Access to Diagnosis and Treatment of Viral Hepatitis

Improving the Response of Global Public Health in a Fast-changing World, Joint UNICEF-UNFPA-WHO meeting with manufacturers and suppliers, 2nd Dec 2019

Dr Nicole Seguy
WHO Regional Office for Europe
STATUS OF HEPATITIS B GLOBALLY

Incidence:
Chronic HBV infection in children under 5 reduced from 4.7% to 1.3% (immunization)

Prevalence:
257 million people living with HBV (68% in Africa /Western Pacific)

Sources – WHO (LSHTM)
**STATUS OF HEPATITIS C GLOBALY**

**Incidence:**
1.75 million new infections / year
(Unsafe health care and injection drug use)

**Prevalence:**
71 million infected, all regions

Sources – WHO (Center for Disease Analysis)
Global Deaths on the rise

Estimated global number of deaths due to viral hepatitis, HIV, malaria and TB, 2000-2015

Number of deaths

- Hepatitis
- Tuberculosis
- HIV
- Malaria
Hepatitis B and C: the biggest killers

In the WHO European Region:

- **B** 15 million people living with HBV
- **B** 56,000 deaths/year
- **B** Universal vaccination in 49/53 countries

- **C** 14 million people living with HCV
- **C** 112,500 deaths/year

Liver fibrosis, cirrhosis, liver cancer

Over 2/3 of cases in EECA countries

Risk Factors:

- Injecting drug use
- Health care settings/unsafe inj
- Unsafe blood transfusion
- HIV infection
- Closed settings, prisons
- Unsafe sex (HBV)
Global and regional agenda: elimination of viral hepatitis as a public health threat by 2030

- 6-10 mio infections (in 2015) to 900,000 infections (by 2030)
- 1.4 mio deaths (in 2015) to under 500,000 deaths (by 2030)
Measuring the progress on vertical transmission prevention is limited by data on pregnant women screening coverage.

**Measuring the progress on HBV treatment is now limited by the absence of data on the proportion of persons eligible.
The number of countries in the European Region with national hepatitis plans increased from 13 (in 2013) to 33 (in 2019).
What to do to Achieve Viral Hepatitis Elimination

• Implement effective interventions to prevent transmission
• Expand testing and treatment access:
  – Diagnostic tests (antibody testing RDT/ EIA, HCV VL, HCV cAg)
  – Tenofovir or Entecavir for HBV
  – Direct acting antivirals (DAA) for HCV
    • Sofosbuvir/ Daclatasvir
    • Sofosbuvir/ Ledipasvir etc....
• Simplify treatment and monitoring
Access to VH drugs and diagnostics
# WHO prequalified IVDs for HCV (oct 2019)

<table>
<thead>
<tr>
<th>Method</th>
<th>Prequalified</th>
<th>Under Review</th>
</tr>
</thead>
<tbody>
<tr>
<td>EIA</td>
<td>INNOTEST HCV Ab IV</td>
<td>Enzygnost Anti-HCV 4.0</td>
</tr>
<tr>
<td></td>
<td>INNO-LIA HCV Score</td>
<td>Monolisa HCV Ag-Ab Ultra</td>
</tr>
<tr>
<td></td>
<td>Bioelisa HCV 4.0</td>
<td></td>
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<tr>
<td></td>
<td>Murex anti-HCV 4.0</td>
<td></td>
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<tr>
<td>RDT</td>
<td>OraQuick HCV (FP, Oral)</td>
<td>Standard Q HCV Ab Test</td>
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<tr>
<td></td>
<td>SD Bioline (FP)</td>
<td></td>
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<tr>
<td></td>
<td>Rapid Anti-HCV (InTec))</td>
<td></td>
</tr>
<tr>
<td>RNA</td>
<td>Xpert HCV VL (plasma)</td>
<td></td>
</tr>
<tr>
<td>HCVcAg</td>
<td>ARCHITECT HCV Ag (Denka Seiken, Japan)</td>
<td></td>
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</tbody>
</table>
### WHO prequalified antiviral drugs for HCV and HBV

<table>
<thead>
<tr>
<th>DAA prequalified</th>
<th>Form and dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sofosbuvir, Mylan India</td>
<td>Tablet, 400mg</td>
</tr>
<tr>
<td>Sofosbuvir, Hetero India</td>
<td>Tablet, 400mg</td>
</tr>
<tr>
<td>Sofosbuvir, European Egyptian Pharm.</td>
<td>Tablet, 400mg</td>
</tr>
<tr>
<td>Sofosbuvir, Cipla</td>
<td>Tablet, 400mg</td>
</tr>
<tr>
<td>Entecavir, Hetero</td>
<td>Tablet, 0.5mg</td>
</tr>
<tr>
<td>Entecavir, Hetero</td>
<td>Tablet, 1mg</td>
</tr>
<tr>
<td>Daclatasvir (dihydrochloride), BMS</td>
<td>Tablet, 30mg</td>
</tr>
<tr>
<td>Daclatasvir (dihydrochloride), BMS</td>
<td>Tablet, 60mg</td>
</tr>
<tr>
<td>Daclatasvir (dihydrochloride), Mylan</td>
<td>Tablet, 30mg</td>
</tr>
<tr>
<td>Daclatasvir (dihydrochloride), Mylan</td>
<td>Tablet, 60mg</td>
</tr>
<tr>
<td>Sofosbuvir/Velpatasvir, Gilead</td>
<td>Tablet, 400mg/100mg</td>
</tr>
</tbody>
</table>
The cost of DAAs has fallen dramatically, making HCV elimination increasingly affordable.

