

NS5A Inhibitor DAA-Experienced (Excluding Glecaprevir/Pibrentasvir Failures), Genotype 1 Patients, With or Without Compensated Cirrhosis

(For [glecaprevir/pibrentasvir treatment failures](#), please see that topic.)

Recommended and alternative regimens listed by evidence level and alphabetically for:

NS5A Inhibitor DAA-Experienced (Excluding Glecaprevir/Pibrentasvir Failures), Genotype 1 Patients, With or Without Compensated Cirrhosis^a



RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg)	12 weeks	I, A
ALTERNATIVE	DURATION	RATING
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) ^b except NS3/4 protease inhibitor inclusive DAA combination regimens	16 weeks	IIa, 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.

Recommended Regimen

Sofosbuvir/Velpatasvir/Voxilaprevir

The placebo-controlled, phase 3 POLARIS-1 trial evaluated a 12-week course of the daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100mg) in patients with a prior NS5A inhibitor-containing DAA regimen. The majority (61%) experienced a failure with a combination regimen of an NS5B inhibitor plus an NS5A inhibitor, such as sofosbuvir/ledipasvir ([Bourliere, 2017](#)). The overall SVR12 was 97% (146/150) in genotype 1 patients. SVR12 rates were 96% (97/101) for participants with genotype 1a and 100% (45/45) for those with genotype 1b. A single genotype 1 patient experienced relapse; this individual had subtype 1a and cirrhosis. Baseline RASs and the presence of cirrhosis were not significant predictors of virologic failure with genotype 1. Serious adverse events were similar in the placebo and treatment arms; only 1 patient discontinued therapy due to an adverse event. Headache, diarrhea, and nausea were more common in those patients receiving sofosbuvir/velpatasvir/voxilaprevir compared to placebo.

Alternative Regimen

Glecaprevir/Pibrentasvir

In parts 1 and 2 of the MAGELLAN-1 trial, 42 genotype 1 patients had previously been treated with either an NS5A inhibitor or an NS3/4A protease inhibitor ([Poordad, 2017](#)); ([Poordad, 2017b](#)). Twenty-four percent of these patients had cirrhosis; 79% had genotype 1a. Patients who were previously treated with an NS5A inhibitor (ledipasvir or daclatasvir) and not concomitantly treated with a NS3/4A protease inhibitor were retreated with the daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) administered as three 100 mg/40 mg fixed-dose combination pills for 16 weeks. Among these patients, 94% (16/17) achieved SVR12. The single patient who did not respond to therapy had an on-treatment virologic failure. Due to the 16-week duration of therapy and limited supporting data, this is recommended as an alternative regimen.

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Related References

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.

Poordad F, Felizarta F, Asatryan A, et al. [Glecaprevir and pibrentasvir for 12 weeks for hepatitis C virus genotype 1 infection and prior direct-acting antiviral treatment](#). Sulkowski MS, Reindollar RW, Landis CS, et al., eds. *Hepatology*. 2017;66(2):389-397.

Poordad F, Pol S, Asatryan A, et al. [MAGELLAN-1, part 2: glecaprevir and pibrentasvir for 12 or 16 weeks in patients with chronic HCV genotype 1 or 4 and prior direct-acting antiviral treatment failure](#). Buti M, Shaw DR, Hezode C, et al., eds. *Gastroenterology*. 2017;152(5):S1057.