Generic HCV DAAs

Economics and sustainability

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HCV DAAs can be made very cheaply

SOF/DCV can be made for under $100 per 12 week course

70 million people with Hepatitis C

Basic cost of treatment is $7 billion, to treat everyone worldwide
Cost per kg of sofosbuvir API exports over time
Cost-based generic price of sofosbuvir (12 weeks)

Cost of API = $1,050/kg

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

API per 12 weeks = $35

Formulation = $0.01/tablet

Formulated drug = $36

Packaging = $0.35/month

Packaged drug = $37

Final generic price = $42

Profit margin and tax = 13%
Cost per kg of daclatasvir API exports over time
Cost-based generic price of daclatasvir (12 weeks)

Cost of API = $973/kg

API needed per person = 5g (60mg x 84 days)

API per 12 weeks = $5

Formulation = $0.01/tablet

Formulated drug = $6

Packaging = $0.35/month

Packaged drug = $7

Profit margin and tax = 13%

Final generic price = $8
Global sales of DAAs: $61 billion from 2014-2017, and rising

- Gilead: $49 Billion
- AbbVie: $3 billion
- BMS: $4 billion
- J&J: $3 billion
- Merck: $2 billion

Total sales = $61 billion
We need to treat more people to overcome the effect of new HCV infections

In 2016, worldwide

1.5 million people were cured (SVR)
300,000 people died from HCV
1.6 million new infections

Countries with 5x more cures than infections

Countries with 5x fewer cures than infections

Hepatitis C: net cure rates in 2016, by country
SVR + deaths – new infections

### Change in the HCV epidemic from cures versus new HCV infections, 2016-2017

<table>
<thead>
<tr>
<th>Region</th>
<th>HCV Epidemic 2016</th>
<th>New HCV infections</th>
<th>Number cured</th>
<th>HCV-related deaths</th>
<th>HCV Epidemic 2017</th>
<th>Net change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia &amp; Pacific</td>
<td>29,564,900</td>
<td>574,330</td>
<td>456,552</td>
<td>179,810</td>
<td>29,502,868</td>
<td>- 62,032</td>
</tr>
<tr>
<td>Central &amp; Eastern Europe</td>
<td>6,507,700</td>
<td>322,800</td>
<td>26,110</td>
<td>15,505</td>
<td>6,788,885</td>
<td>+ 281,185</td>
</tr>
<tr>
<td>Central &amp; South America</td>
<td>3,477,400</td>
<td>27,537</td>
<td>47,859</td>
<td>21,496</td>
<td>3,435,582</td>
<td>- 40,548</td>
</tr>
<tr>
<td>North Africa &amp; Middle East</td>
<td>7,399,470</td>
<td>156,660</td>
<td>542,724</td>
<td>51,944</td>
<td>6,961,462</td>
<td>- 438,008</td>
</tr>
<tr>
<td>North America</td>
<td>2,955,600</td>
<td>31,870</td>
<td>216,731</td>
<td>20,829</td>
<td>2,749,910</td>
<td>- 205,690</td>
</tr>
<tr>
<td>Sub Saharan Africa</td>
<td>5,069,000</td>
<td>130,800</td>
<td>3,805</td>
<td>21,540</td>
<td>5,174,455</td>
<td>+ 105,455</td>
</tr>
<tr>
<td>Western Europe</td>
<td>2,364,430</td>
<td>35,440</td>
<td>105,821</td>
<td>14,951</td>
<td>2,279,098</td>
<td>- 85,332</td>
</tr>
<tr>
<td><strong>Global</strong></td>
<td><strong>69,554,808</strong></td>
<td><strong>1,597,812</strong></td>
<td><strong>1,512,759</strong></td>
<td><strong>383,998</strong></td>
<td><strong>69,255,863</strong></td>
<td><strong>- 298,945</strong></td>
</tr>
</tbody>
</table>

For every person cured of HCV worldwide in 2016, another person was newly infected.
HCV – we need to treat more people

• In 2016, for every person cured of HCV, another person was newly infected

• Rates of treatment are still far too low to allow elimination of HCV worldwide by 2030

• This is despite massive sales of DAAs by pharmaceutical companies (over $61 billion between 2014-2017).

