Oscar Clinical Guideline: Vemlidy (tenofovir alafenamide) (PG010, Ver. 7)

Vemlidy (tenofovir alafenamide)

Summary

Hepatitis B (HBV) is a viral infection that targets the liver, leading to either acute or chronic disease. Acute infections are often self-limiting and do not always require treatment; however, a small fraction can progress to chronic hepatitis B. Chronic infections, defined as the persistence of hepatitis B surface antigens present after 6 months, pose significant health risks as they can result in serious liver complications, such as cirrhosis and hepatocellular carcinoma (HCC). The goal of HBV treatment is to reduce the risk of HCC, however initiation of therapy is based on several factors including presence or absence of cirrhosis, alanine aminotransferase levels (a liver enzyme test, with higher levels indicating liver damage or disease) and HBV DNA levels. Management of chronic HBV includes treatment with either pegylated interferon or nucleoside/nucleotide analogs (i.e., entecavir [Baraclude] or Vemlify [tenofovir alafenamide]).

Vemlidy (tenofovir alafenamide), granted FDA approval in 2016, is a nucleotide analog reverse transcriptase inhibitor employed to manage chronic hepatitis B infection in adults with compensated liver disease. It shares a similar mechanism of action with tenofovir disoproxil fumarate (Viread), another variant of tenofovir used in managing chronic hepatitis B. Yet, Vemlidy (tenofovir alafenamide) is linked to fewer adverse effects on kidneys and bones, making it a preferable treatment option in certain patient populations.

In addition to its role in managing chronic hepatitis B, Vemlidy (tenofovir alafenamide) also has an important place in prophylaxis against HBV reactivation in immunocompromised individuals, and HBV reinfection post liver transplant, further broadening its clinical utility. Reactivation of HBV can result in severe hepatitis and/or hepatic failure in up to 25-50% of cases. Management recommendations in the case of reactivation prophylaxis are the same as for initial chronic HBV infection.

Definitions

"Albumin" is a type of protein made by the liver that often decreases with liver disease.

"ALT and AST" refer to alanine aminotransferase and aspartate aminotransferase, liver enzymes that indicate liver cell injury when elevated.

"Anti-CD20 Therapy" is a type of drug that targets CD20, a protein found on the surface of B cells. It is used in certain types of cancers and autoimmune diseases.

"Antibody to Hepatitis B core Antigen (Anti-HBc)" is an antibody that is part of the body's immune response to a hepatitis B infection.

"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.

"Ascites" refers to an abnormal buildup of fluid in the abdomen, often due to severe liver disease.

"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%).

"Chronic Hepatitis B" is a long-lasting infection of the liver caused by the hepatitis B virus, defined by the persistence of the virus for six months or more. It is typically diagnosed through detection of hepatitis B surface antigen (HBsAg) in the blood.

"Decompensated Liver Disease" is a severe stage of chronic liver disease characterized by the presence of complications such as variceal bleeding, ascites, hepatic encephalopathy, or abnormal liver function tests. It indicates a failure of the liver to perform its normal metabolic and synthetic functions.

"Hepatitis B surface Antigen (HBsAg)" is a surface antigen of the hepatitis B virus; its presence indicates active infection.

"Hepatic Encephalopathy" is a decline in brain function that occurs as a result of severe liver disease. It can lead to symptoms like confusion and poor coordination.

"Hepatitis B Flare" is a sudden increase in liver inflammation, typically measured by a rise in alanine aminotransferase (ALT) levels, in a person with chronic hepatitis B.

"Hepatitis B Virus Reactivation" is a sudden increase in hepatitis B virus in the bloodstream, which can occur spontaneously or as a result of medical or immunological triggers.

"Direct-acting antivirals (DAAs)" are a group of medications used to treat hepatitis C. They directly target the hepatitis C virus to stop it from making copies of itself.

"Immunosuppressive or Cytotoxic Therapy" are treatments that reduce the activity of the body's immune system, often used in conditions like cancer and autoimmune diseases.

"International Normalized Ratio (INR)" is a standardized measurement of the time it takes for blood to clot. It's used to monitor and adjust dosing of anticoagulant therapy.

"Lamivudine-resistance" arises when the hepatitis B virus mutates after exposure to the antiviral drug lamivudine over a prolonged period. These mutations enable the virus to resist the effects of the drug, leading to an increase in viral replication and potentially resulting in the failure of lamivudine treatment.

