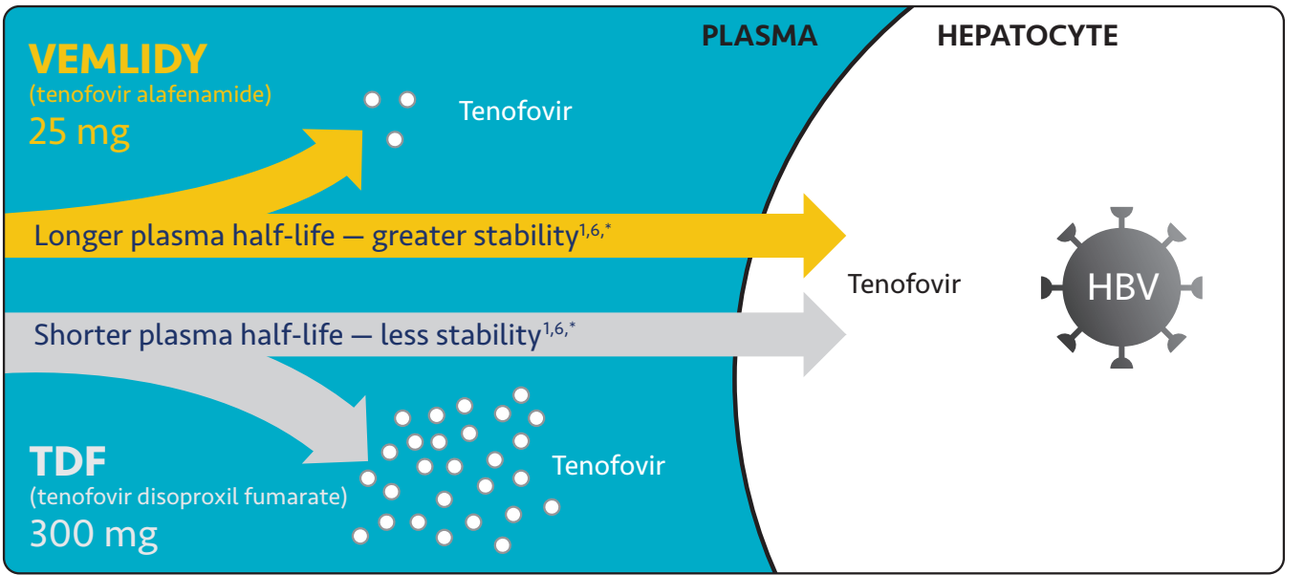
Vemlidy®
tenofovir alafenamide 25mg tablets

VEMLIDY is a novel, targeted prodrug of tenofovir for the treatment of chronic hepatitis B in adults with compensated liver disease[1]

Due to enhanced plasma stability, VEMLIDY demonstrates more efficient delivery of tenofovir to hepatocytes vs tenofovir disoproxil fumarate (TDF).[1-6]

- A 25-mg oral dose of tenofovir alafenamide (TAF) in VEMLIDY resulted in 89% lower plasma concentrations of tenofovir vs a 300-mg oral dose of TDF, thereby reducing systemic exposure[3,6]



*Plasma half-life: VEMLIDY=30.6 minutes (0.51 hour)[1]; TDF=0.41 minutes.[6]

89% **LOWER CONCENTRATIONS OF TENOFOVIR IN PLASMA VS TDF, RESULTING IN REDUCED SYSTEMIC EXPOSURE[3,6]**

INDICATION

VEMLIDY is indicated for the treatment of chronic hepatitis B virus (HBV) infection in adults with compensated liver disease.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: POSTTREATMENT SEVERE ACUTE EXACERBATION OF HEPATITIS B

- **Discontinuation of anti-hepatitis B therapy, including VEMLIDY, may result in severe acute exacerbations of hepatitis B. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who discontinue anti-hepatitis B therapy, including VEMLIDY. If appropriate, resumption of anti-hepatitis B therapy may be warranted.**

Click here for VEMLIDY full Prescribing Information, including **BOXED WARNING**.

VEMLIDY is a **PREFERRED/FIRST-LINE** HBV therapy for chronic HBV patients according to AASLD, AATA, and EASL guidelines[7-9]

Tenofovir alafenamide is more stable than TDF in plasma and delivers the active metabolite to hepatocytes more efficiently, allowing a lower dose to be used with similar antiviral activity, [and] less systemic exposure...

