

# Have a Heart, Save My Liver!

## Where is the Cure Registered?

2021

### State of Hep C Treatment Access

Eight years since the approval of the breakthrough treatment, sofosbuvir, which effectively cures hepatitis C, new direct-acting antivirals (DAAs) regimens have been approved and a variety of treatment access strategies have been used to increase countries' access.

**The fact sheet provides in-country data to further understand where the cure has been registered and to inform advocacy efforts for generating demand that could speed up registration.**

When a country is included in a voluntary licensing agreement, before drugs and pharmaceutical products can be marketed in that country, they must be **registered**—approved for use by that country's regulatory authorities. This is done before aligning new drugs in national treatment guidelines and before widely prescribing them in the health system. While drug registration policies and processes differ by country, data on the quality, safety, efficacy, among other characteristics of the drug usually must be provided to national regulatory authorities for the registration of brand/originator drugs by patent-holding corporations. Whereas some national drug regulatory authorities rely on the data from originator drug developers to approve the registration of generic versions of the drugs based on bioequivalence<sup>1</sup>, other national regulatory authorities require generic manufacturers to conduct additional, local bioequivalence studies or clinical trials, to confirm the safety and efficacy of these drugs. Another factor which delays/hinders drug registration is the fact that some countries have limited capacity and human resources to review the filed dossiers for drug registration—or, in the case of a silent disease like hep C—drug approval is less of a priority if the

disease is seen as not affecting the national population or if it is predominantly affecting stigmatized key populations.

Presently, 105 countries fall under the Gilead voluntary license for sofosbuvir and sofosbuvir-based regimens; 91 often high-burden, high- and middle-income countries are left out. Under the AbbVie voluntary license, 96 countries can access glecaprevir/pibrentasvir (G/P); more than 100 often high-burden, high- and middle-income countries are excluded. The Medicines Patent Pool (MPP) signed separate licensing agreements for daclatasvir and G/P, which allow generic manufacturers to supply these quality-assured medications. There's only one supplier, Mylan, for generic G/P and production was stalled in 2020, due to COVID-19 and limited demand for this hep C generic. The company Bristol Meyers Squibb, which held the patents on Daklinza (daclatasvir), withdrew its marketing authorization in 2020 and allowed its patents to be withdrawn or lapse, including in countries outside the voluntary license territory.<sup>2</sup>

Generics access has also expanded thanks to fierce activism to invoke legal intellectual property mechanisms, such as patent oppositions and compulsory licenses. Patent oppositions in Brazil, China<sup>3</sup>, and at the EU-level challenged patent protection on sofosbuvir, seen as not meeting patentability criteria. The EU patent decision is currently under appeal. In 2018, Malaysia granted a compulsory license on sofosbuvir, which provides royalty compensation to Gilead,<sup>4</sup> and allows for the local production or importation of generic versions of the drug. Generic competition has dramatically reduced the prices to approximately US\$60 per 12-week course, particularly in high-burden countries, such as Egypt, India, and Pakistan.<sup>5</sup> However, many high-burden upper- and middle-income countries (U/MICs) continue to face patent and pricing barriers.

These combined treatment access strategies have contributed to increased treatment uptake and encouraged countries' commitments to meeting global hepatitis targets by 2030. In 2017, the WHO estimated that 5 million (7%) of the 71 million people living with chronic HCV were treated. Since then, estimates put treatment uptake higher at 10-12 million people (14-17%)<sup>6</sup> cured with both branded and generic treatments.

According to the WHO, in 2019 there were 62 low- and middle-income countries with at least one version of sofosbuvir/daclatasvir, sofosbuvir/ledipasvir, or sofosbuvir/velpatasvir registered. According to the MPP, as of Q3 2020, where 28.7% of people living with HCV reside, [10 countries approved](#) generic sofosbuvir/daclatasvir. Of those, [4 countries](#) have sold it: India, Myanmar, Nigeria, and Uganda. Furthermore, [9 countries filed](#) the registration. Of those, [one country](#) has sold it: Vietnam. Sales in the absence of registration could occur through other procurement channels or exemptions. Combined, 52.2% of people living with HCV reside in these 19 high-burden countries.

We provide supplemental evidence, using community and in-country data, to further understand the registration gaps for DAAs. The data highlights the availability and registration of DAAs for community leaders and policy makers to reflect in their national elimination advocacy work.

## Methods

Crowd-sourced data from 82<sup>7</sup> countries, provided by 60 in-country contributors and partner organizations and captured in the free, public [mapCrowd platform](#), was collected from 19 November 2020 to 30 April 2021. We focused on 82 high-burden HCV countries, including 55 PEPFAR-funded countries.

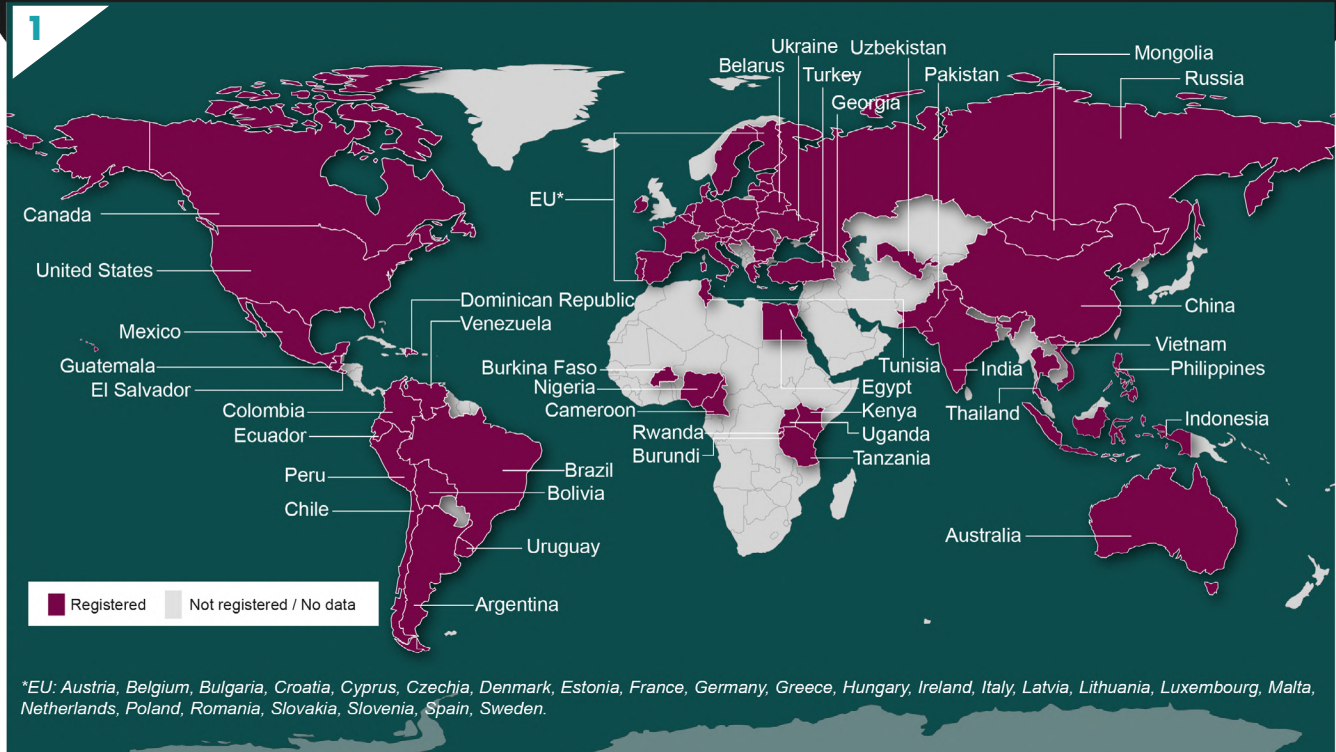
We included PEPFAR countries to inform funding campaigns that urge the inclusion of viral hepatitis and harm reduction in its funding strategy, as part of providing comprehensive care for people living with HIV.

