EPCLUSA®
sofosbuvir/velpatasvir
400 mg/100 mg tablets

EPCLUSA HAS BEEN STUDIED IN A BROAD RANGE OF PATIENTS WITH CHRONIC HCV

INCLUDING PROSPECTIVE STUDIES IN PEOPLE WHO INJECT DRUGS

EPCLUSA is indicated for the treatment of adults with chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis.

IMPORTANT SAFETY INFORMATION

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

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 (DAAs) and were not receiving HBV antiviral therapy. Some cases have resulted in fulminant hepatitis, hepatic failure, and death. Cases have been reported in patients who are HBsAg positive, in patients with serologic evidence of resolved HBV, and also in patients receiving certain immunosuppressant or chemotherapeutic agents; the risk of HBV reactivation associated with treatment with HCV DAAs may be increased in patients taking these other agents. 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.

EPCLUSA DEMONSTRATED SAFETY AND EFFICACY IN SUBJECTS WITH CHRONIC HCV IN THE ASTRAL PIVOTAL TRIALS[1]

98%

overall cure rate in HCV GT 1-6, TN and TE[a] adult subjects without cirrhosis or with CC[1]

(n=1015/1035; ASTRAL-1, -2, & -3)

SVR12 was the primary endpoint and was defined as HCV RNA <15 IU/mL at 12 weeks after the end of treatment.[1] Achieving SVR12 is considered a virologic cure[2]

Active injection drug users (within 12 months) were excluded from the ASTRAL pivotal trials[3]

Trial Safety Data

- Adverse reactions (all grades) reported in ≥5% of all adult subjects receiving 12 weeks of treatment with EPCLUSA (ASTRAL-1) were headache (22%), fatigue (15%), nausea (9%), asthenia (5%), and insomnia (5%)[1]
- The adverse reactions observed in subjects treated with EPCLUSA in ASTRAL-2 & -3 were consistent with those observed in ASTRAL-1[1]
- Irritability was also observed in ≥5% of adult subjects treated with EPCLUSA in ASTRAL-3[1]

0.2% **Discontinuations due to AEs** (ASTRAL-1, -2, & -3)[1]

Please see page 6 for ASTRAL study design details

[a]Prior regimens contained PegIFN alfa + RBV with or without an HCV NS3/4A PI (boceprevir, simeprevir, or telaprevir).[1]
AE=adverse event; CC=compensated cirrhosis; GT=genotype; PegIFN=pegylated interferon; PI=protease inhibitor; RBV=ribavirin; SVR12=sustained virologic response at 12 weeks after the end of treatment; TE=treatment-experienced; TN=treatment-naïve.

SIMPLIFY AND ANCHOR STUDY DESIGNS

SIMPLIFY

SIMPLIFY was an open-label, single-arm, international, Phase 4 trial aimed at evaluating the efficacy and safety of EPCLUSA for 12 weeks in GT 1-6 adults with recent injection drug use (within 6 months) and naïve to NS5A-based HCV therapy (N=103). Participants with HIV and/or decompensated liver disease were excluded. SVR12 was the primary endpoint in SIMPLIFY and was defined as HCV RNA <12 IU/mL at 12 weeks after the end of treatment. Adherence (90%) was a secondary endpoint and was assessed by dividing the number of total doses received by total expected number of doses.[4]

Study Limitations: Weekly clinic visits and weekly electronic blister packs, which participants were incentivized to return, may have led to improved adherence, which may not be generalizable to the larger HCV population. The study population in SIMPLIFY was recruited from hospital-based and community-based clinics/centers; it may not be generalizable to all populations of people with injection drug use.[4]

ANCHOR

ANCHOR was a prospective, open-label, observational, single-site trial evaluating the efficacy of EPCLUSA for 12 weeks in adults with opioid use disorder and reported ongoing injection drug use (within 3 months of screening visit) treated at a harm-reduction center in Washington, DC (N=100). Participants were offered optional buprenorphine initiation. Patients with decompensated liver disease and those who were pregnant or breastfeeding were excluded. The primary endpoint was the proportion of participants with SVR12. Adherence was assessed by monthly pill count, HCV viral load, number of bottles completed, interruptions on treatment (3 days with resumption), and date of last pill taken relative to planned end of treatment date. Imperfect daily adherence was defined as finishing treatment >7 days after the anticipated treatment end date.[5]

Study Limitations: OAT status groups were non-randomized and self-selected. Factors associated with non-update or discontinuation of OAT may have been the same factors that led to HCV treatment failure or loss to follow-up. Results may not be generalizable to the larger HCV population.[5]

The SIMPLIFY and ANCHOR studies are not presented in the EPCLUSA full Prescribing Information.

