Foreword

In November 2013, the Food and Drug Administration (FDA) approved the combination of simeprevir—brand name Olysio, plus pegylated interferon plus ribavirin (RBV) to treat hepatitis C (HCV) genotype 1. This fact sheet will discuss the basics of the Olysio triple therapy. For more detailed information please see the FDA approved Package Insert: Highlights of Prescribing Information. The FDA approval was based on the information from the Quest 1 and 2 and Promise clinical trials.

Sustained Virological Results (SVR- 12 weeks post treatment)/ Cure Rate:

- **Treatment Naïve:**
  - Genotype 1 = 80%
  - Genotype 1a = 75%
    - Without Q80K = 84%
    - With Q80K = 58%
  - Genotype 1b = 85%

*Q80K is a resistant variant of the hepatitis C virus. The FDA recommends screening people with HCV genotype 1a for the Q80K polymorphism.*

- **Treatment Naïve –F0-F2 vs. F3-F4:**
  - Genotype 1 – F0-F2 (no fibrosis/light fibrosis) = 84%
  - Genotype 1 – F3-F4 (severe fibrosis – compensated cirrhosis) = 68%

- **Treatment Experienced—prior relapsers***:
  - Genotype 1 = 79%
  - Genotype 1a = 70%
    - Without Q80K = 78%
    - With Q80K = 47%
  - Genotype 1b = 86%
Genotype 1: Sovaldi (Sofosbuvir) Triple Therapy

- **Treatment experienced – F0-F2 vs. F3-F4:**
  - **Genotype 1 – F0-F2 = 82%**
  - **Genotype 1 – F3-F4 = 73%**

* a person who becomes HCV RNA negative at end of treatment, but becomes HCV detectable within 24 weeks from the end of treatment (EOT)

**Medications and Dose:**
- Simeprevir (brand name Olysio) a HCV protease inhibitor. Olysio is a 150 mg pill taken once-a-day
- Ribavirin (pill) taken twice daily. The dose of ribavirin is based on body weight (<75kg = 1000mg; ≥ 1000kg = 1200mg)
- Pegylated interferon is injected once-a-week

**Dose Modification** — The recommendation is that Olysio should not be dose reduced. If medications used with Olysio are discontinued—Olysio should also be discontinued.

**Food Requirements:**
- Olysio – taken with food
- Ribavirin – taken with food

**Length of Treatment** — The treatment duration is 24 or 48 weeks. Triple therapy of Olysio, pegylated interferon plus ribavirin is taken for 12 weeks. Pegylated interferon plus ribavirin is taken for an additional 12 or 36 weeks. *(See table 1)*

**Discontinuation of Treatment (Stopping Rules)** — Discontinuation of treatment is recommended for people who do not adequately respond during treatment. *(See table 2)*

**Side effects** — The most common side effects from Olysio rash and photosensitivity. Pegylated interferon and ribavirin have many side effects see our Managing Side Effects of HCV Treatment fact sheet.

**Treatment Discontinuation** — The number of patients who discontinued treatment due to side effects was 3% for those who received Olysio plus pegylated interferon and ribavirin.

**Pregnancy** — The prior cautions and warnings of ribavirin also apply to the combination of Olysio pegylated interferon and ribavirin. The use of ribavirin can cause birth defects. Women must have a negative pregnancy test prior to therapy and partners must use at least 2 effective non-hormonal methods of birth control. A woman must have monthly pregnancy tests.

**Drug-Drug Interactions** — Olysio should not be taken with certain medications such as HIV medications, antimycobacterials and anticonvulsants. Olysio should not be taken with St. John’s wort or milk thistle. *(See the complete list in the Highlights of Prescribing Information)*

| Table 1 – Duration of Treatment with Olysio, Peginterferon Alfa and Ribavirin |
|--------------------------------------------------|-----------------|-----------------|-----------------|
| Treatment-naïve and prior relapse patients including those with cirrhosis | Olysio plus PEG/RBV | PEG/RBV | Total Treatment Duration |
| First 12 weeks | Additional 12 weeks | 24 weeks |
| Prior non-responder patients (including partial and null responders) including those with cirrhosis | Frist 12 weeks | Additional 36 weeks | 48 weeks |
Genotype 1: Sovaldi (Sofosbuvir) Triple Therapy

Table 2 – Treatment Stopping Rules in Any Patient with Inadequate On-Treatment Virologic Response

<table>
<thead>
<tr>
<th>HCV RNA</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Week 4: greater than or equal to 25 IU/mL</td>
<td>Discontinue OLYSIO, peginterferon alfa and ribavirin</td>
</tr>
<tr>
<td>Treatment Week 12: greater than or equal to 25 IU/mL</td>
<td>Discontinue peginterferon alfa and ribavirin (treatment with OLYSIO is complete at Week 12)</td>
</tr>
<tr>
<td>Treatment Week 24: greater than or equal to 25 IU/mL</td>
<td>Discontinue peginterferon alfa and ribavirin</td>
</tr>
</tbody>
</table>

Related publications:

- **Olysio (simeprevir) Package Insert** *(Highlights of Prescribing Information)*

- **Sovaldi (sofosbuvir) Package Insert** *(Highlights of Prescribing Information)*
  www.hcvadvocate.org/hepatitis/factsheets_pdf/sovaldi_pi.pdf

- **Patient Assistance Programs**
  www.hcvadvocate.org/hepatitis/factsheets_pdf/Patient_Assistance.pdf

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