Oscar Clinical Guideline: Vemlidy (tenofovir alafenamide) (PG010, Ver. 8)

Vemlidy (tenofovir alafenamide)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

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 Vemlidy [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.

"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.

"Documentation" refers to written information, including but not limited to:

- Up-to-date chart notes, relevant test results, and/or relevant imaging reports to support diagnoses; or
- Prescription claims records, and/or prescription receipts to support prior trials of formulary alternatives.

"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.

"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.

"No evidence of" indicates that the reviewer has not identified any records of the specified item or condition within the submitted materials or claims history. In the absence of such evidence, the member is considered eligible. If any evidence of the item or condition is present upon review of the request, the member does not qualify.

"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.

"[s]" indicates state mandates may apply.

Clinical Indications

Medical Necessity Criteria for Clinical Review

General Medical Necessity Criteria

The Plan considers Vemlidy (tenofovir alafenamide) medically necessary when ALL the following criteria are met:

1. IF the member is coinfected with human immunodeficiency virus (HIV) or chronic hepatitis C virus (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*
2. The member meets ALL of the following:
    a. No evidence of decompensated (Child-Pugh B or C) liver disease*; and*
    b. No evidence of estimated creatinine clearance (CrCl) below 15 mL per minute and is not receiving chronic hemodialysis*; AND*
3. Vemlidy (tenofovir alafenamide) is being prescribed at a dose and frequency that is within FDA approved labeling OR is supported by compendia or evidence-based published dosing guidelines for the requested indication*; AND*

The requested medication is being used within the Plan's Quantity Limit of: 30 tablets every 30 days.

4. The member meets the applicable Medical Necessity Criteria for Initial Clinical Review or Subsequent Clinical Review listed below.

Medical Necessity Criteria for Initial Authorization

Initial Indication-Specific Criteria

Chronic Hepatitis B Virus (HBV) Infection

The Plan considers Vemlidy (tenofovir alafenamide) medically necessary when ALL the following criteria are met:

5. The member meets the above General Medical Necessity Criteria; *AND*
6. The member is 6 years of age or older and weighing at least 25 kg; *AND*
7. The member has a documented diagnosis of chronic hepatitis B virus (HBV) infection, confirmed by appropriate laboratory test(s); *AND*
8. 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)[s]; *or*
    b. The prescriber has provided a clinical rationale for why entecavir (Baraclude) 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/renal impairment, pregnancy); *or*
        ii. Specific drug interactions that preclude the use of entecavir (Baraclude); *or*
        iii. The member has a strain known to have lamivudine resistance variants; *or*
        iv. Prior lamivudine exposure*; or*
        v. Other compelling clinical reasons unique to the member's situation; *or*
    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.

If the above prior authorization criteria are met, the requested product will be approved for up to 6 months.[s]

Hepatitis B Virus (HBV) Reactivation Prophylaxis

The Plan considers Vemlidy (tenofovir alafenamide) medically necessary when ALL the following criteria are met:

5. The member meets the above General Medical Necessity Criteria; *AND*
6. The member is 18 years of age or older*; AND*

7. The medication is 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*
8. Vemlidy (tenofovir alafenamide) is being used for prophylaxis against hepatitis B reactivation*; AND*
9. The member meets 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 A)*; 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 A)*; AND*
10. No evidence the member is currently experiencing a Hepatitis B flare.

If the above prior authorization criteria are met, the requested product will be approved for up to 6 months.[s]

Hepatitis B Virus (HBV) Reinfection Prophylaxis Post Liver Transplant

The Plan considers Vemlidy (tenofovir alafenamide) medically necessary when ALL the following criteria are met:

5. The member meets the above General Medical Necessity Criteria; *AND*
6. The member is 18 years of age or older*; AND*
7. Prescribed by or in consultation with a gastroenterologist, hepatologist, infectious disease specialist, or transplant specialist*; AND*
8. Vemlidy (tenofovir alafenamide) is being used for prophylaxis against HBV reinfection*; AND*
9. The member has a documented history of BOTH of the following:
    a. Hepatitis B infection*; AND*
    b. Has undergone a liver transplant.
10. No evidence the member has contraindications to Vemlidy (tenofovir alafenamide).

If the above prior authorization criteria are met, the requested product will be approved for up to 6 months.[s]

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Indication-Specific Criteria

Chronic Hepatitis B Virus (HBV) Infection

The Plan considers Vemlidy (tenofovir alafenamide) medically necessary when ALL the following criteria are met:

1. The member meets the above applicable General Medical Necessity Criteria and/or Initial Clinical Review; *AND*
2. The member has documented clinical improvement from baseline or maintenance of disease activity as evidenced by ONE of the following:
    a. Decrease or normalization of serum aminotransferases (ALT or AST) levels*; or*
    b. Loss or reduction of HBeAg or HBsAg*; or*
    c. Minimal histologic evidence of liver injury*; or*
    d. Reduction, suppression, or undetectable levels of serum HBV DNA levels.

