"Should I switch to VEMLIDY?"

A guide for speaking with your chronic hepatitis B patients who are considering VEMLIDY

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 on posttreatment severe acute exacerbation of hepatitis B**.

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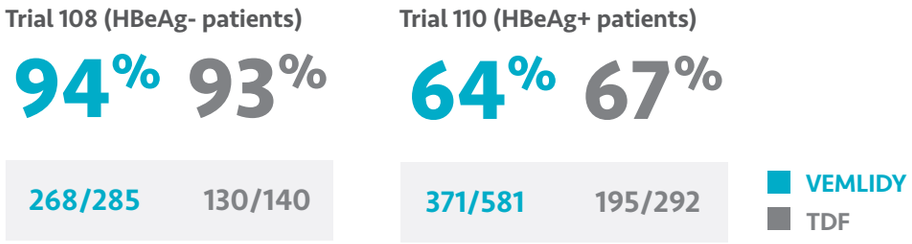
VEMLIDY has efficacy your patients can trust

Powerful antiviral efficacy in chronic hepatitis B patients with compensated liver disease, as demonstrated in clinical trials

Viral suppression (HBV DNA <29 IU/mL) at Week 48 in the pivotal trials[1-3]



Mean baseline plasma HBV DNA was 5.8 log_{10} IU/mL in Trial 108 and 7.6 log_{10} IU/mL in Trial 110.[1]

Primary efficacy endpoint: The proportion of patients with HBV DNA <29 IU/mL and noninferiority to TDF (10% margin; 95% CI approach) at Week 48 for both trials.[1-3]

Most common adverse reactions (incidence ≥5%; all grades) in clinical studies through Week 144 were headache, upper respiratory tract infection, abdominal pain, cough, back pain, arthralgia, fatigue, nausea, diarrhea, dyspepsia, and pyrexia.

Efficacy outcomes in virologically suppressed patients in the switch trial

Trial 4018

	Week 48[1,4]		Week 96[5]	
	Switched to VEMLIDY	Continued on TDF	Continued on VEMLIDY	Switched from TDF to VEMLIDY
HBV DNA ≥20 IU/mL	<1% (1/243)	<1% (1/245)	<1% (1/243)	<1% (1/245)
HBV DNA <20 IU/mL	96% (234/243)	96% (236/245)	95% (230/243)	94% (230/245)

At baseline, median duration of prior TDF treatment was 220 weeks (VEMLIDY) and 224 weeks (TDF).[1]

Primary efficacy endpoint: The proportion of patients with plasma HBV DNA ≥20 IU/mL and noninferiority to TDF (4% margin; 95% CI approach) at Week 48.[1,4]

Adverse reactions observed with VEMLIDY in Trial 4018 at Week 48 were similar to those in Trials 108 and 110 at Week 96. Adverse reactions reported in ≥2% of patients in either treatment group at Week 96: upper respiratory tract infection (5%) in VEMLIDY and TDF switch groups, arthralgia (2%) and back pain (2%) in the TDF switch group.[1,5]

Please see Trial Designs here.

VEMLIDY is a 25-mg pill taken once daily with food[1]

Same dose for patients with:

- Mild, moderate, or severe renal impairment (eCrCl ≥15 mL/min) or end stage renal disease (ESRD; eCrCl <15 mL/min) receiving chronic hemodialysis
  - Not recommended in patients with 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
- Mild hepatic impairment (Child-Pugh A)
  - Not recommended in patients with decompensated (Child-Pugh B or C) hepatic impairment

An important consideration for patients thinking about switching to VEMLIDY

- Explain to patients that VEMLIDY is more stable in plasma than TDF, reaching liver cells more efficiently and allowing for VEMLIDY to be given at one-tenth the dose[3,6]

CI=confidence interval; eCrCl=estimated creatinine clearance; HBeAg=hepatitis B envelope antigen; TDF=tenofovir disoproxil fumarate.

IMPORTANT SAFETY INFORMATION

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:** Postmarketing cases of renal impairment, including acute renal failure, proximal renal tubulopathy (PRT), and Fanconi syndrome have been reported with TAF-containing products. 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.

