VEMLIDY — proven results for the moments that matter

Established efficacy and safety across a broad range* of adult chronic HBV patients with compensated liver disease

For your appropriate treatment-naïve patients, choose VEMLIDY for the long term

Actor portrayals.

See Pivotal and 8-Year Data Inside

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 the baseline characteristics of the broad range of patients in the VEMLIDY trials.

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

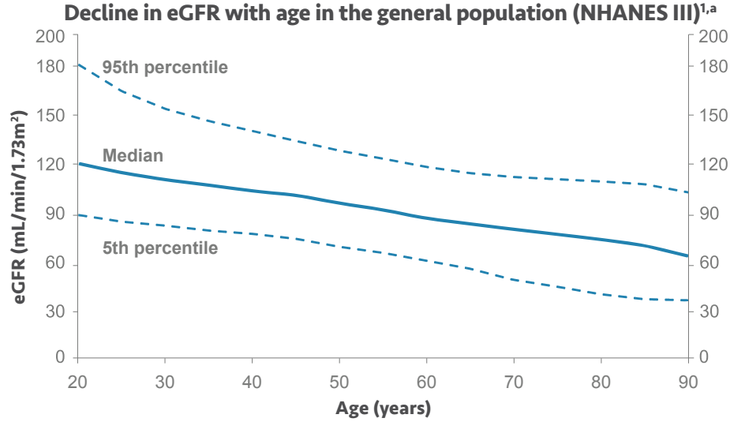
Vemlidy®
tenofovir alafenamide 25mg tablets

It's important to consider renal and bone risk factors when managing your chronic HBV patients

Renal function and bone density may decline over time in the general population due to various factors.

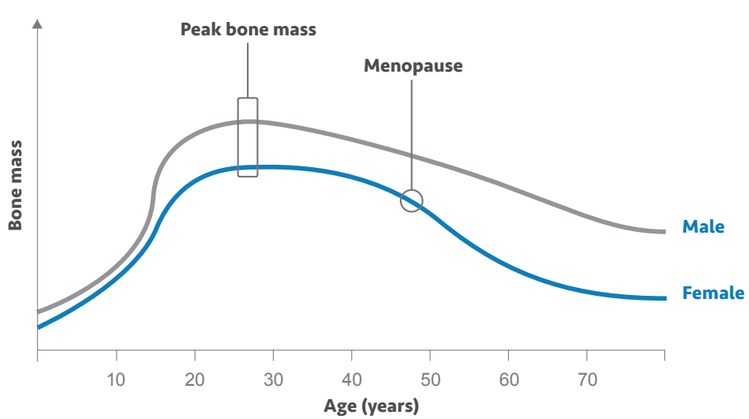
After age ~30, eGFR declines by ~1 mL/min/1.73 m² per year[2]

Decline in eGFR with age in the general population (NHANES III)[1,a]



After age ~40, BMD declines each year

Bone mass throughout the life course[3]



[a]Percentiles of eGFR regressed on age (NHANES III). GFR estimated from serum creatinine clearance using Modification of Diet in Renal Disease (MDRD) study equation based on age, gender, and race. Age ≥20; N=15,600.[2]

In addition, patients with chronic HBV have a higher prevalence of chronic kidney disease and osteoporosis and/or bone fracture than uninfected patients.[4,a]

1.7×-3.5× higher prevalence of chronic kidney disease[4,a]

Up to 1.7× higher prevalence of osteoporosis and/or bone fracture[4,a]

Consider risk factors that impact renal and bone health

Renal function risk factors

- Hypertension[4]
- Obesity[4]
- Diabetes[4]
- NSAIDs[5]
- Smoking[6]
- Sedentary behavior[7]
- Excessive alcohol use[6]
- Proton pump inhibitors[8]

Bone density risk factors

- Gender[9]
- Low BMI[11]
- Ethnicity[10]
- Antidepressants[12]

[a]Retrospective, observational study with case matching of chronic HBV patients without HDV coinfection, based on U.S. administrative healthcare claims from Commercial/Medicare (n=32,523) and Medicaid (n=11,503) databases from 2006 to 2015.[4]

Choose a chronic HBV treatment with long-term bone and renal health in mind

BMD=bone mineral density; BMI=body mass index; eGFR=estimated glomerular filtration rate; NHANES=National Health and Nutrition Examination Survey; NSAID=non-steroidal anti-inflammatory drug.

VEMLIDY—the latest innovation from Gilead's long legacy and commitment to chronic HBV

For over 20 years, Gilead has revolutionized chronic HBV treatment, helping countless patients along the way[13-18]

Timeline of all FDA-approved oral antiviral treatments for chronic hepatitis B[13-18]

1998	LAM (lamivudine)[a]
2002	ADV (adefovir dipivoxil)
2005	ETV (entecavir)[a]
2006	LdT (telbivudine)[a]
2008	TDF (tenofovir disoproxil fumarate)
2016	**VEMLIDY® (tenofovir alafenamide)**

[a]Non-Gilead product.

With over 8 years of experience[19]

FDA approved in 2016, VEMLIDY is the latest treatment from Gilead with 8 years of experience treating adult chronic HBV patients with compensated liver disease.[13,18,19]

Patient featured is compensated by Gilead.

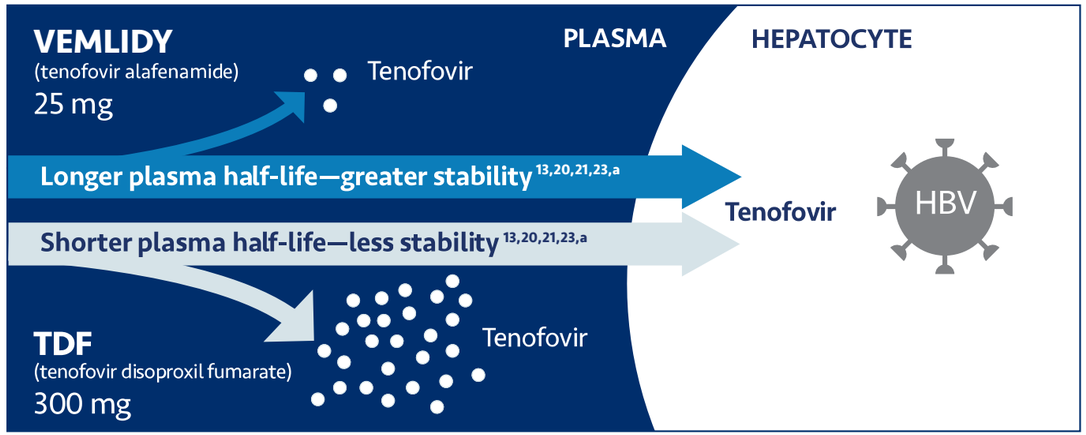
IMPORTANT SAFETY INFORMATION (CONT.)

