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Prior Authorization Criteria Update: Direct Acting Antivirals for Hepatitis C Virus

Purpose of Update:

The purpose of this prior authorization (PA) update is to remove PA criteria for preferred hepatitis C medications for treatment naïve individuals.

There is high quality evidence that direct acting antiviral (DAA) regimens result in pooled sustained virologic response (SVR) rates of 95.5% to 98.9% across genotypes in the treatment of chronic hepatitis C virus (HCV) and have low rates of serious adverse events (1.9%; relative risk [RR] 1.90; 95% confidence interval [CI] 0.73 to 4.95) and withdrawals due to adverse events (0.4%).[1] There is also low quality evidence that SVR is associated with a decreased risk of all-cause mortality (hazard ratio [HR] 0.40; 95% CI 0.28 to 0.56, I^2 52.1%), liver-related mortality (HR 0.11; 95% CI 0.04 to 0.27), cirrhosis (HR 0.36; 95% CI 0.33 to 0.4) and hepatocellular carcinoma (HR 0.29; 95% CI 0.23 to 0.38) after adjustment for potential confounders.[1] Current guidelines from the Veterans Affairs[2], American Association for the Study of Liver Diseases, the Infectious Diseases Society of America[3] and European Association for the Study of the Liver[4] recommend that treatment with DAAs be offered to all patients with recently acquired (acute) or chronic HCV without delay.

The Oregon Drug Use Review/Pharmacy & Therapeutics Committee initially prioritized treatment for the fee-for-service population to patients in greatest need of treatment. Limited real-world experience and data, consideration for the number of patients waiting for treatment, limited provider expertise, and the limited number of alternative treatment options in cases of treatment resistance and patient comorbidities all played a role in prioritizing treatment. As more treatment options became available, real-world experience increased, and the community standard evolved, the P&T Committee has expanded treatment in a stepwise fashion to patients with less severe disease. Since March 2019, Oregon Health Authority (OHA) drug policy approves treatment for patients with chronic HCV regardless of disease severity, level of fibrosis or history of substance use disorder, but also ensures appropriate baseline laboratory screening (hepatitis B virus status, noninvasive screening for cirrhosis and history of previous HCV treatment).

In 2016, the World Health Organization released a proposal to eliminate hepatitis C as a public health threat by 2030. Consistent with this, the OHA includes health equity as a core value and is committed to eliminate health inequities by 2030. Most state Medicaid programs have similarly removed prior authorization (PA) criteria requiring fibrosis, sobriety and prescriber restrictions.[5] Additionally, at least 10 states have removed PA for uncomplicated patients entirely.[5] A previous hepatitis C policy evaluation found that overall utilization of DAAs in the Oregon Health Plan increased over time. Changes to the PA criteria in 2018 (expanded treatment to fibrosis stage 2) and 2019 (removed fibrosis and sobriety requirements) also resulted in an immediate increase in DAA utilization followed by stabilization and an increasing number of primary care prescribers.

Recommendation:

- Remove PA criteria and required case management for preferred DAA regimens for treatment-naïve patients with hepatitis C virus (**Appendix 1**). Continue to require PA for: retreatment of HCV; non-preferred DAAs; and for uses not FDA approved.
- Make sofosbuvir/velpatasvir/voxilaprevir (Vosevi®) non-preferred and continue to reserve it for treatment-experienced individuals.

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- Recommend the Oregon Health Authority continue to facilitate access to and completion of treatments for patients who would benefit from additional support.

