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 selection 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?	**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		
4. Has <u>all</u> of the following pre-treatment testing been documented: a. Genotype testing in past 3 years; b. Baseline HCV RNA level in past 6 months; c. Current HIV status of patient d. Current HBV status of patient e. Pregnancy test in past 30 days for a woman of child-bearing age; <u>and</u> f. History of previous HCV treatment and outcome? 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.	**Yes:** Record results of each test and go to #5 Note: If the patient has HIV or HBV co-infection, it is highly recommended that a specialist be consulted prior to treatment.	**No**: Pass to RPh. Request updated testing.
5. Which regimen is requested?	Document and go to #6	
6. Does the patient have HIV coinfection and is under treatment by a specialist with experience in HIV? Note: persons with HIV/HCV coinfection are at risk for rapidly progressing fibrosis	**Yes:** Go to #11	**No:** Go to #7

Approval Criteria		
7. Does the patient have: a) A biopsy, imaging test (transient elastography [FibroScan®], acoustic radiation force impulse imaging [ARFI], or shear wave elastography [SWE]) to indicate portal fibrosis with septa (METAVIR F2) advanced fibrosis (METAVIR F3) or cirrhosis (METAVIR F4); **OR** Clinical, radiologic or laboratory evidence of complications of cirrhosis (ascites, portal hypertension, hepatic encephalopathy, hepatocellular carcinoma)?	**Yes:** Go to #10 Note: Other imaging and blood tests are not recommended based on evidence of poor sensitivity and specificity compared to liver biopsy. However, if imaging testing is not regionally available, a serum test (FIBROSpect II; Fibrometer; enhanced liver fibrosis [ELF], Fibrosure) can be used to confirm METAVIR F2 or greater but cannot be used for denial. For results falling in a range (e.g. F1 to F2), fibrosis stage should be categorized as the higher F stage for the purpose of treatment, or require one additional, more specific test (per HERC AUROC values http://www.oregon.gov/OHA/HPA/CSI-HERC/Pages/Evidence-based-Reports-Blog.aspx?View=%7b2905450B-49B8-4A9B-AF17-5E1E03AB8B6B%7d&SelectedID=237) to be obtained to determine the stage of fibrosis. However, additional testing cannot be limited to biopsy. After one additional test, if a range still exists, the highest F score in the range will be used for determining coverage.	**No:** Go to #8

Approval Criteria		
8. Does the patient have one of the following extrahepatic manifestations of Hepatitis C (with documentation from a relevant specialist that their condition is related to HCV)? a) Lymphoproliferative disease, including type 2 or 3 cryoglobulinemia with end-organ manifestations (i.e., leukocytoclastic vasculitis); or b) Proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis; or c) Porphyria cutanea tarda or lichen planus d) Lymphomas (B-cell non-Hodgkin lymphoma) e) Type 2 Diabetes with insulin resistance f)	**Yes:** Go to #10	**No:** Go to #9
9. Is the patient in one of the following transplant settings: a) Listed for a transplant and treatment is essential to prevent recurrent hepatitis C infection post-transplant; or b) Post solid organ transplant?	**Yes:** Go to #10	**No:** Pass to RPh. Deny; medical appropriateness.
10. If METAVIR F4: Is the regimen prescribed by, or in consultation with, a hepatologist, gastroenterologist, or infectious disease specialist? **OR** If METAVIR F3: 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? **OR** If METAVIR ≤F2: The regimen does not need to be prescribed by or in consultation with a specialist.	**Yes:** Go to #11	**No:** Pass to RPh. Deny; medical appropriateness. Forward to DMAP for further manual review to determine appropriateness of prescriber.

Approval Criteria		
11. In the previous 6 months: a) Has the patient actively abused alcohol (>14 drinks per week for men or >7 drinks per week for women or binge alcohol use (>4 drinks per occasion at least once a month); OR b) Has the patient been diagnosed with a substance use disorder; OR c) Is the prescriber aware of current alcohol abuse or illicit injectable drug use?	**Yes:** Go to #12	**No:** Go to #13
12. Is the patient enrolled in a treatment program under the care of an addiction/substance use treatment specialist?	**Yes:** Go to #13	**No:** Pass to RPh. Deny; medical appropriateness.
13. Will the patient and provider comply with all case management interventions and adhere to monitoring requirements required by the Oregon Health Authority, including measuring and reporting of a post-treatment viral load?	**Yes**: Go to #14	**No:** Pass to RPh. Deny; medical appropriateness.
14. Is the prescribed drug: a) Elbasvir/grazoprevir for GT 1a infection; <u>or</u> b) Daclatasvir + sofosbuvir for GT 3 infection?	**Yes**: Go to #15	**No:** Go to #16
15. Has the patient had a baseline NS5a resistance test that documents a resistant variant to one of the agents in #16? Note: Baseline NS5A resistance testing is required.	**Yes:** Pass to RPh; deny for appropriateness	**No:** Go to #16 Document test and result.
16. Is the prescribed regimen include a NS3/4a protease inhibitor (elbasvir, glecaprevir, simeprevir, paritaprevir, voxilaprevir)?	**Yes:** Go to #17	**No:** Go to #18

Approval Criteria		
17. Does the patient have moderate-severe hepatic impairment (Child-Pugh B or Child-Pugh C)?	**Yes:** Pass to RPh; deny for appropriateness	**No:** Go to #18
18. Is the prescribed regimen for the retreatment after failure of a DAA due to noncompliance or lost to follow-up?	**Yes:** Pass to RPh; Deny and refer to medical director for review	**No:** Go to #19
19. Is the prescribed drug regimen a recommended regimen based on the patient's genotype, treatment status (retreatment or treatment naïve) and cirrhosis status (see **Table 1**)?	**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 Chronic Hepatitis C.