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.
- **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.

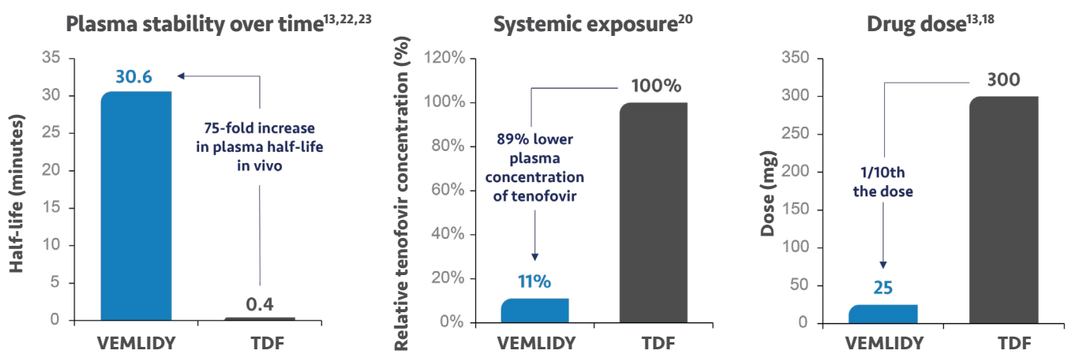
VEMLIDY optimizes tenofovir delivery to the hepatocyte

VEMLIDY demonstrates enhanced plasma stability vs TDF for more efficient delivery of tenofovir to hepatocytes[13,18,20-24]



89% Lower concentrations of tenofovir in the plasma with VEMLIDY vs TDF, **resulting in reduced systemic exposure**[20,23]

VEMLIDY offers increased drug stability with reduced systemic exposure and a lower dose[13,18,20-24]



TDF=tenofovir disoproxil fumarate.
[a]Plasma half-life: VEMLIDY=30.6 minutes (0.51 hour)[1]; TDF=0.41 minutes.[13,18,23]

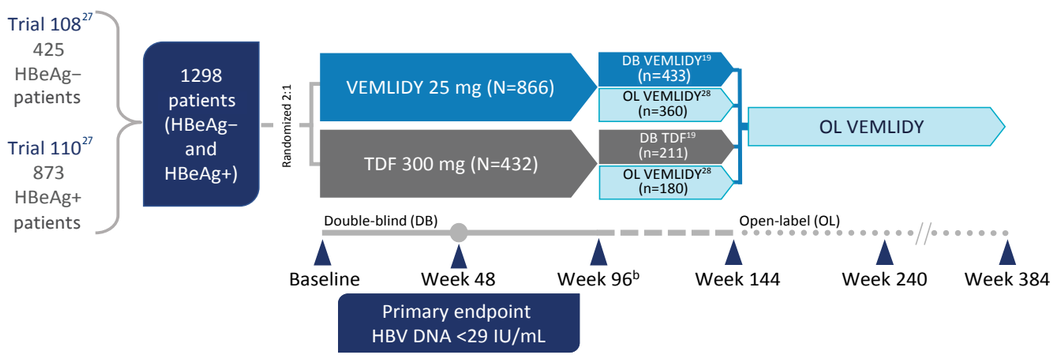
Click here for full Prescribing Information for VEMLIDY, including **BOXED WARNING**.

Vemlidy® tenofovir alafenamide 25mg tablets

The efficacy and safety of VEMLIDY were evaluated in two large clinical trials[13,19]

~75% of patients in pivotal Trials 108/110 were treatment naïve[27]

The efficacy and safety of VEMLIDY in the treatment of adults with chronic HBV infection with compensated liver disease are based on data from 2 randomized, double-blind, active-controlled, noninferiority trials.[13,20,25,26,a]



[a]Key inclusion criteria: HBV DNA ≥20,000 IU/mL; alanine aminotransferase (ALT) >60 U/L (males) or >38 U/L (females) and ≤10 × upper limit of normal (ULN) by central laboratory range.[20,26]

[b]The numbers of patients listed after Week 96 refer to those who entered the open-label phase or remained in the double-blind phase, and exclude patients who prematurely discontinued double-blind study treatment by Week 96.[19]

The primary endpoint for both studies was HBV DNA <29 IU/mL and noninferiority to tenofovir disoproxil fumarate (TDF) (10% margin; 95% confidence interval [CI] approach) at Week 48.[13,20,25]

- Additional efficacy endpoints evaluated at Week 48, Week 96, and Week 144 for both trials included the proportion of patients with HBV DNA <29 IU/mL, ALT normalization, and hepatitis B surface antigen (HBsAg) loss and seroconversion. Hepatitis B e antigen (HBeAg) loss and seroconversion were also assessed in Trial 110[13,20,25]
- The original protocol was amended to extend the double-blind phase from 96 weeks to 144 weeks.[26] However, before implementation of the protocol amendment, 540 patients entered the open-label phase at Week 96 (n=360 remained on VEMLIDY and n=180 switched from TDF to VEMLIDY)[19]
- By Week 144, a total of 1157 patients had entered the open-label phase[27]
- At Week 384, the full analysis set included 1298 patients who were enrolled in the study[27]
- **The 8-year analysis is not presented in the VEMLIDY full Prescribing Information**

Characteristics of the patients in Trials 108 and 110

	Pooled population	
Baseline characteristics[13,19,26,27]	**VEMLIDY** (n=866)	**TDF** (n=432)
Age, years, mean (SD)	**40** (11.8)	41 (12.3)
Male, n (%)	**544** (63)	275 (64)
Asian, n (%)	**687** (79)	333 (77)
HBV genotype A, B, C, D, others[a], %	**6, 19, 48, 26, 1**	7, 20, 46, 24, 2
Mean HBV DNA, $\log_{10}$ IU/mL, mean (SD)	**7** (1.59)	7 (1.63)
Median ALT, U/L (Q1, Q3)	**80** (56, 123)	80 (53, 130)
History of cirrhosis, n (%)[b]	**65** (10)	38 (12)
Treatment naïve, n (%)	**655** (76)	324 (75)
Prior oral antiviral therapy, n (%)[c]		
Entecavir	**109** (13)	49 (11)
Lamivudine	**86** (10)	40 (9)
Adefovir dipivoxil	**35** (4)	14 (3)
Telbivudine	**21** (2)	12 (3)
Other[d]	**14** (2)	6 (1)
Hip BMD osteopenia or osteoporosis, n (%)	**267** (31)	133 (31)
Spine BMD osteopenia or osteoporosis, n (%)	**366** (42)	182 (42)

