# Treatment-Naive Genotype 1b With Compensated Cirrhosis

Recommended regimens listed by pangenotypic, evidence level, and alphabetically for:

## Treatment-Naive Persons With Genotype 1b 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 |
| Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) | 12 weeks | I, A |
| Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) | 12 weeks | I, A |

[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 1 infection in treatment-naive perons based on ASTRAL-1. This placebo-controlled trial involved a 12-week course of sofosbuvir/velpatasvir administered to 624 participants with genotype 1, 2, 4, 5, or 6 infection who were treatment naive (n=423) or previously treated with interferon-based therapy, with or without ribavirin or a protease inhibitor (n=201) (Feld, 2015). Of the 328 participants with genotype 1 infection included in the study, 323 achieved SVR12 with no difference in SVR12 rate observed by subtype (98% 1a; 99% 1b). Among 121 participants (all genotypes) classified as having cirrhosis, 99% (120/121) achieved SVR12. Baseline NS5A RASs (at 15% cutoff)—reported in 11% of genotype 1a and 18% of genotype 1b participant samples tested—did not influence SVR12 rate for genotype 1 (Hézode, 2018). Of the 2 virologic failures in ASTRAL-1 (<1% of treated participants), both were genotype 1 and had baseline RASs. There was no significant difference in the rates of adverse events in the sofosbuvir/velpatasvir vs placebo groups.

The phase 3 POLARIS-2 study randomized 941 DAA-naive persons with genotype 1, 2, 3, 4, 5, or 6 infection—19% of whom had compensated cirrhosis—to receive either 8 weeks of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) or 12 weeks of sofosbuvir/velpatasvir (Jacobson, 2017). Of participants treated with sofosbuvir/velpatasvir, 99% (170/172) with genotype 1a and 97% (57/59) with genotype 1b achieved SVR with a single relapse observed with each subtype.

### Glecaprevir/Pibrentasvir

EXPEDITION-1 investigated use of the daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) administered as three 100 mg/40 mg fixed-dose combination pills in DAA-naive (75%) or DAA-experienced (interferon or peginterferon ± ribavirin, or sofosbuvir plus ribavirin ± peginterferon) persons with compensated cirrhosis. Of 146 participants with genotype 1, 2, 4, 5, or 6 infection given 12 weeks of glecaprevir/pibrentasvir, 99% (145/146) achieved SVR12; all genotype 1b participants achieved SVR (Forns, 2017).

EXPEDITION-2, a study of glecaprevir/pibrentasvir in 153 adults with HIV/HCV coinfection with genotype 1, 2, 3, 4, 5, or 6 infection, utilized 8 weeks of treatment for participants without cirrhosis and 12 weeks for those with cirrhosis (the recommended durations approved by the FDA). The overall SVR12 rate was 98% (150/153); there were no observed virologic failures among the 94 participants with genotype 1 infection (Rockstroh, 2018). In EXPEDITION-1 and EXPEDITION-2, neither subtype (1a versus 1b) nor the presence of baseline RASs impacted SVR12 rate in DAA-naive genotype 1 persons.

EXPEDITION-8 evaluated glecaprevir/pibrentasvir for a reduced duration of 8 weeks in treatment-naive persons with compensated cirrhosis and genotype 1 (n=136, genotype 1b), 2, 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 99% with no virologic failures (Brown, 2020). A meta-analysis of real-world cohorts that examined glecaprevir/pibrentasvir treatment response among adults demonstrated SVR12 rates of 99.6% (n=848) and 98.2% (n=60) among participants with genotype 1 infection without or with compensated cirrhosis, respectively, with 8 weeks of treatment (Lampertico, 2020).

### Elbasvir/Grazoprevir

The recommendation for use of daily fixed-dose elbasvir (50 mg)/grazoprevir (100 mg) in persons with cirrhosis and genotype 1 infection is based on 92 participants (22% of the study cohort) in the phase 3 C-EDGE trial who had Metavir F4 disease (Zeuzem, 2015f). SVR12 rate was 97% in the subgroup of participants with cirrhosis. A similar 97% (28/29) SVR12 rate had previously been demonstrated in treatment-naive persons with genotype 1 infection and cirrhosis treated with 12 weeks of elbasvir/grazoprevir without ribavirin in the open-label phase 2 C-WORTHY trial, which enrolled both persons with HCV monoinfection and HIV/HCV coinfection (Lawitz, 2015c). The presence or absence of cirrhosis does not appear to alter the efficacy of the elbasvir/grazoprevir regimen (Zeuzem, 2017); (Lawitz, 2015c).

### Ledipasvir/Sofosbuvir

The daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) was approved by the FDA for the treatment of genotype 1 infection in treatment-naive persons based on 2 registration trials: ION-1 (865 treatment-naive participants; those with cirrhosis were included) and ION-3 (647 treatment-naive participants; those with cirrhosis were excluded). ION-1 investigated length of treatment (12 weeks versus 24 weeks) and the need for ribavirin (Afdhal, 2014a). SVR12 rates were 97% to 99% across all study arms with no difference in SVR rate based on length of treatment, use of ribavirin, or genotype 1 subtype. Sixteen percent of participants enrolled were classified as cirrhotic. There was no difference in SVR12 rates in persons with cirrhosis (97%) compared with those without cirrhosis (98%).

## Related References


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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.

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Zeuzem S, Ghalib R, Reddy KR, et al. **Grazoprevir-elbasvir combination therapy for treatment-naive cirrhotic and noncirrhotic patients with chronic hepatitis C virus genotype 1, 4, or 6 infection: a randomized trial**. *Ann Intern Med*. 2015;163(1):1-13.

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## Additional Reading

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

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## Treatment-Naive Genotype 2

The following pages include guidance for management of treatment-naive persons with genotype 2 infection.

- Treatment-Naive Genotype 2 Without Cirrhosis
- Treatment-Naive Genotype 2 With Compensated Cirrhosis
- Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis

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