	m2000 RealTime System	CE-Mark	9.60 – 15.55*	FCA
artus HBV RG RT-PCR Kit / artus HBV QS-RGQ Kit	Qiagen	plasma	Rotor-Gene Q or Rotor-Gene Instrument	CE-Mark	NA***	
cobas HBV Test	Roche	plasma, serum	CAP/CTM, cobas 4800/ 5800/ 6800/ 8800 systems	CE-Mark and US FDA	8.90*	CPT
Aptima HBV Quant Assay	Hologic	plasma, serum	Panther System	CE-Mark and US FDA	11.28** (all-inclusive)	DAP
Near point-of-care						
Xpert HBV Viral Care	Cepheid	plasma, serum	Cepheid GeneXpert instruments	CE-Mark	14.90**	EXW
Truenat HBV	Molbio	plasma, serum, whole blood	Truelab Real Time micro-PCR platform (UNO/DUO/ QUATTRO / QUATTRO 4x4)	CE-Mark pending	16.00**	EXW

Source: GFATM List of HIV (and Hepatitis) Diagnostic Products (Updated July 2022)

**Prices are Global Access Prices (Refer to ASLM Diagnostic Pricing Database)*

***Price communicated by the manufacturer*

**** Prices for VL assays for other diseases range from US$8.78 - 11.17 (FCA)*

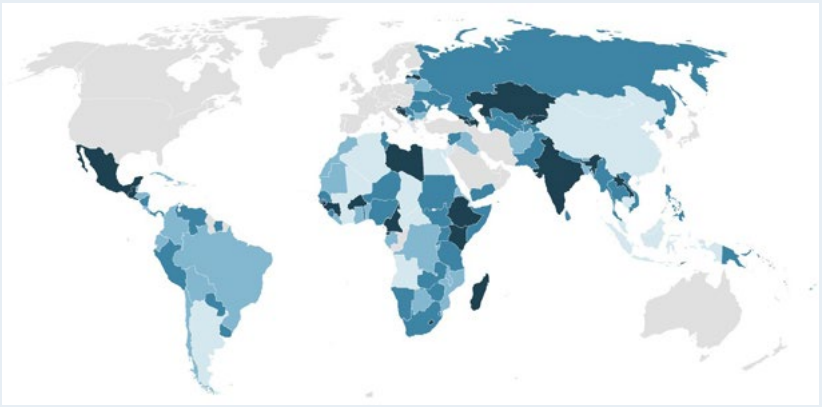
As a note, the above list is a non-exhaustive list of quality-assured products.

13 The Technical Specification Series (TSS) sets out the performance evaluation criteria for meeting prequalification requirements. See here for the draft TSS for IVDs used for quantitative detection of Hepatitis B nucleic acid.

Global Access Program (GAP) Pricing Agreements

Many major suppliers of HBV molecular tests provide pricing programs for global access,[14] making diagnostic products more accessible at reduced prices for LMICs.[15] These prices may be negotiated on a country-by-country basis and depend on several conditions such as the number of device placements, test volumes, service and maintenance, and distribution details. Differences in pricing inclusivity, incoterms, and the supplier-distributor relationship impact the final price paid by countries (see Exhibit 10), which can vary and add significant costs to GAP pricing. Based on an analysis done by CHAI for HBV/HCV assays, 145 countries are eligible for GAP pricing agreements across at least one supplier (see Exhibit 7).

Exhibit 7: GAP Pricing Eligibility for Various Manufacturers' HBV/HCV Tests



Number of GAPs Accessible per Country	Number of Countries Accessing GAP for HCV/HBV Tests
One	46
Two	31
Three	30
Four	38

