GILEAD | Medical Information

Epclusa® (sofosbuvir/velpatasvir) Use With Alcohol

This document is in response to your request for information regarding the use of Epclusa® (sofosbuvir/velpatasvir [SOF/VEL]) with alcohol.

Some data may be outside of the US FDA-approved prescribing information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA-approved prescribing information.

The full indication, important safety information, and boxed warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/liver-disease/epclusa/epclusa_pi.

Summary

Product Labeling[1]

There is no information in the SOF/VEL product labeling about the coadministration of SOF/VEL and alcohol.

PK Analysis on SOF/VEL-Alcohol Interactions

The interaction between the single-tablet regimen SOF/VEL and alcohol has not been studied. Based on the PK profile of each active ingredient within SOF/VEL and alcohol, a PK interaction would not be predicted.

Clinical Data on Alcohol Use With SOF/VEL

The treatment of HCV with SOF/VEL was evaluated in participants who reported any alcohol use, including former or recent hazardous or problematic alcohol use, in three studies.[2-5]

- In a Canadian cohort of patients with GTs 1 to 3 (N=1801), recent or former problematic alcohol use was not associated with a lower SVR rate. Safety results were not reported.[2]
- In the SIMPLIFY study, an open-label, phase 4 study of participants who reported recent IDU (N=103), the frequency of alcohol ingestion was not associated with the achievement of SVR12. The most common (≥10%) AEs reported were fatigue (22%), headache (18%), and nausea (14%).[3]
- The ANCHOR study, a prospective, observational, single-center study of PWID (N=100), found that hazardous drinking was not associated with achievement of SVR12 in the overall population (*P*=0.79). Safety results were not reported.[4,5]

Product Labeling[1]

SOF/VEL PK

Table 1. SOF/VEL Drug Interactions[1]

DDI Mechanism		SOF	VEL
Drug Transporters	P-gp/BCRP	Substrate	Substrate/inhibitor
	OATP1B1	N/A	Inhibitor
	OATP1B3	N/A	Inhibitor
	OATP2B1	N/A	Inhibitor
Drug Metabolizing Enzymes	CYP1A2	N/A	N/A
	CYP2B6	N/A	Substrate
	CYP2C8	N/A	Substrate
	CYP2C9/19	N/A	N/A
	CYP2D6	N/A	N/A
	CYP3A4	N/A	Substrate

Abbreviations: BCRP=breast cancer resistance protein; DDI=drug-drug interaction; OATP=organic anion transporting polypeptide; P-gp=P-glycoprotein.

Relevant SOF/VEL Label Information

There is no information in the SOF/VEL product labeling about the coadministration of SOF/VEL and alcohol.

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 (eg, INR or blood glucose) and dose adjustments of certain concomitant medications may be necessary. For more information, please refer to Section 7.3 of the SOF/VEL US Prescribing Information (Established and Potentially Significant Drug Interactions).

Clinical Data on Alcohol Use With SOF/VEL

Canadian Cohort[2]

Study design and demographics

The British Columbia Hepatitis Testers Cohort was used to evaluate the effectiveness of SOF/VEL ± RBV in patients with GTs 1 to 3. Patients who had received ≥1 prescription for SOF/VEL ± RBV through June 2018 were included. Patients were required to have ≥12 weeks of follow-up to assess treatment completion and ≥12 weeks of post-treatment follow-up for SVR assessment. To allow for variations in clinical practice, SVR was defined as undetectable HCV RNA at ≥10 weeks, instead of 12 weeks, after the end of treatment. Of the 1801 patients included in the analysis, the mean age was 58 years, 1148 (64%) were

male, 236 (13%) were treatment-experienced, 503 (28%) had problematic alcohol use, and GTs 1/2/3 were 35/19/40%, respectively.

Efficacy and safety

SVR rates in the GT 1, GT 2, and GT 3 subgroups were 93% (584/628), 96% (338/351), and 92% (670/725), respectively. Recent or former problematic alcohol use was not associated with a lower SVR rate (Table 2). Safety results were not reported.

