# *It's the moments that matter—choose 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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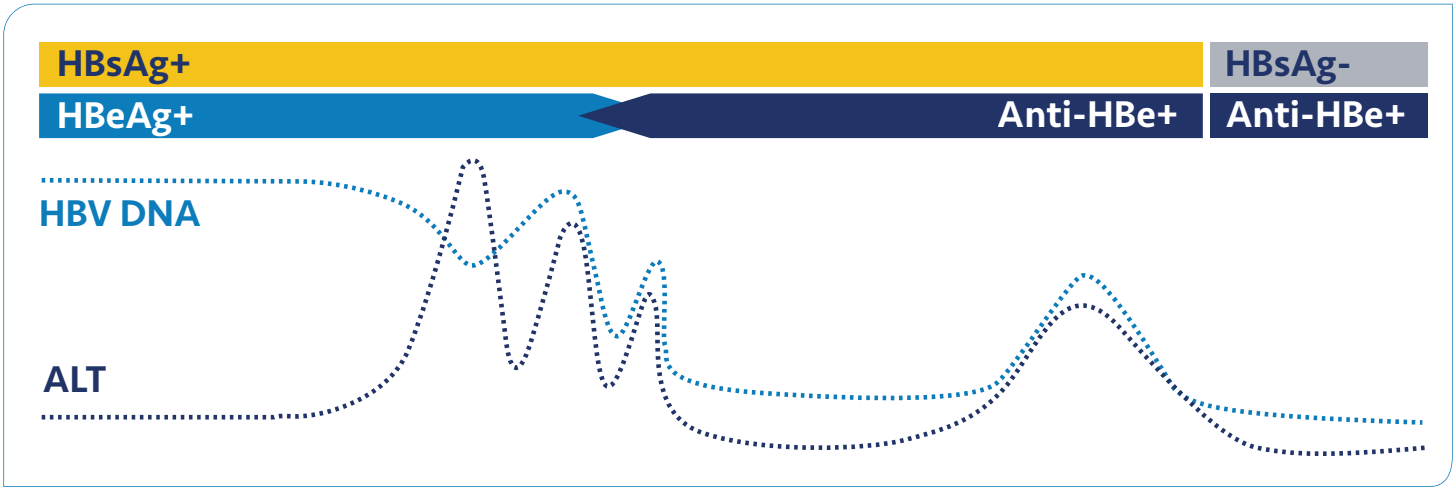
# *Chronic hepatitis B is characterized by serologic markers that relate to specific stages of disease*

| HBsAg | HBV DNA | HBeAg |
|---|---|---|
| Hallmark of infection that is used for screening and diagnosis[1] | Marker of infectivity and risk of major liver disease by tracking viral load and ongoing replication[1] | Associated with high viral load and may correlate with more active disease[2] |

