

SOFOSBUVIR TURNS 5 YEARS OLD: THE VAST MAJORITY OF PEOPLE WITH CHRONIC HEPATITIS C STILL HAVE NOT BEEN TREATED

FACT SHEET

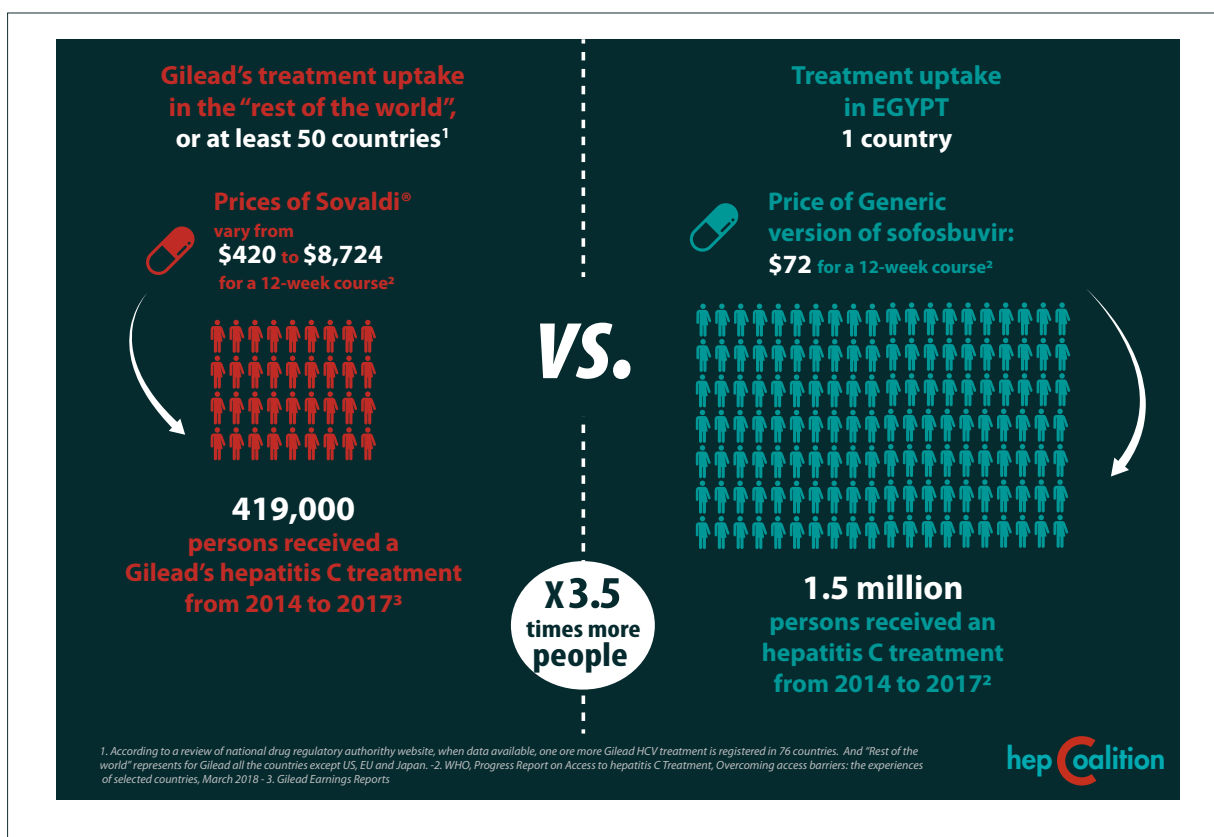


Five years after the U.S. Food and Drug Administration approved the breakthrough hepatitis C cure, sofosbuvir, as an all oral, effective 12-week treatment, the vast majority of the estimated 71 million living with the blood-borne infectious disease have yet to be treated. Pricing barriers in high- and middle-income countries, registration delays in many low- and middle-income countries, patent monopolies on sofosbuvir—challenged as unmerited and not meeting patentability criteria—and the privatization of sofosbuvir after receiving public funds from taxpayers are part of the scandalous factors that impede treatment access and deny patients' treatments, particularly among patients lacking health coverage and people from high-risk, marginalized communities, including people who use drugs.