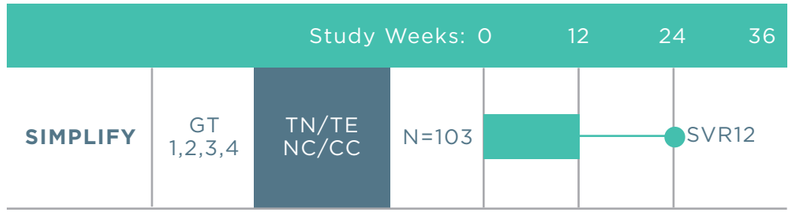
- **Active injection drug users (within 12 months) or those with a positive urine drug test at screening were excluded from the ASTRAL pivotal trials[3]**
- **Patients in SIMPLIFY and ANCHOR were instructed to use EPCLUSA once daily for 12 weeks, as recommended in the EPCLUSA full Prescribing Information[4,5]**
- **In SIMPLIFY, participants received EPCLUSA in weekly blister packs[4]**
- Real-world data are observational in nature and are not based on controlled clinical studies
- **Results from these studies may differ from those observed in clinical practice**
- Funding for SIMPLIFY and ANCHOR was provided by Gilead Sciences, Inc.

OAT=opioid agonist therapy.

Injection drug use is the most common risk factor for HCV infection in the United States, accounting for ~70% of new HCV cases.[6]

SIMPLIFY PROSPECTIVELY STUDIED THE EFFICACY AND SAFETY OF EPCLUSA IN PEOPLE WHO INJECT DRUGS[4]

The SIMPLIFY clinical trial studied the efficacy and safety of EPCLUSA for 12 weeks in adults with chronic HCV and recent injection drug use[a] (within the past 6 months) who were naïve to NS5A-based HCV therapy.



International, multicenter, single-arm, open-label, Phase 4 trial

At baseline:

- **74%** had injected drugs in the past 30 days
- **59%** were receiving medication-assisted treatment

94%

overall cure rate (ITT)

(n=97/103; SIMPLIFY)

SVR12 was the primary endpoint in SIMPLIFY and was defined as HCV RNA <12 IU/mL at 12 weeks after the end of treatment

Trial Safety Data

- Adverse reactions reported in ≥5% of adult participants were fatigue (22%), headache (18%), nausea (14%), insomnia (9%), arthralgia (6%), dizziness (5%), and nasopharyngitis (5%)
- Seven (7%) participants had ≥1 serious AE; 1 (1%) was considered treatment related

1% **Discontinuations due to AEs** (n=1/103)

- **Participants in SIMPLIFY were instructed to use EPCLUSA once daily for 12 weeks, as recommended in the EPCLUSA full Prescribing Information, and received EPCLUSA in weekly blister packs**

[a]Recent injection drug use was defined as self-reported injection drug use within 6 months of enrollment in the clinical study.

IMPORTANT SAFETY INFORMATION (CONT'D)

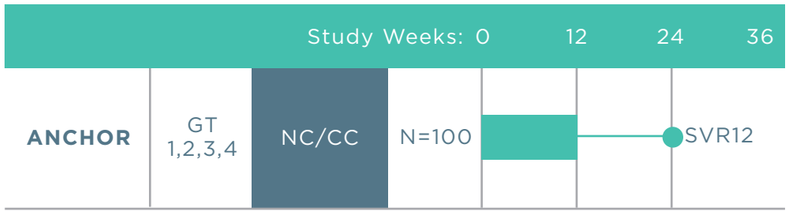
WARNINGS AND PRECAUTIONS

- **Serious Symptomatic Bradycardia When Coadministered with Amiodarone:** Amiodarone is not recommended for use with EPCLUSA due to the risk of symptomatic bradycardia, particularly in patients also taking beta blockers or with underlying cardiac comorbidities and/or with advanced liver disease. A fatal cardiac arrest was reported in a patient taking amiodarone who was coadministered a sofosbuvir-containing regimen. In patients without alternative viable treatment options, cardiac monitoring is recommended. Patients should seek immediate medical evaluation if they develop signs or symptoms of bradycardia.

ITT=intent-to-treat; NC=non-cirrhotic.