We recognize the limitations of the crowd-sourced data which rely on where we have in-country contributors and networks. For example, Scandinavia has registered the branded Gilead DAAs but we do not have contributors there and these countries do not fall within the 82 high-burden and PEPFAR countries that we prioritized.

We focused on 7 available originator and generic DAAs: sofosbuvir and daclatasvir; and fixed-dose combinations of sofosbuvir/daclatasvir; sofosbuvir/velpatasvir; sofosbuvir/ledipasvir and glecaprevir/pibrentasvir. We chose these treatment regimens because they are part of pangenotypic regimens or mostly commonly prescribed in countries.

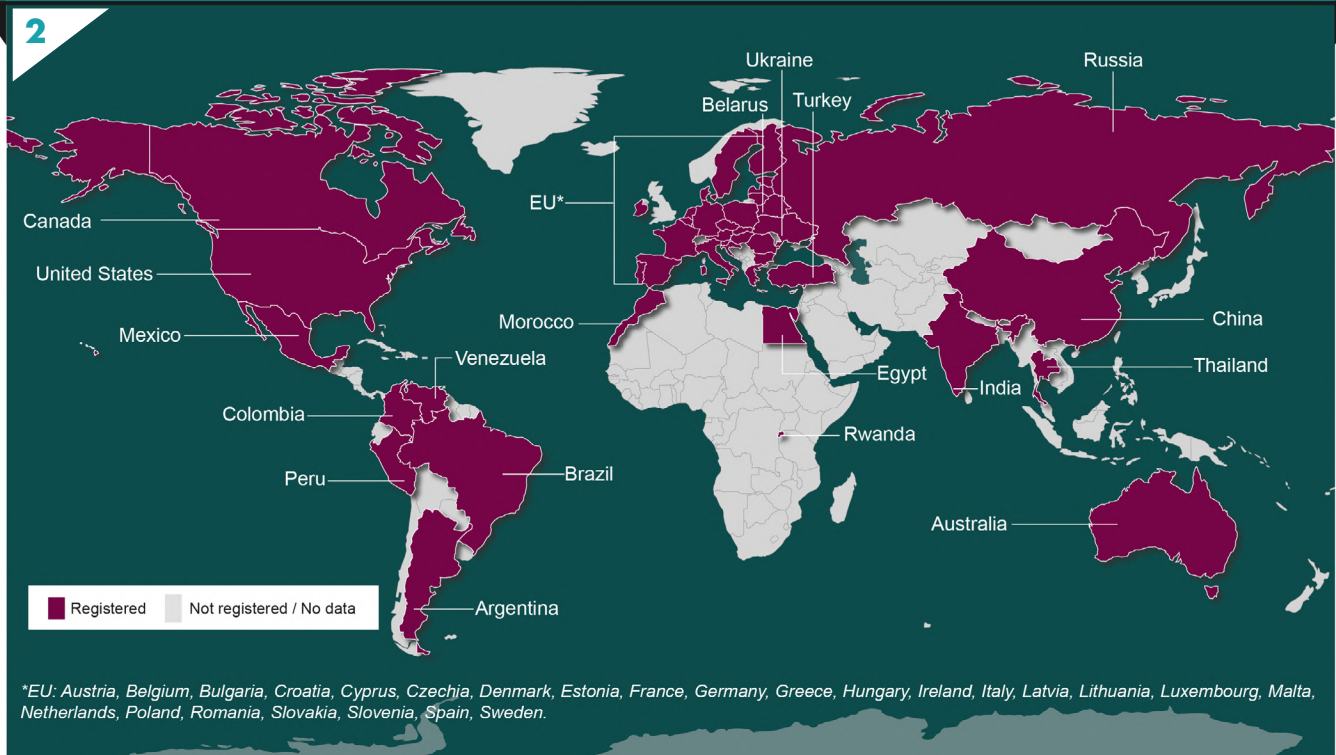


**Sovaldi Registration (40 Countries Plus EU)**



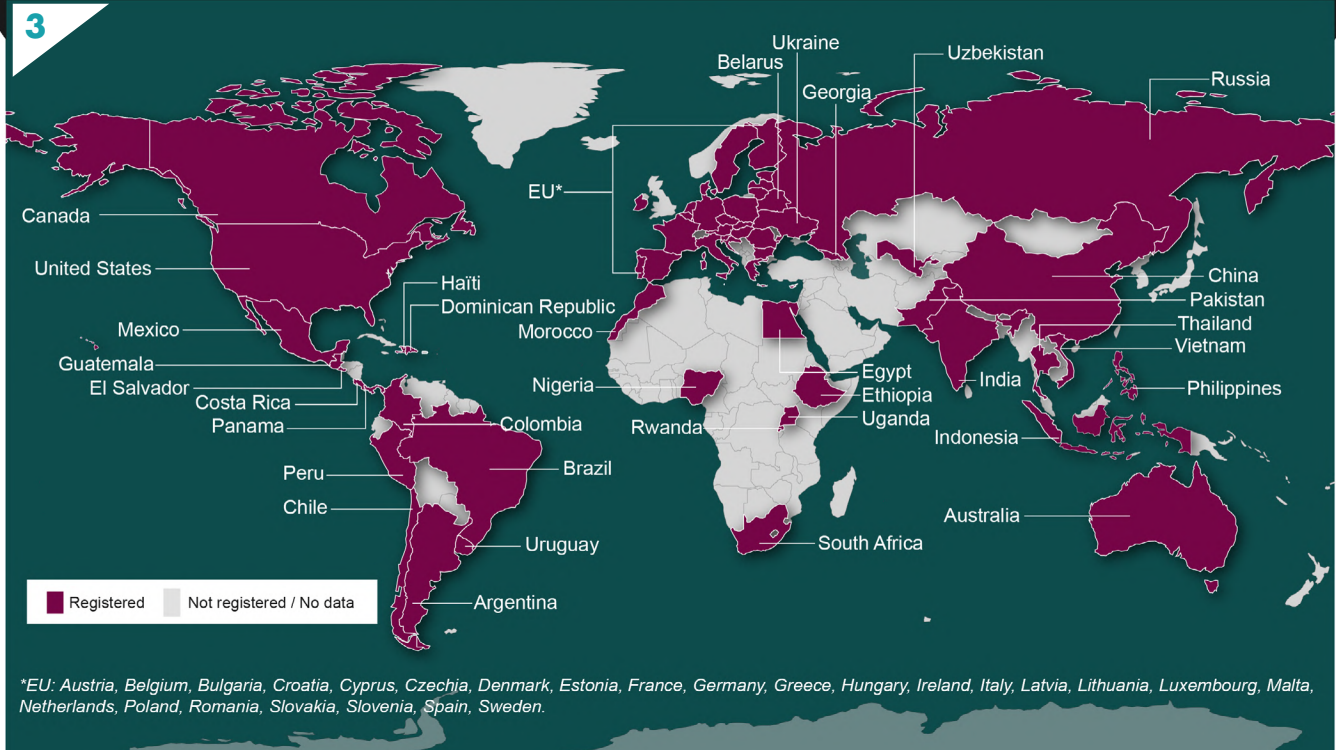
Branded sofosbuvir (Sovaldi) is registered in the EU and 40 of the total 82 (or 48.8%) high-burden and PEPFAR-funded low- and middle-income countries (LMICs) examined.