Treatment History	Cirrhosis Status	Recommended Regimen
Genotype 1		
DAA-Treatment naive	Non-cirrhotic	EBR/GZR x 12 weeks** SOF/VEL x 12 weeks G/P x 8 weeks
	Compensated Cirrhosis	EBR/GZR x 12 weeks** SOF/VEL x 12 weeks G/P x 12 weeks
	Decompensated Cirrhosis	SOF/VEL + RBV x 12 week
Treatment experienced (Prior PEG/RBV)	Non-cirrhotic	EBR/GZR x 12 weeks** SOF/VEL x 12 weeks G/P x 8 weeks
	Compensated cirrhosis	EBV/GRZ 12weeks**

		SOF/VEL x 12 weeks G/P x 12 weeks
Treatment Experienced (Prior sofosbuvir)	Non-cirrhotic or compensated cirrhosis	SOF/VEL x 12 weeks SOF/VEL/VOX x 12 weeks (GT 1 a only without tx h/o NS5A inhibitor) G/P x 12 weeks
Treatment Experienced (Prior NS3A/4A inhibitor)	Non-cirrhotic or compensated cirrhosis	SOF/VEL x 12 weeks EBR/GZR + RBV x 12 weeks** G/P x 12 weeks
Treatment Experienced (prior NS5A-containing regimen)	Non-cirrhotic or compensated cirrhosis	SOF/VEL/VOX x 12 weeks G/P x 16 weeks
Genotype 2		
Naïve	Non-cirrhotic	SOF/VEL x 12 weeks G/P x 8 weeks
	Compensated cirrhosis	SOF/VEL x 12 weeks G/P x 12 weeks
	Decompensated	SOF/VEL + RBV x 12 weeks
Treatment Experienced (prior PEG/RBV)	Non-cirrhotic	SOF/VEL x 12 weeks G/P x 8 weeks
	Compensated cirrhosis	SOF/VEL x 12 weeks G/P x 12 weeks
Treatment Experienced (SOF + RBV)	Non-cirrhotic or compensated cirrhosis	SOF/VEL x 12 weeks G/P x 12 weeks
Treatment Experienced (prior NS5A-containing regimen)	Non-cirrhotic or compensated cirrhosis	SOF/VEL/VOX x 12 weeks
Genotype 3		
Naïve	Non-cirrhotic	SOF/VEL X 12 weeks G/P x 8 weeks
	Compensated cirrhosis	SOF/VEL + RBV x 12 weeks G/P x 12 weeks
	Decompensated Cirrhosis	SOF/VEL + RBV x 12 weeks
Treatment Experienced (prior PEG/RBV only)	Non-cirrhotic or compensated cirrhosis	SOF/VEL x 12 weeks G/P x 16 weeks

Treatment Experienced (SOF + RBV)	Non-cirrhotic or compensated cirrhosis	SOF/VEL/VOX x 12 weeks G/P x 16 weeks
Experienced (prior NS5A-containing regimen)	Non-cirrhotic or compensated cirrhosis	SOF/VEL/VOX x 12 weeks
Genotype 4		
Treatment Naïve	Non-cirrhotic	SOF/VEL x 12 weeks EBV/GZR x 12 weeks G/P x 8 weeks
	Compensated cirrhosis	SOF/VEL x 12 weeks EBV/GZR x 12 weeks G/P x 12 weeks
	Decompensated Cirrhosis	SOF/VEL + RBV x 12 week
Treatment Experienced (prior PEG/RBV only)	Non-cirrhotic	SOF/VEL x 12 weeks EBV/GZR x 12 weeks G/P x 8 weeks
	Compensated cirrhosis	SOF/VEL x 12 weeks EBV/GZR x 12 weeks G/P x 12 weeks
Treatment Experienced (prior NS5A-containing regimen OR sofosbuvir)	Non-cirrhotic or compensated cirrhosis	SOF/VEL/VOX x 12 weeks
Genotype 5/6		
Treatment Naïve or Experienced (prior PEG-IFN/RBV only)	Non-cirrhotic or compensatedcirrhotis	SOF/VEL x 12 weeks G/P x 8 weeks
	Compensated cirrhosis	SOF/VEL x 12 weeks G/P x 12 weeks
	Decompensated cirrhosis	SOF/VEL + RBV x 12 weeks
Experienced (prior NS5A-containing regimen OR sofosbuvir)	Non-cirrhotic or compensated cirrhosis	SOF/VEL/VOX x 12 weeks

Abbreviations: CTP = Child-Turcotte-Pugh; DAA = direct acting antiviral; DCV = daclatasvir; EBV/GZR = elbasvir/grazoprevir;G/P = glecaprevir and pibrentasvir PEG = pegylated interferon;; RAV = resistance-associated variant; RBV = ribavirin; SOF = sofosbuvir; SOF/VEL = sofosbuvir/velpatasvir/voxilaprevir

**No baseline NS5A RAVs. For genotype 1a patients with baseline NAS5A RAVs, extend duration to 16 weeks.
±Evidence is insufficient if the addition of RBV may benefit subjects with GT3 and cirrhosis. If RBV is not used with regimen, then baseline RAV testing should be done prior to treatment to rule out the Y93 polymorphism.

^ 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.
Regimens other than glecaprevir/pibrentasvir (G/P;) and elbasvir/grazoprevir (EBV/GZR) should not be used in patients with severe renal impairment (GRF < 30 mL/min) or end stage renal disease requiring dialysis.
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).

P&T Review: *9/17 (MH); 9/16; 1/16; 5/15; 3/15; 1/15; 9/14; 1/14*
Implementation: *1/1/2018; 2/12/16; 4/15; 1/15*