

## Patients With HIV/HCV Coinfection

This section provides guidance on the treatment of chronic HCV infection in HIV/HCV-coinfected patients. For individuals with acute HCV infection, please refer to the [Acute HCV](#) section. HIV/HCV-coinfected patients suffer from more liver-related morbidity and mortality, nonhepatic organ dysfunction, and overall mortality than HCV-monoinfected patients ([Lo Re, 2014](#)); ([Chen, 2009](#)). Even in the potent HIV antiretroviral therapy era, HIV infection remains independently associated with advanced liver fibrosis and cirrhosis in patients with HIV/HCV coinfection ([Thein, 2008a](#)); ([de Ledinghen, 2008](#)); ([Fierer, 2013](#)); ([Kirk, 2013](#)). As such, treatment of HCV in HIV-infected patients should be a priority for providers, payers, and patients. However, if HCV treatment is delayed for any reason, liver disease progression should be monitored at routine intervals as recommended in the guidance (see [When and in Whom to Initiate Therapy, recommendation for repeat liver disease assessment](#)).


Similar to HCV-monoinfected patients, HIV/HCV-coinfected patients cured with peginterferon/ribavirin have lower rates of hepatic decompensation, hepatocellular carcinoma, and liver-related mortality ([Berenguer, 2009](#)); ([Limketkai, 2012](#)); ([Mira, 2013](#)). Uptake of HCV therapy was lower in the HIV/HCV-coinfected population owing to historically lower response rates, patient comorbidities, patient and practitioner perceptions, and adverse events associated with interferon-based therapy ([Mehta, 2006a](#)); ([Thomas, 2008](#)).

With the availability of HCV direct-acting antivirals (DAAs), efficacy and adverse event rates among those with HIV/HCV coinfection are similar to those observed with HCV monoinfection ([Bhattacharya, 2017](#)); ([Naggie, 2015](#)); ([Sulkowski, 2015](#)); ([Wyles, 2015](#)); ([Wyles, 2017b](#)) and many prior barriers have diminished. However, treatment of HIV/HCV-coinfected patients requires continued awareness and attention to the complex drug interactions that can occur between DAAs and antiretroviral medications. Drug interactions with DAAs and antiretroviral agents are summarized in the text and tables of this section as well as in the US Department of Health and Human Services treatment guidelines (<https://aidsinfo.nih.gov/guidelines>). Another resource for screening for drug-drug interactions with DAAs is the University of Liverpool website ([www.hep-druginteractions.org](http://www.hep-druginteractions.org)).

### Risk for Hepatitis B Virus Reactivation

Due to shared modes of transmission, HIV/HCV-coinfected patients are also at risk for hepatitis B virus (HBV) infection. Reactivation of HBV has been reported in patients starting DAA HCV therapy who are not on active HBV agents. Consistent with general recommendations for the assessment of both HIV- and HCV-infected patients, all patients initiating HCV DAA therapy should be assessed for HBV coinfection with HBsAg, anti-HBs, and anti-HBc testing. HIV-infected patients who have evidence of HBV infection should be on antiretroviral agents with activity against HBV, preferably tenofovir disoproxil fumarate or tenofovir alafenamide. For patients who are only anti-HBc positive and not on tenofovir-based antiretroviral therapy, subsequent monitoring for HBV reactivation should be as detailed in the [Monitoring](#) section of the guidance.

## Recommendations Related to HCV Medication Interactions With HIV Antiretroviral Medications

RECOMMENDED	RATING 
Antiretroviral drug switches, when needed, should be done in collaboration with the HIV practitioner. For HIV antiretroviral and HCV direct-acting antiviral combinations not addressed below, expert consultation is recommended.	I, A
<b>Daclatasvir when used in combination with other antivirals</b> Daclatasvir requires dose adjustment with ritonavir-boosted atazanavir (decrease to 30 mg/d), cobicistat-boosted atazanavir (decrease to 30 mg/d), elvitegravir/cobicistat (decrease to 30 mg/d), and efavirenz or etravirine (increase to 90 mg/d).	IIa, B
<b>Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg)</b> Elbasvir/grazoprevir should be used with antiretroviral drugs with which it does not have clinically significant interactions: abacavir, emtricitabine, enfuvirtide, lamivudine, raltegravir, dolutegravir, rilpivirine, and tenofovir.	IIa, B
<b>Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)<sup>a</sup></b> Glecaprevir/pibrentasvir should be used with antiretroviral drugs with which it does not have clinically significant interactions: abacavir, emtricitabine, enfuvirtide, lamivudine, raltegravir, dolutegravir, rilpivirine, and tenofovir.  Given the limited data on the safety of elvitegravir/cobicistat with glecaprevir/pibrentasvir, monitoring for hepatic toxicity is recommended until additional safety data are available in HIV/HCV-coinfected patients.	IIa, B
<b>Simeprevir used in combination with other antivirals</b> Simeprevir should be used with antiretroviral drugs with which it does not have clinically significant interactions: abacavir, emtricitabine, enfuvirtide, lamivudine, maraviroc, raltegravir, dolutegravir, rilpivirine, and tenofovir.	IIa, B
<b>Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)</b> Sofosbuvir/velpatasvir can be used with most antiretrovirals, but not efavirenz, etravirine, or nevirapine. Because velpatasvir has the potential to increase tenofovir levels when given as tenofovir disoproxil fumarate, concomitant use mandates consideration of renal function and should be avoided in those with an eGFR <60 mL/min.  Due to limited experience with this drug combination, renal monitoring is recommended during the dosing period. Tenofovir alafenamide may be an alternative to tenofovir disoproxil fumarate during sofosbuvir/velpatasvir treatment for patients who take cobicistat or ritonavir as part of their antiretroviral therapy.	IIa, B
<b>Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)</b> Ledipasvir/sofosbuvir can be used with most antiretrovirals. Because this therapy increases tenofovir levels when given as tenofovir disoproxil fumarate, concomitant use mandates consideration of renal function and should be avoided in those with an eGFR <60 mL/min.	IIa, C

