

## A buyers' club to improve access to hepatitis C treatment for vulnerable populations

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### Summary

Hepatitis C is a potentially fatal viral infection that mainly affects vulnerable patient groups. Given the high efficacy of the new direct-acting antivirals (DAAs), the World Health Organization (WHO) aims to eliminate viral hepatitis as a global health threat by 2030. However, due to the high cost of DAAs, this recommendation has put significant pressure on the budgets of countries with mandatory health insurance, such as Switzerland. There are particular challenges related to populations with low socioeconomic status or without residence permits who might not be covered by health insurance, or who forgo health care for economic reasons. This article discusses some of the key issues on this topic, such as reaching the populations most at risk from the hepatitis C virus (HCV) infection, and improving access to care and treatment for underserved, uninsured populations. We suggest a personal importation scheme for unapproved generics of DAA medications, and the use of a buyers' club as a strategy for improving universal access to hepatitis C medicines among vulnerable populations such as uninsured patients, in order to achieve the WHO goals with minimal disruption of the conventional, patent-based business model.

**Keywords:** hepatitis C, universal access, personal importation scheme

### Introduction

The prevalence of the hepatitis C virus (HCV) infection in the general population varies between countries, ranging from 6.3% (4.5–6.7) in Egypt to 0.4–0.5% in Switzerland [1, 2]. The prevalence is higher among vulnerable populations such as people with low socioeconomic status, those who are uninsured, migrants, intravenous (IV) drug users and people living in prison (PLP) [3–6]. Among people receiving opioid substitution therapy, a Swiss study found a high prevalence, 27.8%, of HCV infection before the widespread use of direct-acting antivirals (DAAs) [7]. In Geneva, HCV infection was found in 5.7% of PLP and in

15.54% of those who used illicit drugs, but in only 0.8% of non-users of illicit drugs [8]. The estimated prevalence of HCV infection in Western European prisons is 15.5% [9].

The World Health Organization (WHO) aims to eliminate viral hepatitis as a global health threat by 2030. This means reducing the incidence of new chronic HCV infections by 90% [10, 11]. This objective requires the identification and universal access to treatment of all infected populations, including vulnerable groups who are hard to reach. The Ordinance on the Control of Communicable Diseases of Humans (Epidemic Ordinance, EPO), which came into power on 1 January 2016, has suggested intensifying the screening and treatment of HIV, AIDS and HCV in Switzerland [12].

This recommendation puts pressure on the budgets of countries with mandatory health insurance, as they face difficulties in financing treatment with of all infected patients with costly DAAs. Also, access to treatment is problematic in populations with low socioeconomic status or without residency permits, who may not be covered by health insurance or who forgo healthcare for economic reasons [13, 14].

Yehia et al. identified several gaps in the US healthcare system that contribute to the low (16%) rate of treatment among those with chronic HCV infection in the US, with the main factors being a lack of diagnosis and a lack of access to care [15]. Similarly, Bregenzer et al. found gaps in all steps leading to appropriate access to treatment among drug users in Switzerland [7].

### Treatment policy in Switzerland

When the first DAA, which was associated with an unprecedentedly high cure rate, was marketed in 2014, the Swiss Federal Office of Public Health (FOPH) restricted access to DAAs to patients with advanced fibrosis (F3 and F4). Access was extended to patients with a lower stage of fibrosis (F2) in 2016, and from July 2017 onwards the FOPH lifted restrictions, allowing initially very expensive therapies whose prices had been negotiated down over

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time to be reimbursed to the entire insured population independent of the how advanced the disease (table 1) [11, 16]. In February 2018, FOPH removed sofosbuvir and daclatasvir from the reimbursement list based on the criteria of economic efficiency and the availability of therapeutic alternatives.