>60% of patients were male[27]

~75% of the patients were treatment naïve[27]

>30% of the patients were osteopenic or osteoporotic[27]

Treatment-naïve patients had <12 weeks of previous treatment with any nucleoside/nucleotide analog. Treatment-experienced patients met all entry criteria (including HBV DNA ≥20,000 IU/mL and serum ALT criteria) and had ≥12 weeks of previous treatment with any nucleoside/nucleotide analog.[13,19]

ALT=alanine transaminase.

[a]"Other" includes genotypes E, F, H, and unknown.[27]

[b]Excludes patients with missing values.[19]

[c]Excluding interferon and TDF. Patients may have been on more than one prior therapy.[19]

[d]"Other" category included clevudine, tenofovir alafenamide, and other oral nucleoside/nucleotide agents.[19]


Actor portrayals.

VEMLIDY—confidence in proven efficacy

VEMLIDY demonstrated powerful antiviral efficacy with viral suppression at Weeks 48, 96, and 144 (HBV DNA <29 IU/mL)[13,19,20,25]

Trial 108 (HBeAg– patients)[a,b]

Week 48		Week 144	
94%	**93%**	**87%**	**85%**
268/285	**130/140**	**248/285**	**63/74**

Trial 110 (HBeAg+ patients)[a,b]

Week 48		Week 144	
64%	**67%**	**74%**	**71%**
371/581	**195/292**	**428/581**	**127/178**

■ VEMLIDY ■ TDF

- Trial 108 viral suppression at Week 96: VEMLIDY 90% (257/285), TDF 91% (127/140)[26]
- Trial 110 viral suppression at Week 96: VEMLIDY 73% (423/581), TDF 75% (218/292)[26]

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.[13]

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.[13,20,25]

CI=confidence interval; HBeAg=hepatitis B e-antigen.

[a]Patient populations analyzed included all treatment-naïve and treatment-experienced patients who were randomized into the trial and received at least 1 dose of study drug; a missing=failure approach was used.[13]

[b]The Week 144 analysis did not include the 66 patients from the TDF group in Trial 108 and the 114 patients from the TDF group in Trial 110 who had rolled over from double-blind TDF to open-label VEMLIDY at Week 96 prior to the study amendment.[19]

IMPORTANT SAFETY INFORMATION (CONT.)

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.

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.

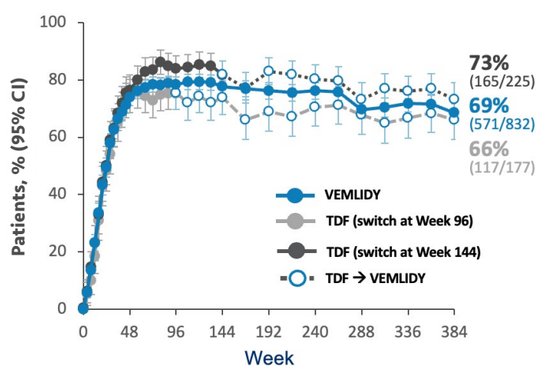
Consult the full prescribing information for VEMLIDY for more information on potentially significant drug interactions, including clinical comments.

Powerful efficacy maintained over the long term with 0% resistance

Long-term viral suppression with VEMLIDY through 8 years

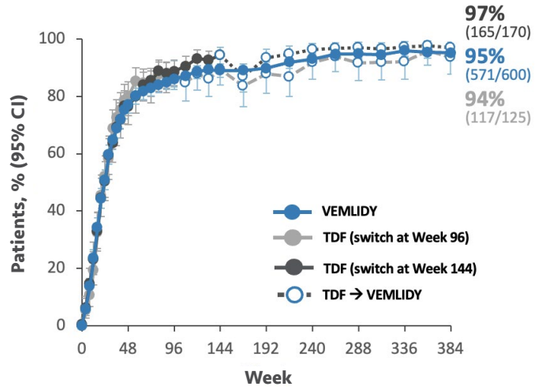
Pooled Week 384 Analysis: Pooled efficacy analysis from Trials 108 and 110 was assessed at Week 384 analysis for patients in the full analysis set. This analysis included 866 patients who continued on VEMLIDY (pooled), 207 patients who switched from TDF to VEMLIDY at Week 96, and 225 patients who switched from TDF to VEMLIDY at Week 144.[19,27,a,b]

Missing=Failure (M=F) analysis from Trials 108/110: HBV DNA <29 IU/mL at Year 8[19,27]



VEMLIDY (n)	640/866	680/866	673/866	635/832	634/832	580/832	597/832	571/832
TDF (W96 switch) (n)	154/207	156/207	153/207	122/177	125/177	120/177	118/177	117/177
TDF (W144 switch) (n)	172/225	189/225	184/225	187/225	181/225	165/225	171/225	165/225

Missing=Excluded (M=E) analysis from Trials 108/110: HBV DNA <29 IU/mL at Year 8[19,27]



VEMLIDY (n)	640/830	680/791	673/755	635/706	634/681	580/611	597/622	571/600
TDF (W96 switch) (n)	154/193	156/177	153/171	122/139	125/136	120/131	118/128	117/125
TDF (W144 switch) (n)	172/225	189/213	184/195	187/200	181/188	165/170	171/176	165/170

Due to early study discontinuations, which were mainly not attributable to lack of efficacy or adverse events, an M=E approach was performed. In the M=E approach, all missing data were excluded in the computations from this analysis.

Limitations: The M=E data are not powered to show statistical significance and should be considered as descriptive only. Neither the M=E data nor the 8-year data are presented in the VEMLIDY full Prescribing Information.

In an M=E analysis, any patients with missing data are excluded from the final analysis. This approach assumes that the missing data are random and not related to treatment outcomes.

In an M=F analysis, missing values are included. This approach accounts for missing data points as a "failure" in the final analysis.

