Daclatasvir/Sofosbuvir (Daklinza®/Sovaldi™) Drug Interactions A Quick Guide for Clinicians – April 2017

John J Faragon, PharmD, BCPS, AAHIVP

Mechanism of Action and Route of Metabolism for Daclatasvir (Daklinza®) and Sofosbuvir (Sovaldi™)

Medication	HCV Mechanism of Action	Route of Metabolism and Drug Interaction Potential
Daclatasvir (Daklinza®)	NS5a inhibitor	• Daclatasvir is a substrate of CYP3A4 and is an inhibitor of P-glycoprotein transporter (P-gp), organic anion transporting polypeptide (OATP) 1B1 and 1B3, and breast cancer resistance protein (BCRP).
Sofosbuvir (Sovaldi ™)	NS5b polymerase inhibitor	• 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.

Daclatasvir (Daklinza®) Drug Interactions with HIV Medications

Concurrent Medication	Recommendation and Clinical Comments
HIV Protease Inhibitors	
Atazanavir/cobicistat (Evotaz®) Atazanavir (Reyataz®) + ritonavir (Norvir®) Indinavir (Crixivan®) unboosted Nelfinavir (Viracept®) Saquinavir (Invirase®) unboosted	• Decrease daclatasvir dose to 30mg once daily
Atazanavir (Reyataz®) unboosted Darunavir/cobicistat (Prezcobix®) Darunavir (Prezista®) + ritonavir (Norvir®) Fosamprenavir (Lexiva®) unboosted Lopinavir/ritonavir (Kaletra®)	• Use daclatasvir 60 mg once daily

Daclatasvir (Daklinza®) Drug Interactions with HIV Medications (continued)

Concurrent Medication	Recommendation and Clinical Comment
HIV Non Nucleoside Reverse Transcriptase Inhibitors	
Efavirenz (Sustiva®, also contained in Atripla®) Etravirine (Intelence®) Nevirapine (Viramune®)	• Increase daclatasvir dose to 90mg once daily
Rilpivirine (Edurant®, also contained in Complera® and Odefsey®)	• Use daclatasvir 60 mg once daily
HIV Integrase Strand Transfer Inhibitors	
Dolutegravir (Tivicay®, also contained in Triumeq®) Raltegravir (Isentress®)	• Use daclatasvir 60 mg once daily
Elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine (Stribild®) and Elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine (Genvoya®)	• Decrease daclatasvir dose to 30mg once daily
HIV Entry Inhibitors	
Maraviroc (Selzentry®)	• Use daclatasvir 60mg once daily
HIV Nucleoside/Nucleotide Reverse Transcriptase Inhibitors	
Abacavir (Ziagen®) Didanosine (Videx EC®) Emtricitabine (Emtriva®) Lamivudine (Epivir®) Tenofovir disoproxil fumarate (Viread®) Tenofovir alafenamide (in Descovy®) Stavudine (Zerit®) Zidovudine (Retrovir®)	• Use daclatasvir 60mg once daily

Non HIV Medications to Avoid with Daclatasvir (Daklinza®)

Medication and or Class	Rationale for Avoiding with daclatasvir
Anticonvulsants – carbamazepine, phenytoin	• Significant decrease in daclatasvir levels expected. Co-administration not recommended.
Antimycobacterials – rifampin	
Herbal products – St. John's Wort	