Accessibility and affordability are key issues that seem to be theoretically solved for the general, insured HCV-infected population in Switzerland in the current policy and pricing context. However, some specific groups may not benefit from such advances for financial and administrative reasons. Indeed, it is estimated that at least 1% of the Swiss population is not covered by the mandatory health insurance scheme (e.g., undocumented migrants, PLP), including economically disadvantaged individuals who forgo healthcare for economic reasons [13, 14, 17]. A recent, reasonable estimate of the migrant population in Switzerland is 76,000 (50,000 to 99,000), accounting for 0.9% (0.6–1.2%) of the total resident population [18]. The number of prisoners is 6863 (2017), of which 71.5% are foreign nationals, a majority of whom are not insured [19]. Additionally, Switzerland is characterized by high out-of-pocket expenses, or direct outlay, by households, at 26% of health expenditures compared with the average for European countries of 19.5% [20, 21]. Therefore, a mandatory health insurance system might not guarantee access to treatment or even appropriate care, as direct or out-of-pocket expenses might be a financial barrier [7]. The proportion of uninsured patients in the group of patients most affected by HCV infection is likely to be much higher. For example, in the HIV consultation of the Geneva University Hospitals, approximately 40% of patients with a new HIV diagnosis had no valid insurance in Switzerland at the time of diagnosis (authors' unpublished data).

Therefore, efficient strategies to combat HCV infection must address the specific needs of the vulnerable populations at risk, including PLP. Indeed, international standards for prison healthcare include the principle of equivalence, meaning that all PLP should benefit from the same quality of care as the population outside prison [22, 23]. Uninsured and/or low income patients and PLP are usually treated by public health institutions. Those health care facilities are under tremendous pressure to keep healthcare expenditures under control in the face of increasing costs, including drug costs and costs related to ageing populations and advances in medicine. According to the OCDE, the Swiss healthcare system is already the second most expensive, after the

United States, accounting for 12.4% of the GDP in 2016 [24].

As in the US, care provision for underserved populations in Switzerland generally relies on public healthcare institutions. These structures play a key role in bridging the gap and achieving the goal of eliminating HCV infection. We aim to present an innovative model of resource allocation in a public hospital caring for vulnerable patients, mostly uninsured and sometimes incarcerated or HIV-positive, that could promote universal access to high-quality, affordable DAA drugs.

### Personal importation scheme

The proposed model was developed using a personal importation scheme that is based on the right of any patient to import any drug into many countries, including Switzerland, for personal use. In the specific context of the personal importation scheme, three categories of drugs are marketed at the same time in different countries and at different prices: the brand patented drug (e.g., brand sofosbuvir), the generic version marketed either after the patent termination or under specific conditions, most of the time in low-income countries, (e.g., generic sofosbuvir) and the unapproved generic. The latter is defined as the generic version imported under a personal importation scheme into a country where a patent guarantees market exclusivity to the brand producer (e.g., unapproved generic sofosbuvir) [25].

Under the Trade-Related Aspects of Intellectual Property Rights agreement, less-developed countries and low- and middle-income countries may have licensing agreements with pharmaceutical industries that allow companies to produce generic formulations [26, 27]. Freeman et al. demonstrated that the worldwide price difference of HCV drugs is wide. For example, the sofosbuvir market access price for a 12 week course of treatment varied from CHF 84,000 in the USA to CHF 900 in India, while the active pharmaceutical ingredient production cost is around CHF 100 [28, 29]. Furthermore, the imported generic formulation has the same efficacy as the corresponding brand-name drug [30, 31].

In Switzerland, the legal importation of drugs is clearly defined in the Federal Act on Medicinal Products and Medical Devices (Therapeutic Products Act, TPA) and the Ordonnance sur les autorisations dans le domaine des médicaments (OAMED). Personal importation can be considered a special access and pricing scheme, since any in-

