GILEAD | Medical Information

Epclusa® (sofosbuvir/velpatasvir) Coadministration with Digoxin

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

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 been conducted between the single-tablet regimen SOF/VEL and digoxin. Coadministration is expected to increase digoxin concentrations, therefore, therapeutic concentration monitoring of digoxin is recommended. Refer to digoxin prescribing information for monitoring and dose modification recommendations for concentration increases of less than 50%. For more information about digoxin, 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]

Coadministration is expected to increase digoxin concentrations. Therapeutic concentration monitoring of digoxin is recommended when coadministered with SOF/VEL. Refer to digoxin prescribing information for monitoring and dose modification recommendations for concentration increases of less than 50%.

Table 1: Changes in PK Parameters for Coadministered Drug in the Presence of SOF, VEL, or EPCLUSA[a]

Coadministered Drug	Dose of Coadministered Drug (mg)	SOF Dose (mg)	VEL Dose (mg)	N	Mean Ratio (90% CI) of Coadministered Drug PK With/Without SOF, VEL, or EPCLUSA No Effect=1.00		
					C_{max}	AUC	C_{min}
Digoxin	0.25 single dose	ND	100	21	1.88 (1.71, 2.08)	1.34 (1.13, 1.60)	NA

NA = not available/not applicable, ND = not dosed

a. All interaction studies conducted in healthy volunteers.

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).

References

1. Enclosed. Gilead Sciences Inc, EPCLUSA® (sofosbuvir and velpatasvir) tablets, for oral use. US Prescribing Information. Foster City, CA

2. Concordia Pharmaceuticals Inc, Lanoxin (digoxin) tablets, for oral use. US Prescribing Information. Dublin, Ireland

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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