

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use EPCLUSA safely and effectively. See full prescribing information for EPCLUSA.

EPCLUSA® (sofosbuvir and velpatasvir) tablets, for oral use
Initial U.S. Approval: 2016

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)	03/2020
Dosage and Administration	
Recommended Treatment Regimen and Duration in Patients 6 Years of Age and Older or Weighing at Least 17 kg (2.2)	03/2020
Recommended Dosage in Adults (2.3)	03/2020
Recommended Dosage in Pediatric Patients 6 Years of Age and Older or Weighing at Least 17 kg (2.4)	03/2020
Renal Impairment (2.5)	11/2019

INDICATIONS AND USAGE

- EPCLUSA is a fixed-dose combination of sofosbuvir, a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor, and velpatasvir, an HCV NS5A inhibitor, and is indicated for the treatment of adult and pediatric patients 6 years of age and older or weighing at least 17 kg with chronic HCV genotype 1, 2, 3, 4, 5, or 6 infection (1):
 - without cirrhosis or with compensated cirrhosis
 - with decompensated cirrhosis for use in combination with ribavirin

DOSAGE AND ADMINISTRATION

- Testing prior to the initiation of therapy: Test all patients for HBV infection by measuring HBsAg and anti-HBc. (2.1)
- See recommended treatment regimen and duration in patients 6 years of age and older or weighing at least 17 kg with genotypes 1, 2, 3, 4, 5, or 6 HCV in table below: (2.2)

Patient Population	Regimen and Duration
Treatment-naïve and treatment-experienced ^a , without cirrhosis and with compensated cirrhosis (Child-Pugh A)	EPCLUSA 12 weeks
Treatment-naïve and treatment-experienced ^a , with decompensated cirrhosis (Child-Pugh B and C)	EPCLUSA + ribavirin 12 weeks

a. In clinical trials, regimens contained peginterferon alfa/ribavirin with or without an HCV NS3/4A protease inhibitor (boceprevir, simeprevir, or telaprevir).

- Recommended dosage in adults: One tablet (400 mg of sofosbuvir and 100 mg of velpatasvir) taken orally once daily with or without food. (2.3)
- Recommended dosage in pediatric patients 6 years and older: Recommended dosage of EPCLUSA in pediatric patients 6 years of age and older or weighing at least 17 kg is based on weight. Refer to Table 2 of the full prescribing information for specific dosing guidelines based on body weight (2.4)

- HCV/HIV-1 coinfection: For patients with HCV/HIV-1 coinfection, follow the dosage recommendations in the table above. (2.2)
- If used in combination with ribavirin, follow the recommendations for ribavirin dosing and dosage modifications. (2.3, 2.4)
- For patients with renal impairment including end stage renal disease on dialysis, follow the dosage recommendations in the table above. (2.5)

DOSAGE FORMS AND STRENGTHS

Tablets: 400 mg of sofosbuvir and 100 mg of velpatasvir; 200 mg of sofosbuvir and 50 mg of velpatasvir. (3)

CONTRAINDICATIONS

EPCLUSA and ribavirin combination regimen is contraindicated in patients for whom ribavirin is contraindicated. (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 coinfecting 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, particularly in patients also receiving beta blockers, or those with underlying cardiac comorbidities and/or advanced liver disease. Coadministration of amiodarone with EPCLUSA is not recommended. In patients without alternative viable treatment options, cardiac monitoring is recommended. (5.2, 7.3)

ADVERSE REACTIONS

- The most common adverse reactions (incidence greater than or equal to 10%, all grades) observed with treatment with EPCLUSA for 12 weeks are headache and fatigue. (6.1)
- The most common adverse reactions (incidence greater than or equal to 10%, all grades) observed with treatment with EPCLUSA and ribavirin for 12 weeks in adult patients with decompensated cirrhosis are fatigue, anemia, nausea, headache, insomnia, and diarrhea. (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

- P-gp inducers and/or moderate to strong CYP inducers (e.g., rifampin, St. John's wort, carbamazepine): May decrease concentrations of sofosbuvir and/or velpatasvir. Use of EPCLUSA with P-gp inducers and/or moderate to strong CYP inducers is not recommended. (5.3, 7)
- Consult the full prescribing information prior to use for potential drug interactions. (5.2, 5.3, 7)
- 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. (7.3)

