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	IIa, B
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg)	12 weeks	IIa, B
For persons with compensated cirrhosis, addition of weight-based ribavirin is recommended.	12 weeks	IIa, C

[a] For persons with decompensated cirrhosis, please refer to that section of the guidance.

Recommended Regimens

Glecaprevir/Pibrentasvir Plus Sofosbuvir and Ribavirin

For the small number of people in whom treatment with glecaprevir/pibrentasvir fails, retreatment with glecaprevir (300 mg)/pibrentasvir (120 mg) plus sofosbuvir (400 mg) and weight-based ribavirin is a retreatment option supported by the MAGELLAN-3 clinical trial (Wyles, 2019). In this study, persons with prior glecaprevir/pibrentasvir failure and genotype 1, 2, 4, 5, or 6 infection without cirrhosis or prior exposure to protease and NS5A inhibitors were retreated with 12 weeks of glecaprevir/pibrentasvir plus sofosbuvir and weight-based ribavirin. Participants with genotype 3 infection and/or compensated cirrhosis and/or previous protease or NS5A inhibitor exposure (prior to their initial glecaprevir/pibrentasvir treatment) were treated for 16 weeks with the same regimen. SVR12 rate was 96% (22/23) with a single relapse in a participant with genotype 1a infection, cirrhosis, and multiple complex baseline NS3 and NS5A RASs.

Sofosbuvir/Velpatasvir/Voxilaprevir

Retreatment with sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) for 12 weeks is another attractive option for people with a prior glecaprevir/pibrentasvir failure. The use of this regimen is supported by a prospective, nonrandomized observational study which demonstrated a 94% (29/31) SVR rate with this regimen among participants who experienced treatment failure with glecaprevir/pibrentasvir (Pearlman, 2019). Three real-world cohort studies that evaluated the efficacy of 12 weeks of sofosbuvir/velpatasvir/voxilaprevir among persons with prior glecaprevir/pibrentasvir failure demonstrated SVR in 92% (49/53) of participants (Graf, 2024); 96% (26/27) of participants (Liu, 2023); and 90% (37/41) of participants (Ruiz-Cobo, 2024). Although the addition of ribavirin was not evaluated in these studies, based on prior retreatment studies of DAA failures, it may be helpful to add weight-based ribavirin for persons with cirrhosis.

Related References

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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. doi: 10.14309/ajg.0000000000000248.

Ruiz-Cobo JC, Llaneras J, Forns X, et al. Real-life effectiveness of sofosbuvir/velpatasvir/voxilaprevir in hepatitis C patients previously treated with sofosbuvir/velpatasvir or glecaprevir/pibrentasvir. *Aliment Pharmacol Ther*. 2024;60(2):201-211. doi: 10.1111/apt.18020.

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.

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