[a]One site did not participate in Protocol amendment 3, and all patients from this site (n=64) discontinued the study on or before year 3 (Week 144); therefore, those patients who completed the planned study treatments were excluded from the M=F analysis for all visits after year 3.[27]

[b]Mean baseline plasma HBV DNA: 5.8 log_{10} IU/mL in Trial 108 and 7.6 log_{10} IU/mL in Trial 110.[13]

Most common adverse reactions (incidence ≥5%; all grades) at Week 384 open-label extension (OLE) were headache, upper respiratory tract infection, nasopharyngitis, hypertension, arthralgia, cough, and back pain.[27]

No known resistance with long-term VEMLIDY treatment

0% resistance

with long-term treatment on VEMLIDY through 8 years[13,27]

In Trials 108 and 110, genotypic resistance analysis was performed on patients experiencing either[13]:

- Virologic breakthrough (2 consecutive visits with HBV DNA ≥69 IU/mL [400 copies/mL] after having been <69 IU/mL, or ≥1.0-log_{10} increase in HBV DNA from nadir)
- Early discontinuation at or after Week 24 with HBV DNA ≥69 IU/mL

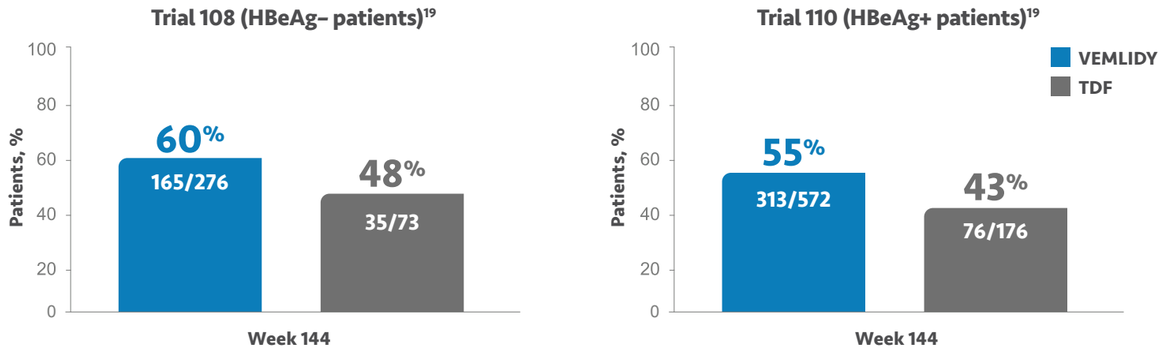
Click here for full Prescribing Information for VEMLIDY, including **BOXED WARNING**.

Vemlidy® tenofovir alafenamide 25mg tablets

VEMLIDY—proven ALT normalization in chronic HBV patients

~75% of patients in pivotal Trials 108/110 were treatment naïve.[19,27]

ALT normalization rates at Weeks 48, 96, and 144 (2016 AASLD criteria)[13,19,26,a,b]



At Week 48: ALT normalization was 50% (137/276) for VEMLIDY vs 32% (44/138) for TDF in Trial 108 and 45% (257/572) for VEMLIDY vs 36% (105/290) for TDF in Trial 110.[13]

At Week 96: ALT normalization was 50% (139/276) for VEMLIDY vs 40% (55/138) for TDF in Trial 108 and 52% (299/572) for VEMLIDY vs 42% (121/290) for TDF in Trial 110.[26]

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.[19]

AASLD=American Association for the Study of Liver Diseases.

[a]The population used for analysis of ALT normalization included only patients with ALT above ULN based on the AASLD 2016 criteria (>30 U/L and >19 U/L for males and females, respectively) at baseline.[13]

[b]The Week 144 analysis did not include the 66 patients from the TDF group in Trial 108 and the 114 patients from the TDF group in Trial 110 who had rolled over from double-blind TDF to open-label VEMLIDY at Week 96 prior to the study amendment.[19]

IMPORTANT SAFETY INFORMATION (CONT.)

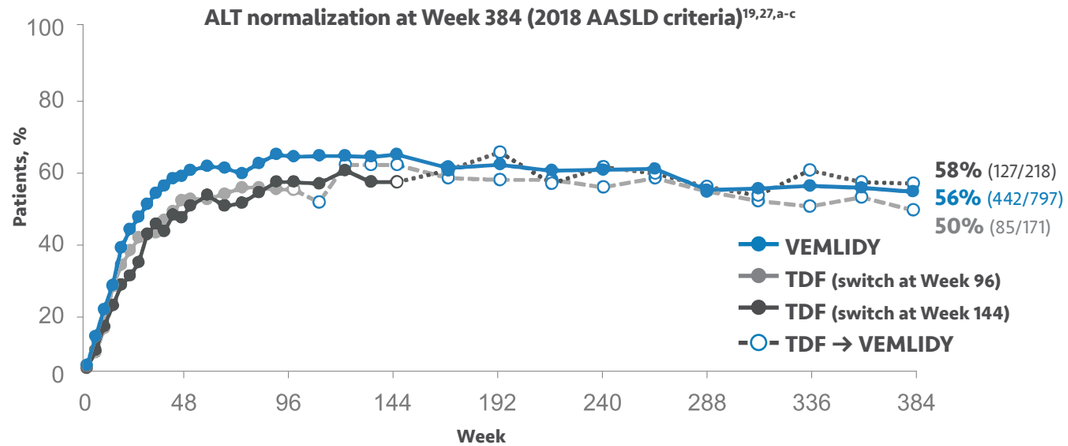
Dosage and Administration

- **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.

Powerful efficacy maintained over the long term with 0% resistance

Long-term ALT normalization with VEMLIDY through 8 years

Pooled Week 384 Analysis: Pooled efficacy analysis from Trials 108 and 110 was assessed at Week 384 analysis for patients in the full analysis set. This analysis includes 866 patients who continued on VEMLIDY (pooled), 207 patients who switched from TDF to VEMLIDY at Week 96, and 225 patients who switched from TDF to VEMLIDY at Week 144. Efficacy in the open-label phase was calculated using a M=F patient analysis.[19,27]



VEMLIDY (n)	506/831	542/831	549/831	503/797	489/797	446/797	456/797	442/797
TDF (W96 switch) (n)	104/199	102/199	123/199	99/171	95/171	94/171	86/171	85/171
TDF (W144 switch) (n)	111/218	126/218	130/218	149/218	138/218	127/218	136/218	127/218

Most common adverse reactions (incidence ≥5%; all grades) at Week 384 OLE were headache, upper respiratory tract infection, nasopharyngitis, hypertension, arthralgia, cough, and back pain.[27]

OLE=open-label extension.