• Harm reduction needs to be intensified, to lower infection rates
Getting to Elimination of HCV - three main problems

1. “Diagnostic burn-out”

2. Lack of WHO pre-qualification / Regulatory “no-mans land”
   - Bioequivalence
   - Batch stability
   - Adherence to Good Manufacturing Practice

3. Voluntary licenses are too restrictive.
“Diagnostic burn-out”

• In many countries, rates of HCV diagnosis are too low to allow elimination of HCV by 2030

• The percentage of people already diagnosed, and newly diagnosed, is highly correlated with Gross National Income

• We will need new HCV testing campaigns to be put in place, similar to “test and treat” strategies for HIV.
HCV Diagnosis worldwide by World Bank Income Group

WHO Target: 90% diagnosed

- **High Income Countries**: 44% diagnosed
- **Upper-Middle Income Countries**: 17% diagnosed
- **Lower-middle Income Countries**: 15% diagnosed
- **Low income countries**: 9% diagnosed

Ref: Polaris observatory database 2017
WHO pre-qualification and quality standards

Generic companies:

India: Natco, Hetero, Mylan, Cipla
Egypt: Pharco
Algeria: Bekar
Bangladesh: Incepta, Beacon
Other companies in Sri Lanka, Iran, Brazil, China, Morocco, Pakistan

Which companies have BE, GMP and batch stability?
Results should be published and presented – this was done for HIV
Even so, generic HCV DAAs work very well

High and consistent SVR rates in a range of programmes.

FixHepC – Australia
Hepatitis C Treatment without Borders – Australia
International Treatment Preparedness Coalition – Russia
SE Asian programme – Thailand

There are many other smaller operations in progress
Generic DAAs are being widely used.
FixHepC programme: SVR4 by Genotype

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Percentage SVR</th>
<th>Number (Total)</th>
</tr>
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<tbody>
<tr>
<td>GT1</td>
<td>96% (288/301)</td>
<td></td>
</tr>
<tr>
<td>GT2</td>
<td>100% (28/28)</td>
<td></td>
</tr>
<tr>
<td>GT3</td>
<td>87% (88/101)</td>
<td></td>
</tr>
<tr>
<td>GT4</td>
<td>91% (10/11)</td>
<td></td>
</tr>
<tr>
<td>GT5/6</td>
<td>100% (7/7)</td>
<td></td>
</tr>
</tbody>
</table>
Russian, Australian and SE Asian buyers clubs: SVR4 by Genotype

% HCV RNA <25 IU/mL

- GT1: 98%
- GT2: 100%
- GT3: 99%
- GT4: 100%
- GT5 & GT6: 100%

HCV Genotype
58% of the HCV epidemic is not covered by the Gilead voluntary licenses.
Other companies are even worse

Bristol-Myers – issued VL for daclatasvir, not helping with registrations in low or middle income countries

AbbVie – where is the VL for glecaprevir/pibrentasvir?

Merck – where is the VL for elbasvir/grazoprevir?
Conclusions – what needs to be done

1. “Diagnostic burn-out” – we need to integrate diagnosis of viral hepatitis into HIV treatment programmes

2. Regulatory “no-mans land” – published, transparent evidence from each generic supplier. Accelerate WHO PQ

3. Voluntary licenses – include more countries, get the drugs registered – needs more support.
Elimination of Hepatitis C as a threat to public health

It has taken 15 years to get to 18 million people on ARV treatment
We have learned a lot from HIV – Hepatitis C should be easier.

We already have the drugs needed to eliminate HCV worldwide
Let’s learn from the past, and repeat this medical success story.