## Recommendations Related to HCV Medication Interactions With HIV Antiretroviral Medications

<p>The absolute tenofovir levels are highest, and may exceed exposures for which there are established renal safety data, when tenofovir disoproxil fumarate is administered with ritonavir- or cobicistat-containing regimens. Due to lack of sufficient safety data with this drug combination, consideration should be given to changing the antiretroviral regimen. If the combination is used, renal monitoring is recommended during the dosing period. Tenofovir alafenamide may be an alternative to tenofovir disoproxil fumarate during ledipasvir/sofosbuvir treatment for patients who take cobicistat or ritonavir as part of their antiretroviral therapy.</p>	
<p>For combinations expected to increase tenofovir levels, baseline and ongoing assessment for tenofovir nephrotoxicity is recommended.</p>	IIa, C
<p><b>Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) with dasabuvir (600 mg) as part of an extended-release regimen or plus twice-daily dosed dasabuvir (250 mg)</b></p> <p>Paritaprevir/ritonavir/ombitasvir plus dasabuvir should be used with antiretroviral drugs with which they do not have substantial interactions: atazanavir, dolutegravir, emtricitabine, enfuvirtide, lamivudine, raltegravir, and tenofovir.</p> <p>The dose of ritonavir used for boosting atazanavir should be held when administered with paritaprevir/ritonavir/ombitasvir plus dasabuvir and then restored when HCV treatment is completed. Atazanavir (300 mg) should be administered at the same time as the fixed-dose HCV combination.</p>	IIa, C
<p><b>Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg)</b></p> <p>Sofosbuvir/velpatasvir/voxilaprevir should be used with antiretroviral drugs with which they do not have substantial interactions: dolutegravir, emtricitabine, enfuvirtide, lamivudine, rilpivirine, and raltegravir.</p> <p>Given increases in voxilaprevir AUC with darunavir/ritonavir or elvitegravir/cobicistat coadministration and lack of clinical safety data, monitoring for hepatic toxicity is recommended until additional safety data are available in HIV/HCV-coinfected patients.</p> <p>Because this therapy has the potential to increase tenofovir levels when given as tenofovir disoproxil fumarate, concomitant use mandates consideration of renal function and should be avoided in those with an eGFR &lt;60 mL/min. In patients receiving sofosbuvir/velpatasvir/voxilaprevir and tenofovir disoproxil fumarate concomitantly, renal monitoring is recommended during the dosing period.</p>	IIa, B
<p><sup>a</sup> This is a 3 tablet coformulation. Please refer to the prescribing information.</p>	

## Regimens Not Recommended for Patients with HIV/HCV Coinfection

NOT RECOMMENDED	RATING <sup>i</sup>
Antiretroviral treatment interruption to allow HCV therapy is <b>not</b> recommended.	III, A
Elbasvir/grazoprevir should <b>not</b> be used with cobicistat, efavirenz, etravirine, nevirapine, or any HIV protease inhibitor.	III, B
Glecaprevir/pibrentasvir should <b>not</b> be used with atazanavir, ritonavir-containing antiretroviral regimens, efavirenz, or etravirine.	III, B
Sofosbuvir/velpatasvir should <b>not</b> be used with efavirenz, etravirine, or nevirapine.	III, B
Sofosbuvir/velpatasvir/voxilaprevir should <b>not</b> be used with ritonavir-boosted atazanavir, efavirenz, etravirine, or nevirapine.	III, B
Sofosbuvir-based regimens should <b>not</b> be used with tipranavir.	III, B
Paritaprevir/ritonavir/ombitasvir plus dasabuvir should <b>not</b> be used with darunavir, efavirenz, ritonavir-boosted lopinavir, ritonavir-boosted tipranavir, etravirine, nevirapine, cobicistat, or rilpivirine.	III, B
Paritaprevir/ritonavir/ombitasvir with or without dasabuvir should <b>not</b> be used in HIV/HCV-coinfected individuals who are not taking antiretroviral therapy.	III, B
Ribavirin should <b>not</b> be used with didanosine, stavudine, or zidovudine.	III, B
Simeprevir should <b>not</b> be used with cobicistat, efavirenz, etravirine, nevirapine, or any HIV protease inhibitor.	III, B

### Clinical Trial, Pharmacokinetic, and Drug Interaction Data

Extensive recommendations for antiretroviral therapy use, including for persons anticipating HCV treatment, are available at [jama.jamanetwork.com](http://jama.jamanetwork.com) and [aidsinfo.nih.gov](http://aidsinfo.nih.gov).

Antiretroviral drug switches may be performed to allow compatibility with DAAs with the goal of maintaining HIV suppression without compromising future options. Considerations include prior treatment history, responses to antiretroviral therapy, resistance profiles, and drug tolerance ([Gunthard, 2014](#)); ([DHHS, 2014](#); [aidsinfo.nih.gov](http://aidsinfo.nih.gov)). Treatment interruption in HIV/HCV-coinfected individuals is not recommended as it is associated with increased cardiovascular events ([SMART, 2006](#)) and increased rates of fibrosis progression and liver-related events ([Tedaldi, 2008](#)); ([Thorpe, 2011](#)). The availability of multiple effective HCV DAA and HIV antiretroviral regimens makes it possible for all HIV/HCV-coinfected patients to safely and successfully receive HCV treatment. Switching an optimized antiretroviral regimen carries risks, including adverse effects and HIV viral breakthrough ([Eron, 2010](#)). HIV viral breakthrough is a particular concern for those with substantial antiretroviral experience or known resistance to antiretroviral drugs. If necessary, antiretroviral therapy switches should be done in close collaboration with the treating HIV provider prior to HCV treatment initiation.

Although fewer HIV/HCV-coinfected patients than HCV-monoinfected patients have been treated in DAA trials, efficacy rates to date have been remarkably similar between the groups ([Sulkowski, 2013](#)); ([Sulkowski, 2014](#)); ([Dieterich, 2014b](#)); ([Rodriguez-Torres, 2015](#)); ([Osinusi, 2015](#)); ([Sulkowski, 2015](#)); ([Dieterich, 2015](#)); ([Naggie, 2015](#)); ([Wyles, 2015](#)). Thus, results from HCV monoinfection studies largely justify the recommendations for HIV/HCV coinfection (discussed in the

[Initial Treatment](#) and [Retreatment](#) sections). Discussion specific to studies of HIV/HCV coinfection is included here.