Volume Trends

Volume Trends of HBV Viral Load

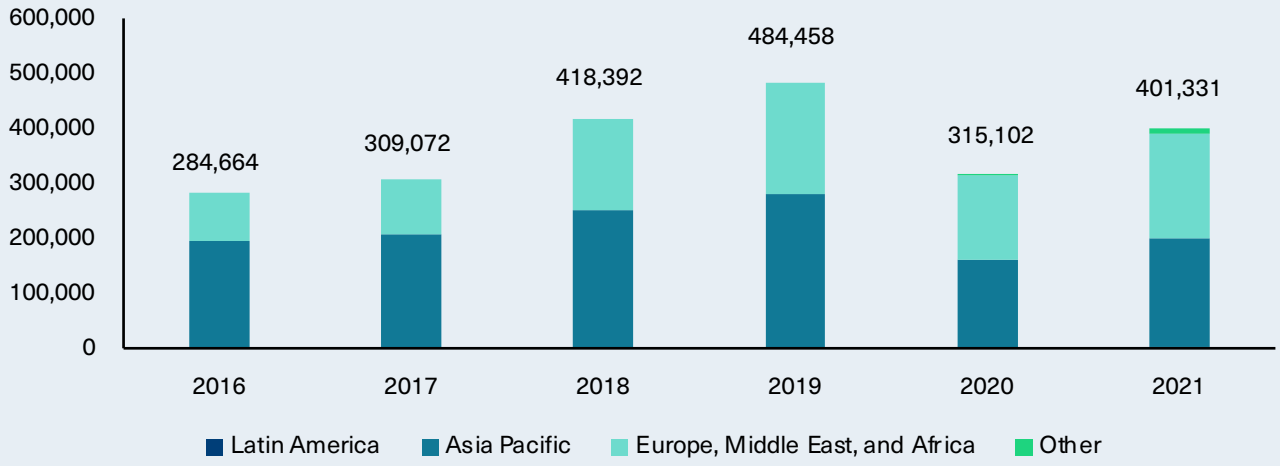
Historic data on volume trends for HBV VL assays have been scarce. The following analysis does not include data on all HBV VL suppliers. Most of the data reflected include procurement data volumes from major VL suppliers for countries which are eligible under specific GAP pricing agreements. The countries included in the GAP pricing agreements vary between suppliers and regions.

Globally, procurement volumes of HBV VL assays have increased with variation over the past six years. Data collected demonstrated that from 2016 to 2019, HBV VL procurement volumes increased by 70 percent (see Exhibit 8) and peaked in 2019 with more than 480,000 tests. In 2020, volume sales declined. This downward trend may be related to the COVID-19 pandemic as countries shifted public health priorities and redirected funding to address the impact of the virus.

Regionally, most sales have been between countries in the Asia Pacific region and within Africa. On average, Asia accounts for 50 to 69 percent whereas Africa, Europe, and Middle East account for 31 to 45 percent of sales volumes in a given year. Beginning in 2020, there have been additional, smaller sale volumes within Latin America, the majority of which have been driven by Brazil; this may reflect the limited countries accessing certain GAP agreements within the region.

14 Please see ASLM Diagnostic Pricing Database for global access prices.
15 For more details on global pricing agreements , please see section Viral load global pricing agreements in HCV Market Intelligence Report 2021 (p. 16)

Exhibit 8: Procurement Volumes of HBV VL by Countries with Global Access Pricing Available from 2016-2021



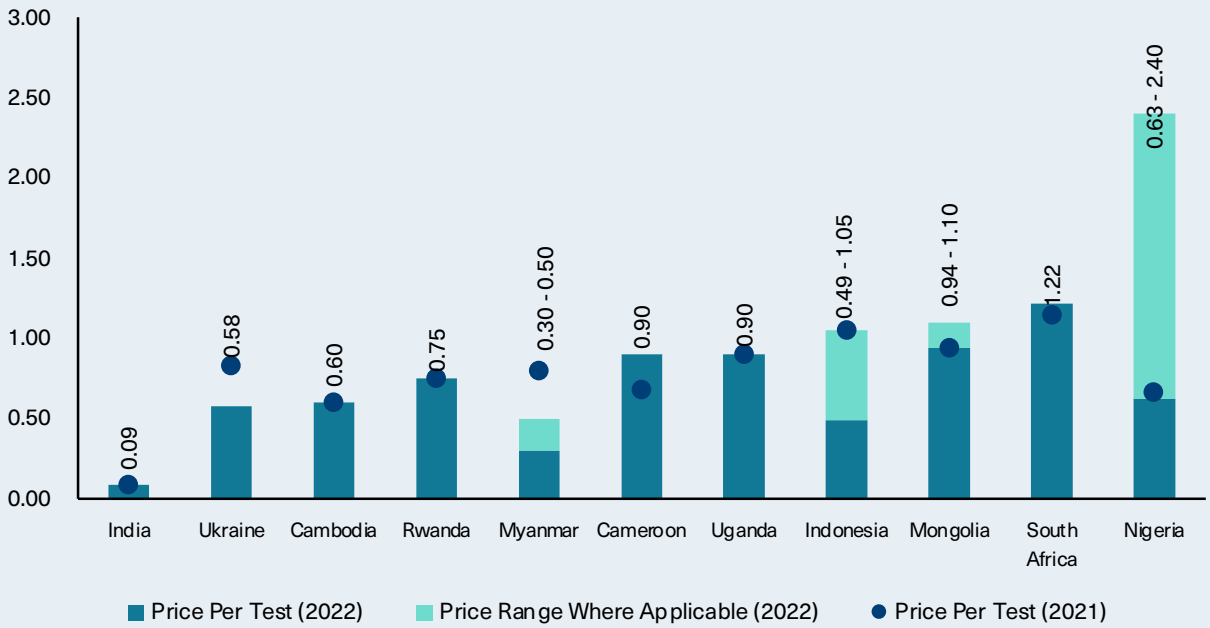
Source: Sale volume data directly communicated by participating HBV VL suppliers (non-exhaustive). Note this data is not exhaustive of the market.

