Hepatitis C Treatment: Back to the Warehouse

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Like many physicians that specialize in hepatitis C virus (HCV) treatment, I have spent the last few years advising many of my patients with chronic HCV infection to defer treatment and wait for new therapies. For those without advanced fibrosis or an extraintestinal manifestation of HCV, this process of “warehousing” patients for future HCV treatment made perfect sense. Why undergo interferon-based therapy, with all of the side effects and marginal results, when it was becoming clear that highly efficacious, interferon-free therapy was close to becoming a reality? Patients, advocacy groups, and physicians closely followed the development of sofosbuvir (Sovaldi), simeprevir (Olysio), sofosbuvir/ledipasvir (Harvoni), and paritaprevir/ritonavir/ombitasvir/dasabuvir (Viekira Pak) among others in eager anticipation of US Food and Drug Administration (FDA) approval and, for most patients, the possibility of a cure of their HCV infection.

However, this eager anticipation morphed into uneasy concern as, along with FDA approval, drug pricing was announced. Realistically, based on the price point set by Merck and Vertex for the first-generation protease inhibitors boceprevir and telaprevir, respectively, it was certain that newly approved HCV treatment would not only be effective, but expensive as well. However, few of us were anticipating the “sticker shock” of an \$84,000 price tag in the United States for Gilead’s Sovaldi followed by \$94,500 for Gilead’s Harvoni and \$83,320 for AbbVie’s Viekira Pak. In no uncertain terms, with that price benchmark set, the prospect of the widespread eradication of HCV evaporated. Healthcare payers, private and public, both in the United States and across the globe, cried foul as they found themselves trapped between consumer and advocate demands for the HCV cure and the real possibility that HCV treatment could lead to a financial crisis in the healthcare system.

The treatment of chronic HCV presents a unique challenge not only due to the cost of the medication, but also due to the disease prevalence, the socioeconomics of HCV infection, and the natural history of HCV infection. Whereas the cost of HCV treatment is shocking in itself, it becomes truly astounding when disease prevalence is taken into account. Worldwide, an estimated 185 million individuals are chronically infected with HCV, including an estimated 3.2 million in the United States. It is easy to see how HCV treatment, if treatment were offered to all those infected, could pose a risk of financial collapse for a healthcare payer. In addition, HCV infection is largely a disease of poverty. Poor and middle income countries suffer the highest burden of HCV infection worldwide. Even in developed countries, HCV disproportionately affects the poor. A National Health and Nutrition Examination Survey (NHANES) study revealed that HCV infection was an independent risk factor for lack of insurance or use of public insurance, such as Medicaid.¹ Likewise, HCV infection is highly prevalent among incarcerated individuals, and can be successfully treated in that setting. In the community setting, these individuals often suffer from financial, social, and mental health challenges that may preclude successful HCV treatment.^{2,3} Finally, the natural history of HCV infection complicates the conundrum of whether it would be worthwhile to attempt to eradicate HCV, because it is estimated that only about 20% of patients with chronic HCV infection will go on to develop cirrhosis and complications such as end-stage liver disease or hepatocellular carcinoma. The caveat regarding this estimate is that we have limited knowledge on the outcome of HCV infection beyond 20 years, although it seems clear that many patients can carry HCV all their lives without coming to any harm.⁴ Thus, health insurance providers feel compelled to highly restrict

Abbreviations: FDA, US Food and Drug Administration; HCV, hepatitis C virus.

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TABLE 1 Healthcare Spending and Sofosbuvir Pricing Compared Between the United States, the United Kingdom, Canada, and Egypt.⁵⁻¹⁵

Country	Sofosbuvir cost, USD*	Total Healthcare Spending 2012 in USD (billions) (%GDP)	Annual healthcare spending per capita (2012) in USD	Sofosbuvir cost/annual healthcare spending per capita 2012	Estimated cost of 12 weeks sofosbuvir for all HCV-infected patients (% total annual healthcare spending)
United States	\$84,000	3007 (17.9%)	\$8865	9.5	~9.0%
United Kingdom	~\$53,000	237 (9.4%)	\$3647	14.5	~5.0%
Canada	~\$47,300	199.1 (10.9%)	\$5741	8.2	~5.7%
Egypt	\$900	13.1 (5%)	\$152	5.9	~80.1%

Abbreviations: GDP, gross domestic product; USD, US dollars.

*Denotes 12-week course

the cure to patients at high risk of developing end-stage complications, lest the financial weight of HCV treatment threaten their solvency.

When the prevalence of chronic HCV infection, the lack of financial resources available to those afflicted with HCV, and the exorbitant cost of medication are taken together, the widespread use of these agents seems an economic impossibility. Even in countries such as Egypt, where an estimated 15% of the population carries antibodies to HCV and sofosbuvir is available at a much publicized 99% discount, the cost of HCV treatment may prohibit its widespread use.^{5,6} Table 1 compares healthcare spending data and sofosbuvir pricing between the United States, the United Kingdom, Canada, and Egypt.⁶⁻¹⁴ Although the \$900 price for a complete course of sofosbuvir negotiated by the Egyptian Government may seem a bargain when compared to prices for the same treatment in the Western world, it is still almost six times more than the estimated \$152 Egypt spent per capita on healthcare in 2012.^{6,7} Whereas this compares somewhat favorably to a cost of 8 to 15 times the healthcare cost per capita for sofosbuvir in the Western countries, when the extraordinary prevalence of HCV infection in Egypt is taken into account, the cost to treat all infected Egyptians with sofosbuvir alone could approach 80% of their total annual healthcare spending!⁶⁻¹⁵ Clearly, even \$900 for sofosbuvir may create problems for poorer countries. Similarly, while it is to Gilead's credit that they have entered licensing agreements with pharmacies to supply sofosbuvir and sofosbuvir-ledipasvir to low-income countries, their agreements exclude middle-income countries such as China and Brazil. Even prices that seem a bar-

gain compared to those in the United States and Europe have to be taken in context with the underlying healthcare economics of a given country.

Recently, there has been at least a glimmer of hope for patients suffering from HCV who lack access to treatment due to cost. With the introduction of Viekira Pak to compete with Harvoni for treatment of genotype 1 infection, much needed competition was introduced into the HCV treatment market. Payers have responded aggressively by negotiating discounted drug costs in exchange for preferred formulary status. Large public health insurance providers like Medicare, Medicaid, and the Veterans Administration, already receiving discounted prices for these medications, will hopefully use their own purchasing power to drive down the cost of treatment for their beneficiaries. Despite this downward pressure on cost, however, most payers are still enforcing strict eligibility criteria for HCV treatment. As a result, barring a truly drastic change in the price of HCV treatment, rationing of these curative new therapies is inevitable, both in Western countries and worldwide. No realistic scenario can be devised where such an unbelievable quantity of resources can be diverted to treating HCV. Thus, as providers, for patients with early stage disease, our only recourse is to acknowledge that the HCV cure is available, but you will have to get sicker to get better. In other words, it's back to the warehouse for now.

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