HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use SOVALDI safely and effectively. See full prescribing information for SOVALDI.

SOVALDI® (sofosbuvir) tablets, for oral use
SOVALDI® (sofosbuvir) oral pellets
Initial U.S. Approval: 2013

WARNING: RISK OF HEPATITIS B VIRUS REACTIVATION IN PATIENTS COINFECTED WITH HCV AND HBV
See full prescribing information for complete boxed warning.

Hepatitis B virus (HBV) reactivation has been reported, in some cases resulting in fulminant hepatitis, hepatic failure, and death. (5.1)

----------RECENT MAJOR CHANGES----------

Indications and Usage (1)	08/2019
Dosage and Administration	
Recommended Dosage in Pediatric Patients 3 Years of Age and Older with Genotype 2 or 3 HCV (2.3)	08/2019
Preparation and Administration of Oral Pellets (2.4)	08/2019

----------INDICATIONS AND USAGE----------

SOVALDI is a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor indicated for the treatment of:

- Adult patients with genotype 1, 2, 3 or 4 chronic HCV infection without cirrhosis or with compensated cirrhosis as a component of a combination antiviral treatment regimen. (1)
- Pediatric patients 3 years of age and older with genotype 2 or 3 chronic HCV infection without cirrhosis or with compensated cirrhosis in combination with ribavirin. (1)

----------DOSAGE AND ADMINISTRATION----------

- Testing Prior to the Initiation of Therapy: Test all patients for HBV infection by measuring HBsAg and anti-HBc. (2.1)
- Recommended dosage in adults: One 400 mg tablet taken once daily with or without food. (2.2)
- Recommended dosage in pediatric patients 3 years of age and older: Recommended dosage of SOVALDI in pediatric patients 3 years of age and older with genotype 2 or 3 HCV using SOVALDI tablets or oral pellets is based on weight. Refer to Table 3 of the full prescribing information for specific dosing guidelines based on body weight. (2.3)
- HCV/HIV-1 coinfection: For adult and pediatric patients with HCV/HIV-1 coinfection, follow the dosage recommendations in the tables below, respectively. (2.2, 2.3)
- Recommended adult treatment regimen and duration: (2.2)

	Adult Patient Population	Regimen and Duration
Genotype 1 or 4	Treatment-naïve without cirrhosis or with compensated cirrhosis (Child-Pugh A)	SOVALDI + peginterferon alfa + ribavirin 12 weeks
Genotype 2	Treatment-naïve and treatment-experienced without cirrhosis or with compensated cirrhosis (Child-Pugh A)	SOVALDI + ribavirin 12 weeks
Genotype 3	Treatment-naïve and treatment-experienced without cirrhosis or with compensated cirrhosis (Child-Pugh A)	SOVALDI + ribavirin 24 weeks

- SOVALDI in combination with ribavirin for 24 weeks can be considered for adult patients with genotype 1 infection who are interferon ineligible. (2.2)
- Should be used in combination with ribavirin for treatment of HCV in adult patients with hepatocellular carcinoma awaiting liver transplantation for up to 48 weeks or until liver transplantation, whichever occurs first. (2.2)
- Recommended treatment regimen and duration for pediatric patients 3 years of age and older: (2.3, 2.4)

	Pediatric Patient Population 3 Years of Age and Older	Regimen and Duration
Genotype 2	Treatment-naïve and treatment-experienced without cirrhosis or with compensated cirrhosis (Child-Pugh A)	SOVALDI + ribavirin 12 weeks
Genotype 3	Treatment-naïve and treatment-experienced without cirrhosis or with compensated cirrhosis (Child-Pugh A)	SOVALDI + ribavirin 24 weeks

- A dosage recommendation cannot be made for patients with severe renal impairment or end stage renal disease. (2.7, 8.6)
- Instructions for Use should be followed for preparation and administration of SOVALDI oral pellets. (2.4)

----------DOSAGE FORMS AND STRENGTHS----------

- Tablets: 400 mg and 200 mg of sofosbuvir. (3)
- Oral Pellets: 200 mg and 150 mg of sofosbuvir. (3)

----------CONTRAINDICATIONS----------

- When used in combination with peginterferon alfa/ribavirin or ribavirin alone, all contraindications to peginterferon alfa and/or ribavirin also apply to SOVALDI combination therapy. (4)