If the above reauthorization criteria are met, the requested product will be authorized for up to 12-months.[s]

Hepatitis B Virus (HBV) Reactivation Prophylaxis

The Plan considers Vemlidy (tenofovir alafenamide) medically necessary when ALL the following criteria are met:

1. The member meets the above applicable General Medical Necessity Criteria and/or Initial Clinical Review; *AND*
2. The member has no evidence of Hepatitis B reactivation.

If the above reauthorization criteria are met, the requested product will be authorized for up to 12-months.[s]

Hepatitis B Virus (HBV) Reinfection Prophylaxis Post Liver Transplant

The Plan considers Vemlidy (tenofovir alafenamide) medically necessary when ALL the following criteria are met:

1. The member meets the above applicable General Medical Necessity Criteria and/or Initial Clinical Review; *AND*
2. The member has no evidence of Hepatitis B virus reinfection.

If the above reauthorization criteria are met, the requested product will be authorized for up to 12-months.[s]

Experimental / Investigational, or unproven[s]

Vemlidy (tenofovir alafenamide) for any other use is considered experimental, investigational, or unproven.

References

1. Agarwal K, Brunetto M, Seto WK, et al. 96 weeks treatment of tenofovir alafenamide vs. tenofovir disoproxil fumarate for hepatitis B virus infection. J Hepatol. 2018 Apr;68(4):672-681. doi: 10.1016/j.jhep.2017.11.039. Epub 2018 Jan 17.
2. Agarwal K, Fung SK, Nguyen TT, et al. Twenty-eight day safety, antiviral activity, and pharmacokinetics of tenofovir alafenamide for treatment of chronic hepatitis B infection. J Hepatol. 2015 Mar;62(3):533-40. doi: 10.1016/j.jhep.2014.10.035. Epub 2014 Oct 30.
3. Ali FS, Nguyen MH, Hernaez R, et al. AGA Clinical Practice Guideline on the Prevention and Treatment of Hepatitis B Virus Reactivation in At-Risk Individuals. Gastroenterology. 2025 Feb;168(2):267-284. doi: 10.1053/j.gastro.2024.11.008.
4. AS Lok et al. Antiviral therapy for chronic hepatitis B viral infection in adults: a systematic review and meta-analysis. Hepatology 2016; 63:284.
5. Buti M, Lim YS, Chan HLY, et al. Eight-year efficacy and safety of tenofovir alafenamide for treatment of chronic hepatitis B virus infection: Final results from two randomised phase 3 trials. Aliment Pharmacol Ther. 2024 Dec;60(11-12):1573-1586. doi: 10.1111/apt.18278. Epub 2024 Sep 27.
6. Byun KS, Choi J, Kim JH, et al. Tenofovir Alafenamide for Drug-Resistant Hepatitis B: A Randomized Trial for Switching From Tenofovir Disoproxil Fumarate. Clin Gastroenterol Hepatol. 2022 Feb;20(2):427-437.e5. doi: 10.1016/j.cgh.2021.04.045. Epub 2021 May 4.
7. Chan HLY, Buti M, Lim YS, et al. Long-Term Treatment With Tenofovir Alafenamide for Chronic Hepatitis B Results in High Rates of Viral Suppression and Favorable Renal and Bone Safety. Am J Gastroenterol. 2024 Mar 1;119(3):486-496. doi: 10.14309/ajg.0000000000002468. Epub 2023 Aug 9.
8. Chan HL, Fung S, Seto WK, et al. Tenofovir alafenamide versus tenofovir disoproxil fumarate for the treatment of HBeAg-positive chronic hepatitis B virus infection: a randomised, double-blind, phase 3, non-inferiority trial. Lancet Gastroenterol Hepatol. 2016 Nov;1(3):185-195. doi: 10.1016/S2468-1253(16)30024-3. Epub 2016 Sep 22. Erratum in: Lancet Gastroenterol Hepatol. 2016 Nov;1(3):e2. doi: 10.1016/S2468-1253(16)30130-3.
9. Choi WM, Choi J, Lim YS. Effects of Tenofovir vs Entecavir on Risk of Hepatocellular Carcinoma in Patients With Chronic HBV Infection: A Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol. 2021 Feb;19(2):246-258.e9. doi: 10.1016/j.cgh.2020.05.008. Epub 2020 May 11.
10. Choi WM, Yip TC, et al. Hepatocellular carcinoma risk in patients with chronic hepatitis B receiving tenofovir- vs. entecavir-based regimens: Individual patient data meta-analysis. J Hepatol. 2023 Mar;78(3):534-542. doi: 10.1016/j.jhep.2022.12.007. Epub 2022 Dec 23.
11. E Murakami et al. Implications of efficient hepatic delivery by tenofovir alafenamide (GS-7340) for hepatitis B virus therapy. Antimicrob Agents Chemother 2015; 59:3563.
12. European Association for the Study of the Liver. EASL Clinical Practice Guidelines on the management of hepatitis B virus infection. J Hepatol. 2025 May 8:S0168-8278(25)00174-6. doi: 10.1016/j.jhep.2025.03.018. Epub ahead of print.
13. Ghany MG, Pan CQ, Lok AS, Feld JJ, Lim JK, Wang SH, Kim AY, Tang AS, Nguyen MH, Naggie S, Sulkowski MS, Norberto RB, Chen J, Murad MH, Mohammad KS, Terrault NA. AASLD ISDA Practice Guideline on treatment of chronic hepatitis B. Hepatology. 2026 Apr 1;83(4):974-997. doi: 10.1097/HEP.0000000000001549. Epub 2025 Nov 4. PMID: 41186418.
14. Guidelines for the prevention, diagnosis, care and treatment for people with chronic hepatitis B infection [Internet]. Geneva: World Health Organization; 2024 Mar. PMID: 40424433.
15. HLY Chan et al. Tenofovir alafenamide versus tenofovir disoproxil fumarate for the treatment of HBeAg-positive chronic hepatitis B virus infection: a randomised, double-blind, phase 3, non-inferiority trial. Lancet Gastroenterol Hepatol 2016; 1:185.
16. Inada K, Kaneko S, Kurosaki M, et al. Tenofovir alafenamide for prevention and treatment of hepatitis B virus reactivation and de novo hepatitis. JGH Open. 2021 Aug 19;5(9):1085-1091. doi: 10.1002/jgh3.12636.