**Table 1:** Evolution of the availability and price of drugs against hepatitis C in Switzerland.

12-week course therapies	Genotype	Market entry date	Price at market entry (CHF)	Price Feb. 2018 (CHF)	Reimbursement policy (Feb. 2018)
Sofosbuvir/ledipasvir (Harvoni®)	1, 4, 5 and 6	01 Feb. 2015	62,363	43,894	Genotype 1
Sofosbuvir/velpatasvir (Epclusa®)	1–6	01 Jan. 2017	60,017	30,952	Genotype 1-6
Ritonavir/ paritaprevir/ombitasvir (Viekirax®) and dasabuvir (Exviera®)	1, 4 (4 without dasabuvir)	01 Feb. 2015	56,576 + (5380)	28,505 + (2790)	Genotype 1, (4)
Grazoprevir/elbasvir (Zepatier®)	1, 4	01 May 2016	47,690	30,952	Genotype 1, 4
Glecaprevir/ pibrentasvir (Maviret®)	1–6	01 Dec. 2017	46,059	46,059	Genotype 1-6
Sofosbuvir (Sovaldi®)	1 (with ribavirin), 4 (with ribavirin and peginterferon-alfa)	01 Aug. 2014	57,626	44,810	Removed from the reimbursement scheme in Feb. 2018
Daclatasvir (Daklinza®)	1,3,4 (in association to ribavirin and peginterferon-alfa)	01 Aug. 2015	34,991	28,902	Removed from the reimbursement scheme in Feb. 2018

dividual, insured or uninsured, has the right to either bring medicines into Switzerland or import them from an overseas supplier for his own consumption in small quantities for a maximum of three consecutive months under specific conditions (article 36 OAMED).

### Buyers' clubs

A personal importation scheme is based on a patient's personal initiative and might be associated with a higher risk of receiving ineffective or even harmful treatment. Indeed, some unapproved imported generics are counterfeit and have been demonstrated to have excessive, insufficient or non-existent active ingredients, or even erroneous and undeclared components [32, 33]. To provide safer access to more affordable drugs, a structure called a buyers' club appeared in the early 1990s, when people were dying of HIV and medicines were not yet approved by the FDA because of gaps in the drug approval process. These unapproved generics were smuggled into Texas and distributed to people who paid not for the drugs but for membership of the club. This story was made into a famous 2013 movie called the 'Dallas Buyers Club', directed by Jean-Marc Vallée. A buyers' club is therefore a structure that aims to help patients import unapproved generic medicines safely, thereby providing treatment access to more patients. The world's largest buyers' club for HCV is FixHepC. To our knowledge, there are two buyers' clubs for HCV in Switzerland. One is managed in Zurich by ARUD and became involved in supporting patients importing unapproved HCV generics for personal use when the FOPH limited access to them for the entire population. The other is managed in Geneva by the Groupe SIDA Genève (GSG), which is involved in helping patients import unapproved HCV and HIV generics. Table 2 compares the price of treatment with the Swiss brand to the price with the corresponding unapproved generic available through a buyers' club.

Several factors may explain why a conventional buyers' club based on a personal initiative may not always be sufficient to increase access to expensive therapies for vulnerable populations. First, it requires that the patient is aware of his/her infection and that the patient is aware of a buyers' club. It depends on the patient's personal initiative to contact a buyers' club, upload a medical prescription, pay with a credit card, provide the address where the drug will be delivered, sign a consent form, pay a minimum amount of CHF 1000 and be able to read English.

As noted above, vulnerable patients likely to benefit from personal importation schemes are usually cared for by public health care facilities. We contend that such institutions could consider developing a partnership with a buyers' club. Hospital physicians retain their traditional role of diagnosing, treating and following up patients, while the buyers' club provides administrative assistance to help pa-

tients import affordable medicines. Such a collaboration may significantly increase access to HCV therapy among those populations with the highest risk of HCV infection by making expensive therapies affordable.

### Relationship between the healthcare facility, the patient and the buyers' club

For groups with a high risk of HCV infection such as IV drug users (past or present), PLP, HIV-positive individuals, migrants coming from regions with a high prevalence of HCV (> 2%) and people with tattoos or piercings performed in poor hygiene settings, the first step is screening for viral infection. Physicians from the health care institution should test two markers of HCV infection, i.e. antibodies to HCV (anti-HCV) (CHF 17.40 per test) followed by HCV RNA (CHF 180 per test) for patients with a positive antibody result [34].

