Gilead Sciences, Inc. is providing this document to you, a US Healthcare Professional, in response to your unsolicited request for medical information.

GILEAD | Medical Information

Vemlidy® (tenofovir alafenamide)
Use in Pregnancy and Lactation

This document is in response to your request for information regarding the use of Vemlidy® (tenofovir alafenamide [TAF]) for the treatment of HBV during pregnancy and lactation. This response was developed according to principles of evidence-based medicine and includes data from registries, meta-analyses, and prospective studies in pregnancy (N≥80) and pregnancy and lactation (N>20).

Some data may be outside of the US FDA-approved prescribing information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA-approved prescribing information.

The full indication, important safety information, and boxed warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/liver-disease/vemlidy/vemlidy_pi.

Summary

Product Labeling[1]

In animal studies, no adverse embryo-fetal developmental effects were observed with TAF.

ARV Pregnancy Exposure Registry[2]

Based on safety data from the APR, the prevalence of birth defects with first-trimester exposure to TAF was 4.1%, and that with second-/third-trimester exposure was 4.6%.

Available Data: TAF Use in Pregnancy and Lactation

In a meta-analysis that included four studies that evaluated TAF use in pregnant participants with CHB, rates of MTCT and pregnancy complications were similar to those observed with TDF (pooled RR, 1.09; 95% CI: 0.16–7.61). Infant safety outcomes were generally similar between the TAF and TDF treatment groups.[3]

In nine studies of pregnant women with HBV,[4-7] treatment with TAF during pregnancy resulted in 0% MTCT at the last follow-up in seven studies.[4,5] In a prospective, multicenter study that evaluated 8 vs 12 weeks of TAF in pregnant women, the MTCT rates in infants at 7 months of age were 7.1% and 0% in the ITT and PP populations, respectively.[7] In another prospective, multicenter study that evaluated effectiveness of TAF vs TDF in pregnant women, 1 infant in each of the TAF (n=81) and TDF (n=55) groups was HBsAg+ at Months 6 and 12.[6]

- Infant growth and development were normal. TAF was generally well tolerated, with no discontinuations due to AEs. Additional safety outcomes are provided below.[4-7]

PK Data: TAF Use in Pregnancy and Lactation

In a PK study that evaluated infant exposure and the PK of TAF and TFV in women with CHB who were breastfeeding, TAF levels were below the LoQ in breast milk and maternal plasma in 7 of the 8 mothers within 6 to 8 hours after a dose. The RID of TAF was 0.005% of the maternal dose.[8]

Product Labeling[1]

Use in Specific Populations

Pregnancy

Animal data

Embryonic fetal development studies performed in rats and rabbits revealed no evidence of impaired fertility or harm to the fetus. The embryo-fetal no observed adverse effect levels in rats and rabbits occurred at TAF exposures similar to and 51 times higher than, respectively, the exposure in humans at the recommended daily dose. TAF is rapidly converted to TFV; the observed TFV exposure in rats and rabbits were 54 (rats) and 85 (rabbits) times higher than human TFV exposures at the recommended daily dose.

TAF was administered orally to pregnant rats (25, 100, or 250 mg/kg/day) and rabbits (10, 30, or 100 mg/kg/day) through organogenesis (on gestation Days 6–17, and 7–20, respectively). No adverse embryo-fetal effects were observed in rats and rabbits at TAF exposures approximately similar to (rats) and 51 (rabbits) times higher than the exposure in humans at the recommended daily dose of TAF. TAF is rapidly converted to TFV; the observed TFV exposures in rats and rabbits were 54 (rats) and 85 (rabbits) times higher than human TFV exposures at the recommended daily dose. Since TAF is rapidly converted to TFV and a lower TFV exposure in rats and mice was observed after TAF administration compared to TDF, another prodrug for TFV administration, a pre/postnatal development study in rats was conducted only with TDF. Doses up to 600 mg/kg/day were administered through lactation; no adverse effects were observed in the offspring on gestation Day 7 (and lactation Day 20) at TFV exposures of approximately 12 (18) times higher than the exposures in humans at the recommended daily dose of TAF.

