Treating epidemics with low-cost generics

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Worldwide deaths from HCV, HBV, HIV, tuberculosis, and malaria in 2013

Deaths per year (thousands)

- HBV & HCV: 1,389,800
  - Cirrhosis: 1,341,000
  - Liver cancer: 1,290,300
  - Acute HCV, 3.5: 854,600

Africa, 1999: mass treatment for HIV/AIDS is not feasible
A key moment in the history of HIV

“My generics company can manufacture HIV antiretrovirals for a dollar per day”

Dr Yussef Hamied
Cipla,
G8 summit,
2000
Could we eliminate Hepatitis B and C worldwide by producing treatments cheaply?
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.
From API cost/kg to target price

API price/kg x grams per treatment course + $0.01 / tablet, + $0.35/month formulation x 10-50% profit margin

10% for mass-produced drugs – e.g. HIV, TB
Target versus Global lowest prices: HIV and TB

weights = kg exported 2Q2016
Exports of sofosbuvir API from India prices are falling rapidly

Total exported volumes equivalent to 344,000 12-week courses
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

Exports of daclatasvir API from India - prices also falling

Target generic price of daclatasvir (12 weeks)

- **Cost of API = $998/kg**
- **API per 12 weeks = $5**
- **Formulated drug = $8**
- **Packaged drug = $9**
- **Final generic price = $14**
- **API needed per person = 5g (60mg x 84 days)**
- **Formulation + excipients = $0.04 per pill**
- **Packaging = $0.35/month**
- **Profit margin = 50%**

Gotham D, Barber M, Fortunak J, Pozniak A, Hill A.
Abstract number A-792-0516-01639, presented at AIDS2016, Durban.

Lowest prices of daclatasvir in selected countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Price for 12-week treatment course</th>
</tr>
</thead>
<tbody>
<tr>
<td>US (list price)</td>
<td>$63,000</td>
</tr>
<tr>
<td>(Veterans Affairs)</td>
<td>$50,653</td>
</tr>
<tr>
<td>France</td>
<td>$39,387</td>
</tr>
<tr>
<td>UK</td>
<td>$37,152</td>
</tr>
<tr>
<td>Spain</td>
<td>$35,174</td>
</tr>
<tr>
<td>Brazil</td>
<td>$2,552</td>
</tr>
<tr>
<td>India</td>
<td>$153</td>
</tr>
<tr>
<td>Target</td>
<td>$14</td>
</tr>
</tbody>
</table>
**HCV DAAs: costs of API, targets and current prices**

<table>
<thead>
<tr>
<th>Drug</th>
<th>API cost/kg</th>
<th>Target price for finished product per treatment</th>
<th>Current lowest Indian market price</th>
<th>Current US price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sofosbuvir (SOF)</td>
<td>$1,094</td>
<td>$62</td>
<td>$324</td>
<td>$49,860-84,000</td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>$998</td>
<td>$14</td>
<td>$153</td>
<td>$50,653-63,000</td>
</tr>
<tr>
<td>Ledipasvir (LDV)</td>
<td>$2,441</td>
<td>$34</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>SOF+LDV</td>
<td>N/A</td>
<td>$96</td>
<td>$507</td>
<td>$56,700-94,500</td>
</tr>
<tr>
<td>Velpatasvir (VEL)</td>
<td>$8,900-11,700</td>
<td>$119-154</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>SOF+VEL</td>
<td>N/A</td>
<td>$181-216</td>
<td>-</td>
<td>$74,760</td>
</tr>
</tbody>
</table>

Sofosbuvir + Daclatasvir ± RBV (12-24 wks)
Percentage of people cured, by Genotype

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Percent SVR</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>96%</td>
<td>1459/1575</td>
</tr>
<tr>
<td>G2</td>
<td>100%</td>
<td>21/22</td>
</tr>
<tr>
<td>G3</td>
<td>90%</td>
<td>628/752</td>
</tr>
<tr>
<td>G4</td>
<td>100%</td>
<td>296/316</td>
</tr>
<tr>
<td>G5</td>
<td>100%</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 of people cured, by Genotype

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<td>100%</td>
</tr>
<tr>
<td>G5</td>
<td>97%</td>
</tr>
<tr>
<td>G6</td>
<td>100%</td>
</tr>
</tbody>
</table>

