

## Popular HCV Drug Combo Wins FDA Backing

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A drug combination widely used off-label to treat hepatitis C (HCV) has been given the nod by the FDA.

The agency approved simeprevir (Olysio) and sofosbuvir (Sovaldi) as a combination for the treatment of chronic genotype 1 HCV, according to Janssen Therapeutics, the maker of simeprevir.

Importantly, the combination can be used without ribavirin or pegylated interferon-alfa, the two drugs that for years were the mainstays of HCV therapy. Both are regarded as difficult to tolerate and sometimes dangerous.

Simeprevir and sofosbuvir were initially approved within 2 weeks of one another last year, but only sofosbuvir was cleared for use without interferon; in some patients, the FDA said it could be used with ribavirin alone.

Simeprevir, on the other hand, was meant to be used only with interferon and ribavirin.

But despite the lack of an indication, many clinicians and patients opted to use the two together, since they target different aspects of viral replication -- simeprevir is an NS3/4A protease inhibitor and sofosbuvir is a nucleotide analog NS5B polymerase inhibitor -- and to avoid using either interferon or ribavirin.

The FDA approval now validates that approach.

The agency's decision was based on data from the so-called COSMOS trial -- a four-armed phase II study in which patients got the combination with or without ribavirin for 12 or 24 weeks.

Participants in the study were either naive to treatment or had failed to respond to prior therapy.

Rates of treatment success, defined as no detectable HCV RNA 12 weeks after the end of treatment or SVR12, were extremely high irrespective of treatment duration or the addition of ribavirin:

91% of patients who got ribavirin reached SVR12, compared with 95% of those who did not. And 94% of those who got 12 weeks of treatment reached SVR12, compared with 91% of those who got 24 weeks.

As well, there was little difference in outcomes between treatment-experienced and -naive patients.

The most common adverse reactions reported by more than 10% of those in the 12-week arms were fatigue (25%), headache (21%), nausea (21%), insomnia (14%), pruritus (11%), rash (11%), and photosensitivity (7%). Among those treated for 24 weeks, dizziness (16%) and diarrhea (16%) were reported.