GILEAD SHAREHOLDERS CASHING IN ON THE HEPATITIS C EPIDEMIC: LOW TREATMENT UPTAKE, STAGGERING NEW INFECTIONS, HIGH MORTALITY DERAIL EFFORTS TO MEET WHO 2030 TARGETS

From 2013-2017, the estimated treatment starts with Gilead's direct-acting antivirals (DAAs), (assuming patients achieved sustained virological rate): **1.85 million**¹

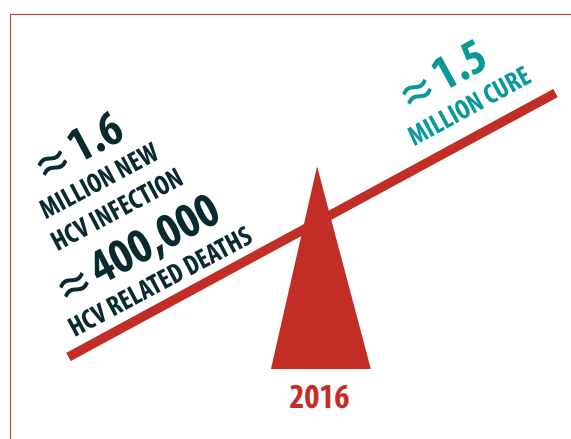
By contrast, despite the significant delay to approve Sovaldi® in high-income markets and the later marketing authorization in developing countries, from 2014-2017, treatment starts with generic versions of the same direct-acting antivirals reached **around 2 million people**². For instance, in Egypt: **1.5 million** received an HCV treatment for the same period.³



Estimated new infections from 2014 to 2018: 8 million (1.6 million per year) compared with **1.85 million** people living with chronic HCV infection who started treatment with Gilead DAAs since December 2013. **23% of new infections are estimated in people who inject drugs.**⁴

Estimated total number of HCV-related deaths (mortality rate) since 2014: 2 million (400,000 per year), of which **33% are people who inject drugs.**

We need to treat 5 million people every year worldwide to achieve HCV elimination by 2030.⁵



1. Gilead earning Reports

2. Data on generics treatment uptake from countries like India and Thailand has not been reported. Since 2014 at least a couple hundred thousand patients have been treated with generic DAAs, including through buyers' clubs, but this data is also not systematically reported. Estimates of treatment uptake with generic versions of sofosbuvir were compiled from mapCrowd data, personal communication, and Table 4.2. Summary of DAA procurement situation in countries, mid-2017 from World Health Organization, Progress report on access to hepatitis C treatment. Overcoming access barriers: the experiences of selected countries. 2018 March. Available from: <http://apps.who.int/iris/bitstream/handle/10665/260445/WHO-CDS-HIV-18.4-eng.pdf?sequence=1> (Accessed 2018 November 29).

3. World Health Organization, Progress report on access to hepatitis C treatment. Overcoming access barriers: the experiences of selected countries. 2018 March. Available from: <http://apps.who.int/iris/bitstream/handle/10665/260445/WHO-CDS-HIV-18.4-eng.pdf?sequence=1> (Accessed 2018 November 29)

4. World Health Organization. Global hepatitis C report. 2017 April. Available from: <http://apps.who.int/iris/bitstream/handle/10665/255016/9789241565455-eng.pdf?jsessionid=E0893DE4445E55C02C42C9CBD3BC74F0?sequence=1> (Accessed 2018 November 29).

5. Hill A. Prices versus costs of medicines in the WHO Essential Medicines List. Presentation at WHO, Geneva. 2018 February 26. Available from: <http://www.who.int/phi/1-AndrewHill.pdf> (Accessed 2018 November 29)