"Prophylaxis" is the prevention of disease. In this context, Vemlidy is being used to prevent the reactivation or reinfection of the hepatitis B virus.

"Variceal Bleeding" refers to bleeding from enlarged veins (varices) usually found in the esophagus or stomach. It is a serious complication of liver cirrhosis.

Medical Necessity Criteria for Initial Authorization

The Plan considers Vemlidy (tenofovir alafenamide) medically necessary when ALL the following criteria are met for the applicable indication listed below:

Treatment of chronic hepatitis B virus infection

1. The member is 6 years of age or older and weighing at least 25 kg; *AND*
2. The member has a documented diagnosis of chronic hepatitis B virus (HBV) infection, confirmed by appropriate laboratory test(s); *AND*

3. If coinfected with HIV or chronic HCV, the member meets ONE of the following:
    a. The member has hepatitis B and HIV coinfection AND will be or is currently receiving a fully suppressive antiretroviral ARV treatment regimen for HIV*; or*
    b. The member is coinfected with hepatitis B and chronic HCV and will be or is currently receiving a hepatitis C direct-acting antiviral (DAA) therapy*; AND*
4. The member meets ONE (1) of the following conditions:
    a. The member has tried and failed treatment with entecavir (Baraclude), OR has a documented intolerance or contraindication to entecavir (Baraclude); *or*
    b. The prescriber has provided a clinical rationale for why entecavir is not appropriate and Vemlidy (tenofovir alafenamide) is necessary, which may include but is not limited to:
        i. Specific member characteristics or comorbidities (e.g., kidney impairment, pregnancy); *or*
        ii. Specific drug interactions that preclude the use of entecavir (Baraclude); *or*
        iii. Other compelling clinical reasons unique to the member's situation; *or*
        iv. The member has a strain known to have lamivudine resistance variants; *AND*
    c. The member has been previously treated with tenofovir disoproxil fumarate (TDF, Viread) and is being switched to Vemlidy due to tolerability or safety concerns; *AND*
5. The member does NOT have decompensated (Child-Pugh B or C) liver disease; *AND*
6. Chart documentation and supporting laboratory work are provided for review to substantiate the above listed requirements.

<u>Hepatitis B Virus Reactivation Prophylaxis</u>

1. The member is 18 years of age or older*; AND*
2. Prescribed by or in consultation with an oncologist, gastroenterologist, hepatologist, infectious disease specialist, transplant specialist, or those with experience managing hepatitis B virus reactivation prophylaxis*; AND*
3. Vemlidy (tenofovir alafenamide) is being used for prophylaxis against hepatitis B reactivation*; AND*
4. The member fulfills ONE (1) of the following conditions:
    a. Is anti-HBc-positive, HBsAg-positive AND are undergoing immunosuppressive or cytotoxic therapy (see moderate-to-high risk assessment per the American Gastroenterology Association (AGA) guidelines, Table 1 in the Appendix)*; or*
    b. Is anti-HBc-positive, HBsAg-negative AND are undergoing stem cell transplantation or receiving anti-CD20 therapy such as rituximab OR immunosuppressive or cytotoxic therapy (see moderate-to-high risk assessment per the AGA guidelines, Table 1 in the Appendix)t*; AND*
5. The member is not currently experiencing a Hepatitis B flare; AND
6. The member does not have decompensated (Child-Pugh B or C) liver disease; AND
7. If coinfected with HIV or chronic HCV, the member meets ONE of the following:

a. The member has hepatitis B and HIV coinfection AND is receiving a fully suppressive antiretroviral treatment regimen for HIV*; or*
b. The member is coinfected with hepatitis B and chronic HCV and is currently receiving a hepatitis C direct-acting antiviral therapy*; AND*

8. Chart documentation and supporting laboratory work are provided for review to substantiate the above listed requirements.

Hepatitis B Virus Reinfection Prophylaxis Post Liver Transplant

1. The member is 18 years of age or older*; AND*
2. Prescribed by or in consultation with a gastroenterologist, hepatologist, infectious disease specialist, or transplant specialist*; AND*
3. Vemlidy (tenofovir alafenamide) is being used for prophylaxis against HBV reinfection*; AND*
4. The member has a documented history of Hepatitis B infection and has undergone a liver transplant*; AND*
5. The member does not have decompensated (Child-Pugh B or C) liver disease*; AND*
6. If coinfected with HIV or chronic HCV, the member meets ONE of the following:
    a. The member has hepatitis B and HIV coinfection AND will be or is currently receiving a fully suppressive ARV treatment regimen for HIV*; or*
    b. The member is coinfected with hepatitis B and chronic HCV AND will be or is currently receiving a hepatitis C DAA therapy*; AND*
7. The member does not have contraindications to Vemlidy (tenofovir alafenamide)*; AND*
8. Chart documentation and supporting laboratory work are provided for review to substantiate the above listed requirements.

