Daclatasvir *(Daklinza)*

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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.

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

Bristol-Myers Squibb

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.

Adverse Effects

Daclatasvir 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.

Key Drug Interactions

Daclatasvir is a moderate inhibitor of P-glycoprotein transporter (P-gp) organic ion transporting polypeptide (OATP) 1B1 and 1B3, and breast cancer resistance protein (BCRP). Daclatasvir has the potential to increase the level of drugs that are substrates of P-gp, OAT 1B1 or 1B3, or BCRP. In addition, daclatasvir is a substrate of CYP3A. When given concomitantly with a strong CYP3A inhibitor, the daclatasvir dose should be reduced to 30 mg once daily; with moderate CYP3A inducers the dose should be increased to 90 mg once daily. Use of daclatasvir is contraindicated for use with drugs that are strong inducers of CYP3A, including phenytoin, carbamazepine, rifampin, and St. John's wort. Additional drug-drug interactions may occur with daclatasvir and other medications and these are detailed in the Daclatasvir (*Daklinza*) Full Prescribing Information.
For complete information on daclatasvir-related drug interactions, see the Drug Interactions section in the Daclatasvir (*Daklinza*) 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