Lactation

Risk summary

Data from the published literature report the presence of TAF and tenofovir in human milk. Data from the published literature have not reported adverse effects of TAF on a breastfed child. There are no data on the effects of TAF on milk production.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TAF and any potential adverse effects on the breastfed infant from TAF or from the underlying maternal condition.

ARV Pregnancy Exposure Registry[2]

Safety data for TAF in pregnant women are derived primarily from outcomes in the HIV-infected population. The APR is an international, voluntary, prospective, exposure-registration cohort study of predominantly women with HIV-1 and no concomitant infections to monitor major teratogenic effects of ARV drugs, including anti-HBV drugs, following exposure during pregnancy. Healthcare providers are encouraged to register patients in the APR (http://www.APRegistry.com).

The APR began to systematically collect HBV infection status in 2003. Since the addition of the HBV indication, the APR has received 1139 prospective reports of patients diagnosed with HBV, with or without concurrent HIV infection, all of which are included in the overall primary prospective analysis. Through July 31, 2025, a total of 896 prospective reports of HBV-monoinfected pregnancies with outcomes have been reported. Among the 896 reports, there were 841 live births, including 686 live births with initial exposure during the first trimester of pregnancy; 3 stillbirths; 33 spontaneous abortions; and 28 induced abortions (including 9 multiple births). Among the 841 live births, 12 birth defect cases were reported. There was no pattern among the types of birth defects reported.

Data from the APR through July 31, 2025, for the overall (n=24,750) prospective reports with follow-up data showed that birth defect prevalence with exposure to any of the ARV therapies included in the registry at any time during pregnancy was 3% (95% CI: 2.7–3.3%; Table 1). This was not substantially different from that reported by the Centers for Disease Control and Prevention Metropolitan Atlanta Congenital Defects Program (2.72 per 100 live births) and the Texas Birth Defects Registry (5.07 per 100 live births).

For TAF, data from the APR showed that there have been 69 first-trimester birth defect cases with exposure to TAF-containing regimens (Table 1). The prevalence of birth defects with first-trimester exposure to TAF-containing regimens was 4.07% (95% CI: 3.18–5.12%). Sufficient numbers of TAF first-trimester exposures have been monitored to detect at least a 1.5-fold increase in the risk of overall birth defects and a 2-fold increase in the risk of birth defects in the cardiovascular and genitourinary systems. No such increases were detected.

In an exposure registration study, rates of drug-associated AEs cannot be extrapolated to reflect true rates in the potential target population. Since reports of exposures in the APR are voluntary, they are subject to numerous potential selection biases.

Table 1. APR: Birth Defect Prevalence by Trimester of Earliest Exposure Through July 31, 2025[2a]

Earliest Drug Exposure	Outcome/Prevalence	All APR-Registered ARVs	TAF-Containing Regimens
First trimester	Defects/live births, n/N	393/13,093	69/1696
	Prevalence, % (95% CI)	3 (2.72–3.31)	4.1 (3.18–5.12)
Second/third trimester	Defects/live births, n/N	296/10,327	20/439
	Prevalence, % (95% CI)	2.9 (2.55–3.21)	4.6 (2.8–6.95)
Any trimester	Defects/live births, n/N	691/23,423	–
	Prevalence, % (95% CI)	3 (2.74–3.18)	–

[a]Exposures are not mutually exclusive across individual ARVs.