**Daklinza Registration (19 Countries)**



Branded Daclatasvir (Daklinza) is registered in the EU and 19 of the total 82 (or 23.2%) countries examined.<sup>8</sup>

**Epclusa Registration (35 Countries Plus EU)**



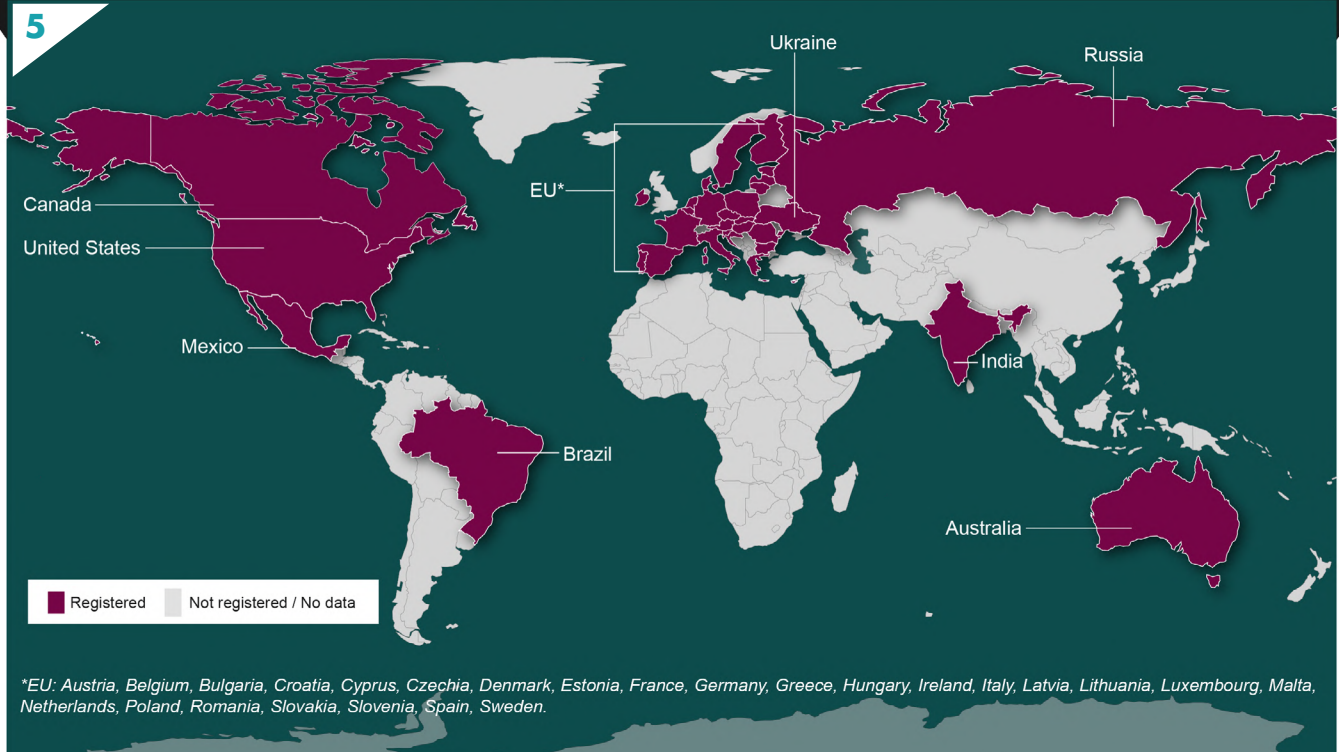
Branded Sofosbuvir/velpatasvir (Epclusa) is registered in the EU and 35 of the total 82 (or 42.6%) countries examined.

**Harvoni Registration (44 Countries Plus EU)**



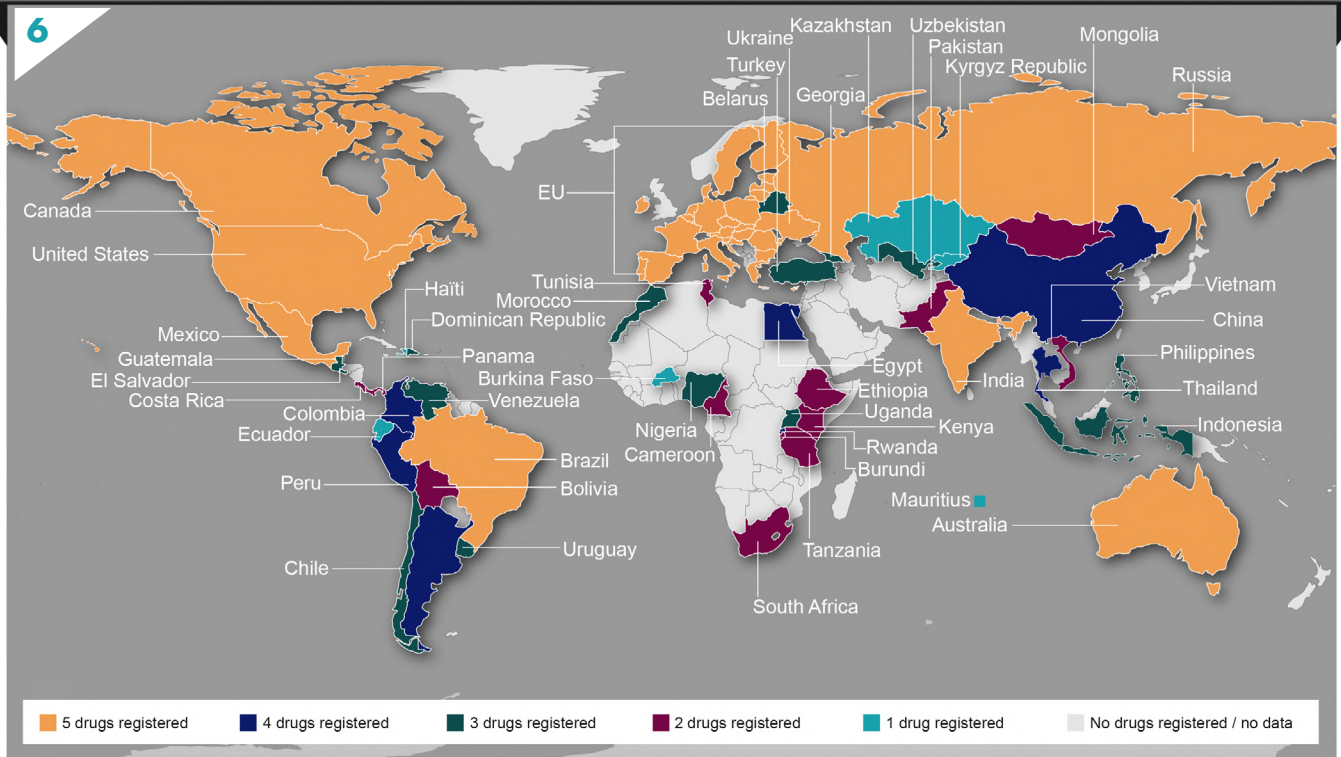
Branded Sofosbuvir/ledipasvir (Harvoni) is registered in the EU and 44 of the total 82 (or 53.6%) countries examined.

Mavyret Registration (8 Countries Plus EU)