## Daclatasvir + Sofosbuvir

The phase 3 ALLY-2 study evaluated the 12-week regimen of daclatasvir plus sofosbuvir in patients with HIV/HCV coinfection with genotype 1, 2, 3, or 4 ([Wyles, 2015](#)). This open-label clinical trial enrolled both treatment-naïve (n=151) and -experienced (n=52) HIV/HCV-coinfected patients. Treatment-naïve patients were randomly assigned (2:1), with stratification by cirrhosis status and genotype, to receive 12 weeks or 8 weeks of once-daily daclatasvir (60 mg dose adjusted based on antiretroviral regimen) and sofosbuvir (400 mg). Treatment-experienced patients received daclatasvir and sofosbuvir for 12 weeks. Genotype distribution was 83%, 9%, 6%, and 2% of patients, respectively, for genotype 1, 2, 3, and 4 HCV infection; 14% of all participants had compensated cirrhosis. Antiretroviral drugs allowed were ritonavir-boosted darunavir, atazanavir, or lopinavir, efavirenz, nevirapine, rilpivirine, raltegravir, and dolutegravir.

The combination of daclatasvir and sofosbuvir once daily for 12 weeks achieved SVR12 in 97% of HIV/HCV-coinfected patients with genotype 1, 2, 3, or 4 infection, and was safe and well tolerated. Ninety-seven percent of treatment-naïve patients and 98% of treatment-experienced patients achieved SVR. However, among patients who received 8 weeks of therapy, only 76% of patients achieved SVR. Factors associated with relapse in this patient group included high baseline HCV RNA level (>2 million IU/mL; 69%), concomitant use of a boosted darunavir-based antiretroviral regimen with 30 mg of daclatasvir (67%), and the presence of compensated cirrhosis (60%).

### Pharmacology and Drug Interaction Data

Daclatasvir is metabolized by cytochrome P450 (CYP) 3A4 and is therefore susceptible to drug interactions with potent inducers and inhibitors of this enzyme. The dose of daclatasvir should be increased from 60 mg to 90 mg when used with efavirenz, etravirine, or nevirapine ([Bifano, 2013](#)). The dose of daclatasvir should be decreased from 60 mg to 30 mg when used with ritonavir-boosted atazanavir, cobicistat-boosted atazanavir, or elvitegravir/cobicistat ([Smolders, 2017](#)). A daclatasvir dose of 60 mg should be used with ritonavir-boosted darunavir and ritonavir-boosted lopinavir ([Gandhi, 2015](#)).

## Elbasvir/Grazoprevir

The safety, tolerability, and efficacy of the second-generation NS3/4A serine protease inhibitor grazoprevir (MK-5172) plus the NS5A inhibitor elbasvir (MK-8742) were assessed in patients with HIV/HCV coinfection in the C-EDGE study. C-EDGE was a phase 3, nonrandomized, open-label, single-arm study in which treatment-naïve patients with genotype 1, 4, or 6 infection and HIV coinfection, with or without compensated cirrhosis, were enrolled in Europe, the US, and Australia ([Rockstroh, 2015](#)). All patients were either naïve to treatment with any antiretroviral therapy (ART) with a CD4 cell count >500/mm<sup>3</sup> (n=7), or stable on current ART for at least 8 weeks with a CD4 cell count >200/mm<sup>3</sup> (n=211) and undetectable HIV RNA. All 218 enrolled patients received the once-daily fixed-dose combination of elbasvir (50 mg) plus grazoprevir (100 mg) for 12 weeks. All 218 patients completed follow-up at week 12. The median baseline CD4 cell count was 568 (424-626)/mm<sup>3</sup>. Limited antiretrovirals were allowed, specifically a nucleoside/nucleotide backbone of abacavir (21.6%) versus tenofovir (75.2%), in combination with raltegravir (52%), dolutegravir (27%), or rilpivirine (17%).

SVR12 was achieved by 96% (210/218) of patients (95% CI, 92.9-98.4). One patient did not achieve SVR12 for a nonvirologic reason and 7 patients without cirrhosis relapsed (2 subsequently confirmed as reinfections, highlighting the requirement of continued harm-reduction strategies after SVR). Thirty-five patients with compensated cirrhosis achieved SVR12. The most common adverse events were fatigue (13%; 29), headache (12%; 27), and nausea (9%; 20). No patient discontinued treatment because of an adverse event. Three out of 6 patients who relapsed before SVR12 had NS3 and/or NS5A resistance-associated substitutions (RASs) while the others had wild type virus at the time of relapse. Two patients receiving ART had transient HIV viremia but subsequently returned to undetectable levels without a change in ART. No significant changes were observed with CD4 cell counts or new opportunistic infections. Elbasvir/grazoprevir without ribavirin seems to be effective and well tolerated among patients coinfecting with HIV, with or without compensated cirrhosis. These data are consistent with previous trials of this regimen in the monoinfected population ([Zeuzem, 2017](#)).

### Pharmacology and Drug Interaction Data



Elbasvir is a substrate for CYP3A4 and the efflux transporter P-glycoprotein (P-gp). Grazoprevir is a substrate for CYP3A4, P-gp, and the liver uptake transporter OATP1B1. Moderate and strong CYP3A and P-gp inducers (including efavirenz) are not recommended for coadministration with elbasvir/grazoprevir. OATP1B1 inhibitors are also not recommended with grazoprevir.

Elbasvir/grazoprevir is not compatible with any ritonavir- or cobicistat-boosted HIV protease inhibitor, elvitegravir/cobicistat, efavirenz, or etravirine ([Feng, 2016](#)).

## Glecaprevir/Pibrentasvir

The safety and efficacy of glecaprevir (ABT-493), a pangenotypic NS3/4A protease inhibitor, coformulated with pibrentasvir (ABT-530), a pangenotypic NS5A inhibitor, were evaluated in the phase 3, multicenter EXPEDITION-2 study ([Rockstroh, 2017](#)). This study evaluated 8 weeks of the daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) administered as three 100 mg/40 mg fixed-dose combination pills in 137 HIV/HCV-coinfected adults without cirrhosis and 12 weeks of glecaprevir/pibrentasvir in 16 HIV/HCV-coinfected patients with compensated cirrhosis. Treatment-naïve and -experienced patients with genotype 1, 2, 3, 4, or 6 infection were enrolled. Patients were either antiretroviral naïve with a CD4 cell count  $\geq 500/\text{mm}^3$ , or on a stable ART regimen for at least 8 weeks with a CD4 cell count  $\geq 200/\text{mm}^3$ . ART drugs included raltegravir, dolutegravir, rilpivirine, tenofovir disoproxil fumarate, tenofovir alafenamide, abacavir, emtricitabine, and lamivudine. One patient received elvitegravir/cobicistat. Overall SVR12 was 98% (136/136 among those without cirrhosis on the 8-week regimen, and 14/15 in those with compensated cirrhosis on the 12-week regimen). Four serious adverse events were reported, none of which were DAA related. One of these led to treatment discontinuation.