----------WARNINGS AND PRECAUTIONS----------

- Risk of Hepatitis B Virus Reactivation: Test all patients for evidence of current or prior HBV infection before initiation of HCV treatment. Monitor HCV/HBV coinfected patients for HBV reactivation and hepatitis flare during HCV treatment and post-treatment follow-up. Initiate appropriate patient management for HBV infection as clinically indicated. (5.1)
- Bradycardia with amiodarone coadministration: Serious symptomatic bradycardia may occur in patients taking amiodarone with a sofosbuvir-containing regimen, particularly in patients also receiving beta blockers, or those with underlying cardiac comorbidities and/or advanced liver disease. Coadministration of amiodarone with SOVALDI is not recommended. In patients without alternative, viable treatment options, cardiac monitoring is recommended. (5.2, 6.2, 7.1)

----------ADVERSE REACTIONS----------

- The most common adverse events (incidence greater than or equal to 20%, all grades) observed with SOVALDI in combination with ribavirin were fatigue and headache. The most common adverse events observed with SOVALDI in combination with peginterferon alfa and ribavirin were fatigue, headache, nausea, insomnia and anemia. (6.1). The most common adverse events observed with SOVALDI in combination with ribavirin oral solution in pediatric patients was decreased appetite. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Gilead Sciences, Inc. at 1-800-GILEAD-5 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

- Coadministration of amiodarone with a sofosbuvir-containing regimen may result in serious symptomatic bradycardia. (5.2, 6.2, 7.1)
- Drugs that are intestinal P-gp inducers (e.g., rifampin, St. John's wort) may alter the concentrations of sofosbuvir. (5.3, 7, 12.3)
- Consult the full prescribing information prior to use for potential drug-drug interactions. (5.2, 5.3, 7, 12.3)
- Clearance of HCV infection with direct acting antivirals may lead to changes in hepatic function, which may impact safe and effective use of concomitant medications. Frequent monitoring of relevant laboratory parameters (INR or blood glucose) and dose adjustments of certain concomitant medications may be necessary. (7.1)

----------USE IN SPECIFIC POPULATIONS----------

- Patients with HCV/HIV-1 coinfection: Safety and efficacy have been studied. (14.4)
- Patients with hepatocellular carcinoma awaiting liver transplantation: Safety and efficacy have been studied. (8.8)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: RISK OF HEPATITIS B VIRUS REACTIVATION IN PATIENTS COINFECTED WITH HCV AND HBV

Test all patients for evidence of current or prior hepatitis B virus (HBV) infection before initiating treatment with SOVALDI. HBV reactivation has been reported in HCV/HBV coinfected patients who were undergoing or had completed treatment with HCV direct acting antivirals and were not receiving HBV antiviral therapy. Some cases have resulted in fulminant hepatitis, hepatic failure, and death. Monitor HCV/HBV coinfected patients for hepatitis flare or HBV reactivation during HCV treatment and post-treatment follow-up. Initiate appropriate patient management for HBV infection as clinically indicated *[see Warnings and Precautions (5.1)]*.

1 INDICATIONS AND USAGE

Adult Patients:

SOVALDI is indicated for the treatment of adult patients with chronic hepatitis C virus (HCV) infection as a component of a combination antiviral treatment regimen *[see Dosage and Administration (2.2), and Clinical Studies (14)]*

- genotype 1 or 4 infection without cirrhosis or with compensated cirrhosis for use in combination with pegylated interferon and ribavirin
- genotype 2 or 3 infection without cirrhosis or with compensated cirrhosis for use in combination with ribavirin.

Pediatric Patients:

SOVALDI is indicated for the treatment of chronic HCV genotype 2 or 3 infection in pediatric patients 3 years of age and older without cirrhosis or with compensated cirrhosis for use in combination with ribavirin *[see Dosage and Administration (2.3) and Clinical Studies (14.5)]*.

2 DOSAGE AND ADMINISTRATION

2.1 Testing Prior to the Initiation of Therapy

Test all patients for evidence of current or prior HBV infection by measuring hepatitis B surface antigen (HBsAg) and hepatitis B core antibody (anti-HBc) before initiating HCV treatment with SOVALDI *[see Warnings and Precautions (5.1)]*.

2.2 Recommended Dosage in Adults

The recommended dosage of SOVALDI is one 400 mg tablet, taken orally, once daily with or without food *[see Clinical Pharmacology (12.3)]*.

Administer SOVALDI in combination with ribavirin or in combination with pegylated interferon and ribavirin for the treatment of HCV. The recommended treatment regimen and duration for SOVALDI combination therapy is provided in Table 1.

For patients with HCV/HIV-1 coinfection, follow the dosage recommendations in Table 1. Refer to *Drug Interactions (7)* for dosage recommendations for concomitant HIV-1 antiviral drugs.