[a]One site did not participate in Protocol amendment 3, and all patients from this site (n=64) discontinued the study on or before Year 3 (Week 144). Therefore, those patients who completed the planned study treatments were excluded from the M=F analysis for all visits after Year 3.[27]

[b]The population used for analysis of ALT normalization included only patients with ALT >ULN per the 2018 AASLD criteria (≤35 U/L for males and ≤25 U/L for females) at baseline.[19]

[c]Efficacy in the open-label phase was calculated using a missing=failure (M=F) patient analysis.

The 8-year analysis is not presented in the VEMLIDY full Prescribing Information.

IMPORTANT SAFETY INFORMATION (CONT.)

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

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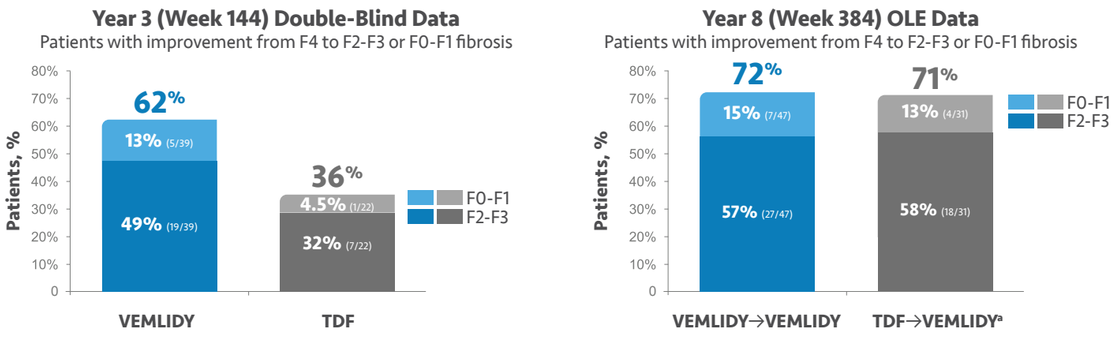
Regression of compensated cirrhosis seen with VEMLIDY through 8 years

Regression of cirrhosis in chronic HBV patients with cirrhosis at baseline[19,27]

Year 3 Data: Among the 1298 randomized and treated patients, 644 remained in the double-blind phase at Week 144, and 398 patients from the VEMLIDY group and 193 patients from the TDF group had FibroTest data available for analysis at both baseline and Week 144. The graphs show the results for those patients who had F4 fibrosis (FibroTest score ≥0.75) at baseline (39 patients in the VEMLIDY group and 22 patients in the TDF group).[19]

Year 8 Data: Among the 1298 randomized and treated patients, 575 patients from the VEMLIDY→VEMLIDY group and 282 patients from the TDF→VEMLIDY groups had FibroTest data available for analysis at both baseline and Week 384. The graphs show the results for those patients who had F4 fibrosis (FibroTest score ≥0.75) at baseline (47 patients in the VEMLIDY→VEMLIDY group and 31 patients in the TDF→VEMLIDY groups).[27]



Limitations: In Trials 108 and 110 at baseline, 10% of VEMLIDY patients and 12% of TDF patients had compensated cirrhosis.[27]

[a]Included data from 11 patients who switched from TDF to VEMLIDY at Week 96 and 20 patients who switched from TDF to VEMLIDY at Week 144.[19]

Additional context regarding the data presented on these pages

Change from baseline in fibrosis assessed by FibroTest score (missing=excluded analysis) for VEMLIDY vs TDF was a secondary endpoint in Trials 108 and 110. Liver biopsies and FibroScan® tests were not conducted as part of Trials 108 and 110.[20,25]

FibroTest is a noninvasive measure of liver fibrosis and combines 5 standard biomarkers: gamma-glutamyl transpeptidase, total bilirubin, alpha-2-macroglobulin, apolipoprotein A1, and haptoglobin. Note that FibroTest does not include ALT. FibroTest has been validated for assessing fibrosis in patients with chronic HBV.[29]

The clinical relevance of these changes in FibroTest scores is not known.[19]

This analysis is not presented in the VEMLIDY full Prescribing Information.

Cirrhosis and fibrosis analyses are not powered for statistical significance, and data should be considered descriptive only.

IMPORTANT SAFETY INFORMATION (CONT.)

Dosage and Administration (cont.)

- **Hepatic Impairment:** Not recommended in patients with decompensated (Child-Pugh B or C) hepatic impairment.

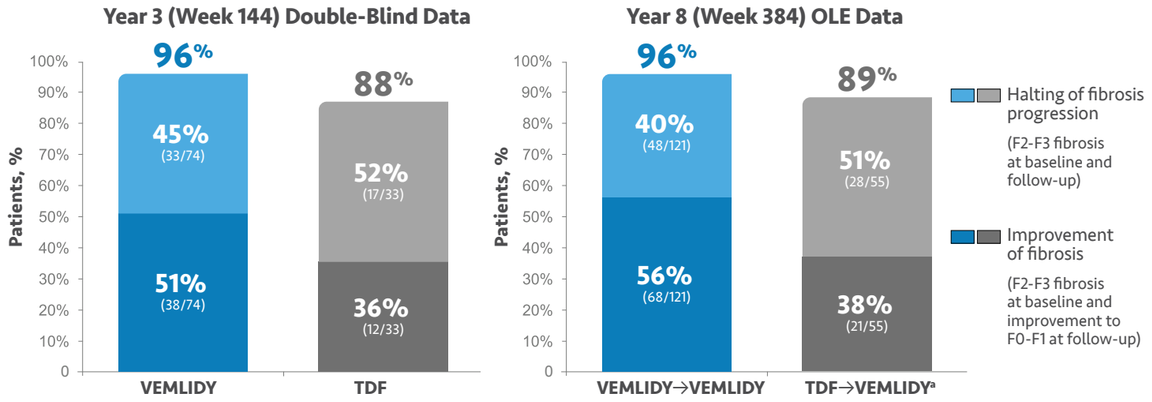
Powerful efficacy maintained over the long term with 0% resistance

