The role of generic drugs in the treatment of viral hepatitis

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What is the best combination of DAAs to mass produce?
Sofosbuvir + Ledipasvir ± RBV (12-24 wks)
Percentage SVR12, by Genotype

G1  |  G2  |  G3  |  G4  |  G5  |  G6  |
---|---|---|---|---|---|
95% | 97% | 78% | 88% | 95% | 96% |
7752/8133 | 33/34 | 281/361 | 61/69 | 39/41 | 24/25
Grazoprevir + Elbasvir ± RBV ± SOF (12-18 wks)
Percentage SVR12, by Genotype

G1: 95% (1807/1904)  
G2: 80% (24/30)  
G3: 96% (24/25)  
G4: 93% (118/127)  
G5: 63% (5/8)  
G6: 74% (26/35)
Sofosbuvir + Daclatasvir ± RBV (12-24 wks)
Percentage SVR12, by Genotype

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Percent SVR12</th>
<th>Samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>93%</td>
<td>1459/1575</td>
</tr>
<tr>
<td>G2</td>
<td>95%</td>
<td>21/22</td>
</tr>
<tr>
<td>G3</td>
<td>84%</td>
<td>628/752</td>
</tr>
<tr>
<td>G4</td>
<td>94%</td>
<td>296/316</td>
</tr>
<tr>
<td>G5</td>
<td>91%</td>
<td>64/70</td>
</tr>
<tr>
<td>G6</td>
<td>100%</td>
<td>5/5</td>
</tr>
</tbody>
</table>
Sofosbuvir + Velpatasvir ± RBV (12-24 wks)
Percentage SVR12, by Genotype

- G1: 96% (749/778)
- G2: 99% (259/261)
- G3: 90% (535/592)
- G4: 100% (128/128)
- G5: 97% (34/35)
- G6: 100% (42/42)
Glecaprevir + Pibrentasvir (12-16 wks)
Percentage SVR12, by Genotype

G1: 99% (331/332)
G2: 99% (195/196)
G3: 95% (125/131)
G4: 99% (75/76)
G5: 100% (26/26)
G6: 100% (19/19)
How cheaply can medicines be produced?
Active Pharmaceutical Ingredient

Raw drug substance

Database [www.indiainfodrive.com](http://www.indiainfodrive.com) shows exports of API from India to other countries, with costs per kilogram of API, for many drugs
Cost/kg of sofosbuvir API exports Jan 2015 to Jul 2016, weighted by size of shipment

From API cost/kg to target price

API price/kg x grams per treatment course

+ $0.04 / tablet for excipients and tableting,
+ $0.35/month for formulation
x 10-50% profit margin

(10% for mass-produced drugs e.g. HIV, TB)
Target generic price of sofosbuvir (12 weeks)

Cost of API = $1,094/kg

API per 12 weeks = $37

API needed per person = 34g (400mg x 84 days)

Formulation + excipients = $0.04 per pill

Formulated drug = $40

Packaging = $0.35/month

Packaged drug = $41

Profit margin = 50%

Final generic price = $62

Gotham D, Barber M, Fortunak J, Pozniak A, Hill A.
Abstract number A-792-0516-01639, presented at AIDS2016, Durban.
Price of sofosbuvir by country (12 weeks)

**Sofosbuvir (Sovaldi)**

**German price:** €50,426  
**Cost price:** €55

Sofosbuvir prices:
3. Germany: medizinfuchs.de
5. UK: British National Formulary 2016
7. Australia: Based on total annual government expenditure (AU$200 million) and 40,000 treated in 2016
## HCV DAAs: Prices in USA and India versus Target

<table>
<thead>
<tr>
<th>Drug</th>
<th>Current US price (lowest)</th>
<th>Current lowest Indian market price</th>
<th>Target price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sofosbuvir</td>
<td>$49,680</td>
<td>$324</td>
<td>$62</td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>$50,653</td>
<td>$153</td>
<td>$14</td>
</tr>
<tr>
<td>SOF+LDV</td>
<td>$56,700</td>
<td>$507</td>
<td>$96</td>
</tr>
<tr>
<td>SOF+VEL</td>
<td>$74,760</td>
<td>-</td>
<td>$181-216</td>
</tr>
</tbody>
</table>

Prices of HCV DAAs keep falling

SOF and DCV API now being exported from China for $800 per kg

This would lower the basic production price to $55 for 12 weeks of SOF/DCV

In Egypt, SOF/DCV is now available for $172 per 12 weeks (WHO 2016 report)
Entecavir for Hepatitis B
one year’s supply (0.2g)
Entecavir for Hepatitis B

cost per person/year by country

US price: $15,111
Cost price: $36

Target versus Global lowest prices: HIV, TB and Hepatitis

weights = kg exported 2Q2016
Mass produced HCV DAAs should fall to <$90 per 12-week course

weights = kg exported 2Q2016
The new “$90 $90 $90” in 2017

There should be standard prices to treat HIV, Hep B/C and TB

- < $90 per year to treat HIV: TDF/3TC/EFV
- < $90 per year to treat Hepatitis B: TDF/3TC or ETV
- < $90 for first-line treatment for TB
- < $90 for 12-weeks course of HCV DAAs: SOF/DCV

TDF/3TC, efavirenz, entecavir and most TB drugs will be generic worldwide in 2017. Prices should then fall in all countries, close to Indian / South African levels.

