Ledipasvir/Sofosbuvir (Harvoni®) Drug Interactions
A Quick Guide for Clinicians – 2023

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Mechanism of Action and Route of Metabolism for Ledipasvir/Sofosbuvir (Harvoni®)

Medication	HCV Mechanism of Action	Route of Metabolism and Drug Interaction Potential
• Ledipasvir/Sofosbuvir (Harvoni®)	NS5a inhibitor and NS5b polymerase inhibitor	• Ledipasvir is an inhibitor of P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP). Unknown metabolism via slow oxidative metabolism has been observed. • Sofosbuvir is a substrate for P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP). The intracellular metabolism of sofosbuvir is mediated by hydrolase and nucleotide phosphorylation pathways.

Ledipasvir/Sofosbuvir (Harvoni®) Drug Interactions with HIV Medications

Concurrent Medication	Recommendation and Clinical Comments
HIV Protease Inhibitors	
• Atazanavir (Reyataz®) + ritonavir (Norvir®) • Atazanavir/cobicistat (Evotaz®) • Darunavir (Prezista®) + ritonavir (Norvir®) • Darunavir/cobicistat (Prezcobix®; in Symtuza®) • Lopinavir/ritonavir (Kaletra®)	• Concurrent use at standard doses appropriate. • If using tenofovir disoproxil fumarate in combination with ledipasvir/sofosbuvir, monitor for tenofovir-associated adverse reactions.
HIV Non-Nucleoside Reverse Transcriptase Inhibitors	
• Efavirenz (Sustiva®; in Atripla®, Symfi®, Symfi Lo®) • Etravirine (Intelence®) • Nevirapine (Viramune®) • Rilpivirine oral (Edurant®; in Complera®, Odefsey®, Juluca®) • Rilpivirine injection (in Cabenuva®) • Doravirine (Pifeltro®; in Delstrigo®)	• Concurrent use at standard doses appropriate. • If using tenofovir disoproxil fumarate in combination with ledipasvir/sofosbuvir, monitor for tenofovir-associated adverse reactions.

Ledipasvir/Sofosbuvir (Harvoni®) Drug Interactions with HIV Medications, continued

Concurrent Medication	Recommendation and Clinical Comment
HIV Integrase Strand Transfer Inhibitors	
• Bictegravir/tenofovir alafenamide/emtricitabine (Biktarvy®) • Dolutegravir (Tivicay®; in Dovato®, Triumeq®, Juluca®) • Elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine (Genvoya®) • Raltegravir (Isentress® Isentress HD®)	• Concurrent use at standard doses appropriate. • If using tenofovir disoproxil fumarate in combination with ledipasvir/sofosbuvir, monitor for tenofovir-associated adverse reactions.
• Elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine (Stribild®)	• Increased tenofovir levels expected. Safety of concurrent ledipasvir/sofosbuvir with elvitegravir, cobicistat, emtricitabine and tenofovir DF has not been established. Do not co-administer.
HIV Nucleoside/Nucleotide Reverse Transcriptase Inhibitors	
• Abacavir (Ziagen®, in Epzicom®, Triumeq®, other STRs) • Emtricitabine (Emtriva®, in other STRs) • Lamivudine (Epivir®, in other STRs) • Tenofovir Disoproxil Fumarate (Viread®; in Cimduo®, Temixys®, Truvada®, other STRs) • Tenofovir Alafenamide (in Descovy®, other STRs)	• Concurrent use at standard doses appropriate. • If using tenofovir disoproxil fumarate in combination with ledipasvir/sofosbuvir, monitor for tenofovir-associated adverse reactions.
HIV Entry Inhibitors, CCR5 Antagonists, gp120-Directed Attachment Inhibitors	
• Fostemsavir (Rukobia®) • Maraviroc (Selzentry®) • Ibalizumab (Trogarzo®)	• Concurrent use at standard doses appropriate.
HIV Capsid Inhibitor	
• Lenacapavir (Sunlenca)	• Concurrent use at standard doses appropriate.

Ledipasvir/Sofosbuvir (Harvoni®) Drug Interactions with Common Primary Care Medications

Medication and or Class	Recommendation and Clinical Comment
• Antacids	• Separate antacids and ledipasvir/sofosbuvir administration by 4 hours.
• H2-receptor antagonists	• Administer simultaneously with or 12 hours apart from ledipasvir/sofosbuvir. Do not exceed doses comparable to famotidine 40 mg twice daily.
• Proton-pump inhibitors	• Doses comparable to omeprazole 20 mg or lower can be administered simultaneously with ledipasvir/sofosbuvir under fasted conditions.

Ledipasvir/Sofosbuvir (Harvoni®) Drug Interactions with Common Primary Care Medication, continued

• Antiarrhythmic – Amiodarone	• Serious, symptomatic bradycardia expected may occur with concurrent use, especially in patients on beta-blockers, underlying cardiac abnormalities, or advanced liver disease. Co-administration not recommended. If concurrent use required, cardiac monitoring is recommended, see package insert for additional information.
• Antiarrhythmic – Digoxin	• Increase in digoxin levels possible. Monitor digoxin levels.
• Anticonvulsants – carbamazepine, oxcarbazepine, phenobarbital, phenytoin	• Significant decrease in ledipasvir/sofosbuvir levels expected. Co-administration not recommended.
• Antimycobacterials – rifampin, rifabutin, rifapentine	• Significant decrease in ledipasvir/sofosbuvir levels expected. Co-administration not recommended.
• Herbal products – St. John's Wort	• Significant decrease in ledipasvir/sofosbuvir levels expected due to intestinal P-glycoprotein (P-gp) induction associated with St. John's Wort. Co-administration not recommended.
• HMG-CoA Reductase Inhibitors – Atorvastatin	• Co-administration may lead to increased risk of myopathy and rhabdomyolysis. Monitor closely.
• HMG-CoA Reductase Inhibitors – Rosuvastatin	• Significant increase in rosuvastatin levels when used with ledipasvir/sofosbuvir leading to increased risk of myopathy, including rhabdomyolysis. Co-administration not recommended.

Disclaimer: The information contained in this table has been developed from various resources, including FDA product information, abstracts and posters presented at national and international meetings, and from Recommendations for the Testing, Managing and Treating of Hepatitis C from AASLD and IDSA located at www.hivguidelines.org. While the tables contained in this guide are complete based upon references reviewed, there may be other medications that may also be contraindicated or should be co-administered with caution. Please consult additional resources as needed.

Funding for this presentation was made possible [in part, if applicable] by U1OHA29291 from the Health Resources and Services Administration HIV/AIDS Bureau. The views expressed do not necessarily reflect the official policies of the Department of Health and Human Services nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government. Any trade/brand names for products mentioned during this presentation are for training and identification purposes only.