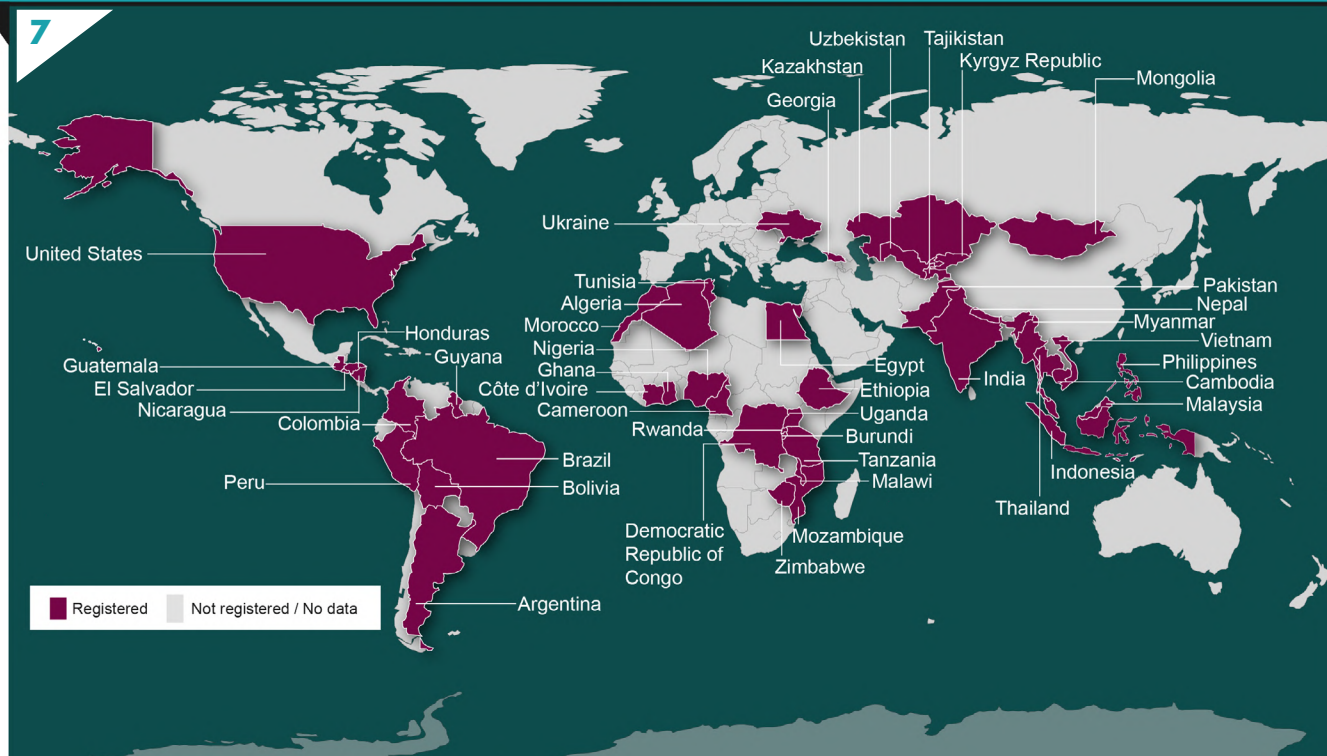


Branded G/P (Mavyret) is registered in the EU and 8 of the total 82 (or 9.8%) countries examined.

Registrations of Branded Sovaldi, Daklinza, Eplclusa, Harvoni, Mavyret

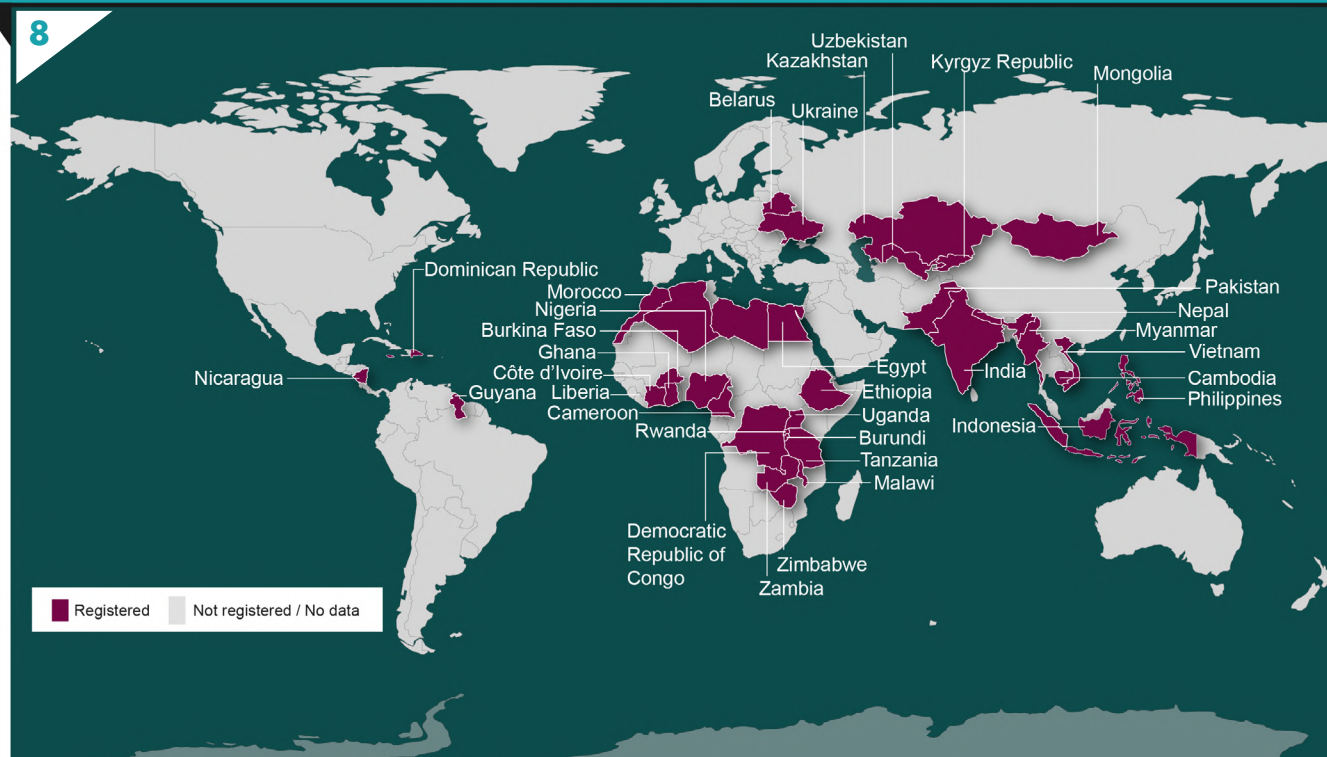


**Sofosbuvir Registration (44 Countries)**



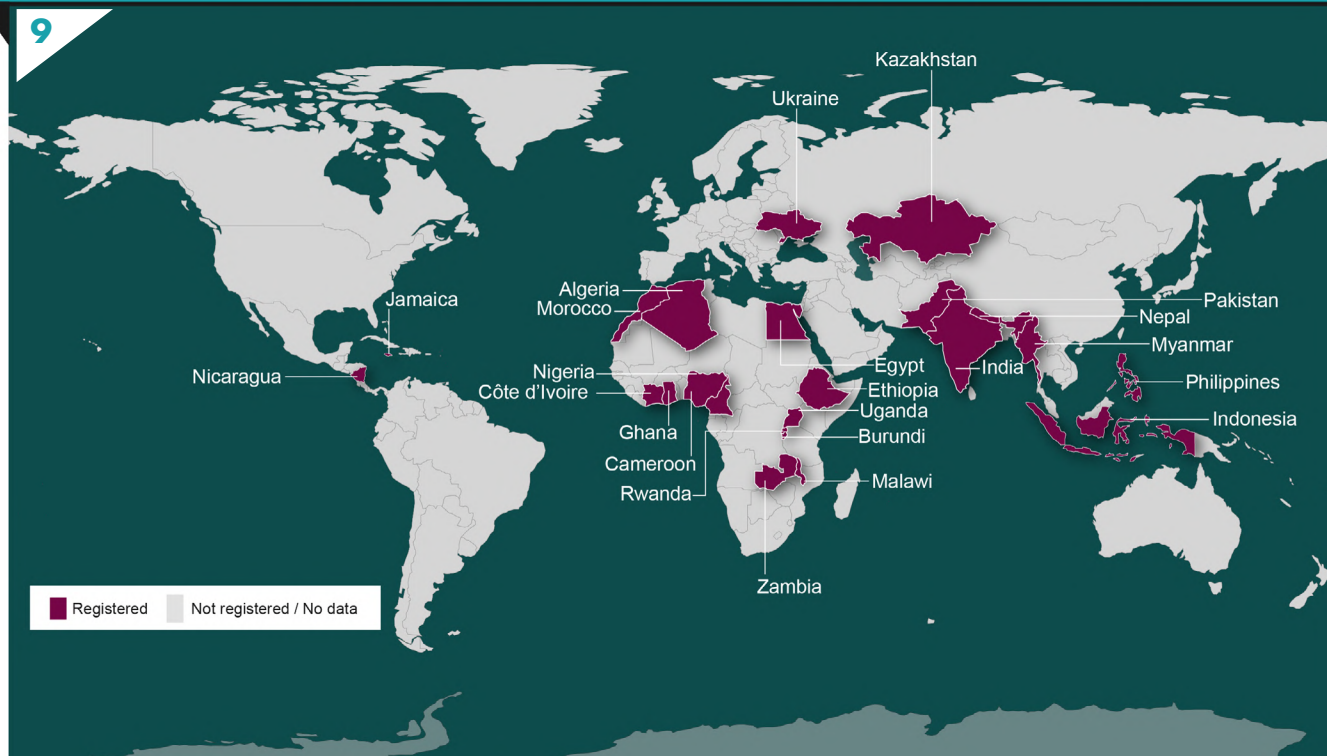
Generic sofosbuvir is registered in 44 of the total 82 (or 53.6%) high-burden and PEPFAR-funded LMICs examined.