Regression or halting of fibrosis progression seen with VEMLIDY through 8 years

Regression or halting of fibrosis progression in chronic HBV patients who were non-cirrhotic at baseline[19,27]

Year 3 Data: Among the 1298 randomized and treated patients, 644 remained in the double-blind phase at Week 144, and 398 patients from the VEMLIDY group and 193 patients from the TDF group had FibroTest data available for analysis at both baseline and Week 144. The graphs show the results for those patients who had F4 fibrosis (FibroTest score ≥0.75) at baseline (39 patients in the VEMLIDY group and 22 patients in the TDF group).[19]

Year 8 Data: Among the 1298 randomized and treated patients, 575 patients from the VEMLIDY→VEMLIDY group and 282 patients from the TDF→VEMLIDY groups had FibroTest data available for analysis at both baseline and Week 384. The graphs show the results for those patients who had F2-F3 fibrosis (FibroTest scores of 0.49 – 0.74) at baseline (121 patients in the VEMLIDY→VEMLIDY group and 55 patients in the TDF→VEMLIDY groups).[27]



Limitations: In Trials 108 and 110 at baseline, 20% of VEMLIDY patients and 19% of TDF patients had F2-F3 fibrosis.[19] Please see additional context regarding the limitations on page 12.

[a]Included data from 29 patients who switched from TDF to VEMLIDY at Week 96 and 26 patients who switched from TDF to VEMLIDY at Week 144.[19]

IMPORTANT SAFETY INFORMATION (CONT.)

Warnings and Precautions (cont.)

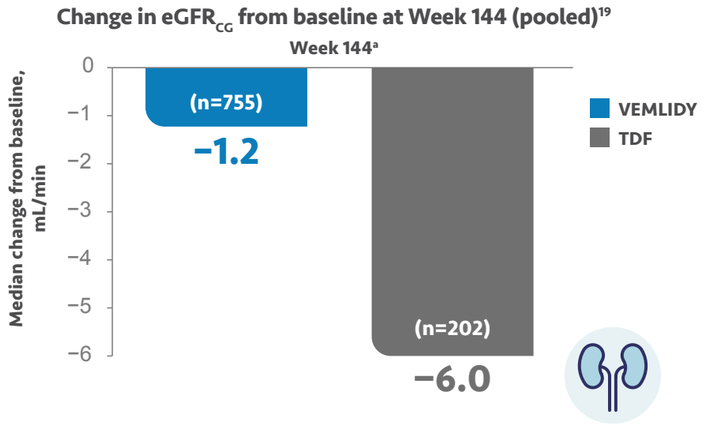
- **Lactic Acidosis and Severe Hepatomegaly with Steatosis:** Fatal cases have been reported with the use of nucleoside analogs, including tenofovir disoproxil fumarate (TDF). Discontinue VEMLIDY if clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity develop, including hepatomegaly and steatosis in the absence of marked transaminase elevations.

VEMLIDY showed reduced impact on renal safety parameters at Week 144

~75% of patients in pivotal Trials 108/110 were treatment naïve.[27]

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

Median baseline $eGFR_{CG}$ was 106 mL/min and 105 mL/min for VEMLIDY and TDF, respectively.[19]



In adult patients with chronic HBV, the mean increase in serum creatinine was 0.1 mg/dL in both treatment groups at both Week 96 and Week 144. The median change in $eGFR_{CG}$ from baseline was smaller for VEMLIDY vs TDF.

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).[13,19]

The long-term clinical significance of these renal laboratory changes on adverse reaction frequencies between VEMLIDY and TDF is not known.[13]

[a]The Week 144 analysis did not include the 180 patients (HBeAg−: 66 patients; HBeAg+: 114 patients) who had rolled over from double-blind TDF to open-label VEMLIDY at Week 96 prior to the trial amendment.[19]

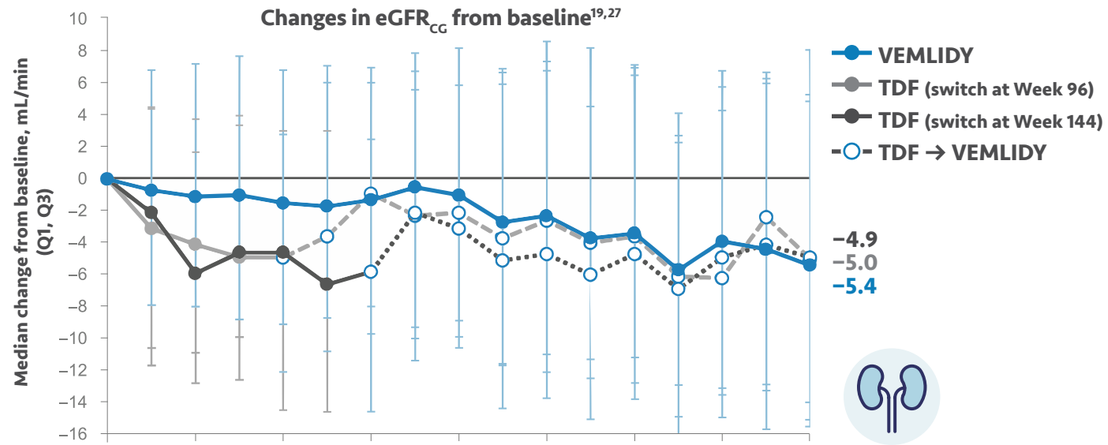
IMPORTANT SAFETY INFORMATION (CONT.)

Dosage and Administration

- **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.

Long-term renal safety parameters remained stable through 8 years in patients taking VEMLIDY

Pooled Safety Analysis (Week 384): Pooled safety analysis (observed data) from Trials 108 and 110 was assessed at Week 384. This analysis includes 866 patients who initiated VEMLIDY at baseline,[a] 207 patients who switched from TDF to VEMLIDY at Week 96, and 225 patients who switched from TDF to VEMLIDY at Week 144.[27]



Week	0	48	96	144	192	240	288	336	384
VEMLIDY (n)	828	789	753	703	677	610	623	592	
TDF (W96 switch) (n)	193	177	172	138	135	130	127	123	
TDF (W144 switch) (n)	225	213	197	198	185	167	174	167	

The long-term clinical significance of these renal laboratory changes on adverse reaction frequencies between VEMLIDY and TDF is not known.[13]

Median change in $eGFR_{CG}$ from Week 96 to 120: −0.6 mL/min in patients who remained on VEMLIDY and +1.8 mL/min in patients who switched from TDF to VEMLIDY.[13]

$eGFR_{CG}$=estimated glomerular filtration rate by Cockcroft-Gault.
[a]VEMLIDY group includes VEMLIDY patients who rolled over to open-label VEMLIDY at Week 96 or Week 144.

