

Disparity in market prices for hepatitis C virus direct-acting drugs

The introduction of direct-acting antiviral drugs (DAAs) is changing the treatment options for hepatitis C virus (HCV). These new medicines were initially marketed at a very high price, but several countries have negotiated favourable price reductions, and, in view of the low cost of production, further price reductions are anticipated, especially as the result of generic competition.¹ Reliable, transparent, and updated information about drug availability and costs are important for policymakers, procurement agencies, providers, and people living with HCV to help ensure equitable access.

We gathered price information in June, 2015, to inform decision making as part of the process of the WHO HCV Guidelines Development. A structured, piloted questionnaire was sent to key informants belonging to the WHO viral hepatitis experts network, including academics, policy makers, and civil society representatives of several countries, to collect information about availability and affordability of sofosbuvir, daclatasvir, ledipasvir-sofosbuvir, simeprevir, ombitasvir-paritaprevir-ritonavir, and dasabuvir. The following information was sought: availability in the public and private sector of originator drugs and generics, market price per bottle (US\$), registration status, and special trading agreements (if applicable). To our knowledge, there are no stringent regulatory authority quality-assured generic sources of DAAs to date.

Information was available for 38 countries, including 14 high-income countries, nine upper middle-income countries, 11 lower middle-income countries, and four low-income countries. The questionnaire was sent to 92 key informants, and 49 respondents agreed to provide information, and some people were

able to provide information for several countries.

The price per bottle of all originator DAAs varied substantially: for sofosbuvir it ranged from \$300 (India, Pakistan) to \$20 590 (Switzerland); for daclatasvir from \$175 (Egypt) to \$14 899 (Germany); for simeprevir from \$241 (Egypt) to \$14 865 (Australia); for ledipasvir-sofosbuvir from \$400 (Egypt and Mongolia) to \$24 890 (Germany); and for ombitasvir-paritaprevir-ritonavir (or 2D regimen) from \$400 (Egypt) to \$20 215 (Switzerland).

The greatest variability was noted in high-income countries, with little correlation between drug prices and

gross national income (figure). In high-income countries, the price per bottle of sofosbuvir ranged from \$14 000 (Spain) to \$20 590 (Switzerland). Prices for daclatasvir ranged from \$1128 (South Korea) to \$14 899 (Germany); those of simeprevir from \$9166 (Spain) to \$14 865 (Australia); those of ledipasvir-sofosbuvir from \$12 604 (USA) to \$24 890 (Germany); and those of the 2D regimen from \$15 344 (UK) to \$20 215 (Switzerland).

In low-income and middle-income countries, prices were generally substantially lower than in high-income countries. However, there