Counts:
- G1: 749/778
- G2: 259/261
- G3: 535/592
- G4: 128/128
- G5: 34/35
- G6: 42/42
Target versus Global lowest prices: HIV, TB and Hepatitis

weights = kg exported 2Q2016

Target price

Global lowest price
Mass produced HCV DAAs should fall to <$90 per 12-week course.
Entecavir for Hepatitis B
one year’s supply (0.2g)
Entecavir for Hepatitis B
cost per person/year by country

Entecavir (Baraclude)
US price: $15,111
Cost price: $36
Price of Moxifloxacin by country

Moxifloxacin

US price: $806

Cost price: $6
Price of Linezolid by country

- US (Pfizer): $4,298
- Spain (Pfizer): $2,011
- UK (Pfizer): $1,862
- South Africa (Pfizer): $1,246
- Russia (Pfizer): $711
- Russia (generic): $690
- GDF Catalogue (generic): $150
- India (SRA-generic): $70
- India (non-SRA-generic): $17
- High Target: $13
- Low Target: $5

Price in USD per month
Imatinib (Gleevec)

US price: $106,322

Cost price: $180
<table>
<thead>
<tr>
<th>Drug</th>
<th>Major indication</th>
<th>Target price</th>
<th>Indian price (or other lowest)</th>
<th>US price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imatinib</td>
<td>Chronic Myeloid Leukaemia</td>
<td>$172</td>
<td>$803</td>
<td>$107,799</td>
</tr>
<tr>
<td>Erlotinib</td>
<td>Non-Small Cell Lung Cancer</td>
<td>$240</td>
<td>$1932</td>
<td>$79,891</td>
</tr>
<tr>
<td>Sorafenib</td>
<td>Renal Cell Carcinoma</td>
<td>$1450</td>
<td>$1332</td>
<td>$139,138</td>
</tr>
<tr>
<td>Lapatinib</td>
<td>Breast Cancer</td>
<td>$4020</td>
<td>$18,603 (Thailand)</td>
<td>$75,161</td>
</tr>
<tr>
<td>Cabazitaxel</td>
<td>Metastatic prostate cancer</td>
<td>$666</td>
<td>$30,810 (South Africa)</td>
<td>$120,613</td>
</tr>
<tr>
<td>Dasatinib</td>
<td>Chronic Myeloid Leukaemia</td>
<td>$15</td>
<td>$1183 (Brazil)</td>
<td>$10,408</td>
</tr>
<tr>
<td>Pazopanib</td>
<td>Renal Cell Carcinoma</td>
<td>$116</td>
<td>$1463 (Brazil)</td>
<td>$8412</td>
</tr>
<tr>
<td>Abiraterone</td>
<td>Metastatic prostate cancer</td>
<td>$3589</td>
<td>$27,570 (Thailand)</td>
<td>$85,877</td>
</tr>
<tr>
<td>Gefitinib</td>
<td>Non-Small Cell Lung Cancer</td>
<td>$16</td>
<td>$139</td>
<td>$6728</td>
</tr>
<tr>
<td>Capecitabine</td>
<td>Metastatic Colorectal Cancer</td>
<td>$73</td>
<td>$126 (Latvia)</td>
<td>$1941</td>
</tr>
</tbody>
</table>
The new $90 $90 $90

There could be standard prices for HIV, Hepatitis B and Hepatitis C in low/middle income countries.

< $90 for 12-weeks course of HCV DAAs – SOF/DCV
< $90 per year to treat HIV – TDF/3TC/EFV
< $90 per year to treat Hepatitis B – TDF/3TC
Widespread access to generics

When patents have expired, drugs should be available worldwide, at close to the cost of production

However, few national health services know these costs

Widespread over-charging

Pricing transparency is needed (WHO panel)

Lower costs for generics could drive down patented drug prices in the same therapeutic area
Paracetamol – UK NHS

NHS spends £87m on paracetamol... at 20 TIMES the high street cost:

Doctors wrote 22.9m prescriptions last year at an average cost of £3.83 each

Average prescription cost 20 times price of 25p box from supermarket

Source: The Daily Mail, 28th July 2016
Value of patented drugs before generics have been approved

Pharmaceutical company negotiates additional value of new drug versus price of current branded version

For example Tenofovir alafenamide (TAF) versus Tenofovir disoproxil fumarate (TDF)
Value of patented drugs after generics have been approved

In 2017, after approval of generic TDF/3TC, price of new drug has to fall, to remain cost-effective versus generic alternative.
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.