If the patient has detectable HCV RNA, the physician will prescribe the appropriate therapeutic option. If the patient does not have access to health insurance and/or cannot cover the out-of-pocket cost of medication, he/she is informed of the option of direct importation of drugs for personal use through a buyers' club which can provide administrative assistance with the process [35]. The patient must sign a consent form acknowledging that he/she has received information about the therapeutic options, the prices of the brand drugs and the unapproved generics available on the market and, finally, the risks and benefits of personal importation [36]. Benefiting from the buyers' club's help requires adherence to the rules established by this group, but those rules cannot include mandatory access to medical records, or the requirement to accept other services from the buyers' club.

Before the unapproved generic is delivered to the patient, the drug source will be checked and quality control will be performed, as the personal importation scheme involves a risk of counterfeit and suboptimal storage conditions. Indeed, buyers' clubs and healthcare facilities should check the supply chain integrity to ensure the quality of the imported medication, as buying any medication over the Internet is associated with higher risks [37]. Obviously, only medicines from controlled sources where quality assurance meets the requirements and expectations should be considered. The buyers' club should therefore preferably purchase drugs from a country with a quality control of production that is equivalent of that of Switzerland, such as Australia, Canada, the US, Japan or EC member states [27, 38]. However, unapproved generics are sometimes not available in such countries and must be imported from countries that are not recognized by the Swiss health authority [32, 33]. One of the many activities of the WHO is to prequalify essential medicines, assuring their quality, safety and efficacy when bought internationally [39]. The

**Table 2:** Comparison of the Swiss cost of treatment using brand medications versus the corresponding unapproved generics available through a buyers' club.

Therapeutic options	Genotype	Swiss brand price 2018 (CHF)	Unapproved generic (CHF)	Fraction of the corresponding brand price	Buyers' club
12 weeks sofosbuvir* + 12 weeks daclatasvir*	1–6	73,713	1250 <sup>‡</sup>	1.70%	GSG FixhepC
12 weeks sofosbuvir/ledipasvir	1, 4–6	43,894	1300 <sup>‡</sup>	2.96%	FixhepC
12 weeks sofosbuvir/velpatasvir	1–6	30,952	1500 <sup>‡</sup>	4.85%	FixhepC

\* Sovaldi<sup>®</sup> and Daklinza<sup>®</sup> were removed from the Swiss reimbursement list in 2018 ‡ We considered an exchange rate of one CHF equal to one USD

second, preferred option is to select medicines that are pre-qualified by the WHO. Currently, the only HCV generics prequalified by the WHO are sofosbuvir 400 mg tablets (Mylan Laboratories, India; Hetero Laboratories, India; Cipla Laboratories, India) and daclatasvir 30 and 60 mg tablets (Bristol Myers Squibb, United Kingdom) [39]. The other options are either to select FDA-approved generics or at least drugs approved by Doctors Without Borders, although approvals by this non-governmental organization are made only under emergency situations.

Nevertheless, to limit the risk of counterfeit associated with the importation of unapproved generics, the buyers' club or the healthcare facility should perform HPLC-UV to ensure the highest quality control of unapproved generics and allowing identification of the batch number for each tablet [25, 40]. Finally, treatment monitoring for potential side effects and efficacy should be provided by the healthcare facility physicians in the same way as for patients treated with brand drugs. For example, the physician should look for the sustained viral response (SVR), defined as the persistent absence of HCV RNA for 12 weeks or more after completing antiviral treatment, which is known to be associated with lower chronic disease progression and mortality [5, 41, 42]. The usual funding scheme to access laboratory monitoring and medical consultation should be used.

### Political and ethical issues

Personal importation schemes raise political and ethical questions. In Switzerland, the pharmaceutical industry is an important stakeholder, accounting for 4.8% of GDP, and it was also a leading exporter in 2016, with one-twelfth of the working population employed in either the chemical and pharmaceutical industry (70,000) or in healthcare facilities (352,000) [43, 44]. The personal importation scheme bypasses the regulatory process associated with the strong intellectual property rights that enable the pharmaceutical industry to protect their market through patents, which give them exclusive territorial rights [45, 46]. A personal importation scheme may disrupt the conventional patent business model, which is a key component of policies designed to foster innovation [47]. Our model, however, does not affect the vast majority of patients covered by health insurance. Rather, being restricted to uninsured patients, it extends universal access to expensive and effective therapies to these vulnerable populations.

