REAL PATIENT UNCERTAINTIES NEED **REAL ANSWERS**

- *End-stage renal disease requiring dialysis*[1,a]
- *Uncertain fibrosis scores*[2]
- *History of injection drug use*[3]
- *Taking certain concomitant medications*[1]
- *New to treatment*[1]

The **BROADEST ACCESS** of any pangenotypic regimen

Based on total covered lives as of August 2020, primarily reflecting coverage in the Commercial and Medicare Part D segments.[4]

Not actual patients.

[a]No safety data are available in pediatric patients with renal impairment.

Confidently treat with EPCLUSA

Sofosbuvir/velpatasvir: **THE ONLY PROTEASE INHIBITOR–FREE**, pangenotypic, panfibrotic chronic HCV regimen[1,2]

INDICATION

EPCLUSA (sofosbuvir 400 mg/velpatasvir 100 mg, sofosbuvir 200 mg/velpatasvir 50 mg tablets) is indicated for the treatment of patients 6 years of age and older or weighing at least 17 kg with chronic hepatitis C virus (HCV) genotype 1-6 infection without cirrhosis or with compensated cirrhosis.

IMPORTANT SAFETY INFORMATION

BOXED 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.

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.

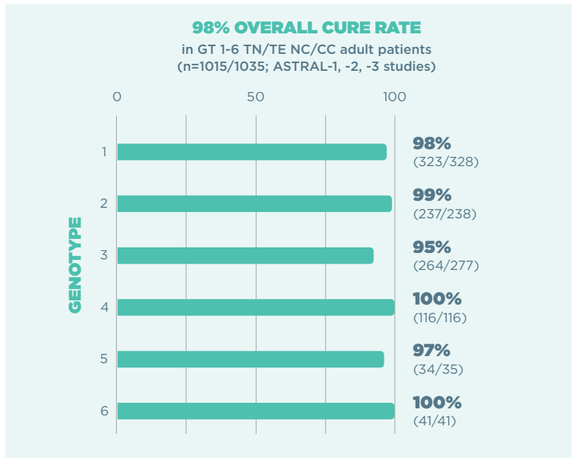
Panfibrotic = fibrosis stages 0-4 (compensated cirrhosis).

Please see additional Important Safety Information throughout, and click here for EPCLUSA full Prescribing Information, including **BOXED WARNING on Hepatitis B reactivation.**

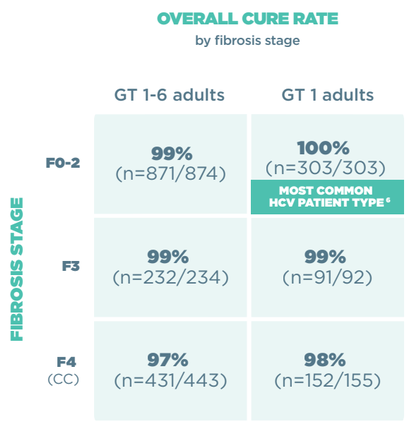
EPCLUSA®
sofosbuvir/velpatasvir
400 mg/100 mg tablets

THE CONFIDENCE OF A PROTEASE INHIBITOR–FREE, **PANGENOTYPIC, PANFIBROTIC REGIMEN**

Consistent outcomes across all genotypes and fibrosis stages[1,2]



Sustained virologic response (SVR12) was the primary endpoint and was defined as HCV RNA <15 IU/mL at 12 weeks after the end of treatment. Achieving SVR12 is considered a virologic cure.[1,5]



Cure rates (SVR12) derived from completer efficacy analysis of ASTRAL-1, -2, and -3 and POLARIS-2 and -3 studies, which included all patients who were randomized, completed assigned study treatment, and had HCV RNA data observed at post-treatment Week 12 or thereafter.[2]

Trial safety data (ASTRAL pivotal trials)

- Adverse reactions (all grades) reported in ≥5% of all adult NC/CC patients receiving 12 weeks of treatment with EPCLUSA (ASTRAL-1, -2, -3): headache, fatigue, nausea, asthenia, and insomnia. Irritability was also observed in ≥5% of adult patients receiving EPCLUSA in ASTRAL-3[1]

Trial safety data (POLARIS clinical trials)

- Diarrhea and arthralgia were observed in 5% of patients receiving EPCLUSA (N=440) in POLARIS-2. Back pain, upper abdominal pain, and myalgia were also observed in 5% of patients treated with EPCLUSA (N=109) in POLARIS-3[7]