### Pharmacology and Drug Interaction Data

Glecaprevir and pibrentasvir area under the curve (AUC) are increased roughly 3-fold and 1.57-fold, respectively, with tenofovir alafenamide/emtricitabine/elvitegravir/cobicistat ([Kosloski, 2017](#)). Only 1 patient received this combination in the EXPEDITION-2 study. Although the increases in AUC of glecaprevir and pibrentasvir when coadministered with elvitegravir/cobicistat are not considered clinically relevant by the manufacturer or the US Food and Drug Administration (FDA), due to lack of sufficient clinical safety data, close monitoring for hepatic toxicity is recommended until additional safety data are available in HIV/HCV-coinfected patients. Consider liver enzyme testing every 4 weeks. Ritonavir-boosted protease inhibitors are not recommended with glecaprevir/pibrentasvir.

Glecaprevir and pibrentasvir AUCs are reduced 25% and 27%, respectively, with abacavir/lamivudine/dolutegravir. These reductions are unlikely to have clinical relevance. Raltegravir and rilpivirine AUCs are increased 47% and 84%, respectively, with glecaprevir/pibrentasvir ([Oberoi, 2016](#)). These interactions do not require dose adjustment. Forty-five and 32 individuals received raltegravir or rilpivirine, respectively, in the EXPEDITION-2 study.

Glecaprevir absorption is pH dependent and glecaprevir exposures are reduced approximately 50% with 40 mg of omeprazole daily.

## Ledipasvir/Sofosbuvir

The safety and efficacy of 12 weeks of ledipasvir/sofosbuvir were evaluated in the phase 2, single-center, open-label ERADICATE trial, which included 50 HIV/HCV-coinfected patients with genotype 1 infection who were treatment naïve without cirrhosis ([Osinusi, 2015](#)). Thirteen patients were not receiving antiretroviral therapy and 37 patients were on protocol-allowed medications (tenofovir, emtricitabine, rilpivirine, raltegravir, and efavirenz). Although the inclusion criteria for patients receiving antiretroviral therapy allowed CD4 cell counts  $> 100/\text{mm}^3$ , the median CD4 cell count was  $576/\text{mm}^3$ . Overall, 98% achieved SVR12 (13/13 in the treatment-naïve arm and 36/37 in the treatment-experienced arm). There were no deaths, discontinuations, or clinically significant, serious adverse events. Renal function was monitored frequently during this trial and after administration of study drugs using a battery of tests (serum creatinine, eGFR, urinary beta-2 microglobulin, proteinuria, and glycosuria). No clinically significant changes in these parameters or renal toxicity were observed.

A larger study, ION-4, reported similar outcomes with ledipasvir/sofosbuvir ([Naggie, 2015](#)). A total of 335 HCV treatment-naïve and -experienced HIV/HCV-coinfecting patients were enrolled in the study and received ledipasvir/sofosbuvir once daily for 12 weeks. Patients received tenofovir disoproxil fumarate and emtricitabine with raltegravir (44%), efavirenz (48%), or rilpivirine (9%). Genotypes included were 1a (75%), 1b (23%), and 4 (2%). Twenty percent of patients had compensated cirrhosis, 34% were black, and 55% had not responded to prior HCV treatment. The overall SVR12 rate was 96% (321/335). Two patients had on-treatment virologic failure judged to be a result of nonadherence, 10 had virologic relapse after discontinuing treatment, 1 died from endocarditis associated with injection drug use, and 1 was lost to follow-up. SVR12 rates were 94% (63/67) among patients with compensated cirrhosis and 97% (179/185) among treatment-experienced patients. No patients discontinued the study drugs because of an adverse event. Although all patients had an eGFR >60 mL/min at study entry, drug interaction studies suggested that patients receiving tenofovir disoproxil fumarate could have increased tenofovir levels. There were 4 patients in whom serum creatinine level rose to ≥0.4 mg/dL. Two remained on tenofovir disoproxil fumarate, 1 had the tenofovir disoproxil fumarate dose reduced, and the other stopped taking tenofovir disoproxil fumarate.

Neither the ERADICATE trial nor the ION-4 study investigators reported clinically significant changes in CD4 cell counts or HIV RNA levels in the study participants. Thus, these data suggest that 12 weeks of ledipasvir/sofosbuvir is a safe and effective regimen for HIV/HCV-coinfecting patients with genotype 1 infection taking selected antiretroviral therapy ([Osinusi, 2015](#)); ([Naggie, 2015](#)). There are limited data regarding an 8-week course of ledipasvir/sofosbuvir in HIV/HCV-coinfecting patients ([Ingiliz, 2016](#)). Additionally, clinical trial data of daclatasvir (an NS5A inhibitor similar to ledipasvir) plus sofosbuvir in HIV/HCV-coinfecting patients demonstrated a lower SVR rate (76%) with 8 weeks of treatment compared to 12 weeks of therapy (97%). Therefore, a shortened treatment course for HIV/HCV-coinfecting persons cannot be recommended at this time.

#### Pharmacology and Drug Interaction Data

Drug interaction studies of ledipasvir (with or without sofosbuvir) with antiretroviral drugs in uninfected persons did not identify clinically significant interactions with abacavir, dolutegravir, emtricitabine, lamivudine, raltegravir, or rilpivirine ([German, 2014](#)); ([Garrison, 2015](#)). Interactions with maraviroc and enfuvirtide are not expected based on their pharmacologic profiles. Ledipasvir AUC is decreased by 34% when coadministered with efavirenz-containing regimens and increased by 96% when coadministered with ritonavir-boosted atazanavir ([German, 2014](#)). No dose adjustments of ledipasvir are recommended to account for these interactions.

Ledipasvir absorption is pH dependent. Refer to product labeling for guidance on temporal separation and dosing of gastric acid modifying agents.

