

Sofosbuvir (*Sovaldi*)

Table of Contents

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

Drug Summary

Sofosbuvir was a breakthrough new medication for the treatment of patients with chronic hepatitis C. Sofosbuvir has a number of ideal properties, including once daily dosing, no meal restrictions, few adverse effects, minimal drug-drug interactions, high genetic barrier to resistance, and relatively good safety and efficacy in patients with advanced liver disease. The use of sofosbuvir in combination with ribavirin was the first FDA-approved all oral therapy for hepatitis C. Of note, the activity against genotype 3 appears less than with genotype 2 and treatment of genotype 3 infection requires a longer all-oral course of treatment than with genotype 2. Sofosbuvir is primarily used now in fixed-dose combinations.

Adverse Effects

Sofosbuvir is generally well-tolerated. The most common adverse effects observed with sofosbuvir, when used in combination with ribavirin, have been fatigue and headache. Sofosbuvir is pregnancy category B. To report suspected adverse reactions, contact (1) Gilead Sciences, Inc. at 1-800-GILEAD-5 or (2) the FDA at 1-800-FDA-1088.

Class and Mechanism

Sofosbuvir is a nucleotide analog inhibitor of hepatitis C virus NS5B polymerase—the key enzyme mediating HCV RNA replication. Sofosbuvir is a prodrug and after ingestion it is rapidly converted to GS-331007, the predominant circulating drug that accounts for greater than 90% of the systemically active drug. The compound GS-331007 is efficiently taken up by hepatocytes, whereby cellular kinases convert GS-331007 to its pharmacologically active uridine analog 5'-triphosphate form (GS-461203). This triphosphate compound mimics the natural cellular uridine nucleotide and is incorporated by the HCV RNA polymerase into the elongating RNA primer strand, resulting in chain termination. The active form GS-461203 targets the NS5B catalytic site and acts as a non-obligate chain terminator. The active compound (GS-461203) does not inhibit host DNA polymerases, RNA polymerases, or mitochondrial RNA polymerase.

Manufacturer for United States

Sofosbuvir is manufactured as *Sovaldi* (soh-VAHL-dee) by Gilead Sciences ([Figure 1](#)) and ([Figure 2](#)). The drug sofosbuvir was previously known as GS-7977 and was originally developed by Pharmasset as compound PSI-7977.

Indications

The following indications for sofosbuvir relate to patients with chronic hepatitis C virus infection.

Sofosbuvir is indicated for treatment of patients with chronic HCV

- Genotype 1 or 4: sofosbuvir plus peginterferon-alfa plus ribavirin for 12 weeks
- Genotype 2: sofosbuvir plus ribavirin for 12 weeks
- Genotype 3: sofosbuvir plus ribavirin for 24 weeks

For the treatment of patients with HCV-HIV-1 coinfection: the recommendations are the same as listed above.

For patents with genotype 1 HCV who are not eligible to receive interferon: sofosbuvir plus ribavirin for 24 weeks can be considered.

For patients with HCV and hepatocellular carcinoma awaiting liver transplantation: sofosbuvir plus ribavirin for a duration of up to 48 weeks or until liver transplantation, whichever occurs first.

Simeprevir in Combination with Sofosbuvir for HCV Infection: for details see the [Simeprevir Drug Summary](#) page and [Simeprevir Full Prescribing Information](#)

Daclatasvir in Combination with Sofosbuvir for HCV Infection: for details see the [Daclatasvir Drug Summary](#) page and [Daclatasvir Full Prescribing Information](#)

Contraindications

When sofosbuvir is used in combination with peginterferon alfa plus ribavirin, or with ribavirin alone, all contraindications that pertain to peginterferon alfa or ribavirin will apply to the combination regimens. The

use of sofosbuvir with amiodarone is not recommended due to the risk of developing serious symptomatic bradycardia; this risk is pronounced in persons also taking a beta-blocker and for those with underlying cardiac comorbidities or advanced liver disease.

Dosing

Sofosbuvir is available as a 400 mg tablet. The recommended dose of sofosbuvir is 400 mg taken orally once daily, with or without food. The 400 mg dose of sofosbuvir should be used, regardless of the patient's genotype and prior hepatitis C treatment experience. No dose adjustment is needed for mild-to-moderate renal impairment or with mild, moderate, or severe hepatic impairment. The prescribing information does not make a recommendation for dosing in patients who have severe renal impairment (eGFR less than 30 ml/min/1.73m²) or end stage renal disease requiring dialysis. Sofosbuvir is also available as a fixed-dose combination pill (ledipasvir 90 mg and sofosbuvir 400 mg) taken once daily.

Clinical Use

Sofosbuvir has FDA approval for the treatment of genotypes 1, 2, 3, and 4. Sofosbuvir is effective in treatment-naive and treatment-experienced patients, including those with HIV-coinfection, compensated cirrhosis, or hepatocellular carcinoma meeting Milan criteria awaiting liver transplantation. Sofosbuvir has been studied in a wide range of populations including persons 65 and older, persons with mild to moderate renal impairment. Sofosbuvir is used in clinical practice with other approved agents, including simeprevir or daclatasvir, as well as in fixed-dose combinations that contain sofosbuvir.

Cost and Medication Access

Gilead Sciences has an active sofosbuvir patient assistance program for eligible patients with hepatitis C who do not have insurance and are not covered by Medicaid or Medicare. Information regarding the Gilead Sciences sofosbuvir patient assistance program can be obtained at the [Support Path](#) website or by calling **1-855-769-7284**.

Resistance

Sofosbuvir has a high genetic barrier for resistance. To date, investigators have identified three amino acid changes in subjects who received sofosbuvir: L159F, S282T, and V321A.

- Investigators identified the L159F and V321A mutations in a small number of individuals with HCV genotype 3a following treatment with sofosbuvir, but these mutations did not lead to phenotypic resistance.
- The L159F mutation has been observed in patients with hepatocellular carcinoma and genotype 1a or 2b who were receiving prolonged courses of sofosbuvir (up to 48 week) while awaiting liver transplant; in these patients, the presence of the L159F and/or C316N mutations at baseline was associated with

virologic breakthrough relapse post-transplant.

- The S282T mutation was detected post sofosbuvir treatment in one patient with genotype 2b, but the patient had received sofosbuvir monotherapy; the isolate with the S282T mutation had a mean 13.5-fold reduced susceptibility to sofosbuvir.

Key Drug Interactions

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

Full Prescribing Information

[Sofosbuvir \(Sovaldi\) Full Prescribing Information](#)

Figures

[Figure 1. Sofosbuvir \(Sovaldi\) Pill Bottle](#)

Photo: Andrew Karpenko, University of Washington

[Figure 2. Sofosbuvir \(Sovaldi\) Pill](#)

Photo: Andrew Karpenko, University of Washington

© [Hepatitis C Online](#)

PDF created September 19, 2021, 7:19 pm

The most up to date version of this content may be obtained from:
<https://www.hepatitisC.uw.edu/page/treatment/drugs/sofosbuvir-drug>