Pricing Trends

Cost of HBsAg RDTs Paid by Country

Pricing for HBV surface antigen tests has remained consistent since 2021, with most high-burden countries procuring the test around the US$1 price point (see Exhibit 9). The global prices for HBsAg RDTs are generally comparable with those of RDTs across other disease areas.

Exhibit 9: Cost of HBsAg RDTs Paid by Public Sector Programs in a Sample of LMICs (US$)

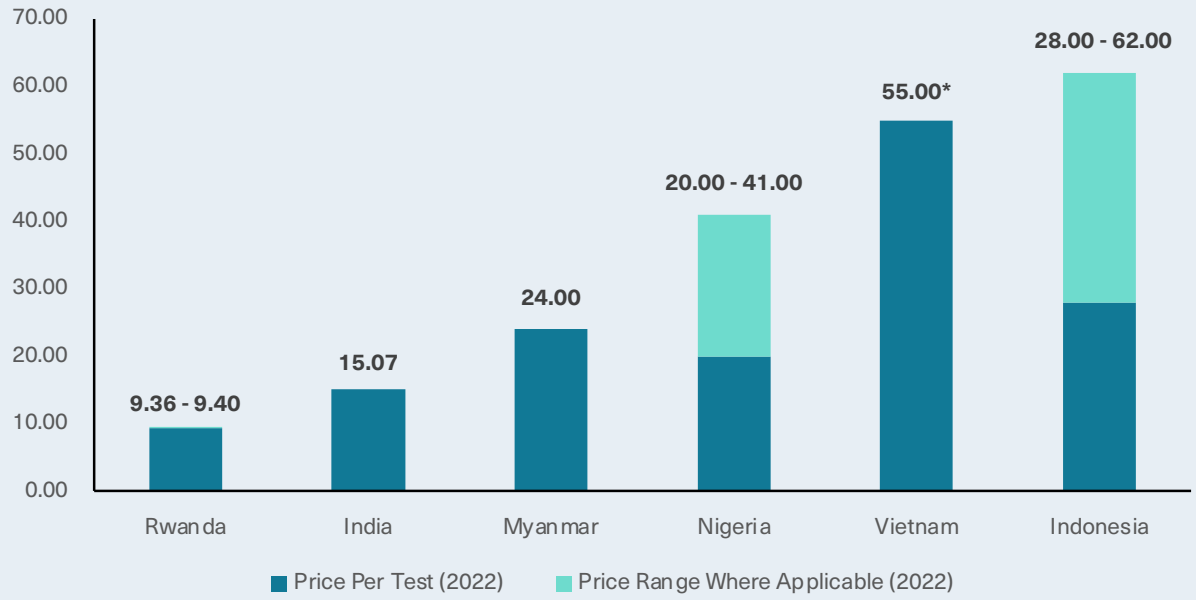


Source: Data collected from CHAI-supported country teams over the course of Q1-2 2022; additional prices were collected from the GFATM Pricing Report Database

Cost of HBV VL Paid by Country

The total cost paid by countries for HBV viral load tests varies across countries (see Exhibit 10) and often exceeds global access prices (refer to Exhibit 6).[16] Programs may also pay for instrument purchase or rental and its service and maintenance, if not already included in the global access option. By leveraging existing molecular testing for HIV, tuberculosis, COVID-19, and other disease programs, governments may integrate diagnostic networks to increase access to HBV VL testing and potentially save costs.

Exhibit 10: Cost of HBV VL Assays Paid by Government in Select CHAI-Supported Hepatitis Programs (US$)



Source: Data collected from CHAI-supported country teams over the course of Q1-2 2022.

**According to the National Social Health Insurance (SHI) scheme, the price of HBV tests is covered 80 percent by the policy and patients pay the remaining 20 percent OOP.*

16 For more details on pricing variations of VL assays, please see section *Complexity of diagnostic cost components, importance of price transparency, and cost comparison of potential testing pathways* in HCV Market Intelligence Report 2021 (p. 20)

Hepatitis B e-Antigen (HBeAg) Market

HBeAg Quality-Assured Products

Based on updated 2020 WHO guidance to prevent vertical transmission, pregnant women who screen positive on HBsAg can receive HBeAg test for determining TDF eligibility, where antenatal HBV VL testing is unavailable.[17] At present, there is no WHO PQ process for HBeAg. Multiple products are in the market (see Exhibits 12 & 13), with options of RDT and laboratory-based immunoassays, which hold SRA approvals. Although recommendations exist for the use of HBeAg as a viable alternative to HBV VL for pregnant women, test performance has varied across settings.