Available Data: TAF Use in Pregnancy and Lactation

Meta-Analysis of TAF vs TDF for MTCT Prevention in Mothers With High VLs

Study design

A systematic review and meta-analysis were conducted to compare the rates of MTCT and safety between TAF-treated, TDF-treated, and control groups within randomized controlled trials (n=6) and controlled, retrospective or prospective cohort (n=25) studies. Eligible studies were those that included pregnant participants with CHB and HBV DNA VL

≥200,000 IU/mL, immunoprophylaxis administration to infants and TAF or TDF to women in one study arm during pregnancy, and reported clinical outcomes, including MTCT rate (HBsAg+ and/or detectable HBV DNA after 6 months) and maternal and infant safety. Study investigators excluded animal or translational studies; studies with participants who had comorbid HIV, HAV, HCV, HDV, or HEV; studies with treatment arms containing <10 participants or those providing second-line treatment with telbivudine, adefovir, or lamivudine; and cohort studies with a high risk of bias (ie, Newcastle Ottawa Scale score <5).[3,9]

Key outcomes assessed included the following: MTCT rates and safety in TAF-treated, TDF-treated, and control groups; infant safety outcomes; infant physical development at birth and beyond postpartum Month 6; maternal outcomes, including ALT level changes; and maternal AEs and obstetric complications.[3]

In the 31 studies included, of the 4468 pregnant women with CHB, 280 participants were TAF treated, 2588 were TDF treated, and 1600 were untreated or received placebo (control group). The cohort of TAF-treated participants included data from 4 studies in which participants received TAF 25 mg or TDF 300 mg once daily. In 3 of the studies, participants began treatment during pregnancy by gestational Week 24.[3]

Results[3]

Among studies that compared MTCT rates between TAF- and TDF-treated participants, similar rates of effectiveness were observed, with a pooled RR of 1.09 (95% CI: 0.16–7.61). In a network meta-analysis (TAF or TDF treatment and infant immunoprophylaxis), comparable efficacy was observed (RR, 0.1 [95% CI: 0.07–0.16]; *P*=0.68). In a pairwise analysis, TAF and TDF were equally effective in MTCT prevention.

Safety

Overall, pregnancy complications were reported in 18 studies, including 48/244 cases (19.7%) in the TAF-treated group; the frequency of complications was comparable between the TAF- and TDF-treated groups (TDF, 378/1493 [25.3%]; RR, 0.93 [95% CI: 0.66–1.31]). One case of CK elevation occurred in the TAF studies, and the rates of postpartum hemorrhage were comparable between the TAF and TDF treatment groups (RR, 0.61; 95% CI: 0.08–4.56).[3,9]

Across the 4 studies that evaluated TAF treatment, there was no association between TAF and negative fetal or infant outcomes. No Grade 3 or 4 AEs or fetal deaths were reported. The RRs (95% CI) for TDF vs TAF for prematurity and fetal death were 0.88 (0.32–2.38) and 1.9 (0.51–6.99), respectively. Safety outcomes, including Apgar score at 1 minute, and physical growth parameters were similar between TAF-treated and TDF-treated groups. No TAF studies reported BMD scores in infants.[3]

Prospective, Randomized Study in China: Perinatal Prophylaxis With 8 vs 12 Weeks of TAF[7]

Study design and demographics

A prospective, open-label, multicenter, randomized controlled study was conducted to compare the safety and efficacy of 12 weeks of TAF with those of a shorter course of TAF (8 weeks) for the prevention of MTCT in pregnant women with CHB. Women aged 20 to 40 years with a gestational age >30 weeks and HBV DNA VLs between 5.3 and

9 $\log_{10}$ IU/mL and normal levels of ALT (ie, <40 U/L) and TB (ie, <17.1 mcmol/L) were eligible for inclusion. Key exclusion criteria were as follows: prior treatment to reduce ALT and TB levels, prior treatment for CHB (except prophylaxis of HBV MTCT during a previous pregnancy that occurred >6 months to the current pregnancy); comorbid HCV, HDV, HEV, or HIV; prior or current hepatocellular carcinoma, cirrhosis, or other systemic disorders; or Hgb level <80 g/L.