GILEAD'S MIND-BOGGLING PROFITS

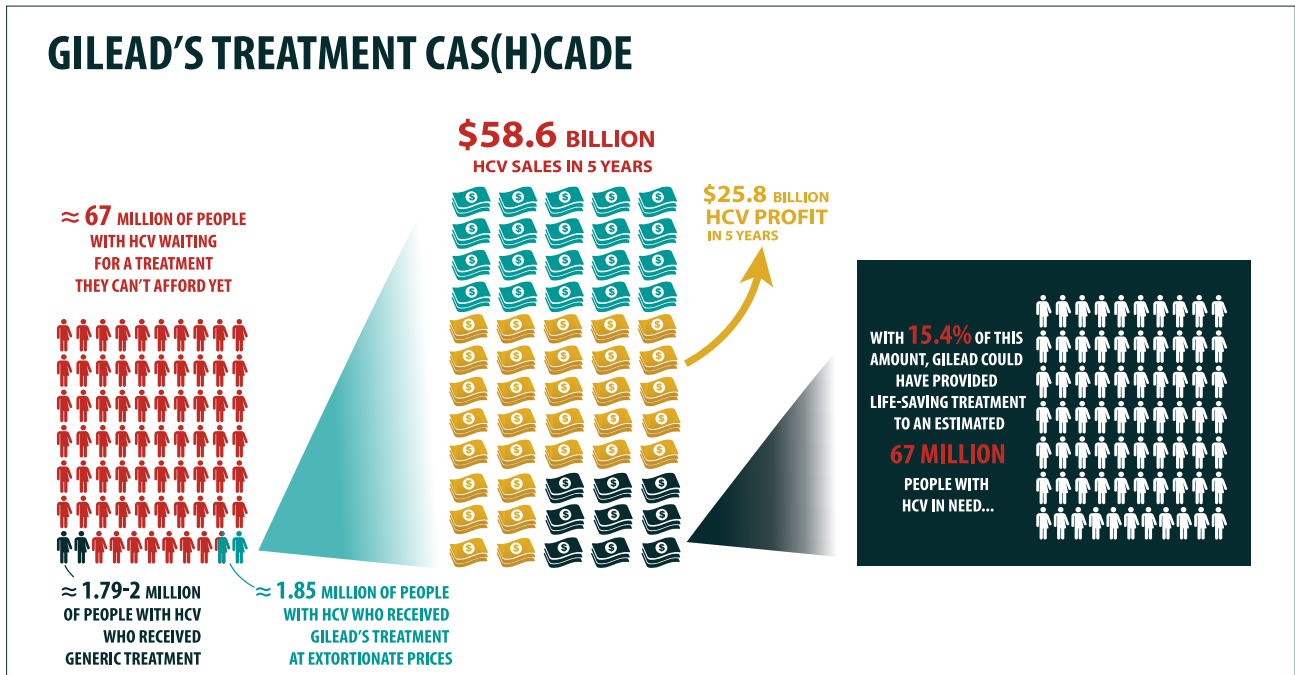
Gilead earnings Q4 2013 to Q3 2018 on HCV sales: **US\$58.6 billion**⁶

The US, Europe, and Japan account for more than 80% of the total HCV sales versus less than 20% for the “rest of the world”.

Estimated profit in 5 years from HCV products: **US\$25.8 billions**⁷

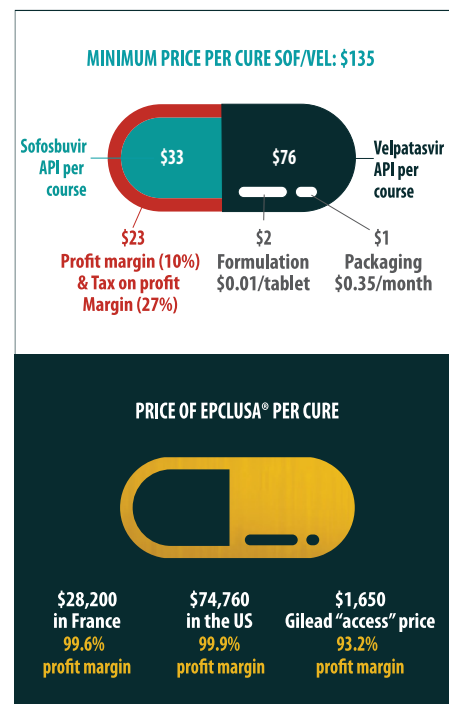
Sales of all pharmaceutical corporations' HCV DAAs combined (Q1 2014- Q3 2018): **US\$77 billion**
—of which 75% are from Gilead sales

With Gilead's HCV profits (US\$25.8 billion) we could treat (at the US\$135 generic price of sofosbuvir/velpatasvir): **all 71 million people, with over US\$16 billion in profits left over.**



COST, PRICE & PROFIT MARGIN

The enormous profits show how medicine prices are artificially constructed and not related to actual drug development costs. In general, cost refers to the amount paid to produce a medicine and represents the sum of the value of the inputs in production, including active pharmaceutical ingredients (API), drug formulation, packaging, labor, capital, and enterprise. Price refers to the money that patients or payors must pay to purchase the medicine. Andrew Hill and researchers at the University of Liverpool calculated the minimum price of a 12-week course of the hepatitis C direct-acting antivirals, according to the cost of production, plus a profit margin of 10% and a 27% tax on the profit margin. For instance, the cost of production of a combination of sofosbuvir/velpatasvir is calculated at US\$112 and its minimum price US\$135⁸. However, Gilead's list price of US\$74,760 for 12-week course of sofosbuvir/velpatasvir (Epclusa®) amounts to a profit margin of 99.9%.



6. Gilead earnings reports.

7. Gilead's profit margin was calculated with the ratio of net income attributable to Gilead divided by the total revenue per year and applied to HCV product sales per year. Yearly figures are coming from Gilead's annual earnings reports.

