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 comorbidities.

Length of Authorization:

- 8-12 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 all 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; and 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.	**Yes:** Record results of each test and go to #5	**No**: Pass to RPh. Request updated testing.
5. Has the patient failed treatment with any of the following HCV NS5A inhibitors: a) Daclatasvir plus sofosbuvir; b) Ledipasvir/sofosbuvir; c) Paritaprevir/ritonavir/ombitasvir plus dasabuvir; d) Elbasvir/grazoprevir; or e) Sofosbuvir/velpatasvir)? Note: Patients who failed treatment with sofosbuvir +/- ribavirin or PEGylated interferon can be retreated (see table below).	**Yes:** Pass to RPh. Deny; medical appropriateness. Note: If urgent retreatment is needed, resistance testing must be done to indicate susceptibility to prescribed regimen. Refer to medical director for review.	**No:** Go to #6
6. Which regimen is requested?	Document and go to #7	

Approval Criteria		
7. Does the patient have HIV coinfection AND: A biopsy, imaging test (transient elastography [FibroScan], acoustic radiation force impulse imaging [ARFI], or shear wave elastography [SWE], or serum test if the above are not available (FIBROSpect II; FibroSure; Fibrometer; enhanced liver fibrosis [ELF]) to indicate fibrosis (METAVIR F2) AND the patient is under treatment by a specialist with experience in HIV?	**Yes:** Go to #12 Note: Other imaging and blood tests are not recommended based on evidence of poor sensitivity and specificity compared to liver biopsy For results falling in a range (e.g. F2 to F3), 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 more specific 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: a) A biopsy, imaging test (transient elastography [FibroScan®], acoustic radiation force impulse imaging [ARFI], or shear wave elastography [SWE]) to indicate 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 #11 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; FbroSure; enhanced liver fibrosis [ELF]) can be used to confirm METAVIR F3 or F4. For results falling in a range (e.g. F2 to F3), 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 more specific test, if a range still exists, the highest F score in the range will be used for determining coverage.	**No:** Go to #9

Approval Criteria		
9. 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) 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	**Yes:** Go to #11	**No:** Go to #10
10. 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 #11	**No:** Pass to RPh. Deny; medical appropriateness.

Approval Criteria		
11. 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 in consultation with, a hepatologist, gastroenterologist, or infectious disease specialist OR is the patient in the process of establishing care 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 #12	**No:** Pass to RPh. Deny; medical appropriateness. Forward to DMAP for further manual review to determine appropriateness of prescriber.
12. In the previous 6 months: • 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 • Has the patient been diagnosed with a substance use disorder; OR • Is the prescriber aware of current alcohol abuse or illicit injectable drug use?	**Yes:** Go to #13	**No:** Go to #14

Approval Criteria		
13. Is the patient enrolled in a treatment program under the care of an addiction/substance use treatment specialist?	**Yes:** Go to #14	**No:** Pass to RPh. Deny; medical appropriateness.
14. Do the patient and provider agree to comply with all case management interventions and adhere to monitoring requirements required by the Oregon Health Authority <link to be added>, including measuring and reporting of a post-treatment viral load?	**Yes**: Go to #15	**No:** Pass to RPh. Deny; medical appropriateness.
15. Is the prescribed drug: a) Elbasvir/grazoprevir for GT 1a infection; <u>or</u> b) Daclatasvir + sofosbuvir for GT 3 infection?	**Yes**: Go to #16	**No:** Go to #17
16. Has the patient had a baseline NS5a resistance test show a resistant variant to one of the agents in #15?	**Yes:** Pass to RPh; deny for appropriateness	**No:** Go to #17
17. Is the prescribed drug regimen a recommended regimen based on the patient's genotype and cirrhosis status?	**Yes:** Approve for 8-12 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.

Genotype	Cirrhosis Status	Recommended Regimen^	Duration of Treatment
Genotype 1			
Treatment-naïve	Non-cirrhotic	• EBR/GZR • LDV/SOF	12 weeks except if LDV/SOF and *HCV RNA < 6 million IU/mL, give for <u>8 weeks</u>*

	Compensated Cirrhosis	• EBR/GZR • LDV/SOF	12 weeks
	Decompensated Cirrhosis	• LDV/SOF + RBV	12 weeks
Treatment-experienced*	Non-cirrhotic	• EBR/GZR • LDV/SOF +/- RBV**	12 weeks
	Compensated Cirrhosis	• EBR/GZR • LDV/SOF + RBV	12 weeks 12 weeks – 24 weeks[c]
	Decompensated Cirrhosis	• LDV/SOF + RBV	24 weeks
Genotype 2			
Naïve or Experienced	Non-cirrhotic	• SOF/VEL	12 weeks
	Compensated Cirrhosis	• SOF/VEL + RBV**	12 weeks
	Decompensated Cirrhosis	• SOF/VEL + RBV	12 weeks
Genotype 3			
Naïve or Experienced	Non-cirrhotic	• LDV/SOF + RBV • SOF/VEL	12 weeks
	Compensated Cirrhosis	• SOF/VEL + RBV±	12 weeks
	Decompensated Cirrhosis	• SOF/VEL + RBV	12 weeks
Genotype 4			
Naïve or Experienced	Non-cirrhotic	• EBR/GZR • LDV/SOF	12 weeks
	Compensated Cirrhosis	• EBR/GZR • LDV/SOF	12 weeks
	Decompensated Cirrhosis	• LDV/SOF + RBV	12 weeks *(24 weeks if prior SOF treatment has failed)*
Genotypes 5 and 6			
Naïve or Experienced	With or Without Compensated Cirrhosis	• LDV/SOF	12 weeks

Abbreviations: EBV/GZR = elbasvir/grazoprevir (Zepatier®) ; LDV/SOF = ledipasvir and sofosbuvir (Harvoni®); RBV = ribavirin; SOF = sofosbuvir (Sovaldi®); SOF/VEL = sofosbuvir/velptasvir (Epclusa®)

*Treatment-experienced defined as previous treatment with PEG/RBV or SOF/RBV only.
**RBV required for previous treatment with SOF but not if PEG/RBV
[c] For those who have failed SOF + RBV with compensated cirrhosis: LDV/SOF + RBV for 24 weeks is recommended
±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.
Sofosbuvir-containing regimens should not be used in patients with severe renal impairment (GRF < 30 mL/min) or end stage renal disease requiring dialysis.
Elbasvir/grazoprevir or ombitasvir/paritaprevir/ritonavir + dasubuvir should not be used in patients with moderate to severe hepatic impairment (CTP and C)

P&T/DUR Review: *9/17(MH); 9/16; 1/16; 5/15; 3/15; 1/15; 9/14; 1/14*
Implementation: *10/1/2017; 6/1/2017; 2/12/16; 4/15; 1/15*