GILEAD | Medical Information

Epclusa® (sofosbuvir/velpatasvir) Coadministration with Oxcarbazepine

This document is in response to your request for information regarding Epclusa® (sofosbuvir/velpatasvir [SOF/VEL]) and coadministration with oxcarbazepine.

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.

PK DDI Evaluation

Drug interaction studies have not been conducted between the single-tablet regimen SOF/VEL and oxcarbazepine. Based on the PK profile of each active ingredient within SOF/VEL and oxcarbazepine, a PK interaction would not be predicted.[1,2]

In a phase 1, open-label, multiple dose, single center study, Lutz et al concluded that oxcarbazepine is predicted to demonstrate weak-to-no induction of P-gp and would not be expected to result in clinically significant changes in the exposure of P-gp substrates.[3]

Additionally, oxcarbazepine was evaluated in human liver microsomes to determine its capacity to inhibit the major cytochrome P450 enzymes. Although inhibition of CYP3A4/5 by oxcarbazepine and its pharmacologically active 10-monohydroxy metabolite (MHD) did occur at high concentrations, it is not likely to be of clinical significance. For more information about oxcarbazepine, please refer to its product labeling.[2]

SOF/VEL PK[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
	CYP2C19/19	N/A	N/A
	CYP2D6	N/A	N/A
	CYP3A4	N/A	Substrate

Relevant SOF/VEL Label Information[1]

In July 2020, the Epclusa® (SOF/VEL) US Prescribing Information was updated and oxcarbazepine was removed from Section 7.3, Table 4 Potentially Significant Drug Interactions.

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. For more information, please refer to Section 7.3 of the SOF/VEL US Prescribing Information (Established and Potentially Significant Drug Interactions).

Case Series/Reports of SOF/VEL & Coadministration With Oxcarbazepine

There are limitations in the interpretation of case reports. Case reports cannot be generalized. Unlike controlled clinical trials, causality cannot be inferred based on uncontrolled observational data. In addition, incidence or prevalence cannot be estimated due to the lack of a representative population sample. Other limitations of case reportsinclude the retrospective design and publication bias.[4]

Retrospective UK Case Series

A retrospective case series from six centres in the UK evaluated treatment outcomes in eleven patients with chronic, treatment-naïve HCV infection prescribed HCV DAAs in combination with enzyme-inducing anti-epileptic drugs. Patient 6 was non-cirrhotic with HCV GT 1a and received 12 weeks of SOF/VEL treatment in combination with oxcarbazepine (300mg twice daily). The patient achieved an end-of-treatment response and SVR12. No adverse events or safety data were reported.[5]

Case Report of a Male Patient With Chronic HCV and Psychotic Personality Disorder

A male patient aged 38 years without cirrhosis with HCV GT 3 received SOF/VEL for 12 weeks and was on treatment with oxcarbazepine (600 mg twice daily) for a psychotic and personality disorder. Concomitant medications included clonazepam 2 mg three times daily, paroxetine 20 mg daily, perphenazine 8 mg daily, and quetiapine 200 mg daily. The patient achieved an end-of-treatment response and SVR12. Plasma DAA concentrations and HCVRNA levels were not analyzed during therapy and no adverse events or dose modifications were reported.[6]

Case Report of a Female Patient With HCV and severe bilateral trigeminal neuralgia and multiple sclerosis

A female patient aged 42 years with HCV infection and severe bilateral trigeminal neuralgia and multiple sclerosis was treated with oxcarbazepine (900 mg, three times daily) for her pain and HCV infection was treated with SOF/VEL for 12 weeks, with the addition of ketoconazole (400 mg daily), as a pharmacokinetic booster. Due to complications with trigeminal neuralgia, four doses of SOF/VEL were missed, however she still achieved SVR12.[7]

References

1. Enclosed. Gilead Sciences Inc, EPCLUSA® (sofosbuvir and velpatasvir) tablets, for oral use. US Prescribing Information. Foster City, CA.
2. Novartis Pharmaceuticals Corporation, TRILEPTAL® (oxcarbazepine) tablets for oral use, oral suspension. US Prescribing Information. East Haover, NJ.
3. Lutz JD, Kirby BJ, Wang L, Song Q, Ling J, Massetto B, Worth A, Kearney BP, Mathias A. Cytochrome P450 3A Induction Predicts P-glycoprotein Induction; Part 2: Prediction of Decreased Substrate Exposure After Rifabutin or Carbamazepine. Clin Pharmacol Ther. 2018 Dec;104(6):1191-1198. doi: 10.1002/cpt.1072.
4. Nissen T, Wynn R. The Clinical Case Report: A Review of Its Merits and Limitations. BMC research notes. 2014;7:264. https://www.ncbi.nlm.nih.gov/pubmed/24758689
5. Boyle A, Marra F, Boothman H et al. Coadministration of hepatitis C direct-acting antivirals and enzyme-inducing antiepileptic drugs: real-world experience from a multi-centre case series. Journal of Hepatology, 2023; 78(S1): S1202.
6. Marcos-Fosch C, Cabezas J, Crespo J et al. Anti-epileptic drugs and hepatitis C therapy: Real-world experience.J Hepatol, 2021; 75(4): 984-5
7. Yin J, Hill L, Mansour M, Collier S, Barman P. Successful treatment of hepatitis C virus infection in patients on anti-epileptics or mood stabilizers using pharmacokinetic enhancers. Br J Clin Pharmacol. 2023 Jun;89(6):1891-1895. doi: 10.1111/bcp.15712. Epub 2023 Mar 22.

Abbreviations

BCRP=breast cancer resistance protein
DDI=drug-drug interaction
OATP=organic anion transporting polypeptide
P-gp=P-glycoprotein
PK=pharmacokinetic(s)
SOF=sofosbuvir
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:
http://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 Pharmacovigilance and Epidemiology ☎ 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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