Sofosbuvir/velpatasvir: A simple dosing regimen for your adult NC/CC patients

ONE DURATION
12 WEEKS[1]

NO FOOD REQUIREMENT
PATIENTS CAN TAKE EITHER WITH OR WITHOUT FOOD[1]

ONE PILL[1]

FEWEST PILLS REQUIRED
OF ANY FIRST-LINE, PANGENOTYPIC CHRONIC HCV REGIMEN[1,8]

ONCE A DAY[1]

Dosing for pediatric patients 6 years and above is based on weight. A lower-dose formulation (sofosbuvir 200 mg/velpatasvir 50 mg tablets) is recommended for certain pediatric patients.[1]

See full Prescribing Information for details on pediatric dosing.

IMPORTANT SAFETY INFORMATION

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.

Please see additional Important Safety Information throughout, and click here for EPCLUSA full Prescribing Information, including **BOXED WARNING on Hepatitis B reactivation.**

CC = compensated cirrhosis; F0-F2 = stages 0-2 fibrosis; F3 = stage 3 fibrosis; F4 = stage 4 fibrosis; GT = genotype; NC = non-cirrhotic.

STUDY **DESIGNS**

ROBUST CLINICAL TRIALS

Randomized trials in TN and TE adult chronic HCV patients without cirrhosis or with compensated cirrhosis.[1]

Patients 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.[9,10]

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

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

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

POLARIS-2: Open-label comparator trial in GT 1-6 DAA-naïve subjects (N=941) who were randomized to receive EPCLUSA for 12 weeks or sofosbuvir/velpatasvir/voxilaprevir for 8 weeks.[7]

POLARIS-3: Open-label comparator trial in DAA-naÏve GT 3 cirrhotic patients (N=219) who were randomized to receive EPCLUSA for 12 weeks or sofosbuvir/velpatasvir/voxilaprevir for 8 weeks.[7]

TE patients had failed a Peg-IFN + RBV-based regimen with or without an HCV NS3/4A protease inhibitor (boceprevir, simeprevir, or telaprevir).[1]

SIMPLIFY[3]

SIMPLIFY was an open-label, single-arm, international Phase 4 trial aimed at evaluating the efficacy, safety, and adherence 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). Patients with HIV and/or decompensated liver disease were excluded. The primary endpoint was the proportion of participants with SVR12. Adherence (≥90%) was a secondary endpoint and was assessed by dividing the number of total doses received by total expected number of doses.

Study Limitations: Weekly clinic visits and weekly electronic blister packs, which patients 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.

ANCHOR[11]

ANCHOR was a prospective, open-label, observational, single-site trial evaluating the efficacy and adherence 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 VL, 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.

Study Limitations: OAT status groups were non-randomized and self-selected. Factors associated with non-uptake 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.

IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

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

DRUG INTERACTIONS

- Coadministration of EPCLUSA is not recommended with topotecan due to increased concentrations of topotecan.

Please see additional Important Safety Information throughout, and click here for EPCLUSA full Prescribing Information, including **BOXED WARNING on Hepatitis B reactivation.**

DAA = direct-acting antiviral; HIV = human immunodeficiency virus; OAT = opioid agonist therapy; Peg-IFN = peginterferon-alfa; RBV = ribavirin; SOF = sofosbuvir; SVR12 = sustained virologic response 12 weeks after treatment completion; TE = treatment-experienced; TN = treatment-naïve; VL = viral load.

EPCLUSA®
sofosbuvir/velpatasvir
400 mg/100 mg tablets

DON'T WAIT **TO CURE**

EPCLUSA MAKES CURE POSSIBLE, EVEN FOR YOUR MOST CHALLENGING PATIENTS[3,11]

ASTRAL PIVOTAL TRIALS

98% **overall cure rate in clinical trials in GT 1-6 TN/TE NC/CC adult patients[1]**
(n=1015/1035; ASTRAL-1, -2, -3 studies)

SVR12 was the primary endpoint in EPCLUSA clinical trials and was defined as HCV RNA <15 IU/mL at 12 weeks after treatment completion.*

EPCLUSA demonstrated high cure rates in people who inject drugs in SIMPLIFY & ANCHOR[3,11]

SIMPLIFY CLINICAL STUDY

94% **cure rate in GT 1-4 NC/CC adult patients[3]**
(n=97/103)

ANCHOR REAL-WORLD STUDY

88% **cure rate in GT 1-4 NC/CC adult patients[11]**
(n=82/93; PP)

