Oscar Clinical Guideline: Direct Acting Antiviral Agents for Hepatitis C (PG045, Ver. 7)

Direct Acting Antiviral Agents for Hepatitis C

Summary

All Antiviral Agents for Hepatitis C require prior authorization:

- The Plan's preferred Hepatitis C medications are included in Table 1 below.
- The Plan requires that members be unable to use, or have tried and failed preferred medication(s) first.
- Requests for non-formulary and non-preferred hepatitis C medications will also be subject to the Plan's Non-Formulary Products Criteria (PG069).

Hepatitis C virus (HCV) infections are of global concern, and can lead to cirrhosis and end stage liver disease if left untreated. Those with HCV can remain asymptomatic until the disease progresses, thus universal screening is often recommended in adults (using antibody and/or RNA testing). Once HCV has been diagnosed, several factors such as viral genotype, liver fibrosis staging, history of prior antiviral therapy, kidney function and current medication use, will dictate which therapy is most appropriate. The goal of therapy is complete viral eradication, and newer direct acting antivirals (DAAs) have made this possible. Most oral regimens are 2- to 3-months in duration and include Epclusa (sofobuvir/velpatasvir), Mavyret (glecaprevir/pibrentasvir), Harvoni (ledipasvir/sofosbuvir), Zepatier (elbasvir/grazoprevir), and Vosevi (sofosbuvir/velpatasvir/voxilaprevir).

Persons with hepatitis C virus who are co-infected with hepatitis B virus (HBV) may be at risk for reactivation of HBV infection during or following HCV treatment. This includes those who are hepatitis B surface antigen (HBsAg) and hepatitis B surface antibody (HBsAb or anti-HBs) negative, but hepatitis B core antibody (HBcAb or anti-HBc) positive. Reactivation of hepatitis B can occur in someone who has a current HBV infection, or who has recovered from a past HBV infection – and can lead to rapid liver failure and death. Providers should test for HBV infection before starting HCV DAA treatment. Providers should also monitor patients during and after hepatitis C treatment for signs of HBV reactivation. HBV reactivation can be managed with appropriate use of antiviral treatment for HBV during HCV treatment with DAAs.

This policy references the most recent FDA prescribing information for each medication as well as guidelines and reports published by the American Association of the Study of Liver Diseases (AASLD) for consideration of approval of these medications. The FDA and AASLD set the patient selection and treatment considerations, choice of regimen, and duration of hepatitis C treatment. Please refer to the FDA website at https://www.fda.gov/drugs and AASLD website at www.hcvguidelines.org.

Table 1: Plan's Preferred Direct Acting Antiviral Agents for Hepatitis C

Drug	FDA-Approved Indications
Epclusa (sofosbuvir/velpatasvir)	for the treatment of adults and pediatric patients 3 years of age and older with chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5, or 6 infection. ● without cirrhosis or with compensated cirrhosis. ● with decompensated cirrhosis for use in combination with ribavirin.
Harvoni (ledipasvir/sofosbuvir)	Adults and pediatric patients 3 years of age and older with chronic HCV infection ● genotype 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis. ● genotype 1 infection with decompensated cirrhosis, for use in combination with ribavirin. ● genotype 1 or 4 infection who are liver transplant recipients without cirrhosis or with compensated cirrhosis, for use in combination with ribavirin.
Vosevi (sofosbuvir/velpatasvir/ voxilaprevir)	Adult patients with chronic hepatitis C virus (HCV) infection without cirrhosis or with compensated cirrhosis (Child-Pugh A) who have: ● genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor. ● genotype 1a or 3 infection and have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor. ○ Additional benefit of sofosbuvir/velpatasvir/voxilaprevir (Vosevi) over sofosbuvir/velpatasvir (Epclusa) was not shown in adults with genotype 1b, 2, 4, 5, or 6 infection previously treated with sofosbuvir without an NS5A inhibitor.

Definitions

"AASLD" refers to the American Association of the Study of Liver Diseases, a professional medical society focused on liver diseases.

"ARV Treatment Regimen" refers to the use of Antiretroviral (ARV) medications, which are a class of drugs utilized in the management and treatment of Human Immunodeficiency Virus (HIV). A fully suppressive regimen is one that effectively minimizes the viral load in a patient's body to levels that are undetectable, thereby helping to prevent progression of the disease and transmission of the virus.

"Child-Pugh" score is a validated scale to assess the severity of chronic liver disease, particularly cirrhosis using common laboratory findings and clinical examination findings. The Child-Pugh score can be used to predict prognosis, and is broken down into three classifications: A (5-6 points, well-compensated disease, 1-year survival of 100%), B (7-9 points, significant functional compromise, 1-year survival of ~80%), and C (10-15 points, decompensated disease, 1-year survival of ~45%).

"Compensated cirrhosis" is a stage of liver cirrhosis classified as Child-Pugh Class A, indicating that the liver is still functioning adequately despite the presence of cirrhosis.

