

Hepatitis C Direct-Acting Antivirals

Goals:

- Approve use of cost-effective treatments supported by the medical evidence.
- Provide consistent patient evaluations across all hepatitis C treatments.
- Ensure appropriate patient regimen based on disease severity, genotype, and patient comorbidities.

Length of Authorization:

- 8-16 weeks

Requires PA:

- All direct-acting antivirals for treatment of Hepatitis C

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Is the request for treatment of chronic Hepatitis C infection (B18.2)? Note: Accurate diagnosis of chronic hepatitis C infection typically includes positive detection of a viral load. Diagnosis should not rely solely on HCV antibody testing.	Yes: Go to #3	No: Pass to RPh. Deny; medical appropriateness.
3. Is expected survival from non-HCV-associated morbidities more than 1 year?	Yes: Go to #4	No: Pass to RPh. Deny; medical appropriateness.

Approval Criteria

<p>4. Has <u>all</u> the following pre-treatment testing been documented:</p> <ol style="list-style-type: none"> Genotype testing in past 3 years is required if the patient has decompensated cirrhosis, prior treatment experience with a DAA regimen, and if prescribed a regimen which is not pan-genotypic Current HBV status of patient History of previous HCV treatment and outcome Presence or absence of cirrhosis as clinically determined (e.g., clinical, laboratory, or radiologic evidence) <p>Note: Direct-acting antiviral agents can re-activate hepatitis B in some patients. Patients with history of HBV should be monitored carefully during and after treatment for flare-up of hepatitis. Prior to treatment with a DAA, all patients should be tested for HBsAG, HBsAb, and HBcAB status. HIV testing is also recommended, and modification of HIV or HCV treatment regimens may be needed if there are drug-drug interactions.</p> <p>Treatment-experienced: Patients who received more than 4 weeks of HCV DAA therapy.</p>	<p>Yes: Record results of each test and go to #5</p> <p>Note: If the patient has HIV or HBV co-infection, it is highly recommended that a specialist be consulted prior to treatment.</p> <p>Currently treatment is not recommended during pregnancy due to lack of safety and efficacy data</p>	<p>No: Pass to RPh. Request updated testing.</p>
<p>5. Which regimen is requested?</p>	<p>Document and go to #6</p>	
<p>6. Does the patient have complications of cirrhosis (ascites, portal hypertension, hepatic encephalopathy, hepatocellular carcinoma, esophageal varices)?</p>	<p>Yes: Go to #7</p>	<p>No: Go to #8</p>
<p>7. Is the regimen prescribed by, OR is the patient in the process of establishing care with or in consultation with a hepatologist, gastroenterologist, or infectious disease specialist?</p>	<p>Yes: Go to #8</p>	<p>No: Pass to RPh. Deny; medical appropriateness.</p> <p>Recommend prescriber document referral to a specialist.</p>

Approval Criteria

<p>8. Is there attestation that the patient and provider will comply with case management to promote the best possible outcome for the patient and adhere to monitoring requirements required by the Oregon Health Authority, including measuring and reporting of a post-treatment viral load OR Is there attestation from the patient and provider that they have opted out of OHA case management?</p> <p>Case management includes assessment of treatment barriers and offer of patient support to mitigate potential barriers to regimen adherence as well as facilitation of SVR12 evaluation to assess treatment success.</p> <p>Patients may opt out of OHA case management with attestation that they understand goals and benefits of the program and responsibilities associated with treatment including adherence to treatment and lab tests. Members may rejoin the program at any time.</p>	<p>Yes: Go to #9</p>	<p>No: Pass to RPh. Deny; medical appropriateness.</p>
<p>9. Is the prescribed drug: a) Elbasvir/grazoprevir for GT 1a infection; <u>or</u> b) Daclatasvir + sofosbuvir for GT 3 infection?</p>	<p>Yes: Go to #10</p>	<p>No: Go to #11</p>
<p>10. Has the patient had a baseline NS5a resistance test that documents a resistant variant to one of the agents in #16?</p> <p>Note: Baseline NS5A resistance testing is required.</p>	<p>Yes: Pass to RPh; deny for appropriateness</p>	<p>No: Go to #11</p> <p>Document test and result.</p>
<p>11. Does the prescribed regimen include a NS3/4a protease inhibitor (elbasvir, glecaprevir, simeprevir, paritaprevir, voxilaprevir)?</p>	<p>Yes: Go to #12</p>	<p>No: Go to #13</p>
<p>12. Does the patient have moderate-severe hepatic impairment (Child-Pugh B or Child-Pugh C)?</p>	<p>Yes: Pass to RPh; deny for appropriateness</p>	<p>No: Go to #13</p>
<p>13. Is the prescribed regimen for the retreatment after failure of a DAA due to noncompliance or loss of follow-up?</p>	<p>Yes: Pass to RPh; Deny and refer to medical director for review</p>	<p>No: Go to #14</p>

