

Daclatasvir (*Daklinza*)

Discontinued. This treatment has been discontinued.

Table of Contents

- [Daclatasvir *Daklinza* Summary](#)
- [Drug Summary](#)
- [Adverse Effects](#)
- [Class and Mechanism](#)
- [Manufacturer for United States](#)
- [FDA Status](#)
- [Indications](#)
- [Contraindications](#)
- [Dosing](#)
- [Clinical Use](#)
- [Cost and Medication Access](#)
- [Resistance](#)
- [Key Drug Interactions](#)
- [Full Prescribing Information](#)
- [Figures](#)

Drug Summary

Daclatasvir plus sofosbuvir, with or without ribavirin, is an all-oral option for the treatment of genotype 1 or 3 chronic HCV across a variety of patient populations. Based on the results of the phase 3 ALLY trials, daclatasvir and sofosbuvir is an effective, albeit very expensive option for patients with genotype 1 or 3 HCV, including those with cirrhosis, HIV coinfection, or post-liver transplantation. The use of daclatasvir with sofosbuvir has provided an important ribavirin-free oral option for genotype 3 patients, but the 12 week dual therapy has limited efficacy in cirrhotic genotype 3 patients. Cost, lack of coformulation, and the recommendation of baseline NS5A testing in genotype 1a cirrhotic patients make daclatasvir plus sofosbuvir a less compelling option in this subset of patients.

Adverse Effects

Daclatasvir (*Daklinza*) has been well tolerated in clinical studies to date. When taken in combination with sofosbuvir, the most common adverse events observed in clinical studies were fatigue (14%), headache (14%), nausea (8%), and diarrhea (5%). Daclatasvir can potentially cause serious bradycardia when coadministered with sofosbuvir and amiodarone, particularly if the patient is also taking a beta-blocker. Coadministration of daclatasvir, sofosbuvir and amiodarone is therefore not advised.

Class and Mechanism

Daclatasvir was discovered as a first-in-class inhibitor of the non-structural viral protein 5A (NS5A), a phosphoprotein that plays an important role in hepatitis C replication. The exact mechanism by which daclatasvir inhibits the NS5A replication complex is unclear, but it is believed that daclatasvir inhibits viral RNA replication and virion assembly. It may also inhibit phosphorylation of the NS4A, and therefore the formation and activation of the HCV replication complex. Based on *in vitro* data, daclatasvir has shown activity against HCV genotypes 1 through 6, with EC50 values ranging from picomolar to low nanomolar against wild type HCV.

Manufacturer for United States

Daclatasvir is manufactured as *Daklinza* (dak lin za) by Bristol-Myers Squibb.

FDA Status

On July 24, 2015, the United States Food and Drug Administration (FDA) initially approved daclatasvir for use with sofosbuvir for the treatment of chronic HCV genotype 3 infection. In February 2016, the FDA modified and expanded the daclatasvir indications—daclatasvir is now indicated for use with sofosbuvir, with or without ribavirin, for patients with chronic HCV genotype 1 or 3. The new indications also include approval for use in patients with HIV-1 infection, those with decompensated cirrhosis, and following liver transplantation.

Indications

Daclatasvir is indicated for use, with sofosbuvir, with or without ribavirin for the treatment of patients with chronic HCV genotype 1 or 3. The use of ribavirin depends on the patient population treated as outlined below. For patients with HCV/HIV-1 coinfection, the dosage and duration are the same as listed below.

Genotype 1

- Genotype 1, without cirrhosis: daclatasvir plus sofosbuvir for 12 weeks
- Genotype 1, compensated (Child-Pugh A) cirrhosis*: daclatasvir plus sofosbuvir for 12 weeks
- Genotype 1, decompensated (Child-Pugh B or C) cirrhosis[^]: daclatasvir plus sofosbuvir plus ribavirin for 12 weeks
- Genotype 1, post-transplant: daclatasvir plus sofosbuvir plus ribavirin for 12 weeks

*For patients with genotype 1a and cirrhosis, consider screening for the presence of baseline NS5A resistance-associated polymorphisms at amino acid positions 28, 30, 31, or 93 prior to initiating treatment.

[^]For HCV genotype 1 patients with Child-Pugh C cirrhosis, the optimal duration of therapy with daclatasvir plus sofosbuvir plus ribavirin has not been established

Genotype 3

- Genotype 3, without cirrhosis: daclatasvir plus sofosbuvir for 12 weeks
- Genotype 3, compensated (Child-Pugh A) or decompensated (Child-Pugh B or C) cirrhosis: daclatasvir plus sofosbuvir plus ribavirin for 12 weeks
- Genotype 3, post-transplant: daclatasvir plus sofosbuvir plus ribavirin for 12 weeks

#For HCV genotype 3 patients with cirrhosis the optimal duration of therapy with daclatasvir plus sofosbuvir, with or without ribavirin, has not been established.