**Daclatasvir Registration (34 Countries)**



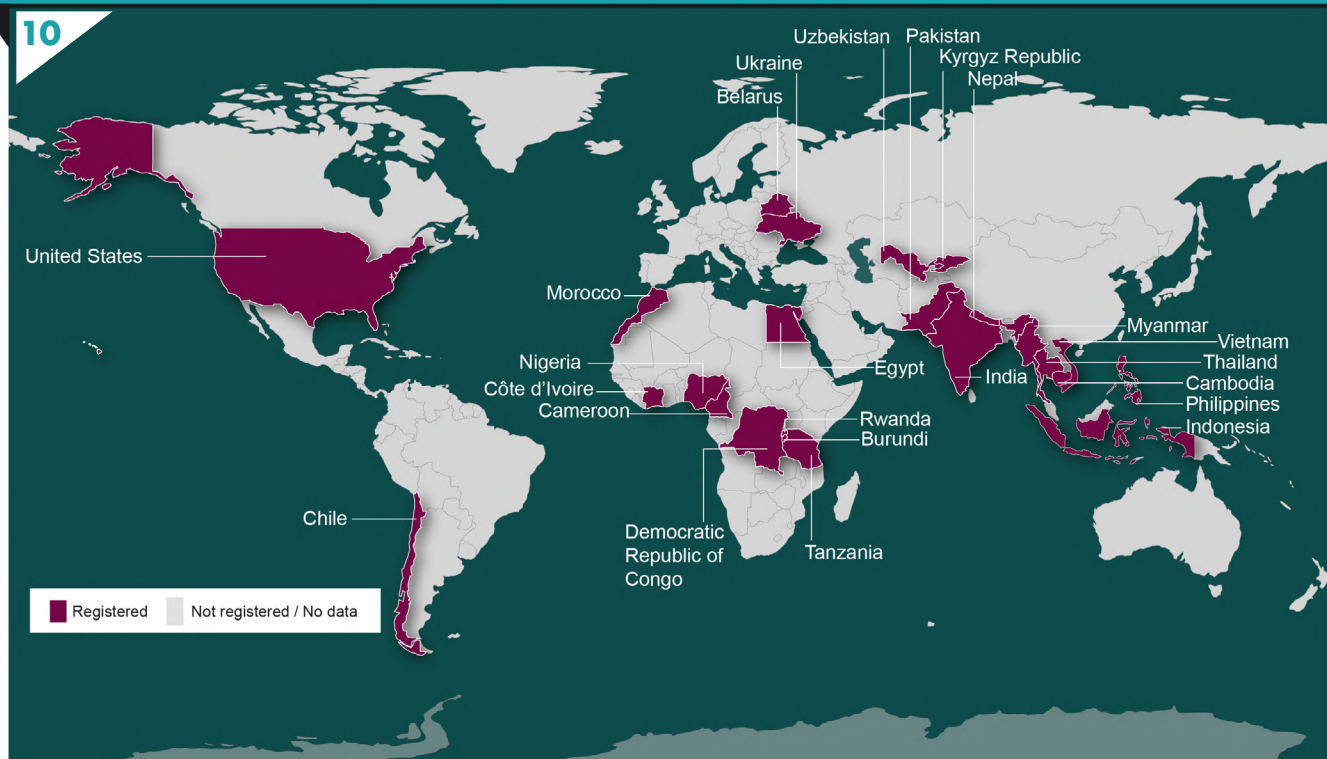
Generic daclatasvir is registered in 34 of the total 82 (or 41.5%) countries examined.

Sofosbuvir/Daclatasvir Fixed-dose Combination Registration (23 Countries)



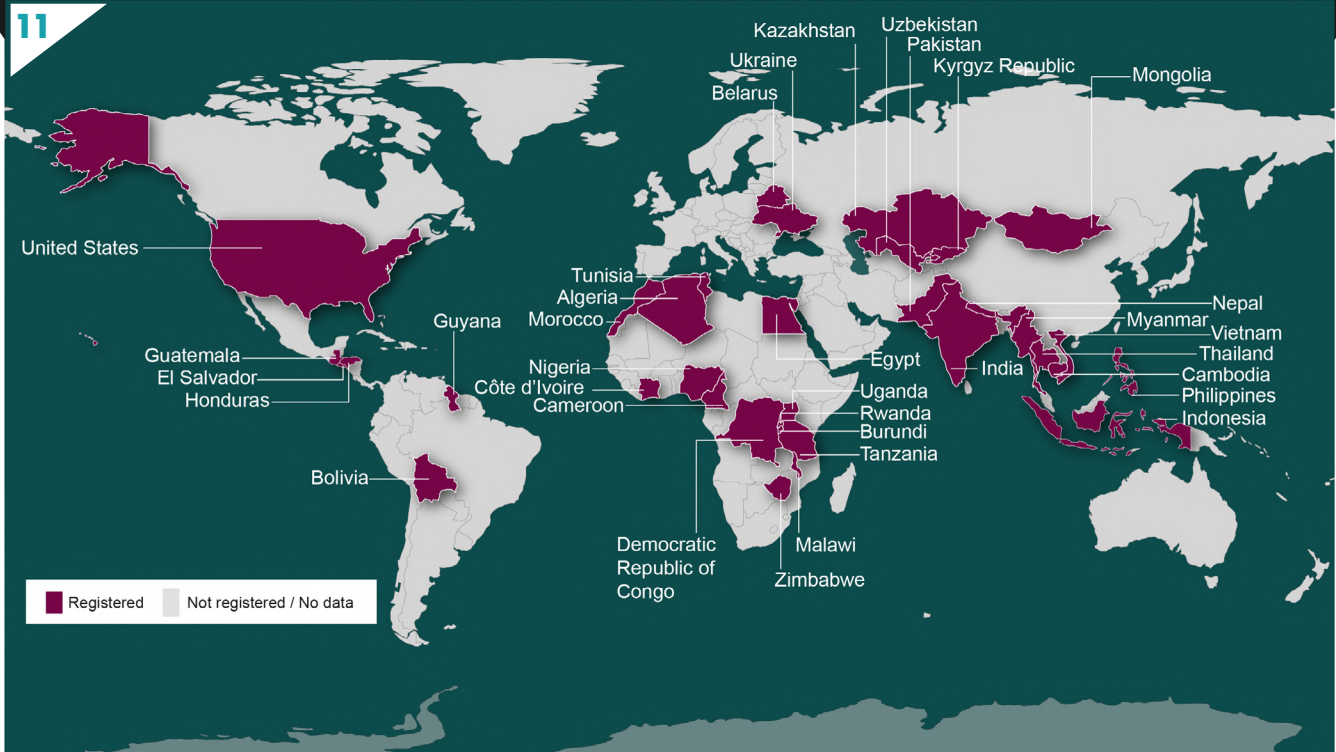
Generic sofosbuvir/daclatasvir fixed-dose combination is registered in 23 of the total 82 (or 28%) countries examined.

Sofosbuvir/Velpatasvir Registration (24 Countries)



Generic sofosbuvir/velpatasvir is registered in 24 of the total 82 (or 29.3%) countries examined.

**Sofosbuvir/Ledipasvir Registration (35 Countries)**



Generic sofosbuvir/ledipasvir is registered in 35 of the total 82 (or 42.6%) countries examined.