8. Hill A et al.: Minimum prices of generic hepatitis C direct acting antivirals fall below US\$50 per person cured. Poster presented at: HIV Drug Therapy, Glasgow, Scotland 2018 October 28-31. Available from: <http://www.hivglasgow.org/wp-content/uploads/2018/02/O323.pdf> (Accessed 2018 November 26).

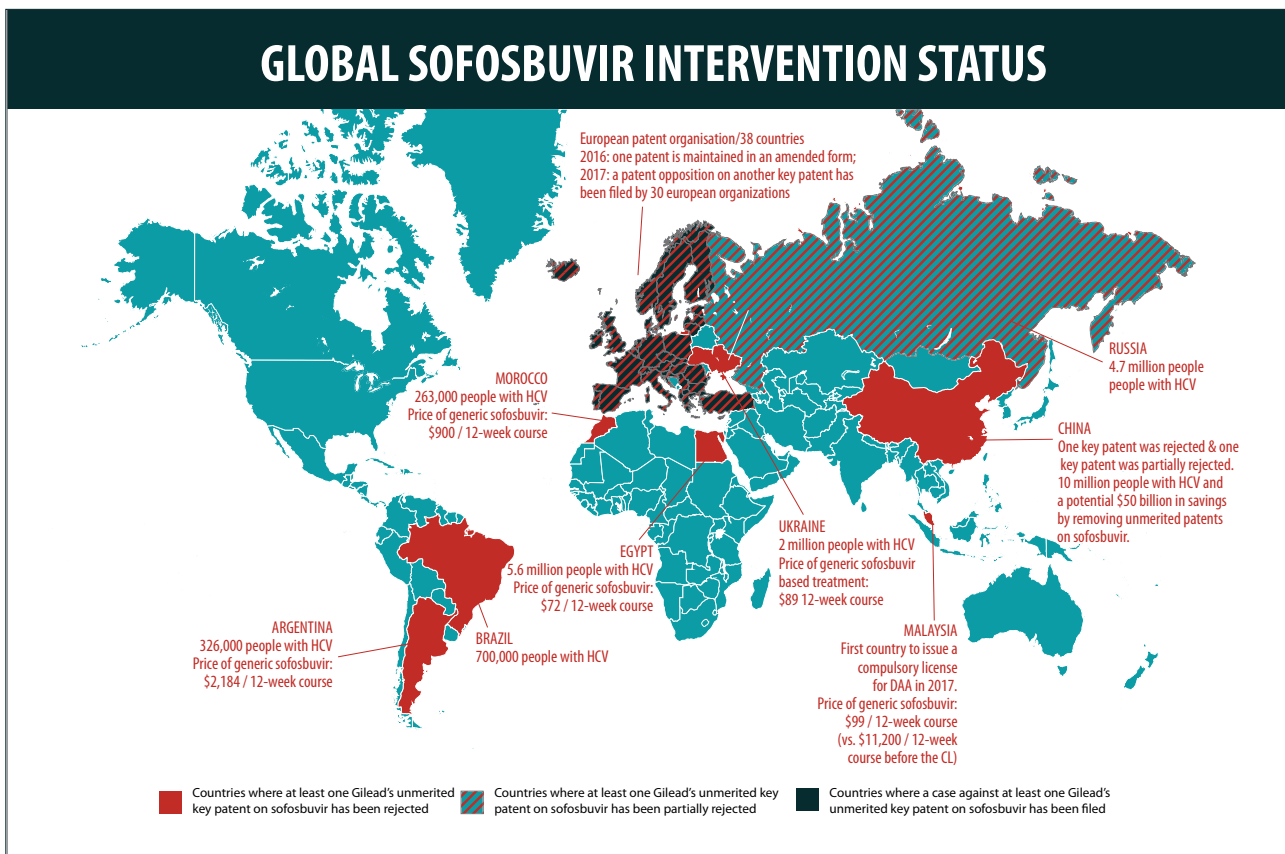
GILEAD'S UNMERITED PATENTS

High prices set by Gilead could be locked in for 20+ years, under their patent protection and data exclusivity for sofosbuvir. To counter this, Gilead's patents and patent applications on sofosbuvir and other sofosbuvir-based direct-acting antivirals have been filed and appealed, citing old science and not meeting patentability criteria. Legal and scientific experts argue that the patents on sofosbuvir do not merit patent protection according to national patent laws in many countries. Pharmaceutical corporations also file secondary patent applications on DAAs, which often lack merit for patentability, which need to be challenged to promote generic competition and wider treatment access. For example, in 2013, the Delhi Network of Positive People (DNP+) and the Initiative for Medicines, Access and Knowledge (I-MAK) filed the first patent challenge for sofosbuvir in India, which was upheld.