ANCHOR PROSPECTIVELY STUDIED EPCLUSA IN PEOPLE WHO INJECT DRUGS WITH REAL CHALLENGES IN A REAL-WORLD SETTING[5]

ANCHOR studied the efficacy of EPCLUSA for 12 weeks in adults with chronic HCV and opioid use disorder and reported ongoing injection drug use (within 3 months of screening visit) treated at a harm-reduction center in Washington, DC.



Prospective, open-label, observational, single-site trial

At baseline:

59% had daily or more frequent injection drug use

33% were receiving medication-assisted treatment

88%

overall cure rate (PP) in the real world
(n=82/93; ANCHOR)

For the total patient population, cure rate was 82% (82/100)

The primary endpoint was the proportion of participants with SVR12

88%

cure rate in adults receiving medication-assisted treatment
(n=29/33)

- **Patients in ANCHOR were instructed to use EPCLUSA once daily for 12 weeks, as recommended in the EPCLUSA full Prescribing Information**
- Real-world data are observational in nature and are not based on controlled clinical studies
- Results from these studies may differ from those observed in clinical practice and are not presented in the EPCLUSA full Prescribing Information

Please see page 2 for ANCHOR study design details

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

- **Risk of Reduced Therapeutic Effect Due to Concomitant Use of EPCLUSA with P-gp Inducers and/or Moderate to Strong Inducers of CYP2B6, CYP2C8 or CYP3A4:** Rifampin, St. John's wort, and carbamazepine are not recommended for use with EPCLUSA as they may significantly decrease sofosbuvir and/or velpatasvir plasma concentrations.

ADVERSE REACTIONS

- The most common adverse reactions (≥10%, all grades) with EPCLUSA were headache and fatigue.

PP=per-protocol.

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EPCLUSA® sofosbuvir/velpatasvir 400 mg/100 mg tablets

HAVE CONFIDENCE IN CONSISTENT OUTCOMES FOR CHALLENGING POPULATIONS

EPCLUSA had a high cure rate and established safety profile in subjects with chronic HCV in the ASTRAL pivotal trials.[1]

EPCLUSA provided a consistent HCV cure in people who inject drugs with varied adherence.[4,5]

CONSIDER EPCLUSA FOR CHRONIC HCV PATIENTS WITH:

Recent or ongoing substance use[4,5]
No known interaction with opioids fentanyl and oxycodone[7]

Medication-assisted treatment[4,5]
High SVR12 rate in people who inject drugs on concurrent medication-assisted treatment[4,5]

Unstable housing[1]
Available in monthly bottles, which may enable patients with unstable housing to be discreet[1]

Food insecurity[1]
No food requirement for NC/CC patients, so patients can take with or without food[1]

Varied compliance[4,5]
One pill, once a day (for NC/CC patients) can help support adherence[1,8,9]
Provided a consistent cure in people who inject drugs with varied adherence[4,5]

IMPORTANT SAFETY INFORMATION (CONT'D)

DRUG INTERACTIONS

- Coadministration of EPCLUSA is not recommended with topotecan due to increased concentrations of topotecan.
- Coadministration of EPCLUSA is not recommended with proton-pump inhibitors, phenobarbital, phenytoin, rifabutin, rifapentine, efavirenz, and tipranavir/ritonavir due to decreased concentrations of sofosbuvir and/or velpatasvir.

Consult the full Prescribing Information for EPCLUSA for more information on potentially significant drug interactions, including clinical comments.

ASTRAL STUDY DESIGNS

Randomized trials in TN and TE[a] subjects without cirrhosis or with compensated cirrhosis.[1]

Subjects who were active injection drug users (use within 12 months), or those with a positive urine drug test at screening, were excluded from the ASTRAL pivotal trials.[3]

ASTRAL-1: Double-blind, placebo-controlled trial in GT 1, 2, 4, 5, or 6 subjects (N=740). GT 1, 2, 4, or 6 subjects were randomized 5:1 to receive EPCLUSA or placebo for 12 weeks; GT 5 subjects received EPCLUSA for 12 weeks.[1]

ASTRAL-2: Open-label trial in GT 2 subjects (N=266). Subjects received EPCLUSA or sofosbuvir + RBV for 12 weeks.[1]

ASTRAL-3: Open-label trial in GT 3 subjects (N=552). Subjects received EPCLUSA for 12 weeks or sofosbuvir + RBV for 24 weeks.[1]

[a]Prior regimens contained PegIFN alfa + RBV with or without an HCV NS3/4A PI (boceprevir, simeprevir, or telaprevir).[1]

References:

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