**Glecaprevir/Pibrentasvir Registration (1 Country)**

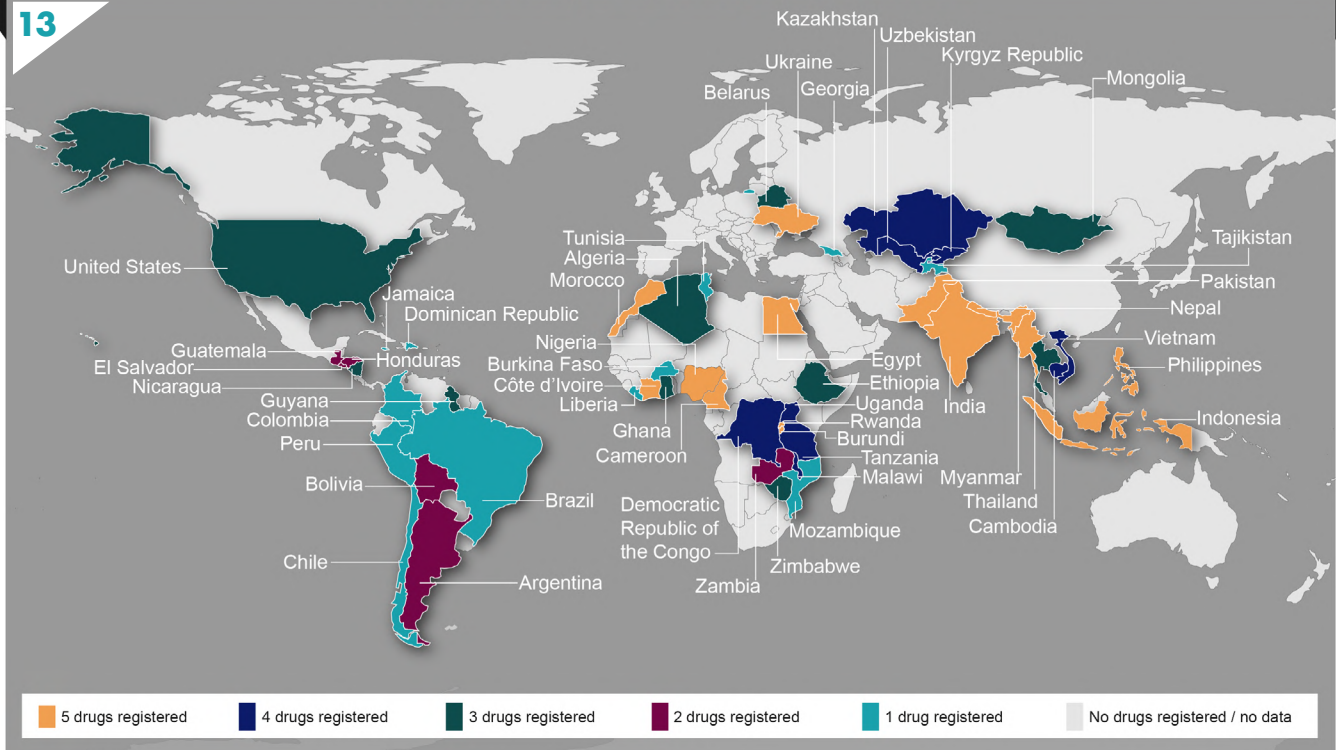


Generic glecaprevir/pibrentasvir is registered in 1 of the total 82 (or 1.2%) countries examined.



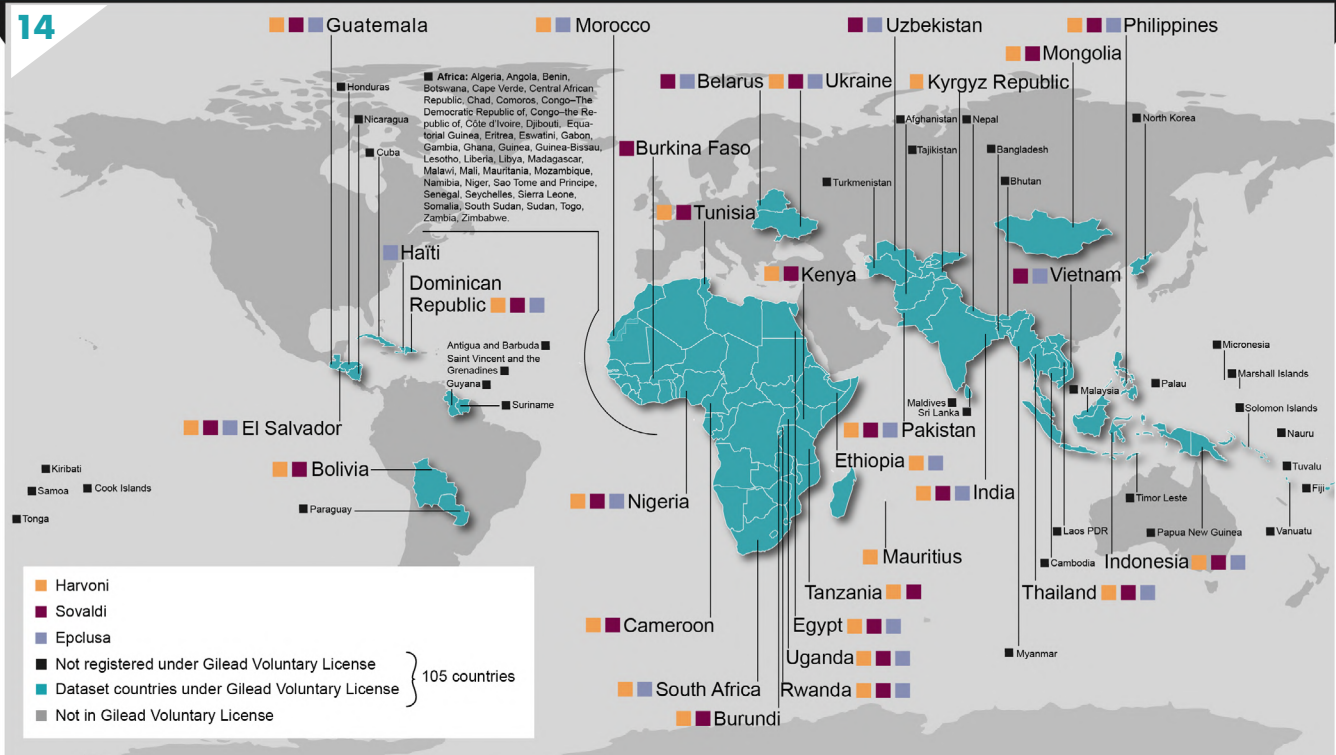
Registrations of Generic Sofosbuvir, Daclatasvir, Sofosbuvir/Daclatasvir, Sofosbuvir/Velpatasvir, Sofosbuvir/Ledipasvir, Glecaprevir/Pibrentasvir