For the total patient population, the cure rate was 82% (n=82/100).[11]

Both studies had a primary endpoint of SVR12 (HCV RNA <LLOQ 12 weeks after treatment completion). Achieving SVR12 is considered a virologic cure.[1,3,11]*

Trial safety data (ASTRAL)[1]

- Adverse reactions (all grades) reported in ≥5% of all adult patients receiving 12 weeks of treatment with EPCLUSA (ASTRAL-1, -2, -3): headache, fatigue, nausea, asthenia, and insomnia. Irritability was also observed in ≥5% of adult patients receiving EPCLUSA in ASTRAL-3

Trial safety data (SIMPLIFY)[3]

- Adverse reactions reported in ≥5% of adult patients were: fatigue (22%), headache (18%), nausea (14%), insomnia (9%), arthralgia (6%), dizziness (5%), and nasopharyngitis (5%)
- Seven (7%) adult patients had at least one serious adverse event and 1 (1%) was considered treatment-related

*See study design details on previous page.

EPCLUSA provided a consistent cure in people who inject drugs with varied adherence[3]

Study Limitations

- Per study protocol, adverse reaction data in ANCHOR were not collected[12]

Patients in SIMPLIFY and ANCHOR were instructed to use EPCLUSA once daily for 12 weeks as recommended in the EPCLUSA full Prescribing Information. In SIMPLIFY, patients received EPCLUSA in weekly blister packs.[1,3,11]

Real-world data are observational in nature and are not based on controlled clinical studies. **Results from SIMPLIFY and ANCHOR may differ from those observed in clinical practice and are not presented in the EPCLUSA Prescribing Information.**

The SIMPLIFY and ANCHOR studies were supported by Gilead Sciences, Inc.

IMPORTANT SAFETY INFORMATION

DRUG INTERACTIONS (cont'd)

- 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.

Please see additional Important Safety Information throughout, and click here for EPCLUSA full Prescribing Information, including **BOXED WARNING on Hepatitis B reactivation.**

LLOQ = lower limit of quantification; PP = per protocol.

References: 1. EPCLUSA [prescribing information]. Foster City, CA: Gilead Sciences, Inc. July 2020. **2.** Lawitz E, Bourlière M, Han L, et al. Poster presented at: International Liver Congress; April 19-23, 2017; Amsterdam, Netherlands. **3.** Grebely J, Dalgard O, Conway B, et al. Sofosbuvir and velpatasvir for hepatitis C virus infection in people with recent injection drug use (SIMPLIFY): an open-label, single-arm, phase 4, multicentre trial. *Lancet Gastroenterol Hepatol*. 2018;3(3):153-161. **4.** Data on file. Gilead Hepatitis C virus coverage status report. August 2020. **5.** US Department of Health and Human Services, Center for Drug Evaluation and Research. Guidance for industry. Chronic hepatitis C virus infection: developing direct-acting antiviral drugs for treatment. November 2017. **6.** Moorman AC, Rupp LB, Gordon SC, et al. Long-term liver disease, treatment, and mortality outcomes among 17,000 persons diagnosed with chronic hepatitis C virus infection: current chronic hepatitis cohort study status and review of findings. *Infect Dis Clin North Am.* 2018;32(2):253-26. **7.** Jacobson IM, Lawitz E, Gane EJ, et al. Efficacy of 8 weeks of sofosbuvir, velpatasvir, and voxilaprevir in patients with chronic HCV infection: 2 phase 3 randomized trials. *Gastroenterology.* July 2017;153(1)113-122. **8.** Mavyret [prescribing information]. North Chicago, IL. AbbVie, Inc.; May 2020. **9.** Feld JJ, Jacobson IM, Hézode C, et al. Sofosbuvir and velpatasvir for HCV genotype 1, 2, 4, 5, and 6 infection. *N Engl J Med.* 2015;373(suppl):2599-2607. **10.** Foster GR, Afdahl N, Roberts SK, et al. Sofosbuvir and velpatasvir for HCV genotype 2 and 3 infection. *N Engl J Med.* 2015;373(suppl):2608-2617. **11.** Rosenthal E, Silk R, Mathur P, et al. Concurrent initiation of hepatitis C and opioid use disorder treatment in people who inject drugs. *Clin Infect Dis.* Published online February 3, 2020; doi: 10.1093/cid/ciaa105. Accessed June 5, 2020. **12.** Data on file. Data for ANCHOR. Accessed October 8, 2020.

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GILEAD