HBeAg RDT products may be more affordable with fewer implementation requirements compared to HBV VL, however, the main barrier to growth for the market is test performance. Studies have demonstrated varied performance in terms of sensitivity and specificity for both HBeAg RDTs and laboratory-based immunoassays, highlighting the need to validate HBeAg testing in settings considering use (see Exhibit 11).

Exhibit 11: Case Study Highlights on HBeAg Test Performance

Study	Findings
Systematic Review and Meta Analysis*	• The pooled sensitivity and specificity of HBeAg for diagnosis of HBV DNA ≥200k IU/mL (threshold in WHO guidance) was 88.2% (95% CI: 83.9–91.5) and 92.6% (95% CI:90–94.5) • In two studies evaluating HBeAg RDTs, there was a pooled sensitivity of 70.1% (95% CI: 58.2–79.9) and specificity of 95.7% (95% CI: 93.3–97.3) for diagnosis of HBV DNA threshold ≥ 200k IU/mL
Thailand**	• HBeAg immunoassay performance in HBsAg-positive pregnant women to determine high HBV DNA ≥ 200k IU/mL demonstrated a 95% sensitivity and 92% specificity • At the time, the cost of HBeAg (US$10) was much lower than the cost of HBV VL (US$65)
Cambodia***	• HBeAg RDT performance in HBsAg-positive pregnant women to determine high HBV DNA level ≥ 200k IU/mL demonstrated a 61.8% sensitivity and 99% specificity" • A novel algorithm of using HBeAg positive or ALT > 40 U/L showed 79.2% sensitivity and 93.3% specificity (for determining HBV DNA ≥ 200k IU/ml)
Malawi**	• In a study evalauating the performance of three commercial HBeAG RDTs in non-pregnant adults, the sensitivity for identifying HBV DNA ≥ 200k IU/mL was 22%, 49% and 54% respectively

** Systematic review of the performance of hepatitis B e antigen test, as an alternative to HBV DNA, to assess eligibility for initiating antiviral therapy during pregnancy, WHO Web Annex B (2020)*

*** Use of Hepatitis B-e Antigen to Identify Pregnant Women With Hepatitis B Virus Infection Who Need Antiviral Therapy for Prevention of Mother-to-child Transmission, Cureus Journal of Medical Science (October 2021)*

**** Hepatitis B e Antigen (HBeAg) Rapid Test and Alanine Aminotransferase Level–Based Algorithm to Identify Pregnant Women at Risk of HBV Mother-to-Child Transmission: The ANRS 12345 TA PROHM Study, Clinical Infectious Diseases (2020)*

***** Diagnostic performance evaluation of hepatitis B e antigen rapid diagnostic tests in Malawi, BMC Infectious Diseases (May 2021)*

Exhibit 12: Market Landscape for HBeAg RDTs

Product	Manufacturer	Sample Type	Time for Detection	Price (US$)	Regulatory Approval
HBeAg Rapid Test	InTec PRODUCTS, INC.	serum, plasma, whole blood	15-20 minutes	0.30 – 0.50*	NA
Insight HBeAg	Tulip Diagnostics	serum	10-15 minutes	0.45*	NA****
OneStep HBeAg	AMS UK Ltd.	serum, plasma	15 minutes	0.70**	CE-Mark
HBeAg Serum Rapid Test (Cassette)	Creative Diagnostics	serum, plasma	10-20 minutes	4.50***	NA
HBeAg Rapid Test	Biopanda Reagents	serum, plasma	15 minutes	0.40***	CE-Mark

17 WHO Prevention of mother-to-child transmission of hepatitis B virus: Guidelines on antiviral prophylaxis in pregnancy (July 2020)

Product	Manufacturer	Sample Type	Time for Detection	Price (US$)	Regulatory Approval
HBeAg Hepatitis B Envelope Antigen Test	Accubio Limited/ Orient Gene	serum, plasma, whole blood	15 minutes	NA	CE-Mark pending
HBeAg Hepatitis B Envelope Antigen Rapid Test	High Top / Shandong Kanghua	serum, plasma, whole blood	15 – 20 minutes	0.22*	NA

** Prices communicated directly by manufacturers (listed in EXW)*

***Source: Poor Sensitivity of Commercial RDTs for HBeAg in Senegal, West Africa*

**** Source: Diagnostic performance evaluation of HBeAg RDTs in Malawi (price reported in 2018)*

***** Product holds regulatory approvals within India (India FDA)*

As a note, the above list is a non-exhaustive list of products.