The 8-year analysis is not presented in the VEMLIDY full Prescribing Information.

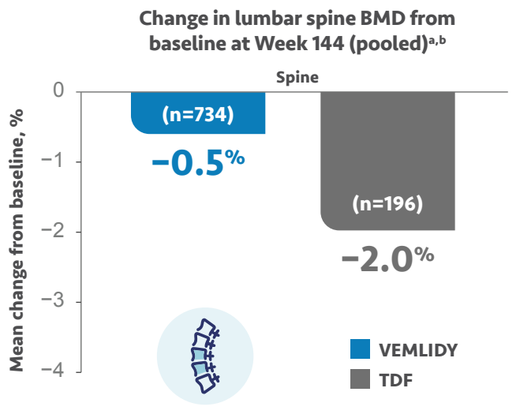
IMPORTANT SAFETY INFORMATION (CONT.)

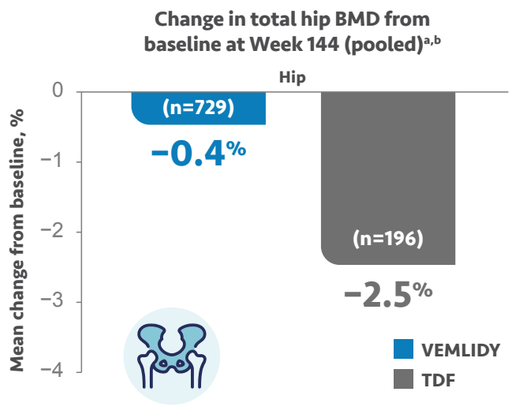
Warnings and Precautions

- **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.

VEMLIDY showed reduced impact on BMD at Week 144

Impacts on spine and hip BMD with VEMLIDY and TDF were compared in Trials 108 and 110[19]





Patients with ≥5% BMD decline in the lumbar spine:
11% (VEMLIDY) vs 25% (TDF) at Week 96[13]
12% (VEMLIDY) vs 24% (TDF) at Week 144[19]

Patients with ≥7% BMD decline in the femoral neck:
5% (VEMLIDY) vs 13% (TDF) at Week 96[13]
9% (VEMLIDY) vs 16% (TDF) at Week 144[19]

The long-term clinical significance of these BMD changes is not known.[13]

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.[13,19]

Key baseline characteristics for pivotal Trials 108 and 110[27]:

- ~75% of patients were treatment naïve
- >30% of patients were osteopenic or osteoporotic
- >60% of patients were male

[a]Only patients with nonmissing baseline data for spine or hip BMD were included in the spine or hip dual-energy x-ray absorptiometry (DXA) analysis set.[19]

[b]The Week 144 analysis did not include the 180 patients (HBeAg−: 66 patients; HBeAg+: 114 patients) who had rolled over from double-blind TDF to open-label VEMLIDY at Week 96 prior to the trial amendment.[19]

IMPORTANT SAFETY INFORMATION (CONT.)

Warnings and Precautions

- **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.

Demonstrated renal and bone safety profile

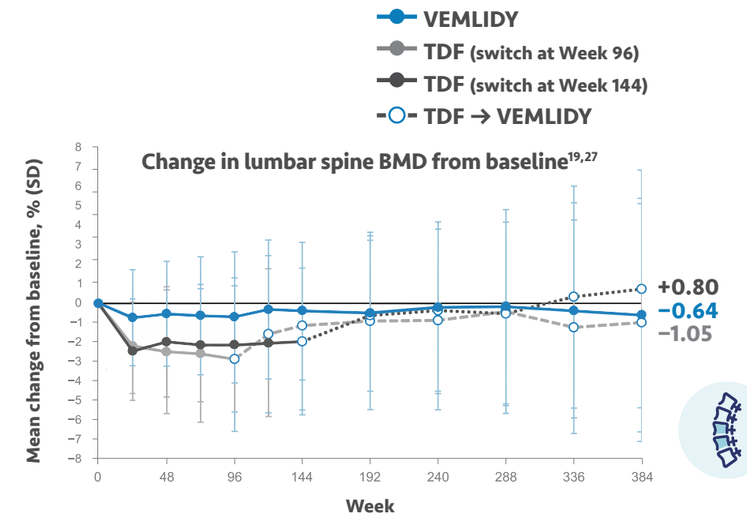
Long-term BMD remained stable through 8 years in patients taking VEMLIDY

Pooled Safety Analysis (Week 384): Pooled safety analysis (observed data) from Trials 108 and 110 was assessed at Week 384. This analysis includes 866 patients who initiated VEMLIDY at baseline,[a] 207 patients who switched from TDF to VEMLIDY at Week 96, and 225 patients who switched from TDF to VEMLIDY at Week 144. Only patients with nonmissing baseline data for spine or hip BMD were included in the spine or hip DXA analysis set.[19,27]

The long-term clinical significance of these BMD changes is not known.[13]

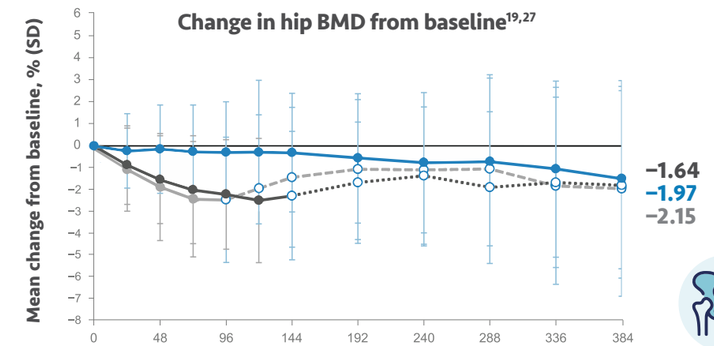
Spine and hip BMD remained stable in VEMLIDY patients, and there was an improvement seen in patients who switched to VEMLIDY from TDF.[19,27]

Mean % change in lumbar spine BMD from Week 96 to Week 120: +0.6% in patients who remained on VEMLIDY; +1.7% in those who switched from TDF to VEMLIDY.[13]



	Week 0	48	96	144	192	240	288	336	384
VEMLIDY (n)	866	816	758	724	685	649	603	590	547
TDF (W96 switch) (n)	207	189	165	169	133	131	123	119	109
TDF (W144 switch) (n)	225	220	207	191	190	176	165	166	157

Mean % change in total hip BMD from Week 96 to Week 120: 0% in patients who remained on VEMLIDY; +0.6% in those who switched from TDF to VEMLIDY.[13]



	Week 0	48	96	144	192	240	288	336	384
VEMLIDY (n)	866	808	745	716	683	645	599	588	532
TDF (W96 switch) (n)	207	186	164	168	133	131	123	118	105
TDF (W144 switch) (n)	225	220	207	187	191	176	166	165	151

[a]VEMLIDY group includes VEMLIDY patients who rolled over to open-label VEMLIDY at Week 96 or Week 144.

