Treatment-Naive Genotype 2 With Compensated Cirrhosis

Recommended regimens listed by evidence level and alphabetically for:

Treatment-Naive Persons With Genotype 2 Infection With Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[b]	8 weeks	I, 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 Regimens

Sofosbuvir/Velpatasvir

The daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) for 12 weeks was approved by the FDA for the treatment of genotype 2 infection in persons without cirrhosis or with compensated cirrhosis. ASTRAL-2 compared 12 weeks of sofosbuvir/velpatasvir to 12 weeks of sofosbuvir plus ribavirin in 266 treatment-naive and treatment-experienced persons without cirrhosis or with compensated cirrhosis. The study showed superior efficacy of sofosbuvir/velpatasvir compared with sofosbuvir plus ribavirin (SVR12 rates of 99% versus 94%); (Foster, 2015a). ASTRAL-1 also included 104 treatment-naive and treatment-experienced participants with genotype 2 infection without cirrhosis or with compensated cirrhosis, all of whom achieved SVR12 (Feld, 2015).

Pooled analysis of all genotype 2 participants in ASTRAL-1 and ASTRAL-2 demonstrated 100% (29/29) SVR12 rate in those with compensated cirrhosis and 99% (194/195) SVR12 rate in treatment-naive participants. Among participants with genotype 2 infection receiving sofosbuvir/velpatasvir, the presence of baseline NS5A or NS5B RASs was not associated with virologic failure (Asselah, 2018).

The POLARIS-2 phase 3 study randomized DAA-naive participants to 8 weeks of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100mg) versus 12 weeks of sofosbuvir/velpatasvir. Fifty-three persons with genotype 2 infection were included in the sofosbuvir/velpatasvir arm and all achieved SVR12 (100%). This study confirms the high efficacy and safety of this 12-week regimen in persons with genotype 2 infection (Jacobson, 2017). A real-world, pooled analysis of 12 cohort studies demonstrated an SVR rate of 98.5% (266/270) among adults with genotype 2 infection and compensated cirrhosis who were treated with 12 weeks of sofosbuvir/velpatasvir (Mangia, 2020).

Glecaprevir/Pibrentasvir

EXPEDITION-1 was a multicenter, open-label, single-arm, phase 3 trial that enrolled 146 treatment-naive or treatment-experienced persons (interferon or peginterferon ± ribavirin, or sofosbuvir plus ribavirin ±

peginterferon) with genotype 1, 2, 4, 5, or 6 infection and compensated cirrhosis. Participants were treated 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 12 weeks. Across all genotypes, 99% (145/146) achieved SVR12 (Forns, 2017). EXPEDITION-1 included 31 treatment-naive and treatment-experienced persons with genotype 2 infection and compensated cirrhosis; all achieved SVR12. Baseline NS5A RASs were detected (by next-generation sequencing using a 15% detection cutoff) in 40% of 133 tested participants. Baseline NS5A RASs had no effect on SVR rates among treatment-naive and treatment-experienced persons with genotype 2 infection.

EXPEDITION-8 evaluated glecaprevir/pibrentasvir for a reduced duration of 8 weeks in treatment-naive participants with compensated cirrhosis and genotype 1, 2 (n=26), 4, 5 or 6 infection. People with a prior history of decompensation, hepatocellular carcinoma, and HIV or HBV coinfection were excluded from this study. SVR12 rate was 100% (26/26) among participants with genotype 2 infection with no virologic failures (Brown, 2020). Real-world data support the use of an 8-week course of glecaprevir/pibrentasvir in persons with compensated cirrhosis (Flamm, 2020).

Related References

Asselah T, Bourgeois S, Pianko S, et al. **Sofosbuvir/velpatasvir in patients with hepatitis C virus genotypes 1-6 and compensated cirrhosis or advanced fibrosis**. *Liver Int*. 2018;38(3):443-450.

Brown RS Jr, Buti M, Rodrigues L, et al. Glecaprevir/pibrentasvir for 8 weeks in treatment-naive patients with chronic HCV genotypes 1-6 and compensated cirrhosis: the EXPEDITION-8 trial. *J Hepatol*. 2020;72(3):441-449. doi: 10.1016/j.jhep.2019.10.020.

Feld JJ, Jacobson IM, Hézode C, et al. **Sofosbuvir and velpatasvir for HCV genotype 1, 2, 4, 5, and 6 infection**. *N Engl J Med*. 2015;373(27):2599-2607.

Flamm SL, Kort J, Marx SE, et al. **Effectiveness of 8-week glecaprevir/pibrentasvir for treatment-naive, compensated cirrhotic patients with chronic hepatitis C infection**. *Adv Ther*. 2020;37(5):2267-2274.

Forns X, Lee SS, Valdes J, et al. **Glecaprevir plus pibrentasvir for chronic hepatitis C virus genotype 1, 2, 4, 5, or 6 infection in adults with compensated cirrhosis (EXPEDITION-1): a single-arm, open-label, multicentre phase 3 trial**. *Lancet Infect Dis*. 2017;17(10):1062-1068.

Foster GR, Afdhal NH, Roberts SK. **Sofosbuvir and velpatasvir for HCV genotype 2 and 3 infection.** *N Engl J Med.* 2015;373(27):2608-2617.

Jacobson IM, Lawitz E, Gane EJ, et al. **Efficacy of 8 weeks of sofosbuvir, velpatasvir, and voxilaprevir in patients with chronic HCV infection: 2 phase 3 randomized trials**. *Gastroenterology*. 2017;153(1):113-122.

Mangia A, Milligan S, Khalili M, et al. **Global real-world evidence of sofosbuvir/velpatasvir as simple, effective HCV treatment: analysis of 5552 patients from 12 cohorts**. *Liver Int*. 2020;40(8):1841-1852.

Additional Reading

- Persons With HIV/HCV Coinfection
- Persons With Renal Impairment
- Management of Acute HCV Infection

Last Update: October 24, 2022 **Last Review:** January 15, 2025

Treatment-Naive Genotype 3

The following pages include guidance for management of treatment-naive persons with genotype 3 infection.

- Treatment-Naive Genotype 3 Without Cirrhosis
- Treatment-Naive Genotype 3 With Compensated Cirrhosis
- Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis

Last Update: October 24, 2022 **Last Review:** January 15, 2025