Table 1 Recommended Treatment Regimen and Duration in Adult Patients with Genotype 1, 2, 3, or 4 HCV

	Patient Population	Treatment Regimen and Duration
Genotype 1 or 4	Treatment-naïve without cirrhosis or with compensated cirrhosis (Child-Pugh A)	SOVALDI + peginterferon alfa[a] + ribavirin[b] 12 weeks
Genotype 2	Treatment-naïve and treatment-experienced[c] without cirrhosis or with compensated cirrhosis (Child-Pugh A)	SOVALDI + ribavirin[b] 12 weeks
Genotype 3	Treatment-naïve and treatment-experienced[c] without cirrhosis or with compensated cirrhosis (Child-Pugh A)	SOVALDI + ribavirin[b] 24 weeks

a. See peginterferon alfa prescribing information for dosage recommendation for patients with genotype 1 or 4 HCV.
b. Dosage of ribavirin is weight-based (<75 kg = 1000 mg and ≥75 kg = 1200 mg). The daily dosage of ribavirin is administered orally in two divided doses with food. Patients with renal impairment (CrCl ≤50 mL/min) require ribavirin dosage reduction; refer to ribavirin tablet prescribing information.
c. Treatment-experienced patients have failed an interferon-based regimen with or without ribavirin.

Patients with Genotype 1 HCV Who are Ineligible to Receive an Interferon-Based Regimen

SOVALDI in combination with ribavirin for 24 weeks can be considered as a therapeutic option for patients with genotype 1 infection who are ineligible to receive an interferon-based regimen *[see Clinical Studies (14.4)]*. Treatment decision should be guided by an assessment of the potential benefits and risks for the individual patient.

Patients with Hepatocellular Carcinoma Awaiting Liver Transplantation

Administer SOVALDI in combination with ribavirin for up to 48 weeks or until the time of liver transplantation, whichever occurs first, to prevent post-transplant HCV reinfection *[see Use in Specific Populations (8.8)]*.

2.3 Recommended Dosage in Pediatric Patients 3 Years of Age and Older with Genotype 2 or 3 HCV

The recommended treatment regimen, duration, and recommended dosage for SOVALDI combination therapy is provided in Table 2 and Table 3. Table 4 provides the weight-based dosage of ribavirin when used in combination with SOVALDI for pediatric patients. For patients with HCV/HIV-1 coinfection, follow the dosage recommendations in Table 3 and Table 4. Refer to *Drug Interactions (7)* for dosage recommendations for concomitant HIV-1 antiviral drugs. In pediatric patients with hepatocellular carcinoma

awaiting liver transplantation, administer SOVALDI in combination with ribavirin for up to 48 weeks or until the time of liver transplantation, whichever occurs first, to prevent post-transplant HCV reinfection *[see Use in Specific Populations (8.8)]*.

Table 2 Recommended Treatment Regimen and Duration in Pediatric Patients 3 Years and Older with Genotype 2 or 3 HCV

	Patient Population	Treatment Regimen and Duration
Genotype 2	Treatment-naïve and treatment-experienced[a] without cirrhosis or with compensated cirrhosis (Child-Pugh A)	SOVALDI + ribavirin[b] 12 weeks
Genotype 3	Treatment-naïve and treatment-experienced[a] without cirrhosis or with compensated cirrhosis (Child-Pugh A)	SOVALDI + ribavirin[b] 24 weeks

a. Treatment-experienced patients have failed an interferon based regimen with or without ribavirin.
b. See Table 4 for weight-based ribavirin dosing recommendations.

The recommended dosage of SOVALDI in pediatric patients 3 years and older with genotype 2 or 3 HCV using SOVALDI tablets or oral pellets (with or without food) is based on weight (Table 3), and is to be taken orally once daily in combination with ribavirin *[see Dosage and Administration (2.4), Use in Specific Populations (8.4), Clinical Pharmacology (12.3), and Clinical Studies (14.5)]*. SOVALDI pellets can be taken by pediatric patients who cannot swallow the tablet formulation *[see Dosage and Administration (2.4)]*.

Table 3 Dosing for Pediatric Patients 3 Years and Older Using SOVALDI Tablets or Oral Pellets

Body Weight (kg)	Dosing of SOVALDI Tablets or Oral Pellets	SOVALDI Daily Dose
at least 35	one 400 mg tablet once daily or two 200 mg tablets once daily or two 200 mg packets of pellets once daily	400 mg per day
17 to less than 35	one 200 mg tablet once daily or one 200 mg packet of pellets once daily	200 mg per day
less than 17	one 150 mg packet of pellets once daily	150 mg per day

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.