Exhibit 13: Market Landscape for Laboratory-Based HBeAg Immunoassays

Product	Manufacturer	Sample Type	Platform	Time for Detection	Price (US$)	Regulatory Approval
ADVIA Centaur HBeAg	Siemens Healthineers	serum, plasma	ADVIA Centaur Immunoassay Systems	57 minutes	2.00*	CE-Mark, US FDA
Atellica IM HBeAg	Siemens Healthineers	serum, plasma	Atellica IM Analyzer	39 minutes	2.00*	CE-Mark, US FDA
VITROS	Ortho-Clinical	serum, plasma	VITROS Systems	NA	NA	NA
Elecsys	Roche	serum, plasma	cobas e 411 analyzer; cobas e 601 and e 602 modules; cobas e 801 and e 402 analytical units	18 minutes	NA	CE-Mark, US FDA
HBeAg ELISA Test Kit	InTec PRODUCTS, INC.	serum, plasma, whole blood	NA	NA	20.00 – 40.00*	NA
HBeAg ELISA	High Top / Shandong Kanghua	serum, plasma	NA	NA	0.20*	NA
Liason XL	DiaSorin	serum, plasma	Liaison Analyzer	30-60 minutes	NA	US FDA

** Prices communicated directly by manufacturers (listed in EXW)*

As a note, the above list is a non-exhaustive list of products.

Emerging Combination RDT Market

Combination RDT Products

At the global level and across multiple countries, there is a concerted effort to make the triple elimination of vertical transmission of HIV, syphilis, and HBV a public health priority. The similarity of interventions to prevent mother-to-child transmission in antenatal care settings represents an opportunity to develop a sustainable, routinized approach to antenatal care. Integrating screening services could facilitate access and uptake of testing across diseases. As countries scale up HBV testing, treatment, and care of pregnant women, there is a growing demand to integrate into existing HIV and syphilis programs to prevent vertical transmission. Several manufacturers have developed products which allow integrated testing in a single RDT (see Exhibit 14). In addition to making triple elimination possible, integrated diagnostics will help streamline procurement and supply chain, simplify workflows, and facilitate the uptake of HBV screening.

The following would enable integrated screening services and new product introduction of a combination RDT:

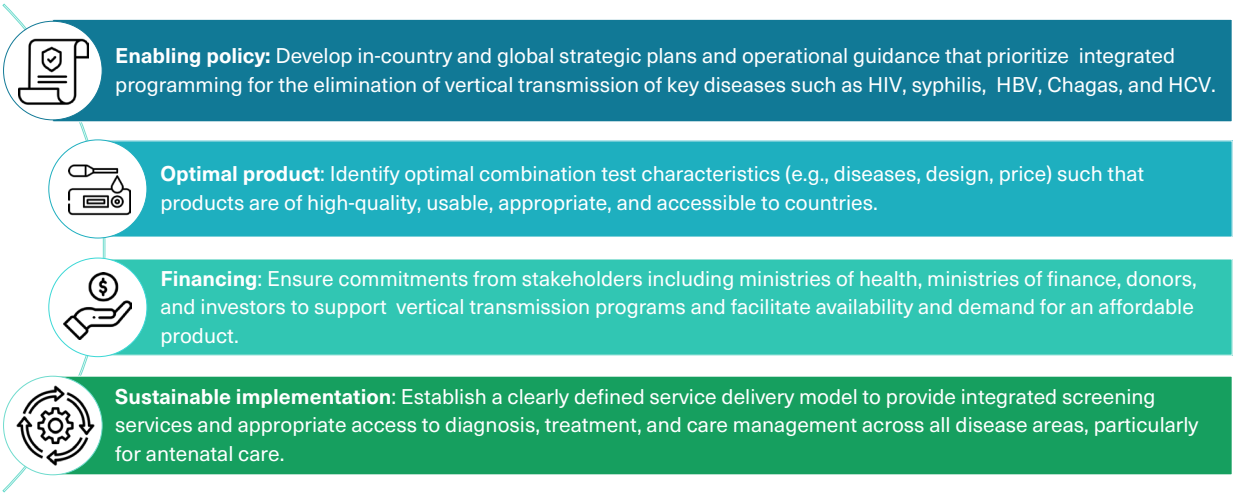


Exhibit 14: Market Landscape for Combination RDT (including HIV, syphilis, and HBV)

Product	Manufacturer	Additional Diseases	Design	Price (US$)	Specimen Type	Regulatory Status
Antenatal Care Panel Test*	Abbott	Malaria (Optional)	3 strips, 1 plastic tray	NA	whole blood	CE-Mark
HIV/Syphilis/ HBV/HCV Panel Rapid Test	CTK Biotech	HCV	2 strips, 2 cassettes	1.45**	whole blood, serum, plasma	Globally released***
HIV Test Paper-TP Syphilis-HBsAg Hepatitis B-HCV Hepatitis C*	Wondfo	HCV	4 strips, 1 cassette, 1 buffer	1.50 – 2.00**	whole blood	NA****
HBsAg/HCV/HIV/ Syphilis Combo Cassette	Accubio Limited/ Orient Gene	HCV	4 strips, 1 cassette, 1 buffer	NA	whole blood, serum, plasma	CE-Mark pending

**Individual tests in the panel have received WHO PQ for the Abbott (Determine HIV Early Detect, Determine HBsAg 2) and Wondfo (OneStep HIV 1/2) products*

***Prices communicated directly by manufacturers (listed in EXW)*

****Product commercialized in select countries*

*****Product holds regulatory approvals within China (NMPA)*

As a note, the above list is a non-exhaustive list of products.