Drug	U.S. Patent Expiration	E.U. Patent Expiration
Sovaldi® (sofosbuvir)	2029	2028
Harvoni® (sofosbuvir/ledipasvir)	2030	2030
Epclusa® (sofosbuvir/velpatasvir)	2032	2032
Vosevi® (sofosbuvir/velpatasvir/voxilaprevir)	2033	?

Médecins Sans Frontières (MSF) along with other civil society organizations and patient groups have recently appealed against the decision by the European Patent Office for rejecting the coalition's opposition against the patent granted to Gilead for sofosbuvir. The extremely high prices in Europe of newer hepatitis C medicines has led civil society organizations to investigate and subsequently challenge the monopoly status and legitimacy of such patents. Rejection of the patent will be a major step toward allowing the production and importation of affordable generic versions of sofosbuvir in Europe and protecting health systems across Europe from illegitimate financial burden due to extortionate corporate pricing of this drug.

Countries that uphold the patents on sofosbuvir will not have generic options until the patents expire—in 11-15 years, or whereby an estimated 4.4-6 million people could die from lack of access to affordable treatment.



Sources of the map: <http://www.i-mak.org> ; <https://www.patentoppositions.org/en/drugs/sofosbuvir> ; <http://www.medspal.org/?keywords=sofosbuvir>

GILEAD'S LICENSE ON HEPATITIS C DRUGS: A FOOL'S BARGAIN

Voluntary licenses may have limits for expanding hepatitis C treatment access. Two-thirds of people with hepatitis C live in low- and middle-income countries, which are excluded from Gilead's voluntary licenses. Voluntary licenses are legal agreements between originator pharmaceutical corporations like Gilead and generics manufacturers or third-party license management organizations, such as the Medicines Patent Pool. The licenses allow the supply of generic versions of a medicine in certain countries under a certain set of terms and conditions. Voluntary licenses often include a royalty paid to the originator—in the case of sofosbuvir the royalty varies between 4-12%. Patent-holding originator corporations determine the geographic scope of countries where generics can be produced and sold. In the case of sofosbuvir, countries such as Brazil and Russia, with a high burden of hepatitis C have been excluded from the voluntary license.

Number of countries under Gilead voluntary license: 105 countries⁹

The 105 countries included in the scope of Gilead's voluntary license is misleading because 15 are small island nations. These countries and the number of people with hepatitis C who live in them are: Antigua & Barbuda (525), Dominica (593), Fiji (16,960), Kiribati (2,020), Maldives (2,850), Nauru (256), Palau (606), Samoa (1,875), Sao Tome & Pr (17,580), Seychelles (289), Solomon Islands (9,560), St Vincent & Grenadines (1,180), Tonga (2,200), Tuvalu (220) and Vanuatu (4,060). The total estimated number of people living with HCV in these 15 countries is **60,774**—whereas almost **10 million people** with hepatitis C live in China, which Gilead has chosen to exclude from its voluntary licensing agreements.¹⁰

It is common for pharmaceutical companies to include small islands to make the scope of their voluntary licenses appear larger. People in these countries deserve the same right to health and medicines as those in any other country, and their size should not be an argument used to deny them this right; however, given the lack of compelling epidemiological data in these countries, it can be inferred that Gilead included them in part to hide the limited scope of their license.

Number of countries excluded from Gilead voluntary license: 65 countries¹¹

Drop the anti-diversion measures!

Furthermore, Gilead is using—and is also requiring generic companies that have signed the voluntary license to adopt—an anti-diversion program which exceeds the typical differential packaging and quantity control measures used for this purpose. Gilead's anti-diversion system is enforced through local distributors and pharmacies and include unethical—and burdensome—requirements: patients and treatment providers may have to disclose the name, address, and other sensitive personal information to companies not directly involved in patient care, and return each empty sofosbuvir bottle to the distributor before they can get more to complete their HCV treatment. In Georgian prescribing clinics and harm reduction sites, patients undergo videotaped direct observed treatment to ensure that prescribed patients are taking the medication and that the medicines are not re-sold. Patients with a history of injecting drug use may be deterred from completing treatment if their identities and confidentiality are compromised, particularly in a country where drug use is criminalized. These conditions violate basic standards of patient confidentiality and autonomy, and interfere with both the doctor-patient and pharmacist-patient relationships. The extra travel requirements or complex alternative pill return and re-supply systems risk interrupting patient care and may even result in default. Certain requirements—such as demonstrating proof of residence or citizenship are likely to exclude high-prevalence, marginalized populations (such as refugees and people who use and inject drugs) who may lack stable living arrangements. These requirements, individually and collectively, interfere with the the human rights to science, health and access to essential medicines codified in international and national law.

