


## Multiple DAA Treatment Failures (All Genotypes), Including Sofosbuvir/Velpatasvir/Voxilaprevir or Sofosbuvir Plus Glecaprevir/Pibrentasvir

Recommended regimens listed by evidence level and alphabetically for:

### Sofosbuvir/Velpatasvir/Voxilaprevir Treatment Failures, With or Without Compensated Cirrhosis<sup>a</sup>

RECOMMENDED	DURATION	RATING 
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) plus daily sofosbuvir (400 mg) and weight-based ribavirin	16 weeks <sup>b</sup>	Ila, B
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) plus weight-based ribavirin	24 weeks	Ila, B

<sup>a</sup> For [decompensated cirrhosis](#), please refer to the appropriate section.

<sup>b</sup> Extension of treatment to 24 weeks should be considered in extremely difficult cases (eg, genotype 3 with cirrhosis) or failure following sofosbuvir plus glecaprevir/pibrentasvir.

## Recommended Regimens

### Glecaprevir/Pibrentasvir Plus Sofosbuvir and Ribavirin

There is 1 case report examining retreatment of patients in whom therapy with sofosbuvir/velpatasvir/voxilaprevir failed. In this study, a quad regimen of sofosbuvir, glecaprevir/pibrentasvir, and ribavirin for 24 weeks was successful ([Bernhard, 2020](#)). Of note, pibrentasvir has improved in vitro activity compared to other NS5A inhibitors against most NS5A RASs ([Ng, 2017b](#)). A small study demonstrated the efficacy of glecaprevir/pibrentasvir plus sofosbuvir and ribavirin for heavily DAA-experienced patients (including those with genotype 3 and/or cirrhosis), although no sofosbuvir/velpatasvir/voxilaprevir failures were included ([Wyles, 2019](#)). Sixteen weeks of glecaprevir/pibrentasvir plus sofosbuvir and ribavirin is recommended based on the improved resistance profile of pibrentasvir and high response rate seen with this duration of therapy among genotype 3 patients in the MAGELLAN-3 trial ([Wyles, 2019](#)). Extension to 24 weeks or longer with this regimen could be considered; while there are case report data using this duration ([Bernhard, 2020](#)); ([Fierer, 2020](#)), no clinical trial data are available to support such an approach.

### Sofosbuvir/Velpatasvir/Voxilaprevir Plus Ribavirin

Although there are no published studies examining retreatment of patients in whom therapy with sofosbuvir/velpatasvir/voxilaprevir failed, in the POLARIS-1 study—which studied sofosbuvir/velpatasvir/voxilaprevir treatment among patients who had a prior DAA therapy failure—treatment failure with this triple antiviral regimen was seen more commonly in persons with cirrhosis (7% cirrhosis vs 1% without cirrhosis), and those with genotype 3 or 4 (5% genotype 3, 9% genotype 4 vs 0% genotype 1) ([Bourliere, 2017](#)). Baseline RASs did not affect SVR nor did failure select for additional RAS variants. The recommendation to treat with longer therapy in conjunction with ribavirin when retreating

with the same DAA regimen (sofosbuvir/velpatasvir/voxilaprevir) is based on extrapolation from prior studies showing benefit with this strategy in different populations ([Gane, 2017](#)).

**Last update:** January 21, 2021

Bernhard B, Stickel F. [Successful fourth line treatment of a relapse patient with chronic hepatitis C virus infection genotype 3a using sofosbuvir, glecaprevir/pibrentasvir, and ribavirin: a case report](#). *Z Gastroenterol*. 2020;58(5):451-455.

Bourliere M, Gordon SC, Flamm SL, et al. [Sofosbuvir, velpatasvir, and voxilaprevir for previously treated HCV infection](#). *N Engl J Med*. 2017;376(22):2134-2146.

Fierer DS, Wyles DL. [Re-treatment of hepatitis C infection after multiple failures of direct-acting antiviral therapy](#). *Open Forum Infect Dis*. 2020;7(4):ofaa095.

Gane EJ, Shiffman ML, Etzkorn K, et al, et al. [Sofosbuvir-velpatasvir with ribavirin for 24 weeks in hepatitis C virus patients previously treated with a direct-acting antiviral regimen](#). *Hepatology*. 2017;66(4):1083-1089.

Ng TI, Krishnan P, Pilot-Matias T, et al. [In vitro antiviral activity and resistance profile of the next-generation hepatitis C virus NS5A inhibitor pibrentasvir](#). *Antimicrob Agents Chemother*. 2017;61(5):pii: e02558-16. doi:10.1128/AAC.02558-16. Print 2017 May.

Wyles D, Weiland O, Yao B, et al. [Retreatment of patients who failed glecaprevir/pibrentasvir treatment for hepatitis C virus infection](#). *J Hepatol*. 2019;70(5):1019-1023. doi:10.1016/j.jhep.2019.01.031.