If the above prior authorization criteria are met, Vemlidy (tenofovir alafenamide) will be approved for up to 6 months.

Medical Necessity Criteria for Reauthorization

Reauthorization of up to 12 months will be granted if the following criteria are met:

For Treatment of Chronic Hepatitis B Virus Infection:

1. The member continues to meet all applicable Medical Necessity Criteria for Initial Authorization*; AND*
2. The member has documented clinical improvement, or maintenance, in disease activity, as evidenced by ANY of the following parameters:
    a. Reduction in HBV DNA levels*; or*
    b. Loss or reduction of HBeAg or HBsAg*; or*
    c. Normalization of ALT levels*; AND*
3. If coinfected with HIV or chronic HCV, the member continues to receive an effective treatment regimen for these conditions*; AND*

4. Chart documentation and supporting laboratory work are provided for review to substantiate the above listed requirements.

For Hepatitis B Virus Reactivation Prophylaxis:

1. The member continues to meet all applicable Medical Necessity Criteria for Initial Authorization*; AND*
2. The member has no evidence of Hepatitis B reactivation*; AND*
3. If coinfected with HIV or chronic HCV, the member continues to receive an effective treatment regimen for these conditions*; AND*
4. Chart documentation and supporting laboratory work are provided for review to substantiate the above listed requirements.

For Hepatitis B Virus Reinfection Prophylaxis Post Liver Transplant:

1. The member continues to meet all applicable Medical Necessity Criteria for Initial Authorization*; AND*
2. The member shows no signs of Hepatitis B virus reinfection*; AND*
3. If coinfected with HIV or chronic HCV, the member continues to receive an effective treatment regimen for these conditions*; AND*
4. Chart documentation and supporting laboratory work are provided for review to substantiate the above listed requirements.

Experimental or Investigational / Not Medically Necessary

Vemlidy (tenofovir alafenamide) for any other indication is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven.

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Appendix

Table 1: American Gastroenterology Association Risk Classification for Hepatitis B Virus Reactivation

	Low risk (<1%)	Moderate Risk (1-10%)	High Risk (>10%)
HBsAg positive	• Corticosteroid therapy (≤ 1 week, dose: low, moderate or high) ↔ • Intra-articular corticosteroid therapy	• Anti-T cell therapy • Corticosteroid therapy (Duration ≥ 4 weeks, dose: low)	• Anthracycline derivatives • Anti-TNF therapy • Anti-IL 6 therapy • B cell-depleting agents • CAR-T cell therapy • Cytokine/integrin inhibitors • TACE • JAK inhibitor therapy • HCV co-infection undergoing DAA therapy • Corticosteroids (Duration ≥ 4 weeks, dose: moderate/high) ↔
HBsAg negative; anti-HBc positive	• Immune checkpoint inhibitors • Anti-TNF therapy • HCV co-infection undergoing DAA therapy • Corticosteroids (Duration≥ 4 weeks,	• Anthracycline derivatives • Anti-IL 6 therapy • Anti-T cell therapy • CAR-T cell therapy • Cytokine/integrin inhibitors • TKI therapy	• B cell-depleting agents

	dose: low) ● Intra-articular corticosteroid therapy ● Corticosteroid therapy (≤ 1 week, dose: low, moderate or high) ↔	● JAK inhibitor therapy ● TACE ● Corticosteroids (Duration ≥ 4 weeks, dose: moderate/high) ↔	

TNF, tumor necrosis factor; HCV, hepatitis C virus; DAA, direct acting antiviral agent(s); IL-6, interleuken-6; TKI, tyrosine kinase inhibitors; JAK, janus kinase; TACE, transcatheter arterial chemoembolization.
↔ Glucocorticoids (prednisone or equivalent): low dose, <10 mg; moderate dose, 10-20 mg; high dose > 20 mg.
A note on duration of use: Antiviral prophylaxis should be started before the start of the risk-imposing therapy and continued for at least 6 months after discontinuation of risk-imposing therapy (at least 12 months for B cell-depleting agents).

Clinical Guideline Revision / History Information

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