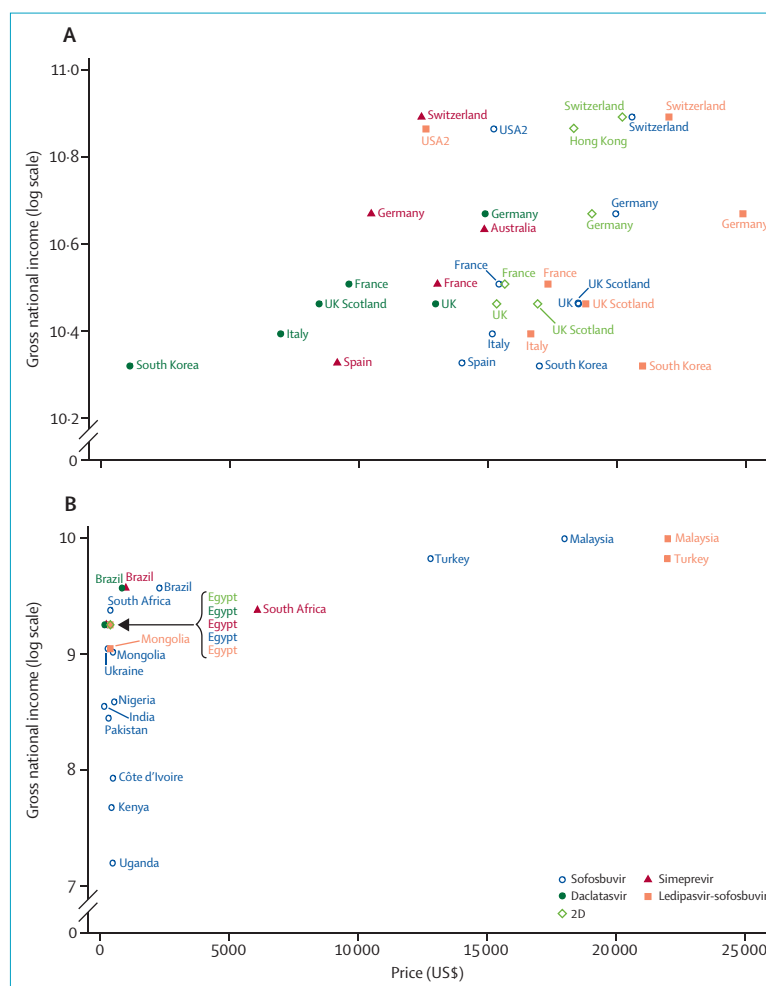


Figure: Correlation between drug prices and gross national income

(A) High-income countries. (B) Low-income and middle-income countries. Information on gross national income was obtained from the United Nations Development Programme.²

were some clear outliers (figure). Côte d'Ivoire is paying almost three times as much for sofosbuvir as is India (\$500 per bottle for the generic drug in Côte d'Ivoire vs \$300 for the originator in India, where the generic drug costs \$312–161) despite having a far lower gross national income (\$2774 for Côte d'Ivoire vs \$5150 for India). South Africa is paying six times more for simeprevir than is Brazil (\$6100 vs \$1000) despite having a lower gross national income (\$11 788 for South Africa vs \$14 275 for Brazil). In Malaysia the cost of sofosbuvir (\$18 000) and ledipasvir-sofosbuvir (\$22 000) is higher than in many high-income countries; similarly, ledipasvir-sofosbuvir (\$21 988) costs more in Turkey than in many high-income countries. In Egypt, a local generic of sofosbuvir is also available at \$343, which is expected to decrease to about \$100. Several sources of generics of sofosbuvir are available in India with prices ranging from \$161 to \$312. With the exception of sofosbuvir, most DAAs were very poorly available in low-income countries.

This survey highlights the high diversity in market prices in low-income, middle-income, and high-income countries. Having access to updated reliable price information can allow country decision makers to negotiate better prices. High-burden countries such as Egypt, Mongolia, India, Pakistan, and Brazil set the scene for increased competition between pharmaceutical companies, including through generic competition.

Gilead has signed voluntary licensing agreements with 11 Indian manufacturers of generic medicines to market generic versions of Gilead's DAAs (such as sofosbuvir and ledipasvir-sofosbuvir) in some low-income and middle-income countries, and Bristol-Myers Squibb is also investigating voluntary license agreements with generic manufacturers. However, these voluntary licenses do not apply to the

majority of middle-income countries, where most of the HCV burden lies. For example, Argentina, Brazil, China, Georgia, Iran, Mexico, Peru, Turkey, and Ukraine are all excluded from Gilead's voluntary license.^{3,4}

Furthermore, prices are still too high and unaffordable in settings in which people have to pay for their treatments or if high numbers of people require treatment in the public system. According to new therapeutic guidelines, treatment duration varies according to the stage of liver disease, with extended treatment durations from 3 to 6 months for patients with compensated cirrhosis.⁵ For example, in Egypt, 3 months' treatment with sofosbuvir-daclatasvir costs \$1350, but the cost will double if a person has cirrhosis and cannot take ribavirin. In Brazil, costs of sofosbuvir-daclatasvir treatment will vary between \$10 947 and \$21 894 according to this same rule. In Germany, ledipasvir-sofosbuvir costs between \$75 000 and \$150 000 and 6 months' treatment with sofosbuvir-daclatasvir costs \$150 366 in France.

Manufacturing costs of DAAs are estimated to be far lower than the current prices. Generic competition from multiple manufacturers is already indicating a downward trend for the prices of sofosbuvir, which should enable low-cost access to quality-assured generic versions of this drug. Several manufacturers are also starting generic production of sofosbuvir-daclatasvir and ledipasvir-sofosbuvir.

Even if countries are excluded from voluntary licenses or face patent barriers, these obstacles do not necessarily preclude them from pursuing access to low-cost generics if adequate legal measures and strategies can be put in place. However, to achieve this access, understanding the patent landscape of key DAAs is a prerequisite, a strict patent examination would prevent granting of weak or invalid DAA patents, and the use of compulsory licenses should be considered where necessary.

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