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.

Other countries may have voluntary licenses but no registration of the drug – so it is not available.

Not all companies set up these licenses.
SOFOSBUVIR VOLUNTARY LICENSE & REGISTRATION

- No voluntary license
- Voluntary license, not registered
- Voluntary license, registration pending/filed
- Voluntary license, registered

Other options if drugs still patented

“Flat rate pricing”- single large payment for unlimited use
Can only be organised in countries with highly centralised procurement – e.g. Australia, HCV DAAs

Compulsory licensing – a country declares a national health emergency and buys drug from generic supplier (e.g. ciprofloxacin in USA after Anthrax scare in 2001)
If drug prices were lower, could pharmaceutical companies still afford to do R&D?
Gilead sales and profits

Cumulative sales of sofosbuvir and Harvoni to end 2015:  
$31.5 billion

Profits in 2015:  
$18 billion
## Pharma profits and tax avoidance

<table>
<thead>
<tr>
<th>Company</th>
<th>Profits held offshore</th>
<th>US Tax 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>
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Gilead: $10 billion in tax avoidance

Washington Post, July 13 2016:

“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
Hepatitis C buyers clubs

There are many companies willing to export generic DAAs into Europe / North America.

Generic sofosbuvir can be bought online in 15 minutes, for approx. $1200 per course. Prices falling rapidly.

But what about quality?

We need systems in place to ensure that supplies are from accredited generic manufacturers.
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 and Bangladesh to countries all over the world
2015: daclatasvir imported into Australia from Mescochem, China
2016: Generics from India and Bangladesh

Incepta (Bangladesh) Twinvir Ledifos
SOF/LDV SOF/LDV

Hetero (India) Ledifos
SOF/LDV

Cipla (India) HepcvirL
SOF/LDV
The FixHepC Buyers Club (www.fixhepc.com)
Published SVR12 Results SOF+LDV and SOF+DCV

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<td>90% (365/406)</td>
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<tr>
<td>GT4</td>
<td>94% (102/109)</td>
</tr>
<tr>
<td>GT5/6</td>
<td>95% (41/43)</td>
</tr>
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REDEMPTION-1 Overall SVR4 Results For Generics

Note: Some small percentage loss of SVR is expected during the SVR4 to SVR12 period
Hepatitis C Treatment Without Borders

36 countries
103 hospitals/clinics/private doctors
South East Asian HCV Buyers Club
Russian HCV Buyers Club
Conclusions - 1

There is now the potential to eliminate Hepatitis B and Hepatitis C using drugs which are cheap to manufacture.

US $10 billion would be enough money to treat everyone with chronic HCV worldwide.

Hepatitis B can be treated with generics costing less than $90 per person-year – patent expiry 2017/8.

By 2017/8, HIV could be treated with generics costing <$90 worldwide (TDF/3TC/EFV).
Conclusions - 2

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:

Flat pricing – unlimited treatment for a fixed price
Voluntary licenses – from all pharma companies

Most drugs are fundamentally cheap to produce, so pharmaceutical companies can still make large profits from selling to large numbers of people at low unit prices.
Conclusions - 3

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 avoided tax alone would provide sufficient funds to treat everyone with Hepatitis C worldwide.
Universal access to HIV treatment is one of the greatest success stories in medicine (>17 million treated).

This should not stand alone, but be repeated for mass treatment of cancer, viral hepatitis and other diseases – this time, more quickly.
Thanks to:

St Stephens AIDS Trust
Anton Pozniak
Marta Boffito

Global Health
Dzintars Gotham
Vicky Houghton-Price
Jake Levi
Roxanna Korologou-Linden
Bryony Simmons
Rachel Smith

Howard University, USA
Joe Fortunak

Hepatitis C Buyers Clubs:
Greg Jeffreys
– HCV Treatment without borders

James Freeman – FixHepC

Sergey Golovin and Julia Dragunova –
- ITPC Russia

Giten Khwairakpan
- SE Asian Buyers Club

- And all the patients who took these generic DAAs especially in the early days