- <$90 price to cure Hepatitis C will only be in low and middle income countries
Could pharmaceutical companies lower their prices, but then treat more people?
Price of sofosbuvir by country (12 weeks)

Sofosbuvir prices:
3. Germany: medizinfuchs.de
5. UK: British National Formulary 2016
7. Australia: Based on total annual government expenditure (AU$200 million) and 40,000 treated in 2016
If drug prices were lower, could pharmaceutical companies still afford to do R&D?
Gilead sales and profits

Cumulative sales of Sovaldi & Harvoni to 3Q 2016:

$40 billion

Profits in 2015:

$18 billion

Reference: Gilead quarterly product sales summaries
Gilead: $10 billion in tax avoidance

Washington Post, July 13 2016. Gilead is using Ireland as a tax haven for global profits.

“The drug company that shocked the world with its prices dodged $10 billion in taxes”

$10 billion is enough money to treat 100 million people with HCV, at the cost price of $100 each

# Pharma profits and tax avoidance

Main tax havens: Bermuda, Cayman Islands, BVI, Bahamas, Luxembourg, Ireland

<table>
<thead>
<tr>
<th>Company</th>
<th>Profits held offshore</th>
<th>US Taxes Avoided</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer</td>
<td>$69 billion</td>
<td>$20 billion</td>
</tr>
<tr>
<td>Merck</td>
<td>$57 billion</td>
<td>$16 billion</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>$51 billion</td>
<td>$14 billion</td>
</tr>
<tr>
<td>Amgen</td>
<td>$26 billion</td>
<td>$9 billion</td>
</tr>
<tr>
<td>Abbott</td>
<td>$24 billion</td>
<td>$7 billion</td>
</tr>
<tr>
<td>BMS</td>
<td>$24 billion</td>
<td>$7 billion</td>
</tr>
</tbody>
</table>

Options if drugs still patented - Voluntary licenses

Some pharmaceutical companies allow cheap generics to be sold in certain low and middle income countries, with voluntary licenses. However:

1. China, South America, Russia and Eastern European countries are not included in most of these agreements. As a result, prices in these countries can be unaffordable.

2. Other countries may have voluntary licenses but if the company does not register the drug for regulatory approval, then the drug cannot be accessed.

3. Merck and AbbVie have no voluntary licenses for their Hepatitis C treatments.
Sofosbuvir voluntary license coverage

A new option for access to treatment: HIV and Hepatitis C buyers clubs

There are many companies willing to export generic PrEP and DAAs into Europe and North America

Several generic ARVs are already approved by the US Food and Drug Administration and the World Health Organization.

Generic PrEP or DAAs can be bought online in 10 minutes. Prices are falling rapidly.

www.alldaychemist.com
www.iwantprepnow.co.uk
www.fixhepc.com
www.myhepc.info
Patented vs Generic drugs for HCV

Harvoni
€45,000

Generic SOF/DCV
€900

Hepatitis C: https://www.youtube.com/watch?v=HBF5cf5zt9U
HIV: https://youtu.be/JXnaHYzyAq4
Routes of export: https://youtu.be/X1QSHkUAP50
The legal basis of personal importation

Article 60 of TRIPS - *De Minimis* Imports – states:  
*Members may exclude from the application of the above provisions small quantities of goods of a non-commercial nature contained in travellers' personal luggage or sent in small consignments.*

In line with Article 60, most countries allow some form of personal medication importation

Medicines are being sent from India, China, Egypt and Bangladesh to countries all over the world
FixHepC Buyer’s Club

N = 438
RVR: 85%
EOT: 99%
SVR4: 89%

[Poster 256 – HIV Glasgow 2016]
Hep C Treatment Without Borders

http://hepatitisctreatment.homestead.com/

N = 151
RVR: 74%
EOT: 93%
SVR4: 96%
SVR12: 96%
South East Asia Buyer’s Club

N = 237
RVR: 99%
EOT: 99%
SVR4: 100%
SVR12: 92%

[Poster 256 – HIV Glasgow 2016]
Russian Buyer’s Club

N = 213  
RVR: 85%  
EOT: 100%  
SVR4: 100%  
SVR12: 98%  

$490 for SOF/DCV, 12 weeks

[Poster 261 – HIV Glasgow 2016]
Conclusions

Elimination of disease is only affordable if drugs can be accessed at low prices, within national health budgets.

We need new approaches to funding mass treatment programmes for Hepatitis C in Europe:

“All you can Treat” pricing – unlimited treatments for a fixed price
Or
Lower fixed prices. Under €4000 per cure for Hepatitis C.

Most drugs are fundamentally cheap to produce, so pharmaceutical companies can still make large profits from selling to larger numbers of people at lower unit prices.
Conclusions

If pharmaceutical companies refuse to lower prices, we need back-up mechanisms to ensure access:

- Compulsory licenses
- Buyers Clubs
- Windfall taxes on tax avoidance

Recovery of Gilead’s $10 billion in avoided tax alone would provide sufficient funds to treat everyone with Hepatitis C worldwide, at cost price of <$90 per person.