We urge Gilead to remove unethical anti-diversion requirements to ensure that they do not limit or impede patient access.



9. Voluntary licenses include mostly small countries and territories without biomedical production capacity. 101 countries were included in the original voluntary licenses in 2014. Belarus, Malaysia, Thailand, Ukraine were added in Aug 2017-Silverman E. Under pressure, Gilead expands Sovaldi licensing deal to four middle-income countries. STATnews [Internet]. 2017 August 24. Available from: <https://www.statnews.com/pharmalot/2017/08/24/gilead-sovaldi-malaysia-ukraine/> (Accessed 2018 November 29).

10. Gilead's License on Hepatitis C drugs, Sofosbuvir and Ledipasvir: a Fool's Bargain. hepCoalition. 2014 October 10. (cited 2018 November 29). Available from: <https://hepcoalition.org/advocate/advocacy-tools/article/gilead-s-license-on-hepatitis-c-drugs-sofosbuvir-and-ledipasvir-a-fool-s>

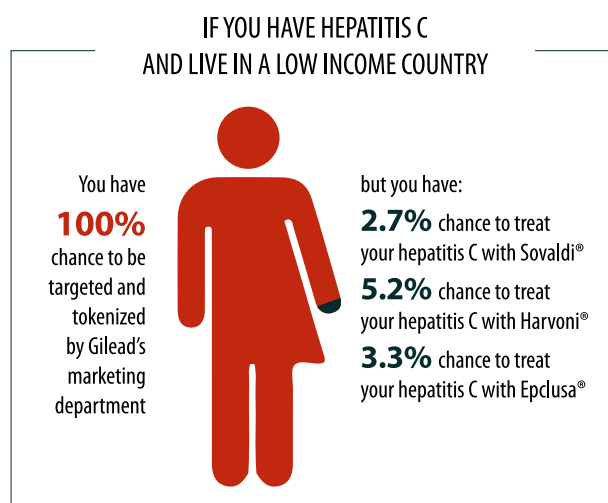
11. Médecins Sans Frontières Access Campaign. Not even close. Issue brief 6. 2016 Available from: https://msfaccess.org/sites/default/files/HepC_Issue-Brief_HEP_C_6.pdf (Accessed 2018 November 24).

GILEAD DRAGGING ITS FEET TO REGISTER?

Therefore, if you have hepatitis C and live in a low-income country, you have **100% chance** to be targeted by Gilead's marketing department, but you have **2.7% chance** to treat your hepatitis C with Sovaldi®.

Even under the voluntary license, countries encounter significant delays due to cumbersome registration processes. Before medicines can be marketed in a country, they must be approved for use by a country's regulatory authorities. If generic versions received prequalification status by the World Health Organization (WHO), national regulatory review can be simplified and sped up. However, as of February 2018, there are only three prequalified generic manufacturers of sofosbuvir by the WHO. Registration policies and processes differ by country, but data on quality, safety, efficacy, and other characteristics of pharmaceutical products usually must be provided. Some regulatory authorities accept data from trials conducted in other countries, but others require originator and generic drug producers to conduct local studies.

Generic competition to accelerate the number of people who start treatment is stalled due to Gilead's and its sub-licensees' delay or failure to register their drugs, blocking access to the cure in countries with some of the highest rates of hepatitis C.



“Gilead’s registration strategy was designed to maintain its monopoly in as many countries as possible. Gilead stopped filing dossiers for registration of sofosbuvir (SOF) once sofosbuvir/ledipasvir (SOF/LDV) was US Food and Drug Administration (FDA)- or European Medicines Agency (EMA)- approved, and halted SOF/LDV registration once sofosbuvir/velpatasvir (SOF/VEL) was US FDA- or EMA-approved.”¹²

—Médecins Sans Frontières Access Campaign

Number (%) countries where sofosbuvir-based DAAs are registered:

Sovaldi is registered at least in **72 countries, 45 high-income countries** (62.5%) according to [mapCrowd data](#)¹³, and according to Gilead: in **25 middle-income countries** (34.7%) and in **2 low-income countries**¹⁴ (2.7%), Tanzania and Rwanda at US\$900 for a 12-week course of sofosbuvir. According to mapCrowd, as of July 2018, **47 countries** registered generic sofosbuvir.

