Simeprevir (*Olysio*)

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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-acting 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.
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.