Ledipasvir/sofosbuvir increases tenofovir levels when given as tenofovir disoproxil fumarate, which may increase the risk of tenofovir-associated renal toxicity. This combination should be avoided in patients with an eGFR <60 mL/min. With the addition of ledipasvir/sofosbuvir, tenofovir levels (when given as tenofovir disoproxil fumarate) are increased with efavirenz, rilpivirine ([German, 2014](#)), dolutegravir, ritonavir-boosted atazanavir, and ritonavir-boosted darunavir ([German, 2015](#)). The absolute tenofovir levels are highest, and may exceed exposures for which there are established renal safety data, when tenofovir disoproxil fumarate is administered with ritonavir- or cobicistat-containing regimens. Due to lack of sufficient safety data with this drug combination, consideration should be given to changing the antiretroviral regimen. Tenofovir alafenamide may be an alternative to tenofovir disoproxil fumarate during ledipasvir/sofosbuvir treatment for patients who take cobicistat or ritonavir as part of their antiretroviral therapy.

In patients with an eGFR <60 mL/min who are taking tenofovir disoproxil fumarate with ledipasvir/sofosbuvir, renal parameters should be checked at baseline and at the end of treatment. Baseline parameters should include measuring creatinine level, electrolytes (including phosphorus), and urinary protein and glucose, according to recent guidelines for the management of chronic kidney disease in those with HIV, which include indications for nephrology consultation ([Lucas, 2014](#)). Changing antiretroviral therapy may be considered for those at high risk for renal toxicity—especially those with an eGFR between 30 mL/min and 60 mL/min or who have preexisting evidence of Fanconi syndrome, and particularly those taking tenofovir disoproxil fumarate and a ritonavir- or cobicistat-containing regimen. Tenofovir disoproxil fumarate should also be properly dosed and adjusted for eGFR at baseline and while on therapy ([Lucas, 2014](#)).

Although there is an absence of data at this time on the renal safety of tenofovir when given as tenofovir alafenamide with

ledipasvir/sofosbuvir, a study of tenofovir pharmacokinetics in healthy volunteers receiving the combination of tenofovir alafenamide, emtricitabine, and cobicistat-boosted elvitegravir with ledipasvir/sofosbuvir found that tenofovir levels were only 20% of the typical tenofovir exposures seen with tenofovir disoproxil fumarate ([Garrison, 2015](#)). Based on these pharmacokinetic data in healthy volunteers, tenofovir alafenamide may be an alternative to tenofovir disoproxil fumarate during ledipasvir/sofosbuvir treatment for patients on ritonavir- or cobicistat-containing regimens.

## Paritaprevir/Ritonavir/Ombitasvir + Dasabuvir

Paritaprevir/ritonavir/ombitasvir plus dasabuvir was approved by the FDA for use in genotype 1a and 1b infection because of its efficacy and safety in treatment-naïve patients and peginterferon/ribavirin treatment-experienced patients, with or without compensated cirrhosis. Available information about response rates with this regimen in HIV/HCV-coinfected patients comes from the first part of the phase 2 TURQUOISE-1 study. In this study, treatment-naïve (n=42) and -experienced (n=21) patients were randomly assigned to 12 weeks or 24 weeks of paritaprevir/ritonavir/ombitasvir plus dasabuvir and weight-based ribavirin (100 mg [ $<75$  kg] to 1200 mg [ $\geq 75$  kg]). Of the 63 study participants, 12 had compensated cirrhosis, 56 had genotype 1a infection, and 7 had genotype 1b infection. Two study-permitted antiretroviral regimens were chosen based on pharmacokinetic data from uninfected volunteers; 35 patients entered taking tenofovir disoproxil fumarate and emtricitabine with raltegravir, and 28 patients entered taking tenofovir disoproxil fumarate and emtricitabine with ritonavir-boosted atazanavir (with the ritonavir coming from the HCV regimen during the time of coadministration). Of the 31 patients who received 12 weeks of paritaprevir/ritonavir/ombitasvir plus dasabuvir and ribavirin, 93.5% (29/31) achieved SVR12, 1 relapsed, and 1 withdrew consent from study participation. Among the 32 patients in the 24-week arm, 90.6% (29/32) achieved SVR12, 1 experienced viral breakthrough, and 2 had apparent HCV reinfection. No treatment-related serious adverse events occurred, and no patients discontinued treatment because of medication intolerance ([Sulkowski, 2015](#)).

### Pharmacology and Drug Interaction Data

Paritaprevir is an inhibitor of the hepatic uptake transporter OATP1B1. Ritonavir is coformulated with paritaprevir and ombitasvir to improve the pharmacokinetics of paritaprevir. As ritonavir has anti-HIV activity, HIV/HCV-coinfected patients should have achieved HIV RNA suppression with an ART regimen prior to initiation of this DAA therapy. Those not taking antiretroviral therapy should not receive this fixed-dose combination due to the potential for low-dose ritonavir to select for HIV protease-inhibitor resistance.

Ritonavir-boosted paritaprevir, ombitasvir, and dasabuvir are metabolized by and inhibitors of CYP enzymes (3A4 and 2C8), P-gp, BCRP, and OATP1B1. Studies of uninfected volunteers did not reveal notable pharmacologic interactions with paritaprevir (150 mg), ritonavir (100 mg), and ombitasvir (25 mg) plus dasabuvir (250 mg), or tenofovir disoproxil fumarate and emtricitabine (when tested separately from other fixed-dose combinations), raltegravir ([Menon, 2015](#)), abacavir, lamivudine, or dolutegravir ([Khatri, 2015](#)). In uninfected volunteers, when paritaprevir/ritonavir/ombitasvir plus dasabuvir was combined with efavirenz, emtricitabine, and tenofovir disoproxil fumarate, clinically significant gastrointestinal and neurologic adverse events occurred, coincident with elevations of alanine aminotransferase levels. When paritaprevir/ritonavir/ombitasvir plus dasabuvir was combined with rilpivirine, exposures to rilpivirine were substantially increased. Therefore, rilpivirine and efavirenz should not be used with paritaprevir/ritonavir/ombitasvir plus dasabuvir.

Because ritonavir is a component of the fixed-dose combination of paritaprevir and ombitasvir, the total daily dose of ritonavir must be carefully considered when using paritaprevir/ritonavir/ombitasvir plus dasabuvir with ritonavir-boosted HIV protease inhibitors. Coadministration with ritonavir-boosted lopinavir would result in a 300 mg daily dose of ritonavir, a dose associated with substantial gastrointestinal adverse effects; this combination is not recommended. In uninfected individuals, darunavir troughs are reduced with paritaprevir/ritonavir/ombitasvir plus dasabuvir. Thus, paritaprevir/ritonavir/ombitasvir plus dasabuvir should not be used with ritonavir-boosted darunavir.

