

Glecaprevir/Pibrentasvir Treatment Failures

Recommended regimens listed by evidence level and alphabetically for:		
Glecaprevir/Pibrentasvir Treatment Failures (All Genotypes), With or Without Compensated Cirrhosis ^a 		
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	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.		

Recommended Regimens

Glecaprevir/Pibrentasvir Plus Sofosbuvir and Ribavirin

For the small number of persons 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 evaluated 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 individuals who experienced virologic failure to glecaprevir/pibrentasvir ([Wyles, 2019](#)). Importantly, many study participants had received other regimens before their nonresponse to glecaprevir/pibrentasvir. 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. Participants with genotype 3, and/or compensated cirrhosis, and/or protease or NS5A inhibitor experience (prior to their initial glecaprevir/pibrentasvir treatment) received 16 weeks of therapy with the same regimen. Overall, 96% (22/23) of these patients achieved SVR12 with a single relapse in a cirrhotic patient with genotype 1a. This individual had prior treatment failures with multiple other regimens and had multiple complex NS3 and NS5A RASs, including NS5A, Q30K, and Y93H prior to treatment. This study provides the rationale to recommend the combination of glecaprevir/pibrentasvir plus sofosbuvir and ribavirin for 16 weeks for persons without cirrhosis or with compensated cirrhosis who experienced treatment failure with initial glecaprevir/pibrentasvir treatment.

Sofosbuvir/Velpatasvir/Voxilaprevir

A prospective, nonrandomized observational study evaluated the efficacy of retreatment with 12 weeks of the daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) among patients who experienced treatment failure with initial glecaprevir/pibrentasvir therapy ([Pearlman, 2019](#)). SVR12 was 94% (29/31). The cohort had higher proportions of patients with factors traditionally associated with virologic failure, including black race, cirrhosis, and genotype 3. Two patients relapsed at week 4 following the completion of therapy. One patient had genotype 3 infection, was noncirrhotic, and had an 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. For patients with cirrhosis, however, it may be helpful to add ribavirin based on prior studies of DAA failures.

Last update: October 24, 2022

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.
