CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

214187Orig1s000

LABELING

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
EPCLUSA® (sofosbuvir and velpatasvir) oral pellets
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)	06/2021
Dosage and Administration	
Recommended Treatment Regimen and Duration in Patients 3 Years of Age and Older (2.2)	06/2021
Recommended Dosage in Pediatric Patients 3 Years of Age and Older (2.4)	06/2021
Preparation and Administration of Oral Pellets (2.5)	06/2021

----------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 inh bitor, and is indicated for the treatment of adults and pediatric patients 3 years of age and older 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 3 years of age and older 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 3 years and older: Recommended dosage is based on weight. Refer to Table 2 of the full prescr bing information for specific dosing guidelines based on body weight. (2.4)
- For pediatric patients less than 6 years of age, administer EPCLUSA oral pellets with food. (2.4)
- Instructions for Use should be followed for preparation and administration of EPCLUSA oral pellets. (2.5)
- HCV/HIV-1 coinfection: For patients with HCV/HIV-1 coinfection, follow the dosage recommendations in the table above. (2.2)
- For treatment-naïve and treatment-experienced liver transplant recipients without cirrhosis or with compensated cirrhosis (Child-Pugh A), the recommended regimen is EPCLUSA once daily for 12 weeks. (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. (2.6)

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

- Tablets: 400 mg of sofosbuvir and 100 mg of velpatasvir; 200 mg of sofosbuvir and 50 mg of velpatasvir. (3)
- Oral Pellets: 200 mg of sofosbuvir and 50 mg of velpatasvir; 150 mg of sofosbuvir and 37.5 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 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, 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 in adults and pediatric subjects 6 years of age and older 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%, grade 1 or 2) observed in pediatric subjects less than 6 years of age are vomiting and product use issue (spitting up the drug). (6.1)
- The most common adverse reactions (incidence greater than or equal to 10%, all grades) observed with treatment with EPCLUSA and r bavirin 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: 06/2021

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 EPCLUSA. 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

EPCLUSA is indicated for the treatment of adults and pediatric patients 3 years of age and older 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 3 Years of Age and Older

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. For treatment-naïve and treatment-experienced liver transplant recipients without cirrhosis or with compensated cirrhosis (Child-Pugh A), the recommended regimen is EPCLUSA once daily for 12 weeks *[see Clinical Studies (14.3 and 14.5)].* Refer to *Drug Interactions (7)* for dosage recommendations for concomitant drugs.

Table 1 Recommended Treatment Regimen and Duration in Patients 3 Years of Age and Older 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 r bavirin 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 3 Years of Age and Older

The recommended dosage of EPCLUSA in pediatric patients 3 years of age and older 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 oral pellets or tablets once daily with or without food. In pediatric patients less than 6 years of age, administer the oral pellets with food to increase tolerability related to palatability *[see Use in Specific Populations (8.4), Clinical Pharmacology (12.3), and Clinical Studies (14.7)]*.

Table 2 Dosing for Pediatric Patients 3 Years and Older with Genotype 1, 2, 3, 4, 5, or 6 HCV Using EPCLUSA Oral Pellets or Tablets

Body Weight (kg)	EPCLUSA Daily Dose	Dosing of EPCLUSA Oral Pellets	Dosing of EPCLUSA Tablet
less than 17	150 mg/37.5 mg per day	one 150 mg/37.5 mg packet of pellets once daily	N/A
17 to less than 30	200 mg/50 mg per day	one 200 mg/50 mg packet of pellets once daily	one 200 mg/50 mg tablet once daily
at least 30	400 mg/100 mg per day	two 200 mg/50 mg packets of pellets once daily	one 400 mg/100 mg tablet once daily[a]

a. Two 200 mg/50 mg tablets once daily can be used for patients who cannot swallow the 400 mg/100 mg tablet.

DOCKET ALARM

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