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

Revised: 03/2020

FULL PRESCRIBING INFORMATION: CONTENTS***WARNING: RISK OF HEPATITIS B VIRUS REACTIVATION IN PATIENTS COINFECTED WITH HCV AND HBV****1 INDICATIONS AND USAGE****2 DOSAGE AND ADMINISTRATION**

- 2.1 Testing Prior to the Initiation of Therapy
- 2.2 Recommended Treatment Regimen and Duration in Patients 6 Years of Age and Older or Weighing at Least 17 kg
- 2.3 Recommended Dosage in Adults
- 2.4 Recommended Dosage in Pediatric Patients 6 Years of Age and Older or Weighing at Least 17 kg
- 2.5 Renal Impairment

3 DOSAGE FORMS AND STRENGTHS**4 CONTRAINDICATIONS****5 WARNINGS AND PRECAUTIONS**

- 5.1 Risk of Hepatitis B Virus Reactivation in Patients Coinfected with HCV and HBV
- 5.2 Serious Symptomatic Bradycardia When Coadministered with Amiodarone
- 5.3 Risk of Reduced Therapeutic Effect Due to Concomitant Use of EPCLUSA with Inducers of P-gp and/or Moderate to Strong Inducers of CYP
- 5.4 Risks Associated with Ribavirin and EPCLUSA Combination Treatment

6 ADVERSE REACTIONS

- 6.1 Clinical Trials Experience
- 6.2 Postmarketing Experience

7 DRUG INTERACTIONS

- 7.1 Potential for Other Drugs to Affect EPCLUSA
- 7.2 Potential for EPCLUSA to Affect Other Drugs
- 7.3 Established and Potentially Significant Drug Interactions

- 7.4 Drugs without Clinically Significant Interactions with EPCLUSA

8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.2 Lactation
- 8.3 Females and Males of Reproductive Potential
- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Renal Impairment
- 8.7 Hepatic Impairment

10 OVERDOSAGE**11 DESCRIPTION****12 CLINICAL PHARMACOLOGY**

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics
- 12.4 Microbiology

13 NONCLINICAL TOXICOLOGY

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

14 CLINICAL STUDIES

- 14.1 Description of Clinical Trials
- 14.2 Clinical Trials in Subjects without Cirrhosis and Subjects with Compensated Cirrhosis
- 14.3 Clinical Trial in Subjects Coinfected with HCV and HIV-1
- 14.4 Clinical Trials in Subjects with Decompensated Cirrhosis
- 14.5 Clinical Trial in Subjects with Severe Renal Impairment Requiring Dialysis
- 14.6 Clinical Trial in Pediatric Subjects

16 HOW SUPPLIED/STORAGE AND HANDLING**17 PATIENT COUNSELING INFORMATION**

* 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 EPCLUSA. HBV reactivation has been reported in HCV/HBV coinfecting 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 coinfecting 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

EPCLUSA is indicated for the treatment of adults and pediatric patients 6 years of age and older or weighing at least 17 kg with chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5, or 6 infection [see *Dosage and Administration (2.2, 2.3, 2.4)* and *Clinical Studies (14)*]:

- without cirrhosis or with compensated cirrhosis
- with decompensated cirrhosis for use in combination with ribavirin.

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 EPCLUSA [see *Warnings and Precautions (5.1)*].

2.2 Recommended Treatment Regimen and Duration in Patients 6 Years of Age and Older or Weighing at Least 17 kg

Table 1 shows the recommended treatment regimen and duration based on patient population.

For patients with HCV/HIV-1 coinfection, follow the dosage recommendations in Table 1 [see *Clinical Studies (14.3)*]. Refer to *Drug Interactions (7)* for dosage recommendations for concomitant HIV-1 antiviral drugs.

Table 1 Recommended Treatment Regimen and Duration in Patients 6 Years of Age and Older or Weighing at Least 17 kg with Genotype 1, 2, 3, 4, 5, or 6 HCV

Patient Population	Treatment Regimen and Duration
Treatment-naïve and treatment-experienced ^a , without cirrhosis and with compensated cirrhosis (Child-Pugh A)	EPCLUSA 12 weeks
Treatment-naïve and treatment-experienced ^a , with decompensated cirrhosis (Child-Pugh B or C)	EPCLUSA + ribavirin ^b 12 weeks

a. In clinical trials in adults, regimens contained peginterferon alfa/ribavirin with or without an HCV NS3/4A protease inhibitor (boceprevir, simeprevir, or telaprevir).

b. See Dosage and Administration 2.3 and 2.4 for ribavirin dosage recommendations.

