FDA Approves 'Game Changer' Hepatitis C Drug Sofosbuvir

Miriam E. Tucker | Disclosures
December 06, 2013

Gilead’s $84,000 Treatment Questioned by U.S. Lawmakers

By Drew Armstrong | Mar 21, 2014 9:07 PM GMT+0100 | 6 Comments

SHOTS - HEALTH NEWS

$1,000 Pill For Hepatitis C Spurs Debate Over Drug Prices

Morning Edition
Feb 06, 2014 | See Full Story

A drug to cure hepatitis C has FDA approval. But at $84,000 per person, who will have access to it?

MSF responds to reports on Gilead pricing for hepatitis C drug sofosbuvir in developing countries
Sofosbuvir

Bought in 2011 by Gilead for 11 billion: "a huge and risky bet on the next generation of hepatitis C treatments" (Reuters)

Patent situation:

- Patents filed widely by Gilead (originally patents filed by Pharmasset) on compound, pro-drug and various combinations with other drugs
- **Patent expiry:** 2024/2028

Regulatory status:

US FDA approval December 2013 (priority review for a new medical entity); EMA approval January 2014; registered in Egypt, other applications pending
HCV Direct-Acting Antivirals (DAAs) in development

Source: Nathan Ford, WHO
Sofosbuvir: Price and access

US: $84,000/12 weeks treatment course (= $1.000/tablet)
(Source: Gilead)

Germany: US$66,000
UK: US$57,000
Egypt: US$900

Turnover: 1st half 2014: 5.75 billion US$

Estimated production costs for a treatment course (84 tablets):
Sofosbuvir: $68 - 136

Source: A. Hill et al. "Minimum costs for producing hepatitis C DAA for use in large-scale treatment access programs in developing countries", Clinical Infectious Diseases, Feb 13, 2014
## Hepatitis C Global Prevalence by Country

<table>
<thead>
<tr>
<th>Country</th>
<th>Income classification</th>
<th>Most prevalent genotypes</th>
<th>Anti-HCV* (%)</th>
<th>No. infected</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>Upper-middle</td>
<td>1,2,6</td>
<td>2.2</td>
<td>29,791,212</td>
</tr>
<tr>
<td>India</td>
<td>Lower-middle</td>
<td>1,3</td>
<td>1.5</td>
<td>18,216,960</td>
</tr>
<tr>
<td>Egypt</td>
<td>Lower-middle</td>
<td>4</td>
<td>14</td>
<td>11,826,360</td>
</tr>
<tr>
<td>Indonesia</td>
<td>Lower-middle</td>
<td>1,2</td>
<td>3.9</td>
<td>9,436,986</td>
</tr>
<tr>
<td>Pakistan</td>
<td>Lower-middle</td>
<td>3</td>
<td>5.9</td>
<td>9,422,402</td>
</tr>
<tr>
<td>Russia</td>
<td>Upper-middle</td>
<td>1,3</td>
<td>4.1</td>
<td>5,796,498</td>
</tr>
<tr>
<td>USA</td>
<td>High</td>
<td>1,2,3</td>
<td>1.8</td>
<td>5,367,834</td>
</tr>
<tr>
<td>Democratic Republic of Congo</td>
<td>Low</td>
<td>4</td>
<td>6.4</td>
<td>4,010,240</td>
</tr>
<tr>
<td>Nigeria</td>
<td>Lower-middle</td>
<td>1,2</td>
<td>2.1</td>
<td>3,323,439</td>
</tr>
<tr>
<td>Japan</td>
<td>High</td>
<td>1,2</td>
<td>2.4</td>
<td>3,058,008</td>
</tr>
<tr>
<td>Cameroon</td>
<td>Lower-middle</td>
<td>1,2,4</td>
<td>13.8</td>
<td>2,754,204</td>
</tr>
<tr>
<td>Brazil</td>
<td>Upper-middle</td>
<td>1,3</td>
<td>1.4</td>
<td>2,609,670</td>
</tr>
<tr>
<td>Uganda</td>
<td>Low</td>
<td>1,4</td>
<td>6.6</td>
<td>2,230,536</td>
</tr>
<tr>
<td>Philippines</td>
<td>Lower-middle</td>
<td>1</td>
<td>2.2</td>
<td>1,932,854</td>
</tr>
<tr>
<td>Italy</td>
<td>High</td>
<td>1,2</td>
<td>3.2</td>
<td>1,923,136</td>
</tr>
<tr>
<td>Ukraine</td>
<td>Lower-middle</td>
<td>1</td>
<td>4.0</td>
<td>1,864,840</td>
</tr>
<tr>
<td>Uzbekistan</td>
<td>Lower-middle</td>
<td>1,3</td>
<td>6.5</td>
<td>1,774,955</td>
</tr>
<tr>
<td>Turkey</td>
<td>Upper-middle</td>
<td>1</td>
<td>2.2</td>
<td>1,549,108</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>Low</td>
<td>1,2,4</td>
<td>1.9</td>
<td>1,500,734</td>
</tr>
<tr>
<td>Thailand</td>
<td>Upper-middle</td>
<td>1,3,6</td>
<td>2.2</td>
<td>1,499,058</td>
</tr>
</tbody>
</table>

| World’s Population           |                       |                          | 2-3%          | 160-180 million   |


*Prevalence of antibody to HCV
What can we learn from HIV?