Table 2. Association of Alcohol Use With SVR Based on Multivariable Modeling (Janjua et al)[2]

Covariate		Adjusted OR (95% CI)
Recent problematic alcohol use	Overall	0.73 (0.38–1.39)
	GT 1	0.64 (0.23–1.75)
	GT 3	0.59 (0.22–1.58)
Former problematic alcohol use	Overall	0.59 (0.34–1.03)
	GT 1	0.46 (0.18–1.16)
	GT 3	0.46 (0.2–1.06)

SIMPLIFY Study

Study design and demographics[3]

SIMPLIFY was an open-label, phase 4 study that assessed the efficacy and safety of SOF/VEL in participants with HCV who reported recent IDU from 19 sites in Australia, Canada, New Zealand, Norway, Switzerland, the UK, and the US (N=103). Each participant received a weekly supply of SOF/VEL in an electronic blister pack with an integrated sensor grid for a 12-week course. The AUDIT-C tool was used to assess participants' alcohol consumption; hazardous consumption was defined as scores ≥3 in women or ≥4 in men.

Table 3. SIMPLIFY Study: Baseline Demographics and Disease Characteristics[3]

Key Demographics and Characteristics		SOF/VEL (N=103)
Age, median (IQR), years		48 (41–53)
Male, n (%)		74 (72)
HCV GT, 1a/1b/2/3/4, n (%)		35 (34)/1 (1)/5 (5)/ 60 (58)/2 (2)
HCV RNA, median (IQR), log IU/mL		6.1 (5.3–6.7)
Liver disease stage, F0–F1/F2–F3/F4,[a] n (%)		59 (61)/27 (28)/9 (9)
Drug and alcohol use history, n (%)	Any alcohol use/hazardous use in the past 30 days	62 (60)/18 (17)
	Any drug use in the past 6 months	103 (100)
	Any non-IDU in the past 30 days	56 (54)
	Any IDU in the past 6 months/30 days	103 (100)/76 (74)
	Use of heroin/methamphetamine/opioids/cocaine/ other in the past 30 days	57 (55)/31 (30)/ 22 (21)/13 (13)/7 (7)
	IDU frequency, never/less than daily/at least daily	27 (26)/49 (48)/27 (26)
History of OST, n (%)		84 (82)
Current OST: methadone/buprenorphine + naloxone/buprenorphine, n (%)		45 (44)/12 (12)/4 (4)

Abbreviation: OST=opioid substitution therapy.
[a]F0–F1: <7.1 kPa; F2–F3: 7.1–12.49 kPa; F4: ≥12.5 kPa.

Efficacy[3]

One hundred participants completed 12 weeks of SOF/VEL. Participants were followed for a median (IQR) of 12 (12–24) weeks after treatment completion. The overall SVR12 rate was 94% (97/103). Three participants did not achieve SVR12: 2 participants were LTFU (including 1 participant who did not have a final sample after treatment); and 1 participant who continued to inject morphine during treatment, was nonviremic following SOF/VEL treatment, and had recurrent viremia at Week 24 experienced HCV reinfection.

The rates of SVR12 by the frequency of alcohol consumption are shown in Figure 1. The frequency of alcohol ingestion was not associated with the achievement of SVR12 (Table 4).

Figure 1. SIMPLIFY Study: SVR12 Rates by Frequency of Alcohol Consumption[3]

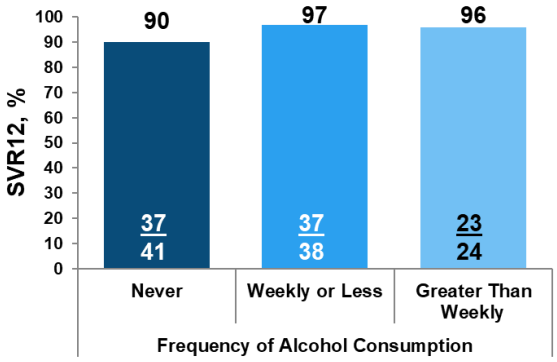

Table 4. SIMPLIFY Study: Unadjusted Analysis of the Frequency of Alcohol Consumption and Associations With SVR12 Achievement[3]

Frequency of Alcohol Consumption	Unadjusted OR (95% CI)	*P*-Value
Weekly or less frequently than weekly	1	-
More frequently than weekly	4 (0.43–37.51)	0.225
Unknown	2.49 (0.26–23.64)	0.428

Safety[3]

One death due to illicit drug overdose was deemed unrelated to SOF/VEL treatment.