## The phases of chronic hepatitis B[3]



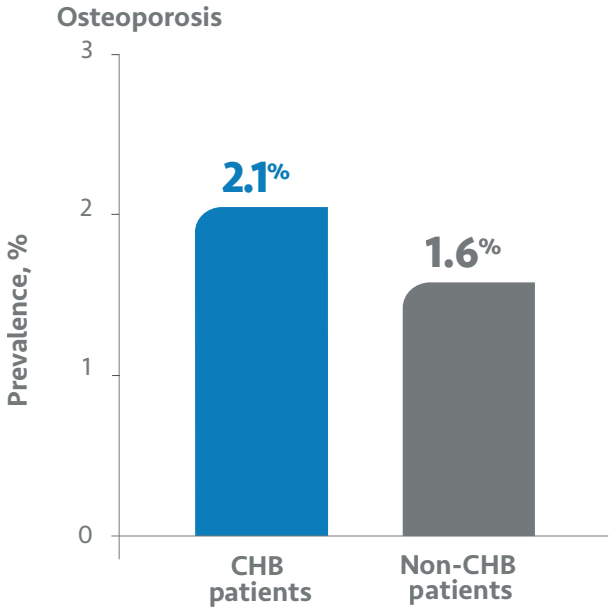

| Immune Tolerant (HBeAg+ chronic infection) | Immune Activation (HBeAg+ chronic hepatitis) | Low Replication (HBeAg- chronic infection) | Reactivation (HBeAg- chronic hepatitis) | Resolution (HBsAg- phase) |
|---|---|---|---|---|
| • Typically caused by perinatal infection[4]<br>• Can last several decades[4]<br>• Associated with very high HBV DNA levels but normal or slightly elevated ALT[4] | • Typically occurs in adolescence or young adulthood[5]<br>• May last for years[5]<br>• Associated with high HBV DNA and ALT[2] | • Marked by HBeAg seroconversion[1]<br>• Associated with low HBV DNA and normalized ALT[1] | • Can be caused by immunosuppression[4]<br>• Usually occurs in older patients with more advanced liver disease[4] | • Occurs in ≤2% of Western patients and <1% of Asians annually[5] |
| **Management considerations** | | | | |
| Risk of fibrosis, cirrhosis, or HCC, especially in patients >40 years with high ALT[1,5] | Potential fibrosis or cirrhosis[5,6] | Cirrhosis or other liver damage from prior phase[4] | Potential cirrhosis or HCC[4] | Potential reactivation[2] |

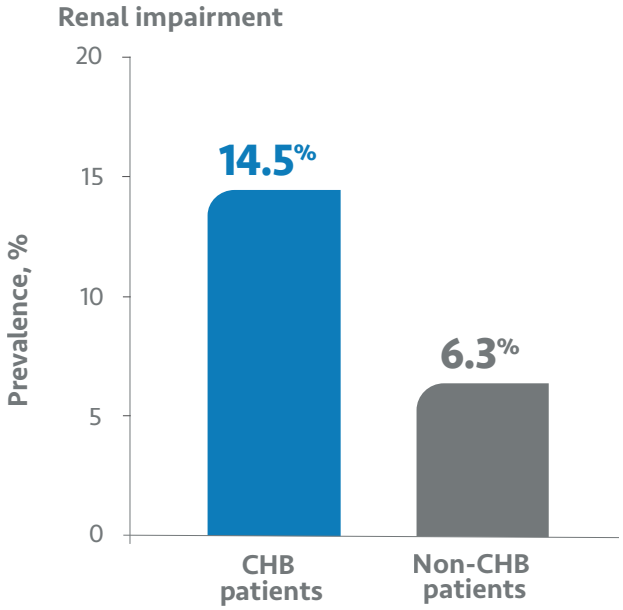
# *The health of patients with chronic hepatitis B can be compromised by comorbidities*[7,8]

## Prevalence of comorbidities

**Chronic hepatitis B patients, compared with the general population, have a higher risk of developing certain comorbidities, including diabetes, metabolic syndrome, and bone and renal conditions**[7-9]

**Proportions of chronic hepatitis B patients with comorbidities, compared with the rest of the population (Commercial, Medicare, and Medicaid, 2015)**[7,a]




**Other comorbidities included**[7]**:**

| Hypertension | Diabetes | Hyperlipidemia |
|---|---|---|
| 37.3% for patients with chronic hepatitis B and 35.8% for the rest of the population | 17.7% for patients with chronic hepatitis B and 15.1% for the rest of the population | 24.0% for patients with chronic hepatitis B and 26.4% for the rest of the population |

ALT=alanine aminotransferase; HBeAg=hepatitis B envelope antigen; HBsAg=hepatitis B surface antigen; HCC=hepatocellular carcinoma.