Factors contributing to lower prices and increased access include:

- Increased funding creating economies of scale (Global Fund, UNITAID, Clinton Foundation et al)
- Possibility to manufacture in India (WTO transition periods allowed delaying pharmaceutical product patents until 2005)
- Political will due to pressure from HIV/AIDS activists and civil society
- WHO standard treatment guidelines
- UN/WHO prequalification programme ensuring quality of generics
- Voluntary license agreements and creation of the Medicines Patent Pool
- Use of compulsory licenses and competition law
- Patent oppositions in key producing countries
- Price reductions/differential pricing by originators and price negotiations
What are the options?

**Local production:** Freedom-to-operate: legal possibility to produce a generic version in a country

- Clarity on patent status needed
- FTO in countries that do not grant patents, e.g. Bangladesh and other least developed countries

**Patent oppositions & local production:** Opposing patents can allow local production

- E.g. I-MAK opposed sofosbuvir patent in India
## Patent landscapes of Hep C medicines

<table>
<thead>
<tr>
<th>Nucleoside polymerase inhibitor</th>
<th>Sponsor</th>
</tr>
</thead>
<tbody>
<tr>
<td>sofosbuvir</td>
<td>Gilead Sciences</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Non-nucleoside polymerase inhibitors</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Dasabuvir (ABT-333)</td>
<td>AbbVie</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NS5A inhibitors</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ombitasvir (ABT-267)</td>
<td>AbbVie</td>
</tr>
<tr>
<td>daclatasvir (BMS-790052)</td>
<td>BMS</td>
</tr>
<tr>
<td>ledipasvir (GS-5885)</td>
<td>Gilead Sciences</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Protease inhibitors</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ABT-450</td>
<td>AbbVie</td>
</tr>
<tr>
<td>simeprevir (TMC435)</td>
<td>Janssen</td>
</tr>
</tbody>
</table>
What are the options?

**Differential pricing**: company charging different prices in different countries according to income level and disease burden.

**e.g.** Sofosbuvir three tiers:
- upper-middle income countries
- lower-middle income countries
- low income countries

Gilead considers China, Georgia, Russia, Ukraine commercial markets

Less effective than competition; often prices in middle-income countries still high in comparison to marginal costs.
What are the options?

License agreements: Gilead signed agreements with seven Indian companies on sofosbuvir allowing exports to 90 countries (+ India)

License agreements through the Medicines Patent Pool: Negotiates licenses for HIV in public interest (currently no mandate for hepatitis); better conditions and broader scope – e.g. atazanavir license: 110 countries and additionally countries where the patent was not granted
What are the options?

**Compulsory licenses:** countries can issue compulsory licenses to locally produce or import a medicine; no emergency necessary; abusive prices can be a legitimate reason

- Producing active pharmaceutical ingredient can be a challenge
- Import requires a source for generic sofosbuvir

**E.g.** in the area of HIV used by Brazil, Ecuador, Indonesia, Thailand and other countries
Prequalification: A UN Programme managed by WHO

Vision: Good quality medicines for everyone

September 2014: Call for Expressions of Interest
Hepatitis C/B

– Sofosbuvir tablet, 400mg
– Simeprevir capsule, 150mg
– Ribavirin capsule, 200mg, 400mg, 600mg
– Entecavir tablet, 0.5mg, 1mg scored
– Tenofovir, tablet 300mg
– *Tenofovir, tablets 150mg, 200mg, preferably dispersible
Technical Assistance

WHO, on request, provides technical assistance to Member States to identify best options to access new treatments. Example Egypt:

- Joint mission of Dep. of HIV/Hepatitis & Dep of Essential Medicines & country office to advise Egypt on new treatments, including negotiations with companies

- Half a day training on IP and health issues in MoH

- 2-days training involving all relevant agencies and Ministries on public health and IP with WIPO and WTO in June 2014
Promoting Access to Medical Technologies and Innovation

www.who.int/phi/promoting_access_medical_innovation/en/

www.who.int/phi/publications/category/en/

Dr Peter Beyer
Senior Advisor
World Health Organization
beyerp@who.int
Tel. +41-22-791 25 07