Paritaprevir/ritonavir/ombitasvir plus dasabuvir can be given with atazanavir but the separate ritonavir-boosting tablet should be held during paritaprevir/ritonavir/ombitasvir plus dasabuvir therapy, and atazanavir (300 mg) should be administered at the same time as the fixed-dose combination of ritonavir-boosted paritaprevir and ombitasvir. Paritaprevir levels are increased 1.5- to 3-fold with atazanavir but no dose adjustment of paritaprevir is recommended ([Khatri, 2016](#)).



Inhibition of OATP1B1 by paritaprevir/ritonavir/ombitasvir plus dasabuvir increases indirect bilirubin concentrations and this effect may be attenuated in individuals taking atazanavir ([Eron, 2014](#)).

## Simeprevir + Sofosbuvir

The combination of simeprevir plus sofosbuvir, with or without ribavirin, has been studied in the phase 2 COSMOS trial in patients with HCV mono-infection ([Lawitz, 2014b](#)). This study is the main basis for the recommendation supporting use of this combination for genotype 1a or 1b mono-infection. Simeprevir plus sofosbuvir has been used anecdotally in patients with HIV/HCV coinfection, with a recent report of achieving SVR in 92% (11/12) of patients ([Del Bello, 2016](#)). Despite the dearth of study data, this regimen may be considered for the treatment of genotype 1 infection in patients with HIV/HCV coinfection who are receiving an antiretroviral therapy regimen that may be coadministered with simeprevir plus sofosbuvir.

Similarly, few data exist for the combination of sofosbuvir plus simeprevir for the retreatment of HCV infection in HIV/HCV-coinfected patients. However, preliminary results obtained for HCV-mono-infected patients, including those with prior treatment failure and advanced fibrosis, support the expectation that this regimen will be highly effective in HIV/HCV-coinfected patients receiving compatible antiretroviral therapy (see [Retreatment](#) section) ([Lawitz, 2014b](#)).

### Pharmacology and Drug Interaction Data

Simeprevir is metabolized primarily by CYP3A4 and is therefore susceptible to drug interactions with inhibitors and inducers of this enzyme. Simeprevir is also an inhibitor of OATP1B1 and P-gp. Drug interaction studies with antiretroviral drugs in HIV-uninfected volunteers suggest no substantial interactions with tenofovir, rilpivirine, dolutegravir, or raltegravir. However, simeprevir concentrations were substantially decreased when dosed with efavirenz, and substantially increased when dosed with ritonavir-boosted darunavir ([MacBrayne, 2017](#)). Use with efavirenz, etravirine, cobicistat, or boosted HIV protease inhibitors is not recommended ([Ouwerkerk-Mahadevan, 2016](#)).

## Sofosbuvir/Velpatasvir

The safety and efficacy of 12 weeks of sofosbuvir/velpatasvir were evaluated in a phase 3 study among 106 antiretroviral-controlled, HIV/HCV-coinfected patients ([Wyles, 2016](#)). Patients with genotype 1, 2, 3, or 4 infection were included; 18% (19/106) had compensated cirrhosis. HIV was controlled on ART including non-nucleoside reverse-transcriptase inhibitor- (rilpivirine), integrase inhibitor- (raltegravir or elvitegravir/cobicistat), or ritonavir-boosted protease inhibitor- (atazanavir, lopinavir, or darunavir) based regimens with either tenofovir/emtricitabine or abacavir/lamivudine. Fifty-three percent (56/106) of participants were on tenofovir disoproxil fumarate with a pharmacologic boosting agent (either ritonavir or cobicistat). Neither efavirenz nor etravirine were allowed in this study as concomitant dosing with sofosbuvir/velpatasvir in healthy volunteers resulted in clinically significant decreases in velpatasvir exposure. SVR12 was 95% with 2 relapses, both occurring in genotype 1a-infected patients. Similar results were noted in patients with compensated cirrhosis and in those with baseline NS5A RASs (n=12 at 15% threshold; SVR12=100%). There were no clinically significant changes in serum creatinine or eGFR, and no patients required a change in their antiretroviral therapy during the study period.

In general, few HIV/HCV-coinfected patients with compensated cirrhosis have been included in clinical trials of DAAs, and no data are available regarding HIV/HCV-coinfected patients with renal insufficiency or who have undergone solid organ transplantation. Despite a lack of data, it is highly likely that response rates are similar to those of HCV-mono-infected patients, as no study to date in the DAA era has showed a lower efficacy for HIV/HCV-coinfected patients. Therefore, the respective guidance from these sections should be followed if treatment is otherwise warranted, with consideration of drug interactions.

### Pharmacology and Drug Interaction Data

Velpatasvir is available only in a fixed-dose combination tablet with sofosbuvir. Velpatasvir is metabolized by CYP3A4, CYP2C8, and CYP2B6. It does not appear to inhibit or induce any CYP enzymes. Velpatasvir is a substrate for P-gp and BCRP, and inhibits P-gp, BCRP, and OATP1B1/1B3 but does not induce any transporters.

Velpatasvir absorption is pH dependent. Refer to product labeling for guidance on temporal separation and dosing of gastric acid modifying agents.

Drug interaction studies with sofosbuvir/velpatasvir have been performed in HIV and HCV seronegative volunteers. As with ledipasvir/sofosbuvir, tenofovir exposures are increased, which may be problematic for individuals with an eGFR <60 mL/min or in those receiving ritonavir- or cobicistat-containing antiretroviral therapy with tenofovir disoproxil fumarate. Fifty-six HIV/HCV-coinfected individuals receiving the combination of tenofovir disoproxil fumarate with ritonavir- or cobicistat-containing antiretroviral therapy were treated with sofosbuvir/velpatasvir in the ASTRAL-5 study with no difference in median creatinine clearance before and after sofosbuvir/velpatasvir treatment (but poor renal function was an exclusion for this study). In individuals with an eGFR <60 mL/min, consider use of tenofovir alafenamide in place of tenofovir disoproxil fumarate in those requiring ritonavir- or cobicistat-containing antiretroviral therapy. If the combination of tenofovir disoproxil fumarate with a ritonavir- or cobicistat-containing antiretroviral therapy is required in patients with an eGFR <60 mL/min, renal parameters should be checked at baseline and regularly thereafter while on sofosbuvir/velpatasvir.

