© Hepatitis C Online
PDF created April 25, 2024, 10:35 pm

Simeprevir *(Olysio)*

Discontinued. This treatment has been discontinued.

Table of Contents

- Simeprevir *Olysio* Summary
- Drug Summary
- Adverse Effects
- Class and Mechanism
- Manufacturer for United States
- FDA Status
- Indications
- Dosing
- Clinical Use
- Cost and Medication Access
- Resistance
- Key Drug Interactions
- Full Prescribing Information
- Figures

Drug Summary

When first introduced, simeprevir provided an excellent alternative to the older first-generation NS3/4A protease inhibitors (boceprevir and telaprevir) for the treatment of patients with genotype 1 HCV. Simeprevir is convenient (once-daily dosing), well-tolerated, and has less extensive drug-drug interactions than the first-generation protease inhibitors. Simeprevir is now infrequently used for the treatment of hepatitis C due to the availability of more effective and better tolerated direct-activing antiviral agents.

Adverse Effects

The most common adverse effects attributable to simeprevir are rash (including a potentially serious photosensitivity reaction), pruritus, and nausea.

- The photosensitivity reaction that can occur with simeprevir most often has an onset during the first 4 weeks of therapy, but can develop at any time on treatment (Figure 3).
- Patients taking simeprevir should limit sun exposure, use protective sun exposure measures, and avoid use of any tanning device.
- If a photosensitivity rash does occur while taking simeprevir, discontinuation of simeprevir should be considered and the patient should have close monitoring until the rash has resolved.

- Rash not related to photosensitivity can also occur and similar to the photosensitivity rash most often develops during the first 4 weeks of therapy.
- Simeprevir contains a sulfonamide moiety, but insufficient data exist to know the risk of taking simeprevir in persons with a prior "sulfa allergy".
- Patients taking simeprevir may experience transient and increases in serum bilirubin levels that peak at week 2 of treatment that are typically mild in severity and not associated with elevated hepatic aminotransferase levels.
- Simeprevir is pregnancy category C.

Class and Mechanism

Simeprevir is a NS3/4A hepatitis C virus (HCV) protease inhibitor. Simeprevir is a macrocyclic compound that non-covalently binds to and inhibits the NS3/4A HCV protease, a protein that is responsible for cleaving and processing the HCV-encoded polyprotein, a critical step in HCV viral life cycle. Simeprevir is considered a second generation HCV protease inhibitor because of the enhanced binding affinity and specificity to NS3/4A when compared with the first-generation protease inhibitors with linear structure.

Manufacturer for United States

Simeprevir is is manufactured as *Olysio* (oh li see oh) by Janssen Research & Development (Figure 1) and (Figure 2). Simeprevir was jointly developed by Janssen Research & Development and Medivir AB, originally known as compound TMC-435. Janssen has a collaborative agreement with Idenix Pharmaceuticals for the clinical development of combination oral direct acting therapies for the treatment of hepatitis C infection and simeprevir is among the drugs included in this agreement.

FDA Status

Simeprevir was approved by the U.S. FDA on November 22, 2013 for the treatment of individuals with genotype 1 chronic hepatitis C as a component of combination therapy with peginterferon-alfa and ribavirin. On November 5, 2014, the U.S. FDA approved the use of simeprevir in combination with sofosbuvir for patients with genotype 1 chronic hepatitis C.

Indications

Simeprevir is indicated as a component of combination antiviral treatment for patients with chronic hepatitis C genotype 1 infection. Simeprevir is approved for use with (a) peginterferon-alfa and ribavirin or (b) in combination with sofosbuvir.

Several limitation exist for the use of simeprevir:

- Simeprevir should not be used as monotherapy.

- Simeprevir is not recommended for use in patients who have previously failed treatment for hepatitis C with a regimen that included simeprevir or another HCV protease inhibitor.
- Simeprevir is not recommended for use in patients with severe hepatic impairment (Child-Pugh Class C) because of substantial increases in simeprevir levels in this setting.
- In patients with genotype 1a, the presence of a baseline NS3A polymorphism Q80K is associated with significantly reduced SVR12 in patients treated with simeprevir plus peginterferon and ribavirin. All patients with genotype 1a infection should have baseline screening for Q80K if simeprevir plus peginterferon plus ribavirin is planned for treatment; if the screening test is positive for Q80K, alternative therapy should strongly be considered.

Dosing

Simeprevir is available in 150 mg capsules (Figure 2). The dose of simeprevir is 150 mg PO once daily with food.