"DAA" are a class of medications used to treat hepatitis C. They specifically target key steps in the hepatitis C virus life cycle, reducing the viral load in the body. Most DAAs are used in combination therapy to enhance their effectiveness.

"Decompensated cirrhosis" is an advanced stage of liver cirrhosis classified as Child-Pugh Class B or C, indicating that the liver is no longer functioning properly and complications have arisen.

"FDA" refers to the Food and Drug Administration, a regulatory agency responsible for approving and monitoring the safety and efficacy of medications in the United States.

"Genotype" refers to the unique genetic makeup of an individual. In the case of a virus, it refers to a type or strain of that virus.

"HBV" refers to the hepatitis B virus, a viral infection that affects the liver.

"HCV" refers to the hepatitis C virus, a bloodborne virus that primarily infects the liver and can cause chronic liver disease.

"HIV" refers to the Human Immunodeficiency Virus, a viral infection that attacks the body's immune system.

"IDSA" refers to the Infectious Diseases Society of America, a professional medical society dedicated to preventing and treating infectious diseases.

"NS5A inhibitor" is a class of direct-acting antiviral medications used in the treatment of hepatitis C. Examples of NS5A inhibitors include elbasvir, ledipasvir, ombitasvir, and velpatasvir.

"Resistance-associated substitutions (RASs)" are genetic mutations in the hepatitis C virus that confer resistance to certain direct-acting antiviral medications. Examples include NS5A RASs, which can impact the effectiveness of regimens containing elbasvir/grazoprevir.

"Viral load" is a quantity (or copies) of a virus in a given volume. Viral load can be a method of assessing disease transmissibility and progression or risk; where higher values as typically associated with more higher risk of a disease being transmissible or progressing to later stages, and lower levels (or undetectable levels) can indicate low risk of transmissibility or suppression of that virus.

Medical Necessity Criteria for Initial Authorization

The Plan considers Direct Acting Antiviral Agents for Hepatitis C medically necessary when the following criteria are met:

1. The requested indication of use, patient selection, treatment consideration, and treatment duration is supported by ONE (1) of the following:
    a. FDA-approved indications and usage; *or*
    b. The most current version of the AASLD/IDSA Clinical Practice Guideline, "*HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection*"; *AND*
2. The requesting prescriber has provided complete and up-to-date clinical documentation showing ALL of the following:
    a. The requested medication is prescribed by a healthcare professional experienced in managing hepatitis C, including:
        i. primary care providers for uncomplicated cases (e.g., compensated cirrhosis)
        ii. specialists (hepatologist, gastroenterologist, liver transplant specialist, infectious disease specialist) in complicated cases (e.g., decompensated cirrhosis, co-infection with HIV, or other significant comorbidities); *and*
    b. The member has a confirmed diagnosis of chronic hepatitis C; *and*
    c. The member is within the appropriate age group for the requested medication based on FDA-labeled indication(s) or the most current AASLD/IDSA recommendations for testing, managing, and treating hepatitis C guidelines; *and*
    d. Clinical chart documentation includes:
        i. Detailed physical examination.
        ii. Disease history.

iii. Viral load.
iv. Treatment history (including previous medications, start and stop dates, and outcomes of each prior treatment).
v. Treatment plan for HCV.
vi. Any concomitant conditions (such as HBV, HIV, or other coexistent liver and/or non-liver diseases).
vii. Specific considerations related to comorbidities such as type 2 diabetes mellitus, HIV, and renal impairment.
viii. Laboratory test results demonstrating hepatitis C viral load within 6 months prior to initiation of HCV treatment.
ix. Laboratory results (i.e., biopsy and/or imaging study) demonstrating the presence or absence of cirrhosis (compensated or decompensated).
x. The member has been assessed for potential nonadherence.

If the above prior authorization criteria are met, approval will be granted for one (1) treatment course for a duration based on FDA-labeled indication(s) or the most current AASLD/IDSA recommendations for testing, managing, and treating hepatitis C guidelines.

Medical Necessity Criteria for Reauthorization or Retreatment

Recommendations for retreatment of HCV in treatment-experienced individuals will be reviewed on a case-by-case basis, taking into consideration the following factors:

- Genotype and subtype, when applicable;
- Presence or absence of compensated cirrhosis;
- Prior regimen that was tried and failed;
- Presence or absence of viral variants harboring resistance-associated substitutions (RASs);
- Comorbidities, including type 2 diabetes mellitus, HIV, and renal impairment; *AND*
- Presence or absence of medication nonadherence.

Regimens for retreatment of HCV will be assessed based on FDA-labeled indication(s) or the most current AASLD/IDSA recommendations for testing, managing, and treating hepatitis C guidelines.

Experimental or Investigational / Not Medically Necessary

The safety and efficacy of Direct Acting Antiviral Agents for Hepatitis C for any indication not supported by FDA-labeled indication(s) or the most current AASLD/IDSA recommendations for testing, managing, and treating hepatitis C guidelines is considered not medically necessary by the Plan. Such indications are deemed to be experimental, investigational, or unproven.

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