As the market expands, suppliers experienced with developing the dual HIV/syphilis RDT are in the process of developing similar products which include a test option for HBsAg. This presents an opportunity to close testing gaps for countries implementing triple elimination of diseases – HIV, syphilis, and hepatitis. Other manufacturers may be developing alternative designs, like SD Bionsensor exploring one lateral flow strip with HIV, syphilis, and HBsAg.

Looking Forward

There is a growing market for quality-assured HBV diagnostic products; many HBsAg diagnostics products are WHO PQ'd, and others hold notable SRA approvals. The cost of HBsAg in countries has remained consistent over the years, averaging US$1 –1.20. These prices are similar to RDT prices across other disease areas.

Although there is no WHO PQ'd HBV VL product, there are several quality-assured products in the market. The anticipated publication of the WHO PQ protocol for HBV VL presents an opportunity for suppliers to submit applications and continue to enter the market for HBV.

Despite a decline in growth in 2020 due to the COVID-19 pandemic, HBV VL sale volumes are forecasted to increase going forward. The cost of HBV VL remains a major barrier in countries that access products above GAP pricing agreements. This highlights an opportunity for new HBV VL products in the LMIC market, which will diversify the range of products available to procurers and make HBV VL more affordable.

Based on WHO guidance, HBeAg is a suitable alternative to HBV VL for determining the treatment eligibility of pregnant women. HBeAg can be less costly than HBV VL and requires less infrastructure to carry out the test. Despite this, barriers to market uptake include limited and variable evidence on test performance and limited visibility on the supplier landscape of quality-assured products.

While some countries are successfully accessing HBV treatment commodities at low prices, many LMICs continue to pay high prices for these commodities. Fragmented demand, small order sizes, lack of centralized procurement, and high OOP expenses have impacted market drivers for HBV drugs, specifically TDF and have led to high in-country prices. In five out of six countries CHAI analyzed, TDF was accessed at a higher price by HBV programs than by HIV programs. In some cases, the price accessed by the HBV program is 12 times the price accessed by the HIV program.

Centralized pooled procurement, using tendering mechanisms to get competitive pricing, and leveraging international pricing benchmarks for procurement emerged as some ways in which HBV programs can and in some cases have been able to access TDF at affordable prices.

Financing continues to be a major barrier to the introduction and growth of HBV programs globally. Countries are now expanding the scope of viral hepatitis programs initially focused on HCV, to now include HBV testing and treatment.

In addition to countries mobilizing domestic resources to support programs, countries can explore donor investments, such as GFATM, to complement programming efforts. GFATM's strategy and guidance documentation[18] for the next funding cycle 2023-2025 articulates support of HBV services among specific populations and presents a critical opportunity for countries to introduce and/or strengthen hepatitis programs. For people living with HIV and key populations[19] countries can request resources for HBV screening, diagnosis, treatment and vaccination within HIV prevention and treatment services, sexual reproductive health services and harm reduction settings. For pregnant women and breastfeeding women, GFATM is supportive of a triple elimination approach that includes HIV, syphilis and HBV screening within the antenatal care setting, confirmatory testing, and prophylaxis treatment. Countries can also explore programmatic investments to support the delivery of the hepatitis B birth dose (hepB BD) vaccine. CHAI will be publishing a Resource Toolkit on GFATM 2023-2025 Funding Opportunities for Hepatitis which provides more detail on HBV products that countries could procure using GFATM resources.

The introduction of new products, such as combination RDTs, has the potential to accelerate triple elimination efforts. As countries scale the elimination of mother-to-child transmission programs across diseases such as HIV and syphilis, they are also integrating HBV testing as part of the package of screening services. This signals potential growth in the hepatitis diagnostics market.