Participants were randomly assigned in a 1:1 ratio to receive TAF 25 mg once daily starting the first day of gestational Week 33 for an expected 8 weeks (ie, discontinuing at delivery; Group 1) or 12 weeks (ie, halting at postpartum Week 4; Group 2). Adherence was evaluated via pill counts; participants were followed through postpartum Month 6. All infants received HBV immunoprophylaxis. The primary endpoint was maternal and infant safety; specifics are presented below. Secondary endpoints included maternal virologic responses throughout the study and infant HBV MTCT at postpartum Month 7.

Table 2. Baseline Demographics and Disease Characteristics (ITT[a]; Zeng et al)[7]

Key Demographics and Characteristics	Group 1: 8 Weeks of TAF (n=119)	Group 2: 12 Weeks of TAF (n=120)
Age, mean (SD), years	28.8 (3.5)	29.2 (4.2)
Primipara, n (%)	73 (61.3)	76 (63.3)
HBV DNA, mean (SD), $\log_{10}$ IU/mL	7.9 (0.6)	7.9 (0.6)
HBsAg, mean (SD), IU/mL	45,269 (20,515.9)	44,776.5 (18,847.2)
ALT, mean (SD), U/L	16.9 (7.1)	16 (6.8)
SCr, mean (SD), mcmol/L	44.6 (8.3)	45.8 (10)
eGFR, mean (SD), mL/min/1.73 m^2	128.2 (8)	127.1 (8.2)

[a]Defined as all enrolled participants, except those who withdrew consent before the assigned treatment started.

At delivery, 115 and 116 mothers had data available in Groups 1 and 2, respectively (4 LTFU due to COVID-19 lockdown in each group), and 115 and 116 infants, respectively, were born to those mothers. After delivery, 110 and 112 mother-infant pairs in Groups 1 and 2, respectively, completed the study (another 4 and 5 pairs were LTFU due to COVID-19 lockdown). At delivery, the mean (SD) durations of TAF exposure were 6.2 (1) weeks and 10.5 (1.1) weeks in Groups 1 and 2, respectively.

Results

Overall, mean HBV DNA VL decreased significantly from 7.86 $\log_{10}$ IU/mL at baseline to 4.05 $\log_{10}$ IU/mL at delivery (P<0.001), and 97% of participants (224/231) had a VL <5.3 $\log_{10}$ IU/mL at delivery. Additionally, significant decreases from baseline to delivery in mean HBsAg (4.6 to 4.55 IU/mL, respectively) and HBeAg (386 to 360.17 PEIU/mL) levels were recorded (each, P<0.001).

In the ITT and PP populations (n=222; excluded infants born to women who withdrew consent, were LTFU, or discontinued TAF due to any reason), the MTCT rates of infants at 7 months were 7.1% (17/239) and 0% (0/222) of participants, respectively. In the PP population, infants were anti-HBs+ in both groups. There was no significant difference between groups for any of the efficacy outcomes at Month 6 postpartum. Efficacy outcomes by group are shown in Table 3.

Table 3. Efficacy Outcomes (Zeng et al)[7]

Outcomes	Group 1: 8 Weeks of TAF		Group 2: 12 Weeks of TAF	
	Delivery (n=115)	Postpartum Month 6 (n=110[a])	Delivery (n=116)	Postpartum Month 6 (n=112[a])
HBV DNA, mean (SD), $\log_{10}$ IU/mL	4 (0.8)	7.8 (0.8)	4.1 (0.5)	7.9 (0.5)
<5.3 $\log_{10}$ IU/mL, n (%)	111 (96.5)	0	113 (97.4)	0
HBsAg, mean (SD), $\log_{10}$ IU/mL	4.5 (0.2)	4.6 (0.2)	4.6 (0.2)	4.6 (0.2)
HBeAg, mean (SD), PEIU/mL	362.8 (105.4)	387.1 (111)	357.6 (108.4)	384.8 (117.2)
ALT, mean (SD), U/L	19.6 (36.4)	23.2 (18.8)	17.3 (7.6)	23.7 (24.5)
>200 U/L, n (%)	1 (0.9)[b]	0	0	0

[a]Two participants in each group restarted TAF due to ALT elevations.
[b]One participant had an ALT level of 399 U/L at delivery and was diagnosed with liver injury due to concomitant treatment with a Chinese herbal supplement. Their ALT level gradually normalized after discontinuation of the supplement.

