Genotype 1: Harvoni Therapy

Foreword
In October 2014, the Food and Drug Administration (FDA) approved the combination of sofosbuvir (polymerase inhibitor) and ledipasvir (NS5a inhibitor)—brand name Harvoni—a two drug fixed-dose combination pill in a single pill to treat hepatitis C (HCV) genotype 1. This fact sheet will discuss the basics of Harvoni therapy for treatment of HCV genotype 1. For more detailed information please see the Harvoni (sofosbuvir/ledipasvir) Full Prescribing Information. The FDA approval was based on the ION-1, 2, and 3 studies.

Dosing:
• One pill dosed once a day

Dose Modification:
• No dose modifications are recommended

Food Requirements:
• Can be taken with or without food

Length of Treatment:
• 8 weeks: Treatment-Naïve with or with cirrhosis can be considered*
• 12 weeks: Treatment-naïve with or without cirrhosis
• 12 weeks: Treatment-experienced without cirrhosis**
• 24 weeks: Treatment-experienced with cirrhosis**

*8 weeks can be considered in treatment-naïve patients without cirrhosis who have pre-treatment HCV RNA less than 6 million IU/mL (Note: in the ION-3 study of Harvoni—treatment of naïve patients treated for 8 or 12 weeks with Harvoni who had an HCV RNA (viral load) of less than 6 million IU/mL—the difference in cure rate was -2.3%).
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**Treatment-experienced patients who have failed treatment with either peginterferon alfa + ribavirin or an HCV protease inhibitor + peginterferon alfa + ribavirin).**

Sustained Virological Results (SVR 12-weeks post treatment)  
— Cure rate listed in table below.

- Side effects
  - The most common side effects were fatigue, headache, nausea, diarrhea, and insomnia

- Treatment Discontinuation
  - In the three trials of Harvoni the treatment discontinuation rates were 0-1%

Additional information

- The patients in the trial who were over 65 yo had similar cure rates to those under 65 yo—no dose adjustments were needed
- No dose adjustment for people with severe renal (kidney) impairment

<table>
<thead>
<tr>
<th>Study name/ Treatment Period</th>
<th>Cirrhosis</th>
<th>Number of Patients</th>
<th>Cure Rates Overall</th>
<th>Cure Rates Genotype 1a</th>
<th>Cure Rates Genotype 1b</th>
</tr>
</thead>
<tbody>
<tr>
<td>ION-1: Treatment Naïve</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 weeks combined</td>
<td>212</td>
<td>99%</td>
<td>98%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>12 weeks no</td>
<td>177</td>
<td>99%</td>
<td></td>
<td></td>
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<tr>
<td>24 weeks yes</td>
<td>34</td>
<td>94%</td>
<td></td>
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<tr>
<td>ION-2: Treatment Experienced*</td>
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<tr>
<td>12 weeks combined</td>
<td>109</td>
<td>94%</td>
<td>95%</td>
<td>87%</td>
<td></td>
</tr>
<tr>
<td>24 weeks combined</td>
<td>109</td>
<td>99%</td>
<td>99%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>12 weeks no</td>
<td>87</td>
<td>95%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 weeks no</td>
<td>86</td>
<td>99%</td>
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<tr>
<td>12 weeks yes</td>
<td>22</td>
<td>86%</td>
<td></td>
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<tr>
<td>24 weeks yes</td>
<td>22</td>
<td>100%</td>
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<td>ION-3: Treatment Naïve</td>
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<td>94%</td>
<td>93%</td>
<td>98%</td>
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</tr>
<tr>
<td>12 weeks no</td>
<td>216</td>
<td>96%</td>
<td>96%</td>
<td>98%</td>
<td></td>
</tr>
</tbody>
</table>

Gilead table adapted from: Full Prescribing Information

*Type of Prior HCV Therapy (including PEG/RBV and protease inhibitor plus PEG/RBV)—12 weeks: 92-95%; 24 weeks: 98-100%
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Pregnancy
Harvoni is pregnancy category B: There are no adequate and well controlled studies with Harvoni in pregnant women. Because animal reproduction studies are not always predictive of human response, Harvoni should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Related publications:

- Harvoni (sofosbuvir/ledipasvir) Full Prescribing Information

- Sovaldi (sofosbuvir) Full Prescribing Information

- Genotype 2 & 3: Sovaldi (Sofosbuvir) Plus Ribavirin

Drug-Drug Interactions
Harvoni should not be taken with certain medications such as HIV medications, antimycobacterials and anticonvulsants. Harvoni should not be taken with the herb—St. John's wort. (See the complete list in the Full Prescribing Information.)

For more information

- American Association for the Study of Liver Diseases
  www.aasld.org

- Centers for Disease Control and Prevention
  www.cdc.gov

- Food and Drug Administration (FDA):
  www.fda.gov

- Mayo Clinic
  www.mayoclinic.com

Visit our websites to learn more about viral hepatitis:

www.hcvadvocate.org • www.hbvadvocate.org
www.hepatitistattoos.org

Get Tested. Get Treated. Get Cured.