


Glecaprevir/Pibrentasvir Treatment Failure (All Genotypes)

Recommended regimens listed by evidence level and alphabetically for:

Patients With Prior Glecaprevir/Pibrentasvir 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	Ila, B
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg)	12 weeks	Ila, B
For patients with compensated cirrhosis, addition of weight-based ribavirin is recommended.	12 weeks	Ila, C

^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

For the small number of patients in whom treatment with the daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) fails, the addition of ribavirin and sofosbuvir is an attractive retreatment option. MAGELLAN-3 is an ongoing phase 3b study evaluating the safety and efficacy of glecaprevir/pibrentasvir in combination with sofosbuvir (400 mg) and weight-based ribavirin as a 12- or 16-week retreatment regimen for patients who experienced virologic failure to glecaprevir/pibrentasvir within the context of a previous AbbVie clinical trial ([Wyles, 2019](#)). Noncirrhotic glecaprevir/pibrentasvir nonresponders with genotype 1, 2, 4, 5, or 6 who were naive to protease and NS5A inhibitors received 12 weeks glecaprevir/pibrentasvir plus sofosbuvir and weight-based ribavirin. Patients with genotype 3, and/or compensated cirrhosis, and/or protease/NS5A experience (prior to their initial glecaprevir/pibrentasvir treatment) received 16 weeks of therapy with the same regimen. In a preliminary analysis, 96% (22/23) of these patients achieved SVR12 with a single relapse in a cirrhotic patient with genotype 1a. Although the number of patients was relatively small and the study population heterogeneous, the presence of baseline RASs did not appear to substantively affect response rates. This study provides the rationale to recommend the combination of glecaprevir/pibrentasvir plus sofosbuvir and ribavirin for 16 weeks for the few patients in whom initial treatment with glecaprevir/pibrentasvir fails.

Sofosbuvir/Velpatasvir/Voxilaprevir

A prospective, nonrandomized observational study of patients in whom treatment with glecaprevir/pibrentasvir failed examined the utility of retreatment with 12 weeks of the daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) ([Pearlman, 2019](#)). SVR12 was achieved in 94% (29/31) of the patients. The cohort had higher proportions of patients traditionally associated with virologic failure, including black race, cirrhosis, and genotype 3. Two patients relapsed at week 4 following completion of therapy. The first patient had genotype 3 infection, was noncirrhotic, and had a A30K mutation at baseline and at relapse. The other patient had genotype 1a infection,

compensated cirrhosis, a Y93 variant detected at baseline, and L31M and Y93 variants at relapse. The addition of ribavirin was not evaluated in this study. However, for patients with cirrhosis, it may be helpful to add ribavirin based on prior studies of DAA failures.

Last update: November 6, 2019

Pearlman B, Perrys M, Hinds A. [Sofosbuvir/velpatasvir/voxilaprevir for previous treatment failures with glecaprevir/pibrentasvir in chronic hepatitis C infection](#). *Am J Gastroenterol*. 2019;114(9):1550-1552.

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.