


Sofosbuvir/Velpatasvir/Voxilaprevir Treatment Failure (All Genotypes)

Recommended regimens listed by evidence level and alphabetically for:

Patients With Prior Sofosbuvir/Velpatasvir/Voxilaprevir Treatment Failure (All Genotypes), With or Without Compensated Cirrhosis^a

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

^a For [decompensated cirrhosis](#), please refer to the appropriate section.

^b Dosing is 3 coformulated tablets (glecaprevir [100 mg]/pibrentasvir [40 mg]) taken once daily. Please refer to the prescribing information.

Glecaprevir/Pibrentasvir Plus Sofosbuvir and Ribavirin

There are no studies examining retreatment of patients in whom therapy with sofosbuvir/velpatasvir/voxilaprevir failed. However, 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 with this regimen could be considered but there are currently no clinical data to support such an approach.

Sofosbuvir/Velpatasvir/Voxilaprevir Plus Ribavirin

Although there are no 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 cirrhotic patients (7% vs 1% in noncirrhotics), those with genotype 3 (5% vs 0% in genotype 1), and those with genotype 4 (9% vs 0% in genotype 1) ([Bourliere, 2017](#)). Pre-existing 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: November 6, 2019

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.

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.