13



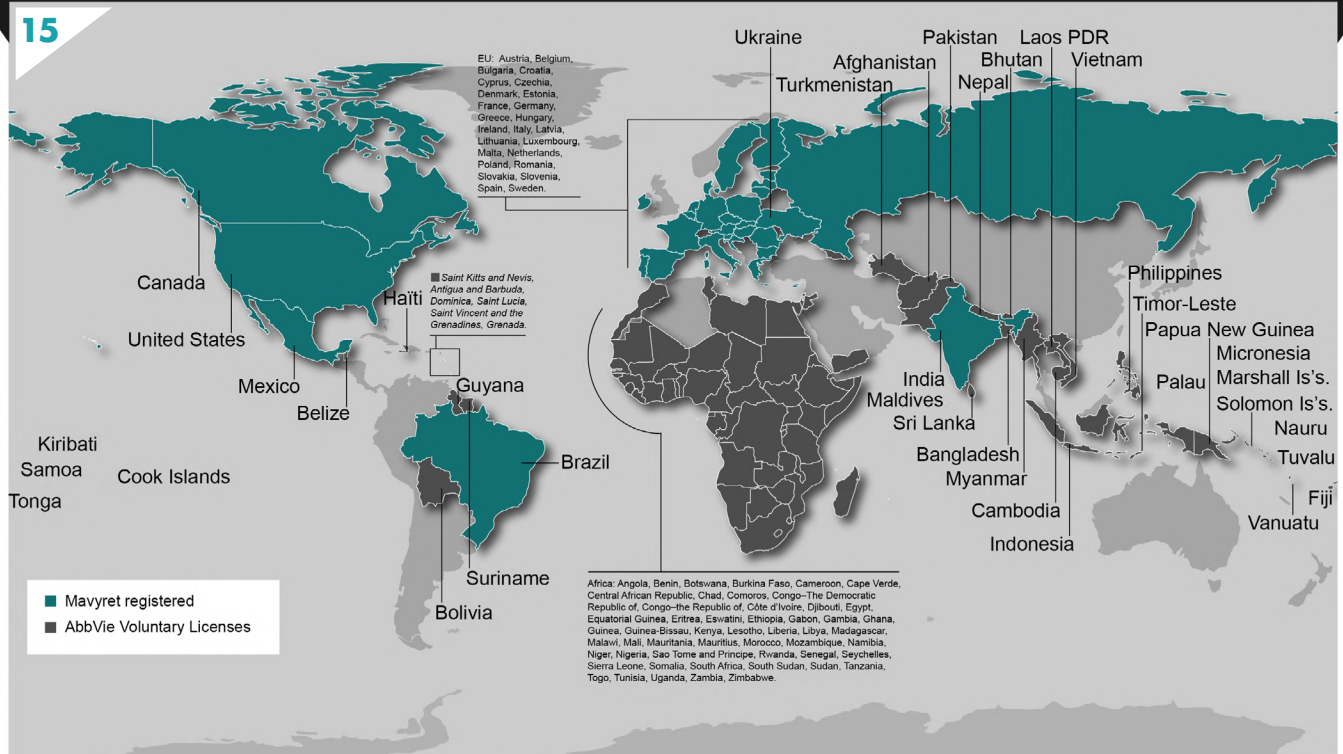
Registration of Branded Sofosbuvir-based DAAs Under Gilead's Voluntary Licenses

14



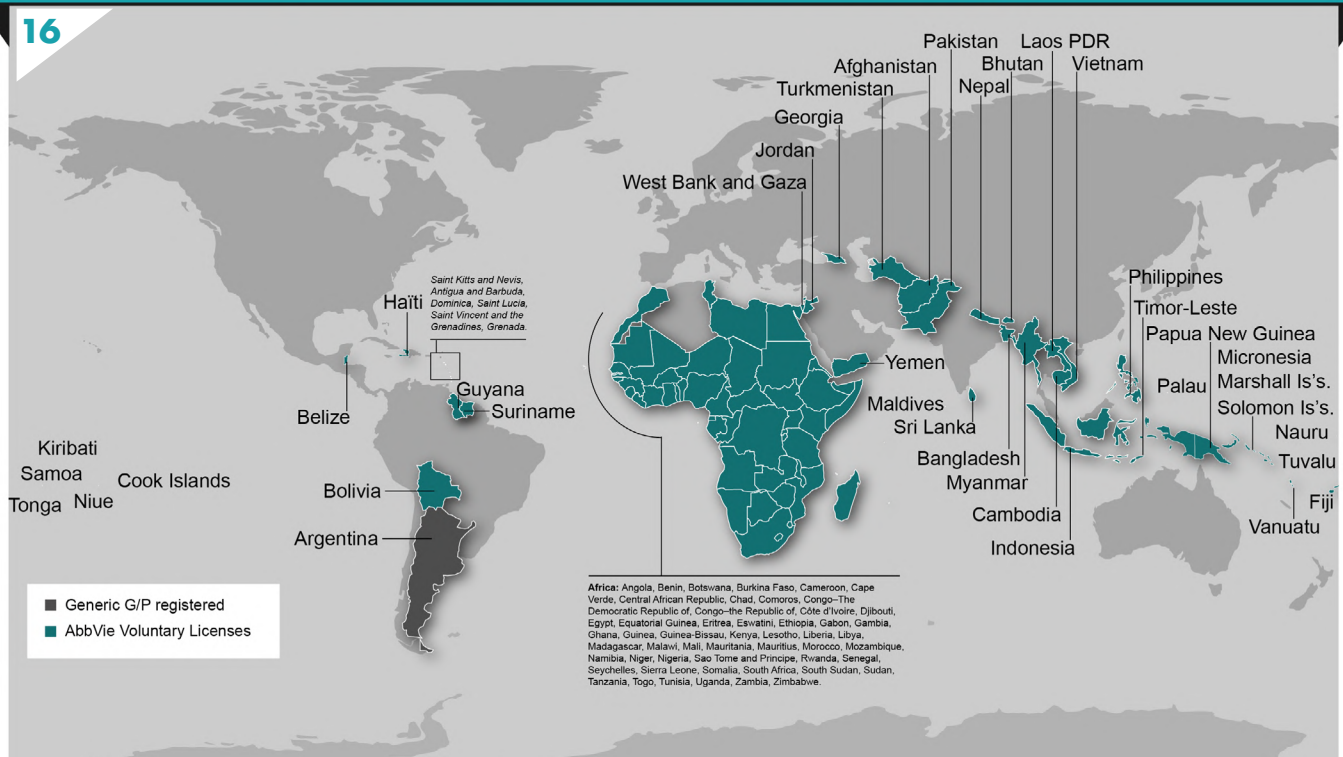
Includes Harvoni, Sovaldi, and Eplusa (105 countries).

Registration of Branded Mavyret Under AbbVie's Voluntary License



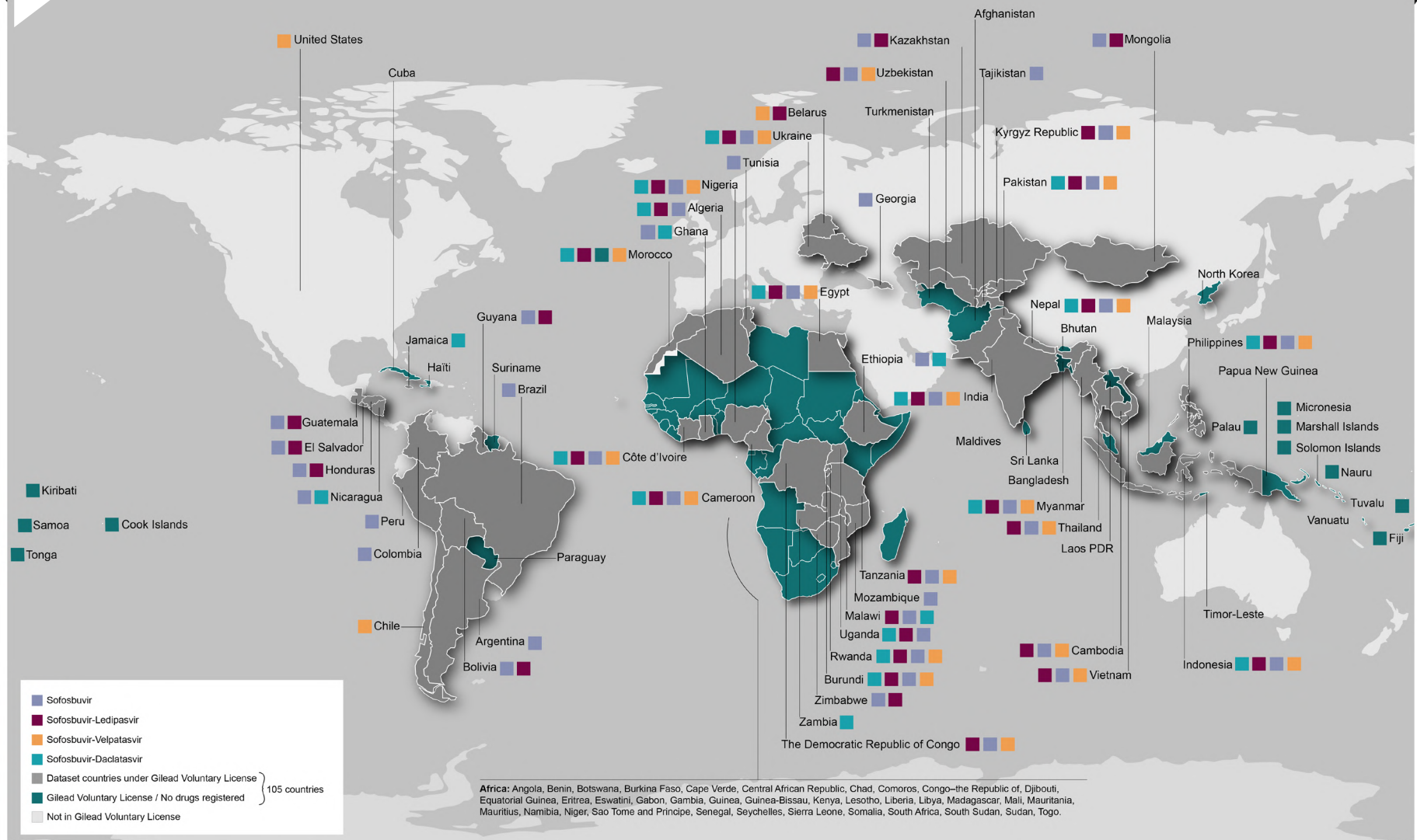
Of the 82 countries we examined, there are no countries that registered branded Mavyret out of the 96 countries under the AbbVie voluntary license.