17. Izumi T, Toshima T, Itoh S, et al. Novel protocol for prevention from hepatitis B reactivation following living-donor liver transplantation. Hepatol Res. 2024 Sep 14. doi: 10.1111/hepr.14110. Epub ahead of print.
18. KK Mugwanya et al. Pre-exposure prophylaxis use by breastfeeding HIV-uninfected women: a prospective short-term study of antiretroviral excretion in breast milk and infant absorption. PLoS Med 2016 September 27 (epub).
19. Kumar M, Satapathy S. A randomized controlled trial of lamivudine to treat acute hepatitis B. Hepatology. 2007;45(1):97.
20. Lim J, Choi WM, Shim JH, et al. Efficacy and safety of tenofovir alafenamide versus tenofovir disoproxil fumarate in treatment-naïve chronic hepatitis B. Liver Int. 2022 Jul;42(7):1517-1527. doi: 10.1111/liv.15261. Epub 2022 Apr 3.
21. M Buti et al. Tenofovir alafenamide versus tenofovir disoproxil fumarate for the treatment of patients with HBeAg-negative chronic hepatitis B virus infection: a randomised, double-blind, phase 3, non-inferiority trial. Lancet Gastroenterol Hepatol 2016; 1:196.
22. NA Terrault et al. AASLD guidelines for treatment of chronic hepatitis B. Hepatology 2016; 63:261.
23. P Martin et al. A treatment algorithm for the management of chronic hepatitis B virus infection in the United States: 2015 update. Clin Gastroenterol Hepatol 2015; 13:2071.
24. PJ Ruane et al. Antiviral activity, safety, and pharmacokinetics/pharmacodynamics of tenofovir alafenamide as 10-day monotherapy in HIV-1-positive adults. J Acquir Immune Defic Syndr 2013; 63:449.
25. Rashidi-Alavijeh J, Straub K, Achterfeld A, Wedemeyer H, Willuweit K, Herzer K. Safety and efficacy of tenofovir alafenamide in liver transplant recipients: a single center experience. Transpl Infect Dis. 2021;23(3):e13522. doi:10.1111/tid.13522
26. Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. Hepatology. 2018;67(4):1560-1599. doi:10.1002/hep.29800
27. Tran TT, Ahn J, Reau NS. ACG Clinical Guideline: Liver Disease and Pregnancy. Am J Gastroenterol. 2016;111(2):176-194. doi: 10.1038/ajg.2015.430.
28. Vemlidy (tenofovir alafenamide) [prescribing information]. Foster City, CA: Gilead Sciences Inc; March 2024.
29. Vemlidy (tenofovir alafenamide) [prescribing information]. Foster City, CA: Gilead Sciences Inc; March 2024.
30. World Health Organization. Guidelines for the prevention, diagnosis, care and treatment for people with chronic hepatitis B infection [Internet]. 2024 [Accessed September 2024]. Available from: https://www.who.int/publications/i/item/9789240090903.

Appendix A

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

	Low risk (<1%)	Moderate Risk (1-10%)	High Risk (>10%)
			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, dose: low) • Intra-articular corticosteroid therapy • Corticosteroid therapy (≤ 1 week, dose: low, moderate or high) ↔	• Anthracycline derivatives • Anti-IL 6 therapy • Anti-T cell therapy • CAR-T cell therapy • Cytokine/integrin inhibitors • TKI therapy • JAK inhibitor therapy • TACE • Corticosteroids (Duration ≥ 4 weeks, dose: moderate/high) ↔	• B cell-depleting agents
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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