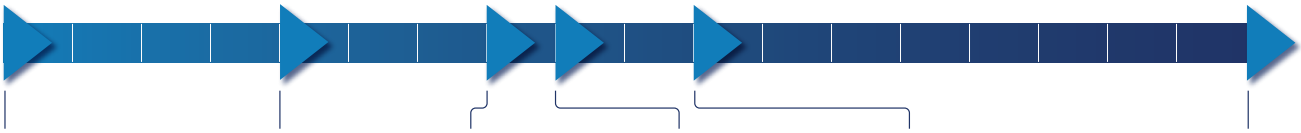
[a]Based on claims from national insurance databases covering Commercial, Medicare, and Medicaid beneficiaries (2006-2015) in 44,026 CHB patients and 121,568 non-CHB patients. The databases contained medical and pharmacy claims for healthcare services performed in both inpatient and outpatient settings. The 2015 cohort included 11,372 CHB patients and 32,110 non-CHB patients.[7]

# *VEMLIDY has been treating chronic hepatitis B since 2016[10]*

## Treatment has evolved over time

**VEMLIDY is the most recently approved oral antiviral for the treatment of chronic hepatitis B in adults with compensated liver disease**

**Timeline of FDA approvals: Oral antiviral treatments for chronic hepatitis B**



**1998** — **LAM** (lamivudine)[11]

**2002** — **ADV** (adefovir dipivoxil)[12]

**2005** — **ETV** (entecavir)[13]

**2006** — **LdT** (telbivudine)[14]

**2008** — **TDF** (tenofovir disoproxil fumarate)[15]

**2016** — **VEMLIDY** (tenofovir alafenamide)[10]


## 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.

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

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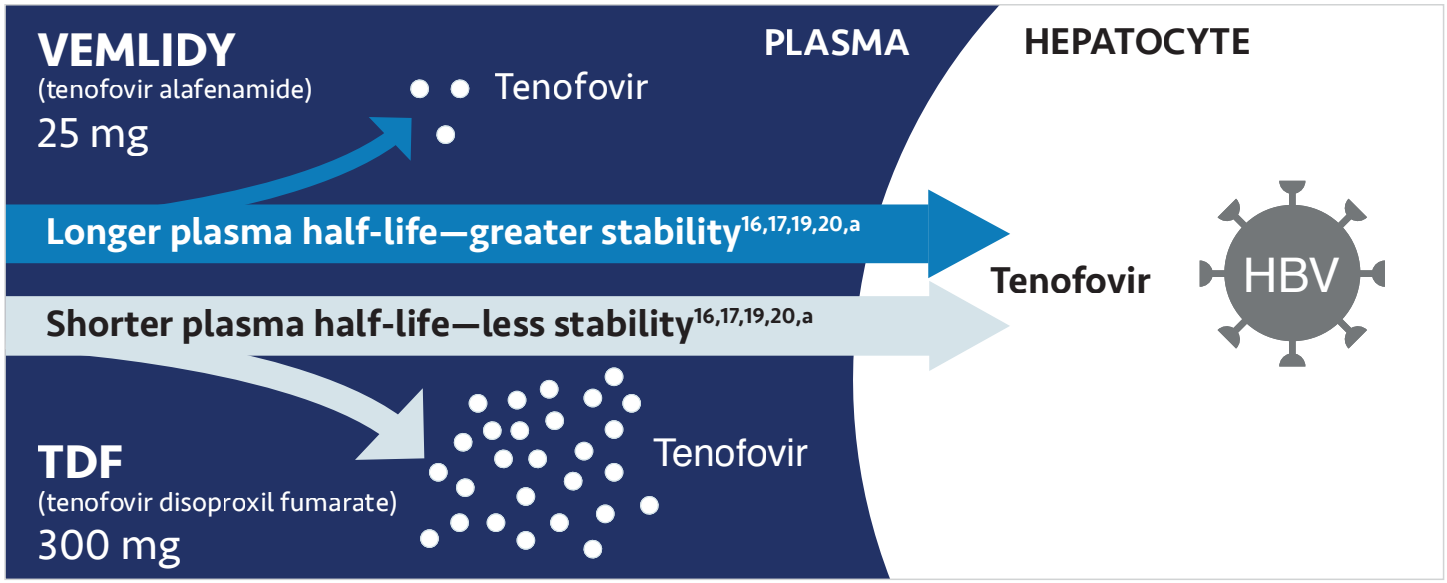
# *VEMLIDY optimizes tenofovir delivery to the hepatocyte*[16]