Velpatasvir exposures are significantly reduced with efavirenz and this combination is not recommended. Etravirine has not been studied with sofosbuvir/velpatasvir and is also not recommended. Indirect bilirubin level increases have been reported when sofosbuvir/velpatasvir was used in patients on atazanavir/ritonavir. These changes are not considered clinically significant.

Based on data from healthy volunteers, tenofovir pharmacokinetics are lower with tenofovir alafenamide relative to tenofovir disoproxil fumarate. Thus, tenofovir alafenamide may be an alternative to tenofovir disoproxil fumarate during sofosbuvir/velpatasvir treatment for patients who take cobicistat or ritonavir as part of their antiretroviral therapy. However, there are no safety data for this combination in HIV/HCV-coinfected patients.

## Sofosbuvir/Velpatasvir/Voxilaprevir

The data supporting use of sofosbuvir/velpatasvir/voxilaprevir are described in the [Initial Treatment of HCV Infection](#) and [Retreatment of Persons in Whom Prior Therapy Has Failed](#) sections of the guidance. This regimen has not been studied in HIV/HCV-coinfected patients. Despite a lack of data, it is highly likely that response rates in HIV/HCV-coinfected patients will be similar to those of HCV-monoinfected patients, as no study to date in the DAA era has shown a lower efficacy for HIV/HCV-coinfected patients. Therefore, the respective guidance from the aforementioned treatment and retreatment sections of the guidance should be followed, with consideration of drug-drug interactions.

### Pharmacology and Drug Interaction Data

Voxilaprevir is a substrate for P-gp, OATP, BCRP, CYP3A, CYP1A2, and CYP2C8. Voxilaprevir inhibits OATP, P-gp, and BCRP. Voxilaprevir AUC is increased 331% with ritonavir-boosted atazanavir and this combination is not recommended ([Garrison, 2017](#)). Voxilaprevir AUC is increased 171% with tenofovir alafenamide/emtricitabine/elvitegravir/cobicistat, and 143% with tenofovir disoproxil fumarate/emtricitabine and ritonavir-boosted darunavir. Although these increases in voxilaprevir AUC were not deemed clinically relevant by the manufacturer or the FDA, due to lack of clinical safety data, close monitoring for hepatic toxicity is recommended until additional safety data are available in HIV/HCV-coinfected patients. Consider liver enzyme testing every 4 weeks.

Tenofovir concentrations are increased with sofosbuvir/velpatasvir/voxilaprevir when given as tenofovir disoproxil fumarate ([Garrison, 2017](#)). In individuals with an eGFR <60 mL/min, consider use of tenofovir alafenamide in place of tenofovir disoproxil fumarate in those requiring ritonavir- or cobicistat-containing antiretroviral therapy. No substantial interactions were observed with dolutegravir, emtricitabine, raltegravir, or rilpivirine.

Velpatasvir absorption is pH dependent. Velpatasvir AUC is reduced approximately 50% when given with omeprazole 20 mg daily as part of the fixed-dose sofosbuvir/velpatasvir/voxilaprevir combination. Refer to product labeling for guidance on temporal separation and dosing of gastric acid modifying agents.

**Table 1. Drug Interactions Between Direct-Acting Antivirals and Antiretroviral Drugs—Preferred Regimens**

Green indicates coadministration is safe; yellow indicates a dose change or additional monitoring is warranted; and red indicates the combination should be avoided.

	Ledipasvir/ Sofosbuvir (LDV/SOF)	Sofosbuvir/ Velpatasvir (SOF/VEL)	Elbasvir/ Grazoprevir (ELB/GRZ)	Glecaprevir/ Pibrentasvir (GLE/PIB)	Sofosbuvir/ Velpatasvir/ Voxilaprevir (SOF/VEL/VOX)
Ritonavir-boosted atazanavir (ATZ)	▲ LDV ▲ ATZ <sup>a</sup>	▲ VEL ▲ ATZ <sup>a</sup>	▲ ELB ▲ GRZ ▲ ATZ	ND	▲ ATZ
Ritonavir-boosted darunavir (DRV)	▲ LDV ◄► DRV <sup>a</sup>	◄► VEL ◄► DRV <sup>a</sup>	▲ ELB ▲ GRZ ◄► DRV	ND	▲ VOX ◄► DRV
Ritonavir-boosted lopinavir (LPV)	ND <sup>a</sup>	◄► VEL ◄► LPV <sup>a</sup>	▲ ELB ▲ GRZ ◄► LPV	ND	ND
Ritonavir-boosted tipranavir (TPV/r)	ND	ND	ND	ND	ND
Efavirenz (EFV)	▼ LDV ▼ EFV <sup>a</sup>	▼ VEL ▼ EFV	▼ ELB ▼ GRZ ▼ EFV	ND	ND
Rilpivirine (RPV)	◄► LDV ◄► RPV	◄► VEL ◄► RPV	◄► ELB ◄► GRZ ◄► RPV	◄► GLE ◄► PIB ▲ RPV	◄► VEL ◄► VOX ◄► RPV
Etravirine (ETV)	ND	ND	ND	ND	ND
Raltegravir (RAL)	◄► LDV ◄► RAL	◄► VEL ◄► RAL	◄► ELB ◄► GRZ ▲ RAL	◄► GLE ◄► PIB ▲ RAL	ND
Cobicistat-boosted elvitegravir (COB)	▲ LDV ▲ COB <sup>a</sup>	▲ VEL ▲ COB <sup>a</sup>	▲ ELB ▲ GRZ ▲ COB	▲ GLE ▲ PIB ▲ COB	▲ VOX ▲ COB <sup>a</sup>
Dolutegravir (DTG)	◄► LDV ◄► DTG	◄► VEL ◄► DTG	◄► ELB ◄► GRZ ▲ DTG	▼ GLE ▼ PIB ▲ DTG	ND

**Table 1. Drug Interactions Between Direct-Acting Antivirals and Antiretroviral Drugs—Preferred Regimens**

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	Ledipasvir/ Sofosbuvir (LDV/SOF)	Sofosbuvir/ Velpatasvir (SOF/VEL)	Elbasvir/ Grazoprevir (ELB/GRZ)	Glecaprevir/ Pibrentasvir (GLE/PIB)	Sofosbuvir/ Velpatasvir/ Voxilaprevir (SOF/VEL/VOX)
<b>Maraviroc (MVC)</b>	ND	ND	ND	ND	ND
<b>Tenofovir (TFV) disoproxil fumarate</b>	↔ LDV ▲ TFV <sup>c</sup>	↔ VEL ▲ TFV	↔ ELB ↔ GRZ ▲ TFV	ND	▲ TFV <sup>b</sup>
<b>Tenofovir (TFV) alafenamide</b>	↔ LDV ▲ TFV <sup>d</sup>	↔ VEL ▲ TFV <sup>d</sup>	ND	↔ GLE ↔ PIB ↔ TFV	▲ TFV <sup>b</sup>

ND, No data; NPD, No pharmacokinetic data.