Different key elements may influence the pricing of a drug, including the amount of investment in R&D, production costs, costs of other failed drugs, marketing costs, the drug's efficacy, safety and route of administration, heat-stable formulations, the duration of treatment, features of comparable treatments, innovation, international benchmarking, market size, and market value as determined by supply and demand [48]. The pharmaceutical industry traditionally uses unit-based pricing linked to the R&D costs, but it may also charge for the price of innovation, or what the market can bear. The latter pricing strategy is often observed in oncology drugs and it is considered unreasonable and unfair by many stakeholders, in part because it raises obstacles to access to drugs, which patients should have and for which industry should strive [49–52]. Regarding HCV treatments, we showed in previous work that the in-

dustry adopted a value-based pricing model over 20 years ago. Indeed, there was a strong correlation between the treatment efficacy, in terms of sustained viral response, and the price of the considered HCV regimen. As efficacy increased, this led to an unaffordable price at the population level even in high-income countries such as Switzerland [11]. This strategic pricing model based on the value for the patient also appears to be applied to drugs with no manufacturing challenges and a low cost of active pharmaceutical ingredients [29]. Rather opportunistically, this strategy tends not to be applied for low-value drugs which could offset the costs of the high-value ones. Finally, these pricing models limit access to innovative drugs, particularly for uninsured patients. Given that a right to access is recognized, this is problematic. These pricing strategies thus require that prices and potential limitations are negotiated over time by the payers (table 1) [11, 53, 54].

The Swiss healthcare system is based on fundamental principles: a mandatory insurance programme promoting universal access to the entire population, with the same good care and access reflecting community solidarity and equity values [17, 55]. The innovative model we discussed, a partnership between the patient, the health care facility and the buyers' club, extends universal access to care and treatment to the uninsured population in accordance with this community solidarity and equity values. Moreover, as the prevalence of HCV is much higher in marginalized groups, an innovative model that increases access for the most vulnerable should present a unique opportunity to treat a more of the HCV-infected population [2, 55, 56].

There are ethical questions about this model related to the dilemma associated with the high costs to institutions that strive to offer access to health care, including to uninsured patients such as undocumented migrants or PLP. These institutions might partner with a buyers' club, which may help to achieve good access to health care for all, in particular through access to expensive drugs, without risking the health care budget dedicated to these populations.

One might also be critical of the fact that disadvantaged and uninsured patients are treated with different drugs to insured patients, even if they are purchased on the patient's individual initiative. Although this model does provide the same drug to some at a lower price, we would argue that it is fair. Within medicine, it is more important to distribute access to care in an equitable manner than to guarantee that costs are the same for all. This is based on equality of opportunity as well as on the human right to health [57, 58]. Indeed, differential costs between richer and poorer countries, which is the current practice of the pharmaceutical industry, also implicitly recognizes this. Although the buyers' club is intended to be limited to uninsured patients, it could also become tempting for institutions that have implemented it to use the same mechanism to purchase cheaper drugs for insured patients. After all, this would lead to more resources being available for other patients as well. Replacement of ordinary market purchases for insured patients with a buyers' club would, however, raise issues of patent disruption that are not raised in a similar manner by a buyers' club limited to uninsured patients. These issues are beyond the scope of this paper, but resolving them would be a prerequisite for any extension of the model.

## Conclusion

High costs are an important barrier to treatment access for vulnerable and often uninsured patients with hepatitis C. We present an initiative designed to allow quasi-universal access to expensive drugs for the vulnerable populations cared for by our public hospitals and not included in our country's standard healthcare insurance scheme. HCV remains an important health problem, but treating all infected patients could eradicate this potentially fatal disease. Therefore, all initiatives which promote access to treatment for patients who cannot afford the costs of antiviral drugs whilst guaranteeing drug safety should be considered ethical, and be promoted to aid the elimination of HCV and to address a major public health problem [2, 15, 59, 60].

## Disclosure statement

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