— AASLD 2018 Hepatitis B Guidance[7]

IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions

- **Risk of Development of HIV-1 Resistance in HBV/HIV-1 Coinfected Patients:** Due to this risk, VEMLIDY alone should not be used for the treatment of HIV-1 infection. Safety and efficacy of VEMLIDY have not been established in HBV/HIV-1 coinfected patients. HIV antibody testing should be offered to all HBV-infected patients before initiating therapy with VEMLIDY, and, if positive, an appropriate antiretroviral combination regimen that is recommended for HBV/HIV-1 coinfected patients should be used.
- **New Onset or Worsening Renal Impairment:** Cases of acute renal failure and Fanconi syndrome have been reported with the use of tenofovir prodrugs. In clinical trials of VEMLIDY, there have been no cases of Fanconi syndrome or proximal renal tubulopathy (PRT). Patients with impaired renal function and/or taking nephrotoxic agents (including NSAIDs) are at increased risk of renal-related adverse reactions. Discontinue VEMLIDY in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome. Monitor renal function in all patients – See Dosage and Administration.
- **Lactic Acidosis and Severe Hepatomegaly with Steatosis:** Fatal cases have been reported with the use of nucleoside analogs, including tenofovir DF. Discontinue VEMLIDY if clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity develop, including hepatomegaly and steatosis in the absence of marked transaminase elevations.

Adverse Reactions

Most common adverse reactions (incidence ≥5%; all grades) were headache, abdominal pain, cough, back pain, fatigue, nausea, arthralgia, diarrhea, and dyspepsia.

Drug Interactions

- Coadministration of VEMLIDY with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of tenofovir and the risk of adverse reactions.
- Coadministration of VEMLIDY is not recommended with the following: oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifampin, rifapentine, or St. John's wort. Such coadministration is expected to decrease the concentration of tenofovir alafenamide, reducing the therapeutic effect of VEMLIDY. Drugs that strongly affect P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP) activity may lead to changes in VEMLIDY absorption.

Consult the full prescribing information for VEMLIDY for more information on potentially significant drug interactions, including clinical comments.

Dosage and Administration

- **Testing Prior to Initiation:** HIV infection.
- **Prior to or when initiating, and during treatment:** On a clinically appropriate schedule, assess serum creatinine, estimated creatinine clearance, urine glucose, and urine protein in all patients. In patients with chronic kidney disease, also assess serum phosphorus.
- **Dosage in Adults:** 1 tablet taken once daily with food.
- **Renal Impairment:** Not recommended in patients with end stage renal disease (ESRD; eCrCl <15 mL/min) who are not receiving chronic hemodialysis; in patients on chronic hemodialysis, on hemodialysis days, administer VEMLIDY after completion of hemodialysis treatment.
- **Hepatic Impairment:** Not recommended in patients with decompensated (Child-Pugh B or C) hepatic impairment.

Click here for VEMLIDY Prescribing Information, including **BOXED WARNING** on **posttreatment severe acute exacerbation of hepatitis B**.

AASLD=American Association for the Study of Liver Diseases; AATA=Asian American Treatment Algorithm (also referred to as an Expert Consensus for the Management of Chronic Hepatitis B in Asian Americans); EASL=European Association for the Study of the Liver.

References: 1. VEMLIDY Prescribing Information, Foster City, CA: Gilead Sciences, Inc; February 2020. **2.** Buti M, Gane E, Seto WK, 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;1:196-206. **3.** Chan H L, 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;1:185-195. **4.** 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;62:533-540. **5.** Murakami E, Wang T, Park Y, et al. Implications of efficient hepatic delivery by tenofovir alafenamide (GS-7340) for hepatitis B virus therapy. *Antimicrob Agents Chemother.* 2015;59:3563-3569. **6.** Lee WA, He G-X, Eisenberg E, et al. Selective intracellular activation of a novel prodrug of the human immunodeficiency virus reverse transcriptase inhibitor tenofovir leads to preferential distribution and accumulation in lymphatic tissue. *Antimicrob Agents Chemother.* 2005;49:1898-1906. **7.** 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;67:1560-1599. **8.** Tong MJ, Pan CQ, Han SB, et al. An expert consensus for the management of chronic hepatitis B in Asian Americans. Aliment Pharmacol Ther. 2018;47:1181-1200. **9.** EASL. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. *Hepatology.* 2017;67:370-398.

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