Approval Criteria

14. Is the prescribed drug regimen a recommended regimen based on the patient's genotype, age, treatment status (retreatment or treatment naïve) and cirrhosis status (see **Table 1 and Table 2**)?

Note: Safety and efficacy of DAAs for children < 3 years of age have not been established
Pediatric dosing available in **Table 3 and Table 4**

Yes: Approve for 8-16 weeks based on duration of treatment indicated for approved regimen

No: Pass to RPh. Deny; medical appropriateness.

Table 1: Recommended Treatment Regimens for Adults, and Adolescents 12 years of age and older with Hepatitis C virus.

Treatment History	Cirrhosis Status	Recommended Regimen
Treatment Naïve (Genotype 1-6)		
Treatment naïve, confirmed reinfection or prior treatment with PEG/RBV	Non-cirrhotic or compensated cirrhosis	SOF/VEL x 12 weeks G/P x 8 weeks
	Compensated cirrhosis	G/P x 8 weeks SOF/VEL x 12 weeks (baseline resistance testing recommended for GT3)
	Decompensated Cirrhosis	SOF/VEL + RBV x 12 weeks SOF/VEL x 24 weeks (if ribavirin ineligible*)
Treatment Experienced (Genotype 1-6)		
Sofosbuvir based regimen treatment failures, including: Sofosbuvir + ribavirin Ledipasvir/sofosbuvir Velpatasvir/sofosbuvir	Non-cirrhotic or compensated cirrhosis	SOF/VEL/VOX x12 weeks G/P x 16 weeks (except GT3)
Elbasvir/grazoprevir treatment failures	Non-cirrhotic or compensated cirrhosis	SOF/VEL/VOX x 12 weeks
Glecaprevir/pibrentasvir treatment failures	Non-cirrhotic or compensated cirrhosis	G/P + SOF + RBV x 16 weeks SOF/VEL/VOX x 12 weeks (plus RBV if compensated cirrhosis)
Multiple DAA Treatment Failures, including: sofosbuvir/velpatasvir/voxilaprevir glecaprevir/pibrentasvir + sofosbuvir	Non-cirrhotic or compensated cirrhosis	G/P + SOF + RBV x 16-24 weeks SOF/VEL/VOX x 24 weeks
Abbreviations: DAA = direct acting antiviral; EBV/GZR = elbasvir/grazoprevir; G/P = glecaprevir and pibrentasvir; PEG = pegylated interferon; RAV = resistance-associated variant; RBV = ribavirin; SOF = sofosbuvir; SOF/VEL = sofosbuvir/velpatasvir; SOF/VEL/VOX = sofosbuvir/velpatasvir/voxilaprevir		
* Ribavirin ineligible/intolerance may include : 1) neutrophils < 750 mm ³ , 2) hemoglobin < 10 g/dl, 3) platelets <50,000 cells/mm ³ , autoimmune hepatitis or other autoimmune condition, hypersensitivity or allergy to ribavirin		
^ Rarely, genotyping assays may indicate the presence of a mixed infection (e.g., genotypes 1a and 2). Treatment data for mixed genotypes with direct-acting antivirals are limited. However, in these cases, a pangenotypic regimen is appropriate.		
Ribavirin-containing regimens are absolutely contraindicated in pregnant women and in the male partners of		