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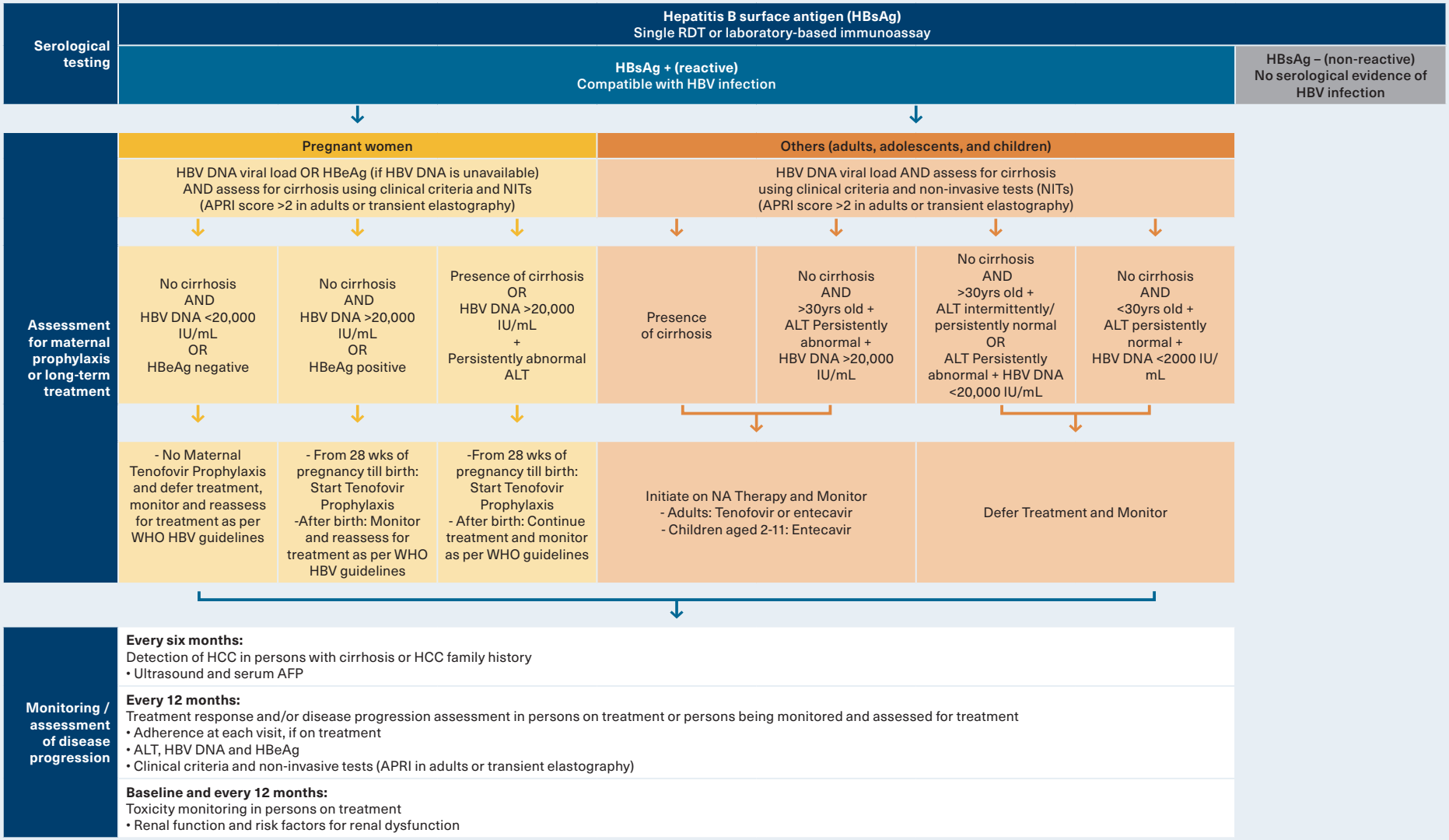
18 GFATM 2023-2028 Strategy; Global Fund (July 2022): HIV Information Note; Global Fund (July 2022) Modular Framework Handbook

19 "Key populations" include those defined by WHO as men who have sex with men, sex workers, people in prisons and other closed settings, people who inject drugs, and trans and gender diverse people

Appendix 1: Summary of WHO-recommended HBV Testing and Treatment Algorithm



Source: 1. Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection. Geneva: WHO; 2015; 2. Guidelines on Hepatitis B and C testing. Geneva: WHO; 2017; 3. Prevention of Mother-to-Child Transmission of Hepatitis B Virus: Guidelines on Antiviral Prophylaxis in Pregnancy. Geneva: WHO; 2020

Appendix 2: India Export Data Analysis Methodology

The volumes for TDF singles have been estimated using India Import Export Data. This database provides details on the volumes and prices of drugs exported from India to the rest of the world. It contains relevant details on the date of export, importer name, the product exported and the country to which it was exported, size of the export order, and the freight on board (FOB) price.

FOB prices are the prices at which the supplier exports the drug from the country. These prices do not include shipping, customs, storage, and distributor-associated costs. Usually, there are in-country costs added to the FOB price, resulting in a higher final price to the buyer.