Safety

Compliance was 100% via self-report, confirmed by pill counts. No participants discontinued treatment due to AEs. Overall, in Groups 1 and 2, the most common AEs and complications were nausea (11.8% vs 10.8%, respectively) and PROM (9.2% and 8.3%); no Grade 3 or 4 AEs were reported (Table 4). Similar rates of mild ALT elevations occurred in each group at delivery and postpartum Months 3 and 6; no ALT flares occurred through postpartum Month 6. Though approximately 90% of participants maintained elevations in total cholesterol and triglycerides at delivery, levels returned to normal after delivery in most women; overall lipid profiles were similar between groups through postpartum Month 6. Overall, in terms of renal function, no significant changes from baseline to delivery in SCr or β2M levels were noted; 1 participant in Group 1 had a mild increase in β2M levels at postpartum Month 6.

Preterm delivery occurred in 3% of cases (7/231), and no infants had congenital defects or malformations or an Apgar score <8 at 1 minute (Table 4). In the PP population, the most common abnormal condition was prolonged neonatal jaundice: Group 1, 14.6% (16/110); Group 2, 16.1% (18/112; P=0.752); each case spontaneously resolved or was cured with phototherapy by postpartum Month 2.

Table 4. Maternal and Infant Safety Outcomes (Zeng et al)[7]

Maternal Safety Parameters, n (%)		Group 1: 8 Weeks of TAF (n=119)	Group 2: 12 Weeks of TAF (n=120)
Any AE		33 (27.7)	32 (26.7)
Grade 1 or 2 AEs that occurred in >5% of participants	Nausea	14 (11.8)	13 (10.8)
	Anorexia	13 (10.9)	13 (10.8)
	Fatigue	11 (9.2)	12 (10)
Any obstetrical complication		14 (11.8)	13 (10.8)
Complications that occurred in >5% of participants	PROM	11 (9.2)	10 (8.3)
Grade 1 or 2 ALT elevation[a] at any time		18 (15.1)	22 (18.3)
Grade 3 ALT elevation[a] at any time		1 (0.8)[b]	0
Hgb <110 g/dL at delivery		34 (29.6)	33 (28.4)

Infant Safety Parameters	Group 1: 8 Weeks of TAF (n=115)	Group 2: 12 Weeks of TAF (n=116)
Gestational age at birth, mean (SD), weeks	39.2 (1)	39.2 (1)
<37 weeks, n (%)	3 (2.6)	4 (3.4)
Cesarean section delivery, n (%)	55 (47.8)	59 (50.9)
Weight, mean (SD), kg	3.41 (0.34)	3.45 (0.34)
Height, mean (SD), cm	50.25 (1.43)	50.25 (1.43)
Head circumference, mean (SD), cm	34.53 (0.84)	34.5 (0.79)
Apgar score at 1 minute, mean (SD)	9.6 (0.6)	9.5 (0.6)
Breastfed, n (%)	64 (55.7)	66 (56.9)

[a]Grade 1 or 2 elevation was defined as an ALT level of 1.1–5 × ULN; Grade 3 elevation was defined as an ALT level of 5–20 × ULN. No Grade 4 ALT laboratory abnormalities occurred in either group.
[b]One participant had an ALT level of 399 U/L at delivery and was diagnosed with liver injury due to concomitant treatment with a Chinese herbal supplement. Their ALT level gradually normalized after discontinuation of the supplement.