Daclatasvir (Daklinza®) Drug Interactions with Common Primary Care Medications

Medication and or Class	Recommendation and Clinical Comment
Strong inhibitors of CYP3A	
Antibiotics – Clarithromycin, telithromycin	• Decrease daclatasvir dose to 30mg once daily
Antifungals – Itraconazole, ketoconazole, posaconazole, voriconazole	
Antidepressant – Nefazodone	
Moderate inducers of CYP3A	
Antibiotic – Nafcillin	• Increase daclatasvir dose to 90mg once daily
Antimycobacterial – Rifapentine	
Corticosteroid – Dexamethasone	
Endothelin Antagonist – Bosentan	
Wakefullness promoting therapy – Modafinil	
Other Medications	
Anticoagulant – Dabigatran	• Potential for increased dabigatran levels in patients with renal impairment. See dabigatran label for further information.
Antiarrhythmic – Amiodarone	• If using with sofosbuvir, serious symptomatic bradycardia may occur, concurrent use not recommended.
Antiarrhythmic – Digoxin	• If receiving daclatasvir and initiating digoxin therapy, use lowest digoxin dose and monitor levels, titrate as needed. • If already receiving digoxin and initiating daclatasavir, measure serum digoxin level prior to starting daclatasvir; reduce digoxin dose by 15% to 30%. Monitor levels, titrate as needed.
HMG-CoA Reductase inhibitors – Atorvastatin, fluvastatin, pitavastatin, pravastatin, rosuvastatin, simvastatin	• Monitor for HMG-CoA reductase inhibitor toxicity such as myopathy.
Opioid Dependence Treatment – Buprenorphine, Buprenorphine/naloxone	• No adjustment required, however monitoring for buprenorphine-associated adverse events recommended.

Sofosbuvir (Sovaldi ™) Drug Interactions with HIV Medications

Concurrent Medication	Recommendation and Clinical Comment
HIV Protease Inhibitors	
Atazanavir (Reyataz®) Darunavir (Prezista®) Fosamprenavir (Lexiva®) Indinavir (Crixivan®) Lopinavir/ritonavir (Kaletra®) Ritonavir (Norvir®) at any dosage Saquinavir (Invirase®)	• Concurrent use at standard doses appropriate.
Tipranavir (Aptivus®) + ritonavir (Norvir®)	• Significant decrease in sofosbuvir levels expected leading to decreased sofosbuvir efficacy. Co-administration not recommended.
HIV Non Nucleoside Reverse Transcriptase Inhibitors	
Efavirenz (Sustiva®)	• Concurrent use at standard doses appropriate.
Etravirine (Intelence®) Nevirapine (Viramune®)	• Concurrent use at standard doses appropriate.
Rilpivirine (Edurant®, also contained in Complera® and Odefsey®)	• Concurrent use at standard doses appropriate.
HIV Integrase Strand Transfer Inhibitors	
Dolutegravir (Tivicay®, also contained in Triumeq®)	• Concurrent use at standard doses appropriate.
Elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine (Stribild®) and Elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine (Genvoya®)	• Concurrent use at standard doses appropriate.
Raltegravir (Isentress®)	• Concurrent use at standard doses appropriate.
HIV Entry Inhibitors	
Maraviroc (Selzentry®)	• Concurrent use at standard doses appropriate.

Sofosbuvir (Sovaldi ™) Drug Interactions with HIV Medications (continued)

HIV Nucleoside/Nucleotide Reverse Transcriptase Inhibitors	
Abacavir (Ziagen®) Emtricitabine (Emtriva®) Lamivudine (Epivir®) Stavudine (Zerit®) Tenofovir disoproxil fumarate (Viread®) Tenofovir alafenamide (in Descoy®)	• Concurrent use at standard doses appropriate.
Didanosine (Videx EC®) Zidovudine (Retrovir®)	• When using ribavirin with daclatasvir/sofosbuvir, the use of didanosine or zidovudine should be avoided due to overlapping toxicity.

Non HIV Medications to Avoid with Sofosbuvir (Sovaldi™) Therapy

Medication and or Class	Rationale for Avoiding with Sofosbuvir
Antiarrhythmic – Amiodarone	• Serious symptomatic bradycardia may occur, concurrent use not recommended. See product information for additional details.
Anticonvulsants – carbamazepine, oxcarbazepine, phenobarbital, phenytoin	• Significant decrease in sofosbuvir levels expected leading to reduced sofosbuvir efficacy. Co-administration not recommended.
Antimycobacterials – rifampin, rifabutin, rifapentin	• Significant decrease in sofosbuvir levels expected leading to reduced sofosbuvir efficacy due to intestinal P-glycoprotein induction from rifampin. Co-administration not recommended.
Herbal products – St. John's Wort	• Significant decrease in sofosbuvir levels expected leading to reduced sofosbuvir efficacy due to intestinal P-glycoprotein induction associated with St. John's Wort. 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.