


Multiple DAA Treatment Failures, Including Sofosbuvir/Velpatasvir/Voxilaprevir or Sofosbuvir Plus Glecaprevir/Pibrentasvir

Recommended regimens listed by evidence level and alphabetically for:

Multiple DAA Treatment Failures (All Genotypes), Including Sofosbuvir/Velpatasvir/Voxilaprevir Treatment Failures or Sofosbuvir Plus Glecaprevir/Pibrentasvir, 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 ^b	Ila, B
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) plus weight-based ribavirin	24 weeks	Ila, B

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

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

Recommended Regimens

Glecaprevir/Pibrentasvir Plus Sofosbuvir and Ribavirin

A small study demonstrated the efficacy of glecaprevir (300 mg)/pibrentasvir (120 mg) plus sofosbuvir (400 mg) and weight-based ribavirin for heavily DAA-experienced persons, although no sofosbuvir/velpatasvir/voxilaprevir failures were included (Wyles, 2019). Among persons who experienced treatment failure with sofosbuvir/velpatasvir/voxilaprevir, 16 weeks of glecaprevir/pibrentasvir plus sofosbuvir and weight-based ribavirin is recommended based on the improved resistance profile of pibrentasvir and high response rate seen with this duration of therapy among persons with genotype 3 infection in the MAGELLAN-3 trial. The overall SVR rate was 96% (22/23), including an SVR rate of 100% (14/14) among those with genotype 3 infection (Wyles, 2019). Extension of treatment duration to 24 weeks or longer with this regimen could be considered. Although no clinical trial data are available to support such an approach, there are real-world data. A real-world cohort study that evaluated 12 weeks to 24 weeks of glecaprevir/pibrentasvir plus sofosbuvir and ribavirin demonstrated an SVR rate of 79% (11/14) among persons with a prior sofosbuvir/velpatasvir/voxilaprevir retreatment failure (Dietz, 2021). Additionally, a pooled analysis of 6 studies reported an SVR12 rate of 88% (28/32) among persons with a prior sofosbuvir/velpatasvir/voxilaprevir treatment failure who were retreated with glecaprevir/pibrentasvir with or without sofosbuvir and/or with or without ribavirin for 12 weeks, 16 weeks, or 24 weeks (Karimi-Sari, 2022).

Sofosbuvir/Velpatasvir/Voxilaprevir Plus Ribavirin

There have been no controlled clinical trials examining retreatment with sofosbuvir/velpatasvir/voxilaprevir-based regimens among people in whom initial therapy with sofosbuvir/velpatasvir/voxilaprevir failed. The recommendation to treat with a longer duration of therapy (24 weeks) in conjunction with weight-based 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](#)). This approach is also supported by very limited real-world data including an SVR rate of 100% (4/4) in 1 cohort (Dietz, 2021).

Related References

Dietz J, Di Maio VC, de Salazar A, et al; HCV virology Italian Resistance network (VIRONET-C) collaborators; Spanish GEHEP-004 collaborators; members of the German HCV resistance study group. Failure on voxilaprevir, velpatasvir, sofosbuvir and efficacy of rescue therapy. *J Hepatol*. 2021;74(4):801-810. doi: 10.1016/j.jhep.2020.11.017.

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.

Karimi-Sari H, Rezaee-Zavareh MS, Falade-Nwulia O, Lim JK. Non-responders to sofosbuvir/velpatasvir/voxilaprevir in the treatment of chronic hepatitis C infection. *J Hepatol*. 2022;77(4):1215-1217. doi: 10.1016/j.jhep.2022.06.024.

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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