Phase 4 Multicenter Cohort Study in China

Study design

A phase 4, single-arm, prospective, multicenter clinical study was conducted in China to assess the safety and efficacy of TAF in preventing MTCT of HBV among pregnant women with CHB who were HBeAg+ and had high levels of HBV DNA (>200,000 IU/mL). Women aged 20 to 35 years and who were 24 to 26 weeks pregnant received TAF 25 mg once daily from 27 to 29 weeks of gestation until delivery,[10] and participants were followed until 6 months postpartum. Infants received combined immunoprophylaxis and were followed through HBV vaccination.[4] Primary outcome measures included the rate of MTCT of HBV from the time of enrollment through the last infant post-HBV vaccination serological test. Secondary outcome measures included the rate of infant birth defects. The study started in April 2021 and was estimated to conclude in December 2023 with approximately 330 participants.[10]

Interim results[4]

The interim analysis included up to 28 weeks of postpartum data from those enrolled up to June 2022, including 134 pregnant participants, 105 of whom gave birth to 108 infants. At delivery, 89% of mothers (89/100) achieved HBV DNA <200,000 IU/mL, and 2% (2/102) had undetectable levels. During treatment, the median (IQR) decreases in serum HBV DNA and HBsAg levels were 4 (3–4) $\log_{10}$ IU/mL and 11,319 (-5909 to +28,534) IU/mL, respectively. All 33 infants who completed the postvaccination serological evaluation tested negative for HBsAg.

At 6 months postpartum, 65.4% of mothers (51/78) had ALT levels >ULN, compared with 2.1% of mothers (2/95) who had ALT levels >ULN during pregnancy. No infants had malformations or congenital defects, and body weight, height, and head circumferences were within normal limits.

Prospective, Multicenter Study in China: TAF in Participants With High HBV DNA VLs[5]

Study design and demographics

A multicenter, prospective study was conducted to assess the safety and effectiveness of TAF initiated during the second trimester for the prevention of MTCT of HBV in 89 pregnant participants with CHB and a high VL. Women aged 20 to 35 years with an HBV DNA VL ≥1 × 10^6 IU/mL who were HBsAg+ and HBeAg+ were eligible for inclusion. Exclusion criteria included comorbid HIV, HCV, or major systemic disease, antiviral treatment at the time of enrollment, congenital fetal abnormalities, or a history of spontaneous abortion. All participants were treated with TAF 25 mg once daily beginning between gestational Weeks 24 and 28 and continuing until postpartum Week 4. All infants received HBV immunoprophylaxis. The primary endpoint was the rate of MTCT (defined as HBsAg+ or HBV DNA >20 IU/mL) at postpartum Month 7. Other outcomes were mother and infant safety.

The mean (SD) TAF treatment duration prior to delivery was 14.3 (1.2) weeks, and treatment began at a mean (SD) gestational age of 25 (1) weeks. Ninety-one infants (male, n=41 [45.1%]; cesarean delivery, n=37 [40.7%]) were born at a mean (SD) gestational age of 39.21 (1.16) weeks, and all mother-infant pairs were followed to postpartum Month 7. Most infants (62.6%, 57/91) were fed with formula, and 17 infants (18.7%) each were fed with breast milk or breast milk and formula.

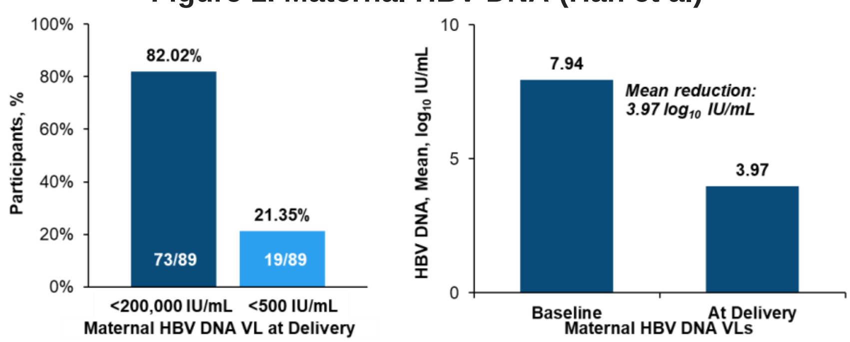
Table 5. Baseline Demographics and Disease Characteristics (Han et al)[5]

