

## Retreatment of Persons in Whom Prior Therapy Failed

This section provides guidance on the retreatment of persons with chronic HCV infection in whom prior therapy failed. The level of the evidence available to inform the best regimen for each patient and the strength of the recommendation vary and are rated accordingly (see [Methods Table 2](#)). In addition, specific recommendations are given when treatment differs for a particular group (e.g., those infected with different viral genotypes). Recommended regimens are those that are favored for most patients in that group based on optimal efficacy, favorable tolerability and toxicity profiles, complexity, and shorter treatment duration.

Alternative regimens are those that are effective but, relative to recommended regimens, have potential disadvantages, limitations for use in certain patient populations, or less supporting data. In certain situations, an alternative regimen may be optimal for a specific patient.

Specific considerations for [pediatric patients](#); [persons with HIV/HCV coinfection](#); [decompensated cirrhosis](#) (moderate or severe hepatic impairment; [Child-Turcotte-Pugh \[CTP\] class B or C](#)); HCV infection [post liver transplantation](#); and [severe renal impairment](#), end-stage renal disease (ESRD), or HCV infection [post kidney transplantation](#) are addressed in other sections of the guidance.

Recommended and alternative regimens are listed in order of level of evidence. When several regimens are at the same recommendation level, they are listed in alphabetical order. Regimen choice should be determined based on patient-specific data, including drug interactions. Persons receiving antiviral therapy require careful pretreatment assessment for comorbidities that may influence treatment response. All patients require careful monitoring during treatment, particularly for anemia if ribavirin is included in the regimen (See [Monitoring](#) section).

### Scope and Need for Direct Acting Antiviral (DAA) Failure Retreatment

Despite the enormous success of DAA therapy, a small percent of patients who fail to achieve SVR with DAA treatment will require retreatment. To simplify and consolidate the guidance, this section no longer contains retreatment recommendations for interferon or interferon plus first-generation protease inhibitor failures because the cure rates with modern DAA regimens in these populations are comparable to treatment-naïve patients. In addition, pangenotypic regimens without the addition of ribavirin have shown high efficacy for patients with prior failure across all genotypes except genotype 3. Therefore, recommendations are categorized by regimen failure.

Prior DAA exposure may result in the selection of resistance-associated substitutions (RASs), particularly in NS5A, which could theoretically compromise the retreatment regimen. To date, however, a negative impact of NS5A RASs on the efficacy of retreatment regimens consisting of 3 DAAs with unique mechanisms of action (e.g., sofosbuvir/velpatasvir/voxilaprevir or sofosbuvir plus glecaprevir/pibrentasvir) has not been demonstrated in clinical trials. Persons experiencing multiple DAA regimen failures with complex RAS patterns in NS3 and/or NS5A represent a unique and understudied population where RASs may impact treatment response. For a full discussion, see [HCV Resistance Primer](#) section.

The following pages include guidance for management of treatment-experienced patients in the following categories:

- [Sofosbuvir-based and elbasvir/grazoprevir treatment failures](#), including:
  - Sofosbuvir/ribavirin ± interferon
  - Sofosbuvir/ledipasvir

- Sofosbuvir/velpatasvir
- Elbasvir/grazoprevir
- [Glecaprevir/pibrentasvir treatment failures](#)
- [Multiple DAA regimen failures, including:](#)
  - Sofosbuvir/velpatasvir/voxilaprevir
  - Sofosbuvir plus glecaprevir/pibrentasvir

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## **Related References**

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