**EVOlUTION OF PRICING FROM THE PRE-DAA ERA TO 2019**

**(PRICE PER PATIENT (PPP) COURSE)**

- **Pre-DAA Pricing (Pre-2014):** >$3,000
- **Innovator Access Pricing (2014):** $750-$900
- **Global Fund Pricing (2019):** <$102 PPP course
- **Rwanda Pricing (2019):** $60 PPP course
- **Egypt/India/Pakistan Pricing (2019):** $39-$45 PPP course

Note: The Global Fund Reference Pricing of $102 is for a 12-week treatment course of SOF/DCV.
Note: Egypt/India/Pakistan pricing shown is for DAAs that follow local quality standards, but have not received WHO PQ status.
62% of people with HCV live in countries which have access to generic DAAs (in green) (2017)
## Licences for Marketed Viral Hepatitis B and C Medicines (2019)

<table>
<thead>
<tr>
<th>Medicine(s)</th>
<th>Brand Name</th>
<th>Indication</th>
<th>MPP Licence</th>
<th>Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenofovir disoproxil fumarate (TDF)</td>
<td>Viread ®</td>
<td>Hepatitis B (and HIV)</td>
<td>YES</td>
<td>116 countries but few patents remaining are expiring in 2018</td>
</tr>
<tr>
<td>Tenofovir Alafenamide (TAF)</td>
<td>Vemlidy ®</td>
<td>Hepatitis B (and HIV)</td>
<td>YES</td>
<td>116 countries</td>
</tr>
<tr>
<td>Daclatasvir Daclatasvir/Sofosbuvir</td>
<td>Daklinza®</td>
<td>Hepatitis C</td>
<td>YES</td>
<td>112 countries +</td>
</tr>
<tr>
<td>Sofosbuvir Sofosbuvir/ledipasvir</td>
<td>Sovaldi®</td>
<td>Hepatitis C</td>
<td>NO (Gilead bileteral licence)</td>
<td>105 countries</td>
</tr>
<tr>
<td></td>
<td>Harvoni®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Eplclusa®</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Glecaprevir/pibrentasvir (G/P)</td>
<td>Maviret®</td>
<td>Hepatitis C</td>
<td>YES</td>
<td>95 countries and 4 territories</td>
</tr>
</tbody>
</table>

Licences negotiated by MPP or issued directly by patent holder (Gilead) have enabled many developing countries to procure more affordable generic treatments.

Over 100 countries should be able to procure a hepatitis C cure for approx. **USD 102** (Global Fund price for 12 weeks SOF + DAC).

Source: [www.medspal.org](http://www.medspal.org)
# The MPP Daclatasvir license in EECA

<table>
<thead>
<tr>
<th>Licence/Patent Status</th>
<th>Countries</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Countries included in MPP daclatasvir licence</td>
<td>Azerbaijan, Georgia, Turkmenistan, Uzbekistan</td>
<td>Can procure generic daclatasvir</td>
</tr>
<tr>
<td>Countries not included but seem to have no patent</td>
<td>Armenia, Belarus (procuring), Kazakhstan (procuring), Kyrgyz Republic, Moldova (procuring), Ukraine (registration), Tajikistan</td>
<td>May be able to procure from generics not using BMS technology, but legal uncertainty around patent status</td>
</tr>
<tr>
<td>Countries not included where product is patented</td>
<td>Russia</td>
<td>Can only procure from MPP licensees if a compulsory licence is issued</td>
</tr>
</tbody>
</table>
## Gilead Sofosbuvir license in EECA

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</tr>
</thead>
<tbody>
<tr>
<td>Countries <strong>included</strong> in Gilead Sofosbuvir licence</td>
<td>Belarus, Kyrgyz Republic, Tajikistan, Turkmenistan, Ukraine, Uzbekistan, Armenia and Kazakhstan</td>
<td>Can procure generic SOF, SOF/LED, SOF/VEL, SOF/VEL/voxilaprevir</td>
</tr>
<tr>
<td>Countries <strong>not included</strong> where product is patented</td>
<td>Russia</td>
<td>cannot procure from Gilead licensees (unless CL is issued), the patent is being challenged</td>
</tr>
</tbody>
</table>
Despite lower volumes, HCV viral load assays are now available to public sector payers/donors at HIV pricing through pan-disease pricing arrangements.

**EVOLUTION OF VIRAL LOAD PRICING (PRICE PER TEST)**

- **Pre-CHAI Quick-Start Pricing (Pre-2016)**: $>100 (Ex-works price with volume commitment)
- **Abbott (2019)**: $13
- **GenXpert (2019)**: $14.90
- **Roche (2019)**: $8.90
- **Hologic (2019)**: $12

Note: Roche price includes Reagents, Controls & Calibrators, Consumables.
Note: Hologic price includes Reagents, Controls & Calibrators, Consumables, Service & Maintenance, Instrument, Inventory Management.
Conclusion

• Some progress has been made in access to diagnosis and treatment of Viral Hepatitis in our Region
• Coverage of diagnosis and treatment remains low
• Solutions have to be identified to improve access and decrease prices in some MICs
Acknowledgement

WHO
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- Colleagues from CHAI
- Colleagues from FIND
- Liudmyla Maistat, MPP
Thank you!!

Contact:
- eurohep@who.int

http://www.euro.who.int/hepatitis
http://www.who.int/hepatitis/en/
Access to generic medicines for HBV

• Tenofovir patents have expired and countries can procure generics

• Quality generic medicines are available for procurement
  • Tenofovir < USD 30 /year
  • Entecavir ~ USD 400 /year
Flowchart guiding access to DAAs (from access report)

Approach to follow in countries that can access generic medicines:

1. Encourage registration of generic manufacturers
2. Open a tender
3. Procure at low price because of competition