Key Demographics and Characteristics	TAF-Treated Mothers (N=89)
Age, mean (SD), years	28.82 (3.61)
Primipara, n (%)	56 (62.9)
Family history of HBV, n (%)	46 (51.7)
Initiated TAF between gestational Weeks 24 and 25, n (%)	64 (71.9)
HBV DNA VL, mean (SD), $\log_{10}$ IU/mL	7.94 (0.6)
HBsAg titer, mean (SD), mIU/mL	30,837.31 (14,170.54)
ALT/AST level, mean (SD), U/L	14.29 (8.09)/18.71 (4.76)

Results

TAF therapy led to maternal HBV DNA VLs <2 × 10^5 IU/mL in 82% of participants at delivery, with a mean (SD) reduction in HBV DNA of 3.97 (1.2) $\log_{10}$ IU/mL (Figure 1).

Figure 1. Maternal HBV DNA (Han et al)[5]



Of the 35 infants with HBeAg and HBsAg serology available at birth, all infants were HBeAg+; 3 of these infants (8.6%) were HBsAg+ at birth, and none had detectable HBV DNA at birth. The MTCT rate (HBsAg+) in 91 infants at 7 months of age was 0%, which included the 3 infants who were HBsAg+ at birth.

Safety

All AEs were mild and did not result in discontinuation of TAF; no serious AEs were reported in the mothers. Maternal complications and AEs are shown in Table 6.

Table 6. Maternal Complications and AEs (Han et al)[5]

Maternal Complications and AEs, n (%)		TAF-Treated Mothers (N=89)
Complications	PROM	9 (10.11)
	Postpartum hemorrhage	7 (7.87)
	Preterm labor	4 (4.49)
	Gestational diabetes mellitus	3 (3.37)
	Gestational hypertension	2 (2.25)
AEs that occurred in >1 participant	Fatigue	5 (5.62)
	Constipation	4 (4.49)
	Insomnia	3 (3.37)
	Nausea	2 (2.25)

Mean (SD) SCr levels increased from 45.97 (5.6) mcmol/L at baseline to 52.23 (8.5) mcmol/L at delivery (*P*<0.05); however, SCr levels remained within normal limits at delivery. Mean (SD) serum phosphorus levels remained stable from baseline to delivery: 1.2 (0.1) mmol/L and 1.21 (0.13) mmol/L, respectively (*P*>0.05). During treatment and pregnancy, no ALT flares were noted. After delivery, 9 participants had mild ALT increases (range, 1.09–1.52 × ULN). Of these participants, 7 did not have an intervention with ALT levels returning to normal in 4 to 8 weeks, and 2 received glutathione with ALT levels returning to normal levels.

No congenital defects or malformations were reported in the infants. Infant measurements at delivery and at postpartum Month 7 are shown in Table 7. After delivery, mean (SD) Apgar scores were the following: at 1 minute, 9.95 (0.23); at 5 minutes, 9.97 (0.16).

Table 7. Infant Measurements at Delivery and at Postpartum Month 7 (Han et al)[5]

Infant Measurements, Mean (SD)	Delivery			Postpartum Month 7	
	Overall	Boys	Girls	Boys	Girls
Weight, kg	3.37 (0.43)	3.49 (0.41)	3.28 (0.43)	8.53 (0.48)	8.14 (0.51)
Height, cm	49.97 (0.92)	50.07 (0.26)[a]	49.9 (1.21)	69.06 (1.95)	68.24 (2.08)
Head circumference, cm	34.72 (0.65)	34.77 (0.44)[a]	34.69 (0.79)[a]	43.47 (1.01)	42.65 (1.46)

[a]*P*<0.05 for comparison with national standards.