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VEMLIDY enables you to treat chronic hepatitis B with a reduced effect on renal and bone trial endpoints when compared to TDF

Renal effects of VEMLIDY and TDF were compared in Trials 108 and 110

- **Median change from baseline to Week 96 in $eGFR_{CG}$ was -1.2 mL/min in the VEMLIDY group** (n=790) **and -4.8 mL/min in those receiving TDF** (n=390)[1,5]

Median baseline $eGFR_{CG}$ was 106 mL/min and 105 mL/min for VEMLIDY and TDF, respectively.[1]

The long-term clinical significance of these renal laboratory changes on adverse reaction frequencies between VEMLIDY and TDF is not known.

- In Trials 108 and 110, mean changes from baseline in low-density lipoprotein cholesterol (LDL-C) (fasted) and triglycerides (TG) (fasted) were +7 mg/dL and +13 mg/dL for VEMLIDY, versus -10mg/dL and -7 mg/dL for TDF at Week 96[1]

IMPORTANT SAFETY INFORMATION

Warnings and Precautions (continued)

- **Lactic Acidosis and Severe Hepatomegaly with Steatosis:** Fatal cases have been reported with the use of nucleoside analogs, including tenofovir disoproxil fumarate (TDF). 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) in clinical studies through week 144 were headache, upper respiratory tract infection, abdominal pain, cough, back pain, arthralgia, fatigue, nausea, diarrhea, dyspepsia, and pyrexia.

AASLD=American Association for the Study of Liver Diseases; ALT=alanine aminotransferase; BMD=bone mineral density; $eGFR_{CG}$=estimated glomerular filtration rate by Cockcroft-Gault method, also referred to as eCrCl; ULN=upper limit of normal.

[a] Key inclusion criteria: HBV DNA ≥20,000 IU/mL; ALT >60 U/L for men and >38 U/L for women (≥2x ULN based on the 2016 AASLD criteria).[2,3]

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Impacts on spine and hip BMD with VEMLIDY and TDF were compared in Trials 108 and 110

- **BMD declines** (≥5%) **at the lumbar spine: 11%** (VEMLIDY) **vs 25%** (TDF) **at Week 96**[1]
- **BMD declines** (≥7%) **at the femoral neck: 5%** (VEMLIDY) **vs 13%** (TDF) **at Week 96**[1]
- **The mean percentage change in BMD from baseline to Week 96 was -0.7% with VEMLIDY** (n=746) **compared to -2.6% with TDF** (n=371) **at the lumbar spine, and -0.3%** (n=740) **compared to -2.5%** (n=369) **at the total hip**[1,5]

The long-term clinical significance of these BMD changes is not known.

Trial designs

Pivotal Trials: 108 and 110

The efficacy and safety of VEMLIDY 25 mg once daily in the treatment of chronic hepatitis B in adults with compensated liver disease were evaluated in 2 randomized, double-blind, active-controlled, noninferiority trials: Trial 108 (N=425 HBeAg- treatment-naïve and treatment-experienced patients) and Trial 110 (N=873 HBeAg+ treatment-naïve and treatment-experienced patients).[a] The primary efficacy endpoint for both trials was the proportion of patients with plasma HBV DNA levels below 29 IU/mL at Week 48.[1-3]

Switch Trial 4018

The efficacy and safety of switching from TDF 300 mg once daily to VEMLIDY 25 mg once daily in virologically suppressed adults with chronic hepatitis B infection were evaluated in a randomized, double-blind, active-controlled, noninferiority trial: Trial 4018 (N=488). Patients must have been taking TDF 300 mg once daily for ≥12 months, with HBV DNA less than the Lower Limit of Quantitation by local laboratory assessment for ≥12 weeks prior to screening and HBV DNA <20 IU/mL at screening. The primary efficacy endpoint was the proportion of patients with plasma HBV DNA ≥20 IU/mL at Week 48. Additional efficacy endpoints included the proportion of patients with HBV DNA <20 IU/mL. At Week 48, all patients who were randomized to TDF for the controlled portion of the trial were switched to VEMLIDY for the open-label extension through Week 96.[1,4,5]

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Important considerations for patients thinking about switching to VEMLIDY

- The efficacy data for VEMLIDY show it can treat their chronic hepatitis B **as effectively as TDF**[1]