References:

1. Chou R, Dana T, Fu R, et al. U.S. Preventive Services Task Force Evidence Syntheses, formerly Systematic Evidence Reviews. *Screening for Hepatitis C Virus Infection in Adolescents and Adults: A Systematic Review Update for the US Preventive Services Task Force*. Agency for Healthcare Research and Quality (US); 2020.
2. Department of Veterans Affairs HIV, Hepatitis, and Related Conditions Program. Chronic Hepatitis C Virus Infection: Treatment Considerations. March 2021. Available at: https://www.hepatitis.va.gov/pdf/Treatment-Considerations-2021-03-18-508.pdf.
3. The American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. HCV Guidance: Recommendations for testing, managing and treating hepatitis C. January 2021. Available at: www.hcvguidelines.org.
4. EASL recommendations on treatment of hepatitis C: Final update of the series(☆). *Journal of hepatology*. Nov 2020;73(5):1170-1218. doi:10.1016/j.jhep.2020.08.018
5. The Center for Health Law and Policy Innovation of Harvard Law School (CHLPI) and the National Viral Hepatitis Roundtable (NVHR) Hepatitis C: The State of Medicaid Access 2022 Progress Report. Available at: https://stateofhepc.org/report/. Accessed: February 1, 2022.

Appendix 1: Prior Authorization Criteria

Hepatitis C Direct-Acting Antivirals

Goals:

- Approve use of cost-effective treatments supported by the medical evidence.
- Provide consistent patient evaluations across hepatitis C treatments.
- Ensure appropriate patient regimen based on prior treatment experience and genotype.

Length of Authorization:

- 8-24 weeks

Requires PA:

- Non-preferred direct acting antivirals (DAAs)
- Preferred regimens for patients with treatment experience with a DAA

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Is the request for treatment of Hepatitis C infection?	**Yes:** Go to #3 Document baseline quantitative HCV RNA level _____	**No:** Pass to RPh. Deny; medical appropriateness.

Approval Criteria		
3. Has <u>all</u> the following pre-treatment testing been documented: a. Genotype testing in past 3 years is required if the patient has decompensated cirrhosis, <u>prior treatment experience</u> with a DAA regimen, and if prescribed a regimen which is not pan-genotypic b. History of previous HCV treatment, viral load after treatment, and outcome are required only if there is documentation of treatment experience	**Yes:** Record results of each test and go to #4	**No**: Pass to RPh. Request updated testing.
4. Which regimen is requested?	Document and go to #5	
5. Has the patient been treated with a direct acting antiviral regimen previously?	**Yes:** Go to #6	**No:** Go to #8
6. Did the patient achieve a sustained virological response (SVR) at week 12 or longer following the completion of their last DAA regimen?	**Yes:** Go to #7	**No:** Document as treatment failure and treat as indicated for treatment experienced. Go to #8
7. Is this likely a reinfection, indicated by at least one of the following: a. Does the patient have ongoing risk factors for hepatitis C reinfection (e.g. sexually active men who have sex with men, persons who inject drugs), OR b. Is the hepatitis C infection a different genotype than previous	**Yes:** Document as reinfection. Use regimens recommended for treatment naïve patients. Go to #8	**No:** Document as treatment failure and treat as indicated for treatment experienced. Go to #8

Approval Criteria		
8. Is the prescribed drug: a) Elbasvir/grazoprevir for GT 1a infection; or b) Ledipasvir/sofosbuvir for GT 1a treatment-experienced infection; or c) Sofosbuvir/velpatasvir for GT 3 in cirrhosis or treatment-experienced infection	**Yes:** Go to #9	**No:** Go to #10
9. Has the patient had a baseline NS5a resistance test that documents a resistant variant to one of the agents in #10? Note: Baseline NS5A resistance testing is required.	**Yes:** Pass to RPh; deny for appropriateness	**No:** Go to #10 Document test and result.
10. 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 8-24 weeks based on duration of treatment indicated for approved regimen Referral will be made for optional case management (patient may choose to opt-in).	**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 PEGylated interferon/ribavirin	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 pegylated interferon/ribavirin	Non-cirrhotic or compensated cirrhosis	SOF/VEL x 12 weeks G/P x 8 weeks
	Decompensated Cirrhosis	SOF/VEL + RBV x 12 weeks

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 • 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 mg50 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: *4/22 (MH); 10/21; 6/20; 9/19; 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: *TBD; 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*