Similarly, **Harvoni** is registered at least in **76 countries, 45 high-income countries** (59.2%) according to [mapCrowd data](#)¹³, and according to Gilead: in **27 middle-income countries** (35.5%), and in **4 low-income countries**¹⁵ (5.2%) Ethiopia, Tanzania, Rwanda and Uganda.

As for **Eplclusa**, this pangenotypic treatment is registered in at least in **60 countries, 45 high-income countries** (75%) according to [mapCrowd data](#)¹³, and according to Gilead: in **13 middle-income countries** (21.4%) and in **2 low-income countries**¹⁶ (3.3%), Ethiopia and Uganda.

12. Médecins Sans Frontières Access Campaign. Not even close. Issue brief 6. 2016 Available from: https://msfaccess.org/sites/default/files/HepC_Issue-Brief_HEP_C_6.pdf (Accessed 2018 November 24).

13. Database of mapCrowd. New York, NY: mapCrowd.org; 2018. Available from: www.mapcrowd.org Information related to registration of Gilead's hepatitis C products was not available in the following high-income countries: Andorra, Antigua and Barbuda, Aruba, Bahamas, Barbados, Bermuda, Brunei, Cayman Islands, Curacao, Faroe Islands, Gibraltar, Greenland, Guam, Isle of Man, Liechtenstein, Macao, Northern Mariana Islands, Palau, Panama, Saint Kitts and Nevis, San Marino, Seychelles, Sint Maarten, Trinidad and Tobago, Turks and Caicos Islands, British Virgin Islands, and US Virgin Islands.

14. Sovaldi® registration in the developing world, September 2018 https://www.gilead.com/-/media/files/pdfs/aoem-registrations/sovaldi_registration.pdf?la=en&hash=A1C56DDC36C8388E5D08EC9355A0C320 (accessed 2018 November 28)

15. Harvoni® registration in the developing world, September 2018 https://www.gilead.com/-/media/files/pdfs/aoem-registrations/harvoni_registration.pdf?la=en&hash=9D9E167E17132DDDB1A9E9A039D630D50 (accessed 2018 November 28)

16. Eplclusa® registration in the developing world, September 2018 https://www.gilead.com/-/media/files/pdfs/aoem-registrations/eplclusa_registration.pdf?la=en&hash=83CDB4E0C2D7FBF3DE87E9E5F5C60BE6 (accessed 2018 November 28)

HISTORY OF GILEAD'S DIRECT-ACTING ANTIVIRALS

The development of sofosbuvir has a scandalous history. The principal investigator, Raymond Schinazi earned a salary, funded by taxpayers, at the Veterans Administration, while leading the research at a private biopharmaceutical firm, Pharmasset which relied on publicly funded research. After completing the riskier stages of development and showing promise in late-stage clinical trials, Gilead bought Pharmasset and took sofosbuvir through the final stages of development and regulatory approval. The first oral, direct-acting antiviral was then privatized, locked under patent, and set at a list price of US\$84,000 for a 12-week course, or US\$1,000 per pill.

The jaw-dropping list price has resulted in payors and health systems in high-income countries putting into place treatment restrictions that contradict clinical treatment guidelines, such as those issued by the European Association for the Study of the Liver and the American Association for the Study of Liver Diseases. In 2018, in the US, 13 states still have liver disease progression (fibrosis) restrictions, sobriety restrictions remain in 37 states, and 31 states uphold prescriber restrictions for Medicaid programs, or health coverage for low-income patients.¹⁷ In 2017, in 35 EU countries, nearly half (46%) of countries had fibrosis restrictions, nearly all (94%) countries had prescriber restrictions, and 17% had sobriety restrictions.¹⁸

The timeline of Gilead's DAAs show the strategies to generate enormous profits and shareholder rewards, while leaving behind the tens of millions of people living with hepatitis C, despite the availability of the first-ever cure. **On 6 December, 2018, global hepatitis C advocates demand the lifting of pricing, patent, regulatory, and health system barriers so that everyone who needs treatment can benefit—and to ensure this monumental breakthrough does not become a failure in medical history.**

Gilead's DAAs Timeline:

1998: Pharmasset, Inc. is founded in Tucker, Georgia.

Before 2004: Beginning at Emory University with US\$880 million in public funds from the National Institutes of Health, Raymond Schinazi's research leads to the development of sofosbuvir.

2004: Schinazi starts the drug company Pharmasset, while earning a salary, funded by taxpayers, at the Veterans Administration. Begins the earliest phase of medical discovery of the sofosbuvir molecule.