This methodology is limited as it doesn't account for the use or export of TDF and entecavir manufactured outside India, such as Uganda. It also does not include sales or donations by originators. These limitations may lead to underestimating the volume of drugs procured across LMICs.

For more details, please refer to Appendix 6 of Hepatitis C Market Report 2021.

Appendix 3: Global Fund In-Country Price Estimate		
	Percent (%)	**Cost (USD)**
EXW price (per pack)		2.40
PSA reference fees[2]	1.50%	0.04
Freight (Ocean)[3]	8%	0.19
Insurance[4]	0.14%	0.0036
Indicative in-country price		2.63

Notes:

1. These costs are indicative and can vary from country to country. They are calculated based on actual international freight cost transactional data from the Global Fund's Pooled Procurement Mechanism over a two-year period (2020-2022) and forecasts freight, insurance and quality assurance reference costs based on current knowledge.

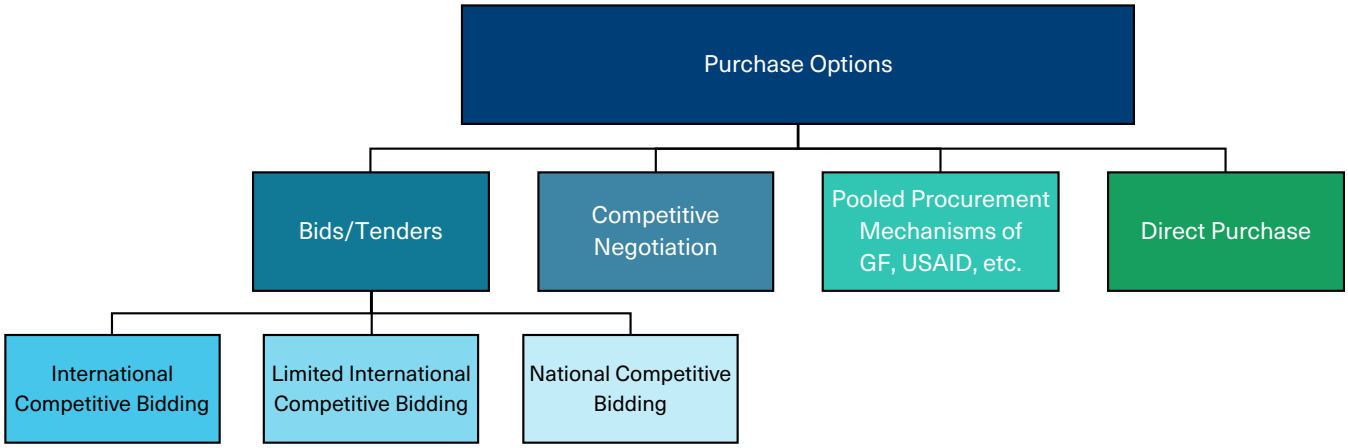
2. PSA reference fee is levied on the vendor's unit price stated on the purchase order, excluding customs duty and other taxes, transport, and insurance.

3. The GFATM recommends that almost all products should be shipped by the ocean if shipment volumes are sufficient, products' shelf-life is not too short or when low-temperature-controlled transit conditions can be met as air freight can be many times more expensive than ocean freight; 75th percentile rates were used for estimation here.

4. Indicative insurance costs are given as a proportion of product value and freight cost

Source: Global Fund

Appendix 4: TDF Purchasing Options Used by Programs And Hospitals Across LMICs



Tenders/Bidding Process: Its primary purpose is to provide the purchaser with a wide range of bids from competing suppliers. The increased pool of bidding suppliers fosters a competitive environment often leading to lower commodity prices. When a tender allows suppliers from outside the country to bid, it is known as International Competitive Bidding. If a program limits the number of bidders by allowing only pre-qualified bidders to bid, they are engaging in Limited International Competitive Bidding. Sometimes, countries may choose not to allow foreign suppliers to bid. In that case, they are utilizing National Competitive Bidding.

Competitive Negotiation: In this process, a purchaser invites a preselected number of suppliers to submit price offers, followed by negotiation to establish a better price or service arrangement. Typically, for a bid value below a certain threshold, countries allow public procurement through competitive negotiation rather than bid/tender.

Pooled Procurement Mechanisms of GF/USAID: Pooled procurement mechanisms of GF/USAID are used by programs to purchase commodities typically funded by international donors. It is important to highlight that in many cases, governments cannot utilize their budgets to purchase commodities directly through such international procurement mechanisms due to local procurement restrictions. Hence, flexible laws and national policies can allow governments to access a wider variety of procurement channels and leverage international mechanisms.

Direct Purchase: It is used for low-value products where hospitals procure healthcare commodities from a single supplier at a list price with some discount.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