women who are pregnant. Documented use of two forms of birth control in patients and sex partners for whom a ribavirin containing regimen is chosen is required.
All regimens containing a protease inhibitor (elbasvir, glecaprevir, simeprevir, paritaprevir, voxilaprevir) should not be used in patients with moderate to severe hepatic impairment (CTP B and C).
There is limited data supporting DAA regimens in treatment- experienced patients with decompensated cirrhosis. These patients should be handled on a case by case basis with the patient, prescriber, and CCO or FFS medical director.
Definitions of Treatment Candidates • Treatment-naïve: Patients without prior HCV treatment. • Treat as treatment-naïve: Patients who discontinued HCV DAA therapy within 4 weeks of initiation or have confirmed reinfection after achieving SVR following HCV treatment. • Treatment-experienced: Patients who received more than 4 weeks of HCV DAA therapy.

Table 2: Recommended Treatment Regimens for children ages 3 - 12 years of age with Hepatitis C virus.

Treatment History	Cirrhosis Status	Recommended Regimen
Treatment Naïve Genotype 1-6		
Treatment naïve, confirmed reinfection or prior treatment with PEG/RBV	Non-cirrhotic or compensated cirrhosis	SOF/VEL x 12 weeks G/P x 8 weeks
	Decompensated Cirrhosis	SOF/VEL + RBV x 12 week
Treatment Experienced with DAA regimen		
Note: Efficacy and safety extremely limited in treatment experienced to other DAAs in this population. Can consider recommended treatment regimens in adults if FDA approved for pediatric use. Recommend consulting with hepatologist.		
Abbreviations: DAA = direct acting antiviral; G/P = glecaprevir and pibrentasvir; RBV = ribavirin; SOF = sofosbuvir; SOF/VEL = sofosbuvir/velpatasvir		
<ul style="list-style-type: none"> All regimens containing a protease inhibitor (elbasvir, glecaprevir, simeprevir, paritaprevir, voxilaprevir) should not be used in patients with moderate to severe hepatic impairment (CTP B and C). There is limited data supporting DAA regimens in treatment- experienced patients with decompensated cirrhosis. These patients should be handled on a case by case basis with the patient, prescriber, and CCO or FFS medical director. 		

Table 3: Recommended dosage of sofosbuvir/velpatasvir in pediatric patients 3 years of age and older:

Body weight	Dosing of sofosbuvir/velpatasvir
Less than 17 kg	One 150 mg/37.5 mg pellet packet once daily
17 kg to less than 30 kg	One 200 mg/50 mg pellet packet OR tablet once daily
At least 30 kg	Two 200 mg/50 mg pellet packets once daily OR one 400 mg/100 mg tablet once daily

Table 4: Recommended dosage of glecaprevir/pibrentasvir in pediatric patients 3 years of age and older:

Body weight	Dosing of sofosbuvir/velpatasvir
Less than 20 kg	Three 50mg/20 mg pellet packets once daily
20 kg to less than 30 kg	Four 50 mg/20 mg pellet packets once daily
30 kg to less than 45 kg	Five 50 mg/20 mg pellet packets once daily
45 kg and greater OR 12 years of age and older	Three 100mg/40 mg tablets once daily

P&T Review: 10/21 (MH); 6/20; 9/19 (MH); 1/19; 11/18; 9/18; 1/18; 9/17; 9/16; 1/16; 5/15; 3/15; 1/15; 9/14; 1/14
Implementation: 1/1/2022; 7/1/20; 1/1/20; 3/1/2019; 1/1/2019; 3/1/2018; 1/1/2018; 2/12/16; 4/15; 1/15