Simeprevir in Combination with Peginterferon-alfa and Ribavirin:

- Treatment-naive and prior relapsers: 12 weeks of simeprevir in combination with peginterferon alfa and ribavirin followed by an additional 12 weeks of peginterferon alfa and ribavirin
- Prior non-responders (including partial and null responders): 12 weeks of simeprevir in combination with peginterferon-alfa and ribavirin followed by an additional 36 weeks of peginterferon alfa and ribavirin

Simeprevir in Combination with Sofosbuvir:

- Treatment-naive or treatment experienced patients without cirrhosis: 12 weeks of simeprevir and sofosbuvir
- Treatment-naive or treatment experienced patients with cirrhosis: 24 weeks of simeprevir and sofosbuvir

Simeprevir in Patients with Renal or Hepatic Impairment:

- The dose of simeprevir does not need adjusting in patients with mild, moderate, or severe renal insufficiency.
- Since simeprevir is highly protein-bound, dialysis is unlikely to significantly impact simeprevir levels.
- The dose of simeprevir does not need adjusting in patients with mild hepatic impairment (Child-Pugh Class A).
- Simeprevir is metabolized primarily in the liver and patients with moderate or severe hepatic impairment (Child-Pugh Class B or C) would be expected to have higher levels of simeprevir. No dosing recommendation for simeprevir is given for patient with moderate to severe hepatic impairment.

Clinical Use

Simeprevir is FDA-approved only for patients with genotype 1 infection. The duration of therapy with simeprevir plus peginterferon and ribavirin depends on prior treatment experience and prior response to treatment. Duration of therapy is not based on response guided therapy, but continuation of therapy assumes

the patient does not meet stopping rules:

- For any patient on a regimen of simeprevir combined with peginterferon and ribavirin, therapy should be discontinued if the patient has an HCV RNA level of 25 IU/ml or greater at treatment week 4, 12, or 24.
- Most experts recommend not using simeprevir in combination with peginterferon plus ribavirin if the patient has a baseline Q80K polymorphism at baseline. The Q80K mutation does not appear to significantly impact the treatment response with simeprevir plus sofosbuvir, with or without ribavirin.

Cost and Medication Access

The wholesale acquisition cost (WAC) for simeprevir is $790 per 150 mg capsule. The cost for a 28-days supply of simeprevir is $22,120 and a 12-week supply is $66,360. Thus, a typical 12-week treatment course of simeprevir when used with a total of 24-weeks of peginterferon plus ribavirin will cost approximately $85,000. A 12-week course of simeprevir plus sofosbuvir costs approximately $150,000. Janssen has a simeprevir patient assistance program for treatment eligible patients with hepatitis C who are not able to obtain access to simeprevir. Medical providers and patients can learn more about this program by visiting the Janssen Prescription Assistance Program website or by calling 1-855-565-9746.

Resistance

Similar to other protease inhibitors, resistance and cross-resistance is a significant problem with simeprevir.

- Among patients on a triple therapy, simeprevir-containing regimen who failed to achieve a sustained virologic response at 12 weeks post-treatment (SVR12), more than 90% developed emergent NS3/4 protease mutations.
- The most common mutations were at the NS3 positions: Q80, S122, R155, and D168. Overall, the most common mutations to emerge with treatment failure were D168V and R155K.
- For genotype 1a, the most common mutation to emerge with simeprevir treatment failure is the R155K mutation (alone or in combination with mutations at codons Q80, S122, and D168).
- For genotype 1b, the most common mutation to emerge is the D168V mutation.
- The mutations R155K and I170T, which have emerged on simeprevir therapy, have cross resistance with boceprevir and telaprevir.
- The R155K and A156T/V mutations can emerge on boceprevir or teleprevir therapy and these mutations potentially cause cross-resistance to simeprevir.
- Simeprevir is not recommended for patients who failed to achieve an SVR with boceprevir or telaprevir, particularly those with genotype 1A.

Key Drug Interactions

For complete information on simeprevir-related drug interactions, see the Drug Interactions section in the Simeprevir (*Olysio*) Prescribing Information.

Full Prescribing Information

Simeprevir (*Olysio*) Full Prescribing Information

Figures

Figure 1. Capsules - Simeprevir (*Olysio*)

Photo: Andrew Karpenko, University of Washington

Figure 2. Bottle - Simeprevir (*Olysio*)

Photo: Andrew Karpenko, University of Washington

Figure 3. Simeprevir Rash

Pruritic rash on hands of patient that started 2 weeks into treatment with simeprevir plus sofosbuvir. The photograph is taken 10 weeks into treatment. The rash only manifested in sun exposed areas.

This photograph is courtesy of Dr. John D. Scott, MD.

© Hepatitis C Online
PDF created April 25, 2024, 10:35 pm

The most up to date version of this content may be obtained from:
https://www.hepatitisC.uw.edu/page/treatment/drugs/simeprevir-drug