The 8-year analysis is not presented in the VEMLIDY full Prescribing Information.

Adverse events

Trials 108 and 110 (pooled)

The proportion of patients who discontinued treatment at Week 96 due to adverse reactions (ARs) of any severity was 1.5% with VEMLIDY and 0.9% with TDF.[13] At Week 144, the discontinuation rates due to ARs of any severity were 1.6% with VEMLIDY and 1.6% with TDF.[19]

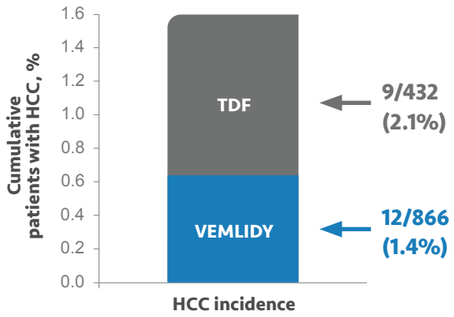
Adverse reactions[a] (all grades) reported in ≥5% of patients on VEMLIDY in Trials 108 and 110 (Week 96 and Week 144 analyses)

	VEMLIDY pooled population (n=866)	
Adverse reactions[13,19]	**Week 96**	**Week 144**
Headache	12%	13%
Upper respiratory tract infection	11%	13%
Abdominal pain[b]	9%	10%
Cough	8%	9%
Back pain	6%	7%
Fatigue	6%	7%
Nausea	6%	7%
Arthralgia	5%	7%
Diarrhea	5%	6%
Dyspepsia	5%	5%
Pyrexia	5%	5%

Pooled safety analysis (Week 384) of 1157 patients who completed the double-blind treatment and entered the VEMLIDY open-label extension[27]

- Incidence ≥5% (all grades) were headache, upper respiratory tract infection, nasopharyngitis, hypertension, arthralgia, cough, and back pain

At Week 384, **21 cases (1.6% incidence)** of hepatocellular carcinoma (HCC) were observed in Trials 108 and 110.[27,a,c]



HCC surveillance was included as part of the 96-week protocol amendments for Trials 108/110. These trials were not powered to look at any treatment effect on HCC, and no results should be drawn based on these observations. This information is not in the VEMLIDY Prescribing Information.[19]

[a]Frequencies of adverse reactions are based on all treatment-emergent adverse events, regardless of relationship to study drug.[13]
[b]Grouped term including abdominal pain upper, abdominal pain, abdominal pain lower, and abdominal tenderness.[13]
[c]3 cases of HCC were observed in the open-label TDF→VEMLIDY group, all of which developed before Week 48 of the open-label phase.[19]

The 8-year analysis is not presented in the VEMLIDY full Prescribing Information.

Lipids

Differences were observed between VEMLIDY and TDF in certain lipid parameters

In Trials 108 and 110:

- **Week 96:** 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 vs −10 mg/dL and −7 mg/dL for TDF[13]
- **Week 144:** Mean changes from baseline in LDL-C (fasted) and TG (fasted) were +8 mg/dL and +18 mg/dL for VEMLIDY vs −8 mg/dL and −2 mg/dL for TDF[19]
- **Week 384:** Among patients receiving VEMLIDY, the median change in LDL-C (fasted) was +16 mg/dL and TG (fasted) was +9 mg/dL. Among patients who switched from TDF to VEMLIDY at Week 96, the median change in LDL-C (fasted) was +17 mg/dL and TG (fasted) was +11 mg/dL. Among patients who switched from TDF to VEMLIDY at Week 144, the median change in LDL-C (fasted) was +11 mg/dL and TG (fasted) was +14 mg/dL[27]

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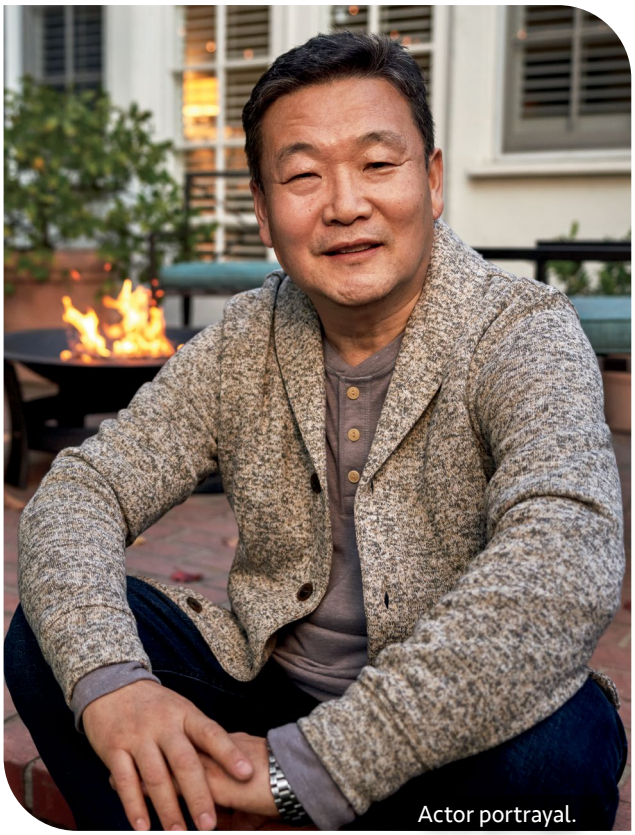
Actor portrayal.

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[c]Data on File as of February 2025, VEMLIDY Co-pay Coupon Program. Gilead Sciences, Inc.

Vemlidy® tenofovir alafenamide 25mg tablets

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

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