2006: Pharmasset becomes a publicly traded company.

2007: The promising sofosbuvir molecule is discovered by Pharmasset.

2011: Pharmasset's clinical trials show that sofosbuvir is safe and far more effective than previous hepatitis C treatments. Gilead buys Pharmasset, including sofosbuvir, for US\$11.2 billion.

6 December 2013: Receiving Food and Drug Administration (FDA) approval, Gilead Sciences releases Sovaldi® (sofosbuvir). It is priced at US\$84,000 for a 12-week treatment course, or US\$1,000 per pill.

24 July 2014: Global activists, as part of the hepCoalition, hold action at International AIDS Conference to protest Gilead's extortionately priced hepatitis C drug, Sovaldi® (sofosbuvir).

12 November 2015: Harvoni® (sofosbuvir/ledipasvir) is released as a once-daily, all-oral, single tablet regimen which is priced at US\$94,500 for a 12-week treatment course, or US\$1,125 per pill.

2015: Annual revenues from both drugs rise to nearly US\$20 billion.

28 July 2016: Eplclusa® (sofosbuvir/velpatasvir) is approved as the first once-daily, all-oral, pangenotypic, single tablet regimen for the treatment of adults with genotype 1-6 chronic HCV infection. Eplclusa® is also the first single tablet regimen approved for the treatment of patients

with HCV genotypes 2 and 3, without the need for ribavirin. Eplclusa® is priced at US\$74,760 for a 12-week course, or US\$890 per pill.

28 July 2016: NOhep campaign launched on World Hepatitis Day.

7 April 2017: FDA approves supplemental indications for Sovaldi® and Harvoni® for the treatment of HCV in certain pediatric patients. Harvoni is approved for the treatment of genotypes 1, 4, 5 or 6 chronic HCV infection in adolescents without cirrhosis or with compensated cirrhosis, 12 years of age or older, or at least 35 kilograms.

1 August 2017: FDA approves expanded labeling for Eplclusa® to include use in patients co-infected with HIV.

18 July 2017: Vosevi® (sofosbuvir/velpatasvir/voxilaprevir) is approved for adults with chronic hepatitis C virus (HCV) genotypes 1-6 without cirrhosis (liver disease) or with mild cirrhosis. Gilead markets Vosevi® as a "salvage" treatment for patients who failed previous treatment regimens or who require retreatment.

25 September 2017: China grants regulatory approval of Sovaldi®.

31 December, 2017: Sales of Sovaldi®, Harvoni®, Eplclusa®, and Vosevi®, for the treatment of HCV, account for approximately 36% of total product sales.

24 September 2018: Gilead launches authorized generic versions of Eplclusa® (sofosbuvir/velpatasvir) and Harvoni® (sofosbuvir/ledipasvir) to be made available in the U.S. in January 2019, at a list price of US\$24,000 for a 12-week treatment course.

As of 6 December 2018: The most recently available estimates show US\$58.6 billions in HCV sales; an estimated 1.85 million patients treated with Gilead DAAs worldwide.

17. NASTAD. Hepatitis C: The state of Medicaid access. November 2018. DC: NASTAD. Available from: https://www.nastad.org/sites/default/files/Uploads/2018/hcv_state_of_medicaid_access_update_11-8-18.pdf (Accessed 2018 November 30).

18. Marshall AD, Pawlotsky JM, Lazarus JV et al. The removal of DAA restrictions in Europe – One step closer to eliminating HCV as a major public health threat. *J Hepatol* 2018 Nov;69(5):1188-96. doi:10.1016/j.jhep.2018.06.016.

WE DEMAND:

Gilead:

- Drop patents in all low- and middle-income countries!
- Drop the prices of Sovaldi® in high-income countries and immediately register sofosbuvir in all low and middle-income countries!
- Remove unethical anti-diversion requirements to ensure that they do not limit or impede patient access!

Generic companies:

- Register generic direct-acting antivirals in all the countries!

Governments:

- Develop national treatment programs and procure affordable generic direct-acting antivirals!
- Enforce strict patentability criteria and issue compulsory licenses to overcome patents blocking access to affordable treatment!
- Develop alternative and more sustainable models for medical research and development!

World Health Organization:

- Prioritize the prequalification process of generic DAAs!

International donors:

- Stop ignoring the HCV epidemic and allocate funding to respond to the global epidemic!

To learn more about the global movement to expand access to affordable hepatitis C treatments and diagnostics, visit:

www.hepCoalition.org; www.mapCrowd.org