Registration of Generic Mavyret Under AbbVie's Voluntary License



Registration of Generic Sofosbuvir-based DAAs Under Gilead's Voluntary Licenses

17



There are 27 countries where generic sofosbuvir-based DAAs are registered out of 105 countries in the Gilead voluntary licenses.

To ensure generic pangenotypic DAA options, registration should be sped up in Middle East and North Africa (e.g., Iraq, Tunisia), southern, western and eastern African countries (e.g., Burkina Faso, Senegal, Zambia) and Latin America (e.g., Ecuador, Guatemala) countries.

## Demands

We hope that by providing details on the DAA registration gaps we can hone advocacy efforts in countries that are missing treatment—particularly generic pangenotypic—options. By summarizing the registration gaps, we hope we can encourage in-country advocates to further explore the bottlenecks, from both industry and government sides, and strategize best treatment access strategies and practices to overcome them.

## We demand governments:

- Through regulatory agencies, to speed up the approvals of pending filings;
- Optimize the availability of WHO prequalified and high-quality generic DAAs, with goals to expand generic pangenotypic options;
- Through procurement agencies, pool procurement of DAAs with COVID-19, HIV, TB, and malaria medications relevant to the national epidemiological profile;
- Apply harmonized registration procedures, such as through the WHO Collaborative Registration Procedure; and
- Leverage HIV, reproductive/sexual health, and harm reduction infrastructure and funding; COVID disrupted programs and reappropriated funding, staff, and resources. Due to the lack of global HCV funding, it is possible to include HCV in the Global Fund and PEPFAR country proposals. Proposals can be framed as part of meeting the needs of people coinfecting with HIV and viral hepatitis, and as part of providing wraparound services for people using HIV, reproductive/sexual health, and harm reduction services.



## Other sources

Clinton Health Access Initiative. Hepatitis C Market Report. Boston, MA: CHAI; 2020 May 26. [https://3cdmh310dov3470e6x160esb-wpengine.netdna-ssl.com/wp-content/uploads/2020/05/Hepatitis-C-Market-Report\\_Issue-I\\_Web.pdf](https://3cdmh310dov3470e6x160esb-wpengine.netdna-ssl.com/wp-content/uploads/2020/05/Hepatitis-C-Market-Report_Issue-I_Web.pdf)

Emails with: International Treatment Preparedness Coalition, Latin America Community Advisory Board, and Treatment Action Group. Personal correspondence. 2021 March 16-24. mapCrowd database [Internet]. New York (NY): mapCrowd; 2021 [cited 2021 April 30]. Available from: <https://mapcrowd.org/>

Gilead (Press release). Chronic Hepatitis C Treatment Expansion: Generic Manufacturing for Developing Countries. 15 September 2014. [cited 2021 April 30]. Available from: <https://www.gilead.com/~media/Files/pdfs/other/HCV%20Generic%20Agreement%20Fast%20Facts%20102214.pdf>

Medicines Patent Pool [https://medicinespatentpool.org/uploads/2021/04/MPP\\_DAC\\_licence\\_implementation\\_update\\_April\\_2021.pdf](https://medicinespatentpool.org/uploads/2021/04/MPP_DAC_licence_implementation_update_April_2021.pdf)

Medicines Patent Pool. MPP-AbbVie HCV Form Sublicense Agreement. 2019 June [cited 2021 April 30]. Available from: <https://medicinespatentpool.org/uploads/2020/04/MPP-AbbVie-HCV-Form-Sublicense-Agreement-June-2019.pdf>

World Health Organization. Accelerating Access to Hepatitis C Diagnostics and Treatment: Overcoming Barriers in Low-and Middle-Income Countries. Geneva: WHO; 2021 January 21. <https://www.who.int/publications/i/item/9789240019003%20>

<sup>1</sup> This means they must contain the same active pharmaceutical ingredients, route of administration (e.g., oral), formulation (e.g., capsule or tablet), dosing (e.g., once-daily), and rate of absorption.

<sup>2</sup> Medicines Patent Pool (Press release). Affordable versions of hepatitis C treatment daclatasvir soon available in additional countries. 16 March 2021. Available from: <https://medicinespatentpool.org/news-publications-post/affordable-versions-of-hepatitis-c-medicine-daclatasvir-soon-available-in-additional-countries/>.

<sup>3</sup> Following the patent opposition in China, only some of the patent claims were withdrawn, hence, it is unclear to the extent which generic sofosbuvir is available. Generic sofosbuvir is being used for research purposes and there are several generic combinations under investigation, for domestic use only.

<sup>4</sup> Generic sofosbuvir is available in Malaysia but Malaysia is not included in our scope of countries.

<sup>5</sup> For more detailed pricing by country, see World Health Organization. Accelerating Access to Hepatitis C Diagnostics and Treatment: Overcoming Barriers in Low-and Middle-Income Countries Global Progress Report. Geneva: World Health Organization; 2021 January 21. <https://www.who.int/publications/i/item/9789240019003>.

<sup>6</sup> Emails with: Drugs for Neglected Diseases initiative; HCV Partnership data as of 2021 April 30.

<sup>7</sup> The list of countries in our data set are: Algeria, Angola, Argentina, Australia, Barbados, Belarus, Bolivia, Botswana, Brazil, Burkina Faso, Burundi, Cambodia, Cameroon, Canada, Chile, China, Colombia, Congo–Democratic Republic of, Costa Rica, Cote d’Ivoire, Dominican Republic, Ecuador, Egypt, El Salvador, Eswatini, Ethiopia, Georgia, Ghana, Guatemala, Guyana, Haiti, Honduras, India, Indonesia, Jamaica, Kazakhstan, Kenya, Kyrgyz Republic, Lao PDR, Lesotho, Liberia, Malaysia, Malawi, Mali, Mauritius, Mexico, Mongolia, Morocco, Mozambique, Myanmar, Namibia, Nepal, Nicaragua, Nigeria, Pakistan, Panama, Papua New Guinea, Paraguay, Peru, Philippines, Russia, Rwanda, Senegal, Sierra Leone, South Africa, South Sudan, Suriname, Tajikistan, Tanzania, Thailand, Togo, Trinidad and Tobago, Tunisia, Turkey, Uganda, Ukraine, United States, Uruguay, Uzbekistan, Venezuela, Vietnam, Zambia, Zimbabwe, and the EU.

<sup>8</sup> Please note that the company Bristol Meyers Squibb, which held the patents on Daklinza (daclatasvir), withdrew its marketing authorization in 2020 and allowed its patents to be withdrawn or lapse, including in countries outside the voluntary license territory. This could broaden access to daclatasvir for eligible countries.