

VA Outpatient Pharmacy Checklist for HCV Prescriptions document

Background:

- For Veterans initiating HCV treatment, ombitasvir/paritaprevir/ritonavir plus dasabuvir (Viekira Pak) ± ribavirin should be considered first, if clinically appropriate, for all Veterans infected with HCV Genotype 1.
- If ledipasvir/sofosbuvir (Harvoni) is prescribed, it is strongly encouraged that the prescription is evaluated to determine if clinically appropriate to change prescription to Viekira Pak.
- Below are checklist for inclusion and exclusion for Viekira Pak and Harvoni as well as Dosage Regimens. Please refer to [PBM HCV CFUs](#) and [VHA Office of Public Health HCV Treatment Considerations](#) for more detailed information.

CHECKLIST FOR VIEKIRA PAK: Evaluate both inclusion and exclusion criteria for eligibility

Exclusion: If one of the following criteria is met, Viekira Pak should NOT be prescribed:

- Co-administration of drugs 1) highly dependent on CYP3A for clearance such as lovastatin and simvastatin and for which elevated plasma concentrations are associated with serious and/or life-threatening events; 2) drugs that are strong inducers of CYP3A and CYP2C8 such as rifampin or St. John's wort and may lead to reduced efficacy of ombitasvir, paritaprevir/ritonavir and dasabuvir; OR 3) drugs such as gemfibrozil that are strong inhibitors of CYP2C8 and may increase dasabuvir plasma concentrations and the risk of QT prolongation. **NOTE: Please note that these are listed as contraindications in PI; however, there are additional medications that may need significant modification in dosage regimen and/or monitoring if co-administered with Viekira Pak. Conduct thorough drug-drug interaction review.** (<http://www.hep-druginteractions.org/>)
- Patient receiving ethinyl estradiol containing product(s)
- HIV/HCV co-infection in patients not receiving antiretroviral therapy OR where antiretroviral drug-interactions preclude the use of Viekira Pak such as efavirenz, darunavir/ritonavir, lopinavir/ritonavir or rilpivirine
- Decompensated liver disease ([Child-Pugh B and C](#))
- Previous virologic failure to NS3-4A protease-inhibitor (i.e. boceprevir, telaprevir, simeprevir), sofosbuvir-containing regimen or NS5a inhibitors (i.e. ledipasvir, ombitasvir, daclatasvir)
- If co-administered with ribavirin, contraindication and/or intolerance to ribavirin
 - Contraindication and/or intolerance to ribavirin: Contraindication is defined as history of significant or unstable cardiac disease, known pregnancy, positive pregnancy test, and men whose female partner is pregnant or plan to become pregnant, known hypersensitivity reaction, autoimmune hepatitis, hemoglobinopathies) and/or intolerance (i.e. baseline hemoglobin <12g/dL) and/or history of *significant* adverse events with previous ribavirin-containing regimen.

Inclusion: If the following criterion is met, Viekira Pak ± ribavirin may be prescribed:

- Hepatitis C Virus Genotype 1 infection

NOTE: If patient does not meet Viekira eligibility, please evaluate if Harvoni is an option.

CHECKLIST FOR HARVONI: Evaluate both inclusion and exclusion criteria for eligibility

Exclusion: If one of the following criteria is met, Harvoni should NOT be prescribed:

- Patients with severe renal impairment (eGFR<30mL/min/1.73m²), end-stage renal disease or on hemodialysis.
- Patients who have failed prior treatment with NS5a inhibitors (i.e. ledipasvir, ombitasvir, or daclatasvir)
- Co-administration with rifampin, rifabutin, rifapentine, St. John's wort, carbamazepine, phenytoin, phenobarbital, oxcarbazepine, elvitegravir/cobicistat/emtricitabine/tenofovir, tipranavir/ritonavir, simeprevir, rosuvastatin, or amiodarone.
- If co-administered with ribavirin, any contraindications and/or intolerance to ribavirin as described above

Inclusion: If one of the following criteria is met, Harvoni ± ribavirin may be prescribed:

- Presence of potentially serious drug interactions with Viekira Pak for which there is no alternative (<http://www.hep-druginteractions.org/>)
- HIV/HCV co-infection in patients not receiving antiretroviral therapy OR where antiretroviral drug-interactions preclude the use of Viekira Pak
- Decompensated liver disease ([Child-Pugh B and C](#))
- Recipient of solid organ transplant
- Previous virologic failure to NS3-4A protease-inhibitor (i.e. boceprevir, telaprevir, simeprevir) or sofosbuvir-based regimen
- Patients who cannot receive ribavirin with Viekira Pak due to contraindications to ribavirin (if applicable)
 - Contraindication and/or intolerance to ribavirin: Contraindication is defined as history of significant or unstable cardiac disease, known pregnancy, positive pregnancy test, and men whose female partner is pregnant or plan to become pregnant, known hypersensitivity reaction, autoimmune hepatitis, hemoglobinopathies) and/or intolerance (i.e. baseline hemoglobin <12g/dL) and/or history of *significant* adverse events with previous ribavirin-containing regimen.
- In genotype 1a patient with cirrhosis and history of prior null responder (i.e., no measureable decrease in HCV RNA with prior treatment to peginterferon/ribavirin) or who are known to have the IL-28B T/T polymorphism (if applicable)

Issues for Consideration

If co-administered with proton-pump inhibitor, H2-receptor antagonists, or antacids, the prescribing information must be followed:

- Separate antacids and Harvoni administration by 4 hours.
- H2-receptor antagonists may be administered simultaneously with or 12 hours apart from Harvoni at a dose that does not exceed doses comparable to famotidine 40mg twice daily
- Proton-pump inhibitor doses comparable to omeprazole 20mg or lower can be administered simultaneously with Harvoni under fasted conditions.

Harvoni Dosage Regimen for HCV Genotype 1

Population includes patients with HCV monoinfected, HCV/HIV-1 co-infected, or hepatocellular carcinoma (HCC) ^a	Dosage Regimens	Total treatment duration
HCV Genotype 1		
Treatment-naïve without cirrhosis		
HCV RNA <6 million IU/mL	Ledipasvir/sofosbuvir	8 weeks
HCV RNA ≥6 million IU/mL	Ledipasvir/sofosbuvir	12 weeks
Treatment-naïve with cirrhosis		
	Ledipasvir/sofosbuvir	12 weeks
Treatment-experienced^b without cirrhosis		
	Ledipasvir/sofosbuvir	12 weeks
Treatment-experienced^b with cirrhosis^c		
	Ledipasvir/sofosbuvir OR Ledipasvir/sofosbuvir and ribavirin	24 weeks 12 weeks
Decompensated cirrhosis^c		
	Ledipasvir/sofosbuvir and ribavirin (initiate ribavirin at 600mg/day and titrate up as tolerated) OR Ledipasvir/sofosbuvir (if unable to tolerate ribavirin)	12 weeks 24 weeks

^aRefer to CFU Issues for Consideration for alternative treatment options including patients with decompensated cirrhosis, and pre- and post-transplant.

^bIn clinical trials, treatment-experienced was defined as previous peginterferon/ribavirin with or without an NS3-4a protease inhibitor

^cRefer to CFU Issues for Consideration for additional information

Viekira Pak Dosage Regimen for HCV Genotype 1

Population includes patients with HCV monoinfected, HCV/HIV-1 co-infected stabilized on certain antiretroviral regimens or hepatocellular carcinoma (HCC) ^{a,b,c}	Dosage Regimens	Total Treatment Duration
Genotype 1a without cirrhosis	Viekira Pak plus ribavirin	12 weeks
Genotype 1a with cirrhosis	Viekira Pak plus ribavirin	24 weeks ^d
Genotype 1b without cirrhosis	Viekira Pak	12 weeks
Genotype 1b with cirrhosis	Viekira Pak plus ribavirin	12 weeks

^aRefer to CFU Issues for consideration for alternative treatment options including pre- and post-transplant patients

^bFollow the genotype 1a dosing recommendations in patients with an unknown genotype 1 subtype or with mixed genotype 1 infection.

^cPopulation includes treatment-naïve and treatment-experienced patients with peginterferon/ribavirin.

^dViekira Pak plus ribavirin for 12 weeks may be considered for patients who are treatment naïve OR in patients with prior relapse or partial response to previous peginterferon/ribavirin treatment; Refer to Issues for Consideration for more detail.