## A novel, targeted prodrug of tenofovir[17,18]

**Due to enhanced plasma stability, VEMLIDY demonstrates[18]:**

- More efficient delivery of tenofovir to the hepatocytes vs TDF[16]
- Reduced systemic exposure, with 89% less tenofovir circulating in the plasma vs TDF[18]




[a]Plasma half-life: VEMLIDY=30.6 minutes (0.51 hour); TDF=0.41 minutes.[17,19]

### 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.

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

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# *VEMLIDY is recommended by treatment guidelines*

## A recommended treatment option in many clinical situations

| Categories for treatment of adults with chronic hepatitis B | AASLD 2018[1] | AATA 2018[3] | EASL 2017[2] |
|---|---|---|---|
| **Initial/first-line** | A preferred treatment option for patients with immune-active disease | A recommended treatment option for HBeAg+ or HBeAg- patients with HBV DNA >2000 IU/mL and ALT >ULN | A preferred treatment option |
| **TDF alternative/switch** | A recommended treatment option for patients with TDF-associated renal dysfunction and/or bone disease | | A recommended switch option for patients who might develop or already have underlying renal and/or bone disease |
| **Substitution for entecavir, lamivudine, or telbivudine** | A recommended treatment option for patients experiencing virological breakthrough | | A recommended treatment option for patients experiencing resistance |
| **Hepatic/renal** | A preferred treatment option for patients with cirrhosis and viremia <2000 IU/mL | A recommended treatment option for patients with compensated cirrhosis and detectable HBV DNA | A recommended treatment option for HBsAg+ patients receiving dialysis or renal transplant |
| **Quotes on VEMLIDY** | **"[VEMLIDY] joins the list of preferred therapies"** | **"Based on [the]...safety profile and non-inferiority of efficacy endpoints, [VEMLIDY] represents an attractive alternative to TDF"** | **"In the two registrational TAF trials, [VEMLIDY] compared to TDF demonstrated superiority in...several markers of renal function...and bone turnover"** |

AASLD=American Association for the Study of Liver Diseases; AATA=Asian American Treatment Algorithm; EASL=European Association for the Study of the Liver; TAF=tenofovir alafenamide; ULN=upper limit of normal.

## 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.**

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# *VEMLIDY is a 25-mg pill taken once daily with food*[17]

## VEMLIDY is a pill that's 8 mm in diameter


Pill image not to scale.

**No recommended dosing change for patients with mild hepatic impairment (Child-Pugh A)**[17]

- Not recommended in patients with decompensated (Child-Pugh B or C) hepatic impairment

## The only oral antiviral for chronic hepatitis B *without* required renal dosage adjustment [13,17,21]

- Mild, moderate, or severe renal impairment (eCrCl ≥15 mL/min) or ESRD (eCrCl <15 mL/min) receiving chronic hemodialysis[17]
  - In patients on chronic hemodialysis, on hemodialysis days, administer VEMLIDY after completion of hemodialysis treatment[17]
  - VEMLIDY is not recommended in patients with ESRD who are not receiving chronic hemodialysis[17]

eCrCl=estimated creatinine clearance.