NOTE: For the use of dasabuvir and sofosbuvir in genotype 3 patients with cirrhosis, the AASLD/IDSA guidance recommends 24 weeks of therapy, with or without ribavirin.

Contraindications

Daclatasvir is contraindicated when coadministered with drugs that are strong inducers of CYP3A, including phenytoin, carbamazepine, rifampin, and St. John's wort (*Hypericum perforatum*); use of these combinations may result in lower exposure of daclatasvir, with potential reduced daclatasvir efficacy and virologic failure. If daclatasvir is used with sofosbuvir, the concomitant use of amiodarone is not recommended due to the risk of severe bradycardia with coadministration of sofosbuvir and amiodarone.

Dosing

Daclatasvir is available as a 60 mg tablet (light green in color) and 30 mg tablet (green in color) ([Figure 1](#)). The recommended standard dose of daclatasvir is 60 mg orally once daily, with or without food. The recommended dose of sofosbuvir, when used with daclatasvir is 400 mg once daily, with or without food.

Dose Modifications of Daclatasvir with CYP3 Inhibitors and Inducers

- With Strong CYP3A Inhibitor and Certain HIV Antiviral Agents: The daclatasvir levels are expected to increase and thus the daclatasvir dose should be reduced to 30 mg once daily.
- With Moderate CYP3A Inducers and Nevirapine: The daclatasvir levels are expected to decrease and the daclatasvir dose should be increased to 90 mg once daily.
- With Strong CYP3A Inducers: Daclatasvir is contraindicated.
- Patients with Renal Impairment: The dose of daclatasvir does not need to be adjusted in patients with any degree of renal impairment. In addition, because daclatasvir is highly protein bound, it is unlikely to be removed by dialysis.
- Patients with Hepatic Impairment: No dose adjustment is recommended for hepatic impairment, including patients with mild (Child-Pugh A), moderate (Child-Pugh B), or severe (Child-Pugh C) hepatic impairment.

Recommended Ribavirin Dosing

- When ribavirin is used in patients with HCV genotype 1 or 3 and either Child-Pugh B or C cirrhosis or post-transplantation patients, the recommended initial dose of ribavirin is 600 mg once daily, increasing up to 1000 mg daily as tolerated. In this scenario, the ribavirin starting dose and on-treatment dose can be decreased based on hemoglobin and creatinine clearance.
- When ribavirin is used in combination with daclatasvir and sofosbuvir in patients with HCV genotype 3

and compensated cirrhosis (Child-Pugh A), the recommended ribavirin dose is weight based (1000 mg for patients weighing less than 75 kg and 1200 mg for those weighing at least 75 kg) and is administered in two divided doses.

Clinical Use

The primary use for daclatasvir, at present, will be in combination with sofosbuvir, with or without ribavirin, for treatment-naïve and treatment-experience patients with chronic HCV genotype 1 or 3 infection, including those with cirrhosis and those with HIV coinfection. This regimen is the only FDA-approved all-oral 12-week regimen for the treatment of genotype 3 infection and regimen is a once-daily regimen. The regimen of daclatasvir plus sofosbuvir plus ribavirin will likely be a preferred option for treating patients post-liver transplantation.

Cost and Medication Access

The wholesale acquisition cost (WAC) cost for a 12-week course of daclatasvir is \$63,000. Bristol-Myers Squibb has a program for support and financial help related to medication access; see the web site [Patient Support Connect](#), which has information for both patients and professionals. In addition, patients and physicians may call 844-442-6663 for assistance with access to a range of support services for patients and healthcare professionals.

Resistance

Data from the ALLY-1 and ALLY-2 trials showed that 2 (33%) of 6 patients with genotype 1a and cirrhosis achieved an SVR in response to treatment with daclatasvir plus sofosbuvir, with or without ribavirin, if they had one or more baseline NS5A amino acid polymorphisms at position M28, Q30, L31, or Y93. Based on pooled clinical trials data, the prevalence of one or more of the NS5A polymorphisms at position M28, Q30, L31, or Y93 in patients with genotype 1a HCV in the United States is 11%. There are very limited data on the impact of daclatasvir resistance-associated mutations and response to therapy in patients with genotype 3 infection.

Key Drug Interactions

For complete information on daclatasvir-related drug interactions, see the [Drug Interactions section in the Daclatasvir \(Daklinza\) Prescribing Information](#).

Full Prescribing Information

[Daclatasvir \(Daklinza\) Full Prescribing Information.](#)

Figures

[Figure 1. Daclatasvir Pills](#)

Daclatasvir is available as a 60 mg tablet (light green in color) and 30 mg tablet (darker green in color).

Photographs courtesy of Bristol-Myers Squibb