<sup>a</sup> Caution only with tenofovir disoproxil fumarate

<sup>b</sup> Increase in tenofovir depends on which additional concomitant antiretroviral agents are administered.

<sup>c</sup> Avoid tenofovir disoproxil fumarate in patients with an eGFR <60 mL/min; tenofovir concentrations may exceed those with established renal safety data in individuals on ritonavir- or cobicistat-containing regimens.

<sup>d</sup> Studied as part of fixed-dose combinations with ledipasvir/sofosbuvir or sofosbuvir/velpatasvir plus TAF, emtricitabine, elvitegravir, and cobicistat.

## Table 2. Drug Interactions Between Direct-Acting Antivirals and Antiretroviral Drugs—Alternative Regimens

Green indicates coadministration is safe; yellow indicates a dose change or additional monitoring is warranted; and red indicates the combination should be avoided.

	Simeprevir/ Sofosbuvir (SMV/SOF)	Daclatasvir/ Sofosbuvir (DCV/SOF)	Paritaprevir/ Ritonavir/ Ombitasvir + Dasabuvir (PrOD)	Paritaprevir/ Ritonavir/ Ombitasvir (PrO)
Ritonavir-boosted atazanavir (ATZ)	ND	▲ DCV <sup>a</sup>	▲ PRV ▲ ATZ	▲ PRV ◄► ATZ
Ritonavir-boosted darunavir (DRV)	▲ SMV ◄► DRV	▲ DCV ◄► DRV	▼▲ PRV ▼ DRV	▲ PRV ◄► DRV
Ritonavir-boosted lopinavir (LPV)	ND	▲ DCV ◄► LPV	▲ PRV ◄► LPV	▲ PRV ◄► LPV
Ritonavir-boosted tipranavir (TPV/r)	ND	ND	ND	ND
Efavirenz (EFV)	▼ SMV ◄► EFV	▼ DCV <sup>b</sup>	NPD <sup>c</sup>	ND
Rilpivirine (RPV)	◄► SMV ◄► RPV	ND	▲ PRV ▲ RPV	ND
Etravirine (ETV)	ND	▼ DCV <sup>b</sup>	ND	ND
Raltegravir (RAL)	◄► SMV ◄► RAL	ND	◄► PrOD ▲ RAL	◄► PrO ▲ RAL
Cobicistat-boosted elvitegravir (COB)	ND	▲ DCV <sup>a</sup>	ND	ND
Dolutegravir (DTG)	◄► SMV ◄► DTG	◄► DCV ▲ DTG	▼ PRV ▲ DTG	ND
Maraviroc (MVC)	ND	ND	ND	ND



## Table 2. Drug Interactions Between Direct-Acting Antivirals and Antiretroviral Drugs—Alternative Regimens

Green indicates coadministration is safe; yellow indicates a dose change or additional monitoring is warranted; and red indicates the combination should be avoided.

	Simeprevir/ Sofosbuvir (SMV/SOF)	Daclatasvir/ Sofosbuvir (DCV/SOF)	Paritaprevir/ Ritonavir/ Ombitasvir + Dasabuvir (PrOD)	Paritaprevir/ Ritonavir/ Ombitasvir (PrO)
Tenofovir (TFV)  disoproxil fumarate	◀▶ SMV ◀▶ TFV	◀▶ DCV ◀▶ TFV	◀▶ PrOD ◀▶ TFV	◀▶ PrO ◀▶ TFV
Tenofovir (TFV)  alafenamide	ND	ND	ND	ND

ND, No data


<sup>a</sup> Daclatasvir dose should be reduced to 30 mg.

<sup>b</sup> Daclatasvir dose should be increased to 90 mg.


### Ribavirin

Ribavirin has the potential for dangerous drug interactions with didanosine, resulting in mitochondrial toxicity with hepatomegaly and steatosis, pancreatitis, and lactic acidosis. Thus, concomitant administration of these 2 drugs is contraindicated ([Fleischer, 2004](#)). The combined use of ribavirin and zidovudine has been reported to increase the rates of anemia and the need for ribavirin dose reduction. Thus, zidovudine is not recommended for use with ribavirin ([Alvarez, 2006](#)).

## Treatment Recommendations for Patients With HIV/HCV Coinfection

RECOMMENDED	RATING 
HIV/HCV-coinfected persons should be treated and retreated the same as persons without HIV infection, after recognizing and managing interactions with antiretroviral medications (see <a href="#">Initial Treatment of HCV Infection</a> and <a href="#">Retreatment of Persons in Whom Prior Therapy Has Failed</a> ).	I, B
Daily daclatasvir (refer to information <a href="#">above</a> for dose) plus sofosbuvir (400 mg), with or without ribavirin, is a recommended regimen when antiretroviral regimen changes cannot be made to accommodate alternative HCV direct-acting antivirals. Refer to <a href="#">Initial Treatment of HCV Infection</a> and <a href="#">Retreatment of Persons in Whom Prior Therapy Has Failed</a> sections for treatment duration.	I, B

**Regimens Not Recommended for Patients With HIV/HCV Coinfection**

NOT RECOMMENDED	RATING 
Ledipasvir/sofosbuvir for 8 weeks is <b>not</b> recommended, regardless of baseline HCV RNA level.	IIb, C

**Mixed Genotypes**

Rarely, genotyping assays may indicate the presence of a mixed infection (eg, genotypes 1a and 2). Treatment data for mixed genotypes with direct-acting antivirals are sparse but utilization of a pangenotypic regimen should be considered. When the correct combination or duration of treatment is unclear, expert consultation should be sought.

**Last update:** September 21, 2017