Multiple highly potent, DAA combination regimens are recommended for patients with genotype 1 infection. There are
differences in the recommended regimens based on viral subtype, the presence or absence of baseline NS5A resistance-
associated substitutions (RASs), the presence or absence of compensated cirrhosis, and the type of prior failed
regimen(s). Genotype 1 infection that cannot be subtyped should be treated as genotype 1a.

Approximately 10% to 15% of genotype 1 patients without prior exposure to NS5A inhibitors have detectable NS5A RASs
prior to treatment. The clinical impact of NS5A RASs varies across regimens and baseline patient characteristics. In
patients with genotype 1a, the presence of baseline NS5A RASs that cause a large reduction in the activity of NS5A
inhibitors (>5 fold) adversely impacts response to some NS5A inhibitor-containing regimens (Zeuzem, 2017); (Jacobson,
2015b). These RASs are found by population sequencing in roughly 5% to 10% of patients; relevant RASs vary by DAA
regimen. Given that baseline NS5A RASs are one of the strongest pretreatment predictors of therapeutic outcome with
certain regimens in genotype 1a patients, testing for these RASs prior to deciding on a therapeutic course is
recommended in selected situations (Zeuzem, 2015c). For further guidance, please see the Resistance Primer section.

Compared to interferon-based therapy, DAAs are associated with a higher rate of drug interactions with concomitant
medications. With combinations of DAAs in the various treatment regimens, attention to drug-drug interactions is that
much more important (see Drug Interactions table). The product prescribing information and other resources
(eg, http://www.hep-druginteractions.org) should be consulted regularly to ensure safety when prescribing DAA regimens.
Important interactions with commonly used medications (eg, antacids, lipid-lowering drugs, anti-epileptics, antiretrovirals,
etc) exist for all regimens discussed.

The following pages include guidance for management of treatment-experienced patients with genotype 1.

- Peginterferon/Ribavirin-Experienced, Genotype 1a Patients Without Cirrhosis
- Peginterferon/Ribavirin-Experienced, Genotype 1a Patients With Compensated Cirrhosis
- Peginterferon/Ribavirin-Experienced, Genotype 1b Patients Without Cirrhosis
- Peginterferon/Ribavirin-Experienced, Genotype 1b Patients With Compensated Cirrhosis
- NS3 Protease Inhibitor + Peginterferon/Ribavirin-Experienced, Genotype 1 Patients Without Cirrhosis
- NS3 Protease Inhibitor + Peginterferon/Ribavirin-Experienced, Genotype 1 Patients With Compensated Cirrhosis
- Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced, Genotype 1 Patients Without Cirrhosis
- Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced, Genotype 1 Patients With Compensated Cirrhosis
- NS5A Inhibitor DAA-Experienced (Excluding Glecaprevir/Pibrentasvir Failures), Genotype 1 Patients, With or
  Without Compensated Cirrhosis
- Glecaprevir/Pibrentasvir Treatment Failures (All Genotypes)
- Sofosbuvir/Velpatasvir/Voxilaprevir Treatment Failure (All Genotypes)

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Related References

(RAVs) on the efficacy of elbasvir/grazoprevir (EBR/GZR) against GT1a infection [abstract LB-22]. The Liver Meeting.
2015.

Zeuzem S, Rockstroh JK, Kwo PY, et al. Predictors of response to grazoprevir/elbasvir among HCV genotype 1