### 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.

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## VEMLIDY is:

- The most recently approved oral antiviral for the treatment of chronic hepatitis B in adults with compensated liver disease[10-15]
- A novel, targeted prodrug of tenofovir[17,18]
- A recommended option in multiple treatment guidelines[1-3]
- A 25-mg pill taken once daily with food[17]


## IMPORTANT SAFETY INFORMATION

### 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.

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

**References: 1.** 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. **2.** European Association for the Study of the Liver. EASL 2017 clinical practice guidelines on the management of hepatitis B virus infection. *J Hepatol*. 2017;67(2):370-398. DOI: 10.1016/j.jhep.2017.03.021. **3.** Tong MJ, Pan CQ, Han S-HB, et al. An expert consensus for the management of chronic hepatitis B in Asian Americans. *Aliment Pharmacol Ther*. 2018;47(8):1181-1200. DOI: 10.1111/apt.14577. **4.** Sarin SK, Kumar M, Lau GK, et al. Asian-Pacific clinical practice guidelines on the management of hepatitis B: a 2015 update. *Hepatol Int*. 2016;10(1):1-98. DOI: 10.1007/s12072-015-9675-4. **5.** Burns GS, Thompson AJ. Viral hepatitis B: clinical and epidemiological characteristics. *Cold Spring Harb Perspect Med*. 2014;4(12):a024935. DOI: 10.1101/cshperspect.a024935. **6.** Croagh CMN, Lubel JS. Natural history of chronic hepatitis B: phases in a complex relationship. *World J Gastroenterol*. 2014;20(30):10395-10404. DOI: 10.3748/wjg.v20.i30.10395. **7.** Nguyen MH, Lim JK, Ozbay AB, et al. Advancing age and comorbidity in a US insured population-based cohort of patients with chronic hepatitis B. *Hepatology*. 2019;69(3):959-973. DOI: 10.1002/hep.30246. **8.** Ning L, Lin W, Hu X, et al. Prevalence of chronic kidney disease in patients with chronic hepatitis B: a cross-sectional survey. *J Viral Hepat*. 2017;24(11):1043-1051. DOI: 10.1111/jvh.12733. **9.** Chen CH, Lin CL, Kao CH. Association between chronic hepatitis B virus infection and risk of osteoporosis: a nationwide population-based study. *Medicine (Baltimore)*. 2015;94(50):e2276. DOI: 10.1097/MD.0000000000002276. **10.** VEMLIDY approval letter, Silver Spring, MD: US Department of Health and Human Services; November 10, 2016. Accessed March 17, 2021. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2016/208464Orig1s000ltr.pdf. **11.** Epivir-HBV (lamivudine) approval letter, Rockville, MD: US Department of Health and Human Services; December 8, 1998. Accessed March 17, 2021. https://www.accessdata.fda.gov/drugsatfda_docs/nda/98/21003_Epivir-HBV_Approv.pdf. **12.** Hepsera Prescribing Information. Gilead Sciences, Inc.; 2018. Accessed March 17, 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/021449s024lbl.pdf. **13.** Baraclude. Prescribing Information. Bristol-Myers Squibb; 2019. Accessed March 17, 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021797s023,021798s024lbl.pdf. **14.** Tyzeka. Prescribing Information. Novartis; 2018. Accessed March 17, 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/022011s022,022154s019lbl.pdf. **15.** TDF (tenofovir disoproxil fumarate) supplemental approval letter, Rockville, MD: US Department of Health and Human Services; August 11, 2008. Accessed March 17, 2021. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2008/021356s025ltr.pdf. **16.** 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(6):3563-3569. DOI: 10.1128/AAC.00128-15. **17.** VEMLIDY. Prescribing Information. Gilead Sciences, Inc.; 2024. Accessed March 17, 2024. https://www.gilead.com/~/media/files/pdfs/medicines/liver-disease/vemlidy/vemlidy_pi.pdf?la=en. **18.** Chan HLY, Fung S, Seto WK, et al; 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(3):185-195. DOI: 10.1016/S2468-1253(16)30024-3. **19.** Lee WA, He GX, 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(5):1898-1906. DOI: 10.1128/AAC.49.5.1898-1906.2005. **20.** 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(3):533-540. DOI: 10.1016/j.jhep.2014.10.035. **21.** Viread. Prescribing Information. Gilead Sciences, Inc.; 2019. Accessed March 17, 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021356s058,022577s014lbl.pdf.

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