- Talk to patients about how **their kidneys and bones may be affected by age and chronic hepatitis B**.[7-9] VEMLIDY has been shown in studies to have **less impact on kidney and bone safety parameters compared to TDF**[1]
  - The clinical significance of these changes is unknown

- Let commercially insured patients[a] concerned about cost know they may be eligible to reduce their out-of-pocket cost to **as little as $0 co-pay** (up to $6000 per year) through the VEMLIDY Co-pay Coupon Program

[a] Co-pay coupon support is available for commercially insured eligible patients only. Additional restrictions may apply. Subject to change; for full terms and conditions, visit www.mysupportpath.com/providers. This is not health insurance. Only accepted at participating pharmacies.

IMPORTANT SAFETY INFORMATION

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.

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

Addressing questions that may arise

Please see below for some potential questions from your patients, along with responses to help start the conversation. These have been developed with the help of leading clinicians who have a lot of experience prescribing VEMLIDY.

"Why do you want to switch me to VEMLIDY now? Does this mean my hepatitis is getting worse?" Your chronic hepatitis B is well controlled for now, but hepatitis B is a chronic condition, so we need to consider all of the effects of treatment. VEMLIDY has been proven effective, with a demonstrated safety profile in many patients, which is why VEMLIDY might be a good option for you now.[1]

"Does this mean I've been on the wrong treatment all along?" Your current treatment has been working well, but as patients get older, their kidney and bone health may become a bigger concern.[7,9] VEMLIDY is a newer medication than the drug you're currently taking. In clinical studies of VEMLIDY, it was shown to have less impact on kidney function lab tests and bone density compared to TDF.[1] That is one of the important reasons why I'm recommending a switch.

"Is there a program to help with payment?" Support Path® offers information and resources to help patients understand coverage and financial options. Visit www.mysupportpath.com/providers.

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Help ensure your patients get VEMLIDY

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VEMLIDY is a yellow, round, film-coated tablet. Tell your patients to let you know if they don't think they received VEMLIDY at the pharmacy. Also make sure they understand they should take VEMLIDY once daily with food.[1]

Due to enhanced plasma stability, VEMLIDY demonstrates[3]:

- More efficient delivery of tenofovir to hepatocytes vs TDF[6]
- Reduced systemic exposure, with 89% less tenofovir circulating in the plasma vs TDF[3]

VEMLIDY
Size 8 mm.
Pill image not to scale.

IMPORTANT SAFETY INFORMATION

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.

Pregnancy and Lactation

- **Pregnancy:** A pregnancy registry has been established for VEMLIDY. Available clinical trial data show no significant difference in the overall risk of birth defects for VEMLIDY compared with the background rate of major birth defects in the U.S. reference population.
- **Lactation:** TAF and tenofovir can pass into breast milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for VEMLIDY and any potential adverse effects on the breastfed infant from VEMLIDY or from the underlying maternal condition.

References: 1. VEMLIDY Prescribing Information, Foster City, CA: Gilead Sciences, Inc.; March 2024. **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 HLY, Fung S, Seto WK, et al; and the GS-US-320-0110 investigators. 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.** Lampertico P, Buti M, Fung S, et al. Switching from tenofovir disoproxil fumarate to tenofovir alafenamide in virologically suppressed patients with chronic hepatitis B: a randomised, double-blind, phase 3, multicentre non-inferiority study. *Lancet Gastroenterol Hepatol.* 2020;5:441-453. **5.** Data on file. Gilead Sciences, Inc. **6.** 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. **7.** Cooper C, Ferrari S, on behalf of the International Osteoporosis Foundation Board and Executive Committee. *IOF Compendium of Osteoporosis.* Nyon, Switzerland: International Osteoporosis Foundation; 2017. **8.** Nguyen MH, Lim JK, Ozbay AB, et al. Advancing age and comorbidity in a United States insured population-based cohort of patients with chronic hepatitis B. *Hepatology.* 2019;69:959-973. **9.** Stevens LA, Viswanathan G, Weiner DE. Chronic kidney disease and end-stage renal disease in the elderly population: current prevalence, future projections, and clinical significance. *Adv Chronic Kidney Dis.* 2010;17:293-301.

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