Table 5. SIMPLIFY Study: Safety Outcomes[3]

Safety Outcomes, n (%)		SOF/VEL (N=103)
Experienced ≥1 AE		85 (83)
Most common AEs (≥10%)	Fatigue	23 (22)
	Headache	19 (18)
	Nausea	14 (14)
Serious AEs		7 (7)
Treatment-related AE		48 (47)
Treatment-related serious AE		1 (1)
Discontinuation due to AE		1 (1)

Adherence[6]

In an adherence substudy to SIMPLIFY, hazardous alcohol consumption at baseline was not associated with <90% adherence (OR, 0.55; 95% CI: 0.17–1.83; *P*=0.331), nor was hazardous alcohol consumption during treatment (OR, 0.43; 95% CI: 0.13–1.4; *P*=0.161).

ANCHOR Study[4,5]

Study design and demographics

The ANCHOR study was a prospective, observational, single-center study that evaluated adherence to direct-acting antiviral treatment among PWID (ongoing IDU; N=100) and its effect on the achievement of SVR12. Participants with decompensated cirrhosis were excluded. The mean age was 58 years, 76% were male, 93% had HCV GT 1, and 59% reported greater-than-daily IDU. Forty percent of participants had a hazardous consumption of alcohol as assessed with the AUDIT-C tool.

Efficacy and safety

Overall, 82% of participants (82/100) achieved SVR12. In the ITT population (n=93), 78% of participants achieved SVR12; in the PP population (n=82), 89% of participants achieved SVR12. In the overall population, 18 participants did not achieve SVR12, which included 11 participants who experienced virologic relapse, 3 participants who were LTFU, 3 participants who died, and 1 participant who was incarcerated.

SVR12 rates were similar between participants who reported hazardous alcohol use at baseline and those who did not (80% [32/40] vs 83% [50/60]). Hazardous drinking was not associated with achievement of SVR12 in the overall population (*P*=0.79), ITT population (*P*=1), or the PP population (*P*=0.47). Safety results were not reported.

References

1. Enclosed. Gilead Sciences Inc, EPCLUSA® (sofosbuvir and velpatasvir) tablets, for oral use. US Prescribing Information. Foster City, CA.
2. Janjua NZ, Wong S, Yu A, et al. Effectiveness of Sofosbuvir / Velpatasvir in Treating Hepatitis C Virus Infection in Real-World Setting [Poster 608]. Paper presented at: AASLD; 09-13 November, 2018; San Francisco, CA.
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. https://www.ncbi.nlm.nih.gov/pubmed/29310928
4. Kattakuzhy S, Mathur P, Gross C, et al. High SVR in PWID with HCV Despite Imperfect Medication Adherence: Data from the ANCHOR Study [Presentation]. Paper presented at: AASLD; 09-13 November, 2018; San Francisco, CA.
5. Rosenthal ES, Silk R, Mathur P, et al. Concurrent Initiation of Hepatitis C and Opioid Use Disorder Treatment in People Who Inject Drugs. *Clin Infect Dis.* 2020. https://www.ncbi.nlm.nih.gov/pubmed/32009165
6. Cunningham EB, Amin J, Feld JJ, et al. Adherence to Sofosbuvir and Velpatasvir Among People with Chronic HCV Infection and Recent Injection Drug Use: The SIMPLIFY Study. *The International journal on drug policy.* 2018;62:14-23. https://www.ncbi.nlm.nih.gov/pubmed/30352330

Abbreviations

AE=adverse event
AUDIT-C=Alcohol Use Disorders Identification Test-Consumption
GT=genotype
IDU=injection drug use
LTFU=lost to follow-up
OR=odds ratio
PP=per protocol
PWID=people who inject drugs
RBV=ribavirin
SOF=sofosbuvir
SVR=sustained virologic response
SVR12=sustained virologic response 12 weeks after end of treatment
VEL=velpatasvir

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Epclusa US Prescribing Information available at:
www.gilead.com/-/media/files/pdfs/medicines/liver-disease/epclusa/epclusa_pi

Follow-Up

For any additional questions, please contact Gilead Medical Information at:

☎1-866-MEDI-GSI (1-866-633-4474) or 🖱 www.askgileadmedical.com

Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or
🖱 www.gilead.com/utility/contact/report-an-adverse-event

FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖱 www.accessdata.fda.gov/scripts/medwatch

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