2.3 Recommended Dosage in Adults

The recommended dosage of EPCLUSA in adults is one tablet (400 mg sofosbuvir and 100 mg velpatasvir) taken orally once daily with or without food [see *Clinical Pharmacology* (12.3)].

When administered with EPCLUSA, the recommended dosage of ribavirin is based on weight (administered with food): 1,000 mg per day for patients less than 75 kg and 1,200 mg for those weighing at least 75 kg, divided and administered twice daily. The starting dosage and on-treatment dosage of ribavirin can be decreased based on hemoglobin and creatinine clearance. For ribavirin dosage modifications refer to the ribavirin prescribing information [see *Use in Specific Populations* (8.6) and *Clinical Studies* (14.4)].

2.4 Recommended Dosage in Pediatric Patients 6 Years of Age and Older or Weighing at Least 17 kg

The recommended dosage of EPCLUSA in pediatric patients 6 years of age and older or weighing at least 17 kg is based on weight and provided in Table 2. Table 3 provides the weight-based dosage of ribavirin when used in combination with EPCLUSA for pediatric patients. Take EPCLUSA once daily with or without food [see *Use in Specific Populations* (8.4), *Clinical Pharmacology* (12.3), and *Clinical Studies* (14.6)].

Table 2 Dosing for Pediatric Patients 6 Years and Older or Weighing at Least 17 kg with Genotype 1, 2, 3, 4, 5, or 6 HCV

Body Weight (kg)	Dosing of EPCLUSA	EPCLUSA Daily Dose
at least 30	one 400 mg/100 mg tablet once daily or two 200 mg/50 mg tablets once daily	400 mg/100 mg per day
17 to less than 30	one 200 mg/50 mg tablet once daily	200 mg/50 mg per day

Table 3 Recommended Dosing for Ribavirin in Combination Therapy with EPCLUSA for Pediatric Patients 6 Years and Older

Body Weight (kg)	Oral Ribavirin Daily Dosage ^a
less than 47	15 mg per kg per day (divided dose AM and PM)
47–49	600 mg per day (1 x 200 mg AM, 2 x 200 mg PM)
50–65	800 mg per day (2 x 200 mg AM, 2 x 200 mg PM)
66–80	1,000 mg per day (2 x 200 mg AM, 3 x 200 mg PM)
greater than 80	1,200 mg per day (3 x 200 mg AM, 3 x 200 mg PM)

a. The daily dosage of ribavirin is weight-based and is administered orally in two divided doses with food.

2.5 Renal Impairment

No dosage adjustment of EPCLUSA is recommended in patients with any degree of renal impairment, including patients requiring dialysis. Administer EPCLUSA with or without ribavirin according to the recommendations in Table 1 [see *Adverse Reactions (6.1)*, *Use in Specific Populations (8.6)*, and *Clinical Studies (14.5)*]. Refer to ribavirin tablet prescribing information for ribavirin dosage modification for patients with CrCl less than or equal to 50 mL per minute.

3 DOSAGE FORMS AND STRENGTHS

EPCLUSA tablets are available in two dose strengths:

- 400 mg/100 mg Tablets: pink, diamond-shaped, film-coated tablet debossed with “GSI” on one side and “7916” on the other side. Each tablet contains 400 mg of sofosbuvir and 100 mg of velpatasvir.
- 200 mg/50 mg Tablets: pink, oval-shaped, film-coated tablet debossed with “GSI” on one side and “S/V” on the other side. Each tablet contains 200 mg of sofosbuvir and 50 mg of velpatasvir.

4 CONTRAINDICATIONS

EPCLUSA and ribavirin combination regimen is contraindicated in patients for whom ribavirin is contraindicated. Refer to the ribavirin prescribing information for a list of contraindications for ribavirin [see *Dosage and Administration (2.2, 2.3, 2.4)*].

5 WARNINGS AND PRECAUTIONS

5.1 Risk of Hepatitis B Virus Reactivation in Patients Coinfected with HCV and HBV

Hepatitis B virus (HBV) reactivation has been reported in HCV/HBV coinfecting patients who were undergoing or had completed treatment with HCV direct acting antivirals, and

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.