PreMIT: Prospective Taiwanese Study of TAF vs TDF[6]

Study design and demographics

A multicenter, prospective cohort study was conducted to assess the safety and effectiveness of TAF compared with TDF for the prevention of MTCT of HBV in pregnant women. Women aged 20 to 45 years with HBV DNA 6 $\log_{10}$ IU/mL who were HBsAg+ and HBeAg+, had ALT levels <40 U/L, did not have HIV or HCV, and did not receive antiviral treatment during pregnancy were eligible for enrollment in this study. Exclusion criteria included systemic disease, fetal anomalies, cirrhosis, and malignant liver tumors. The TAF group comprised mothers treated with TAF 25 mg once daily from the third trimester to 2 weeks after the delivery date between 2019 and 2021 (n=78). Outcomes for TAF-treated mothers and their children were compared with outcomes for those who were treated with TDF 300 mg once daily from the third trimester to 2 weeks postpartum between 2016 and 2018 (TDF P2W group, n=53). All infants received passive/active HBV immunoprophylaxis.

Maternal outcomes included evaluations of prepartum and postpartum HBV DNA and ALT levels through postpartum Month 6; infant outcomes included HBsAg status testing at birth and postpartum Months 6 and 12. Safety outcomes were evaluated in mothers and infants. Additional outcomes were compared with those of an earlier cohort of TDF-treated mothers who received TDF 300 mg once daily from the third trimester to 4 weeks postpartum between 2011 and 2015 (TDF P4W group, n=101) or no antivirals (control group). In the TAF and TDF P2W groups, 27.5% and 26%, respectively, were exclusively breastfed; 22.5% and 32% of infants were fed with breast milk and formula.

Table 8. Baseline Demographics, Disease and Treatment Characteristics, and Maternal and Infant Disposition (Chen et al)[6]

Key Demographics and Characteristics	TAF Group (n=78)	TDF P2W Group (n=53)
Age, mean (SD), years	35.84 (4.57)	34.56 (3.65)
Prepartum treatment duration, mean (SD), weeks	12.6 (2.1)	11 (1.3)
Duration >4 weeks/>8 weeks, n (%)	77 (98.7)/70 (89.7)	53 (100)/45 (84.9)
CK, mean (SD), U/L	52.74 (40.21)	68.62 (79.95)
SCr, mean (SD), mg/dL	0.47 (0.1)	0.45 (0.08)
Participant Disposition	**TAF Group (n=78)**	**TDF P2W Group (n=53)**
Completed postpartum Month 6 follow-up, n	77	53
Infants born/completed postpartum Month 12 follow-up, n	81/78	55/55

Results

The mean decreases in HBV DNA levels from baseline to delivery were similar between TAF- and TDF-treated mothers, although HBV DNA VLs were significantly lower at postpartum Month 6 in the TAF group than in the TDF P2W group (P<0.0001; Table 9). In addition, no differences were observed between groups in the proportion of participants who achieved HBV DNA levels <6 $\log_{10}$ IU/mL at delivery (Table 9). Significantly more TAF-treated than TDF-treated participants continued or restarted antiviral treatment by postpartum Month 6: 11.54% vs 1.89%, respectively (P=0.04).

Table 9. Maternal Efficacy Results (Chen et al)[6]

Maternal Efficacy Parameters		TAF Group (n=78)	TDF P2W Group (n=53)	*P*-Value
HBV DNA VL, mean (SD), $\log_{10}$ IU/mL	Baseline	7.87 (0.59)	8.3 (0.36)	<0.0001
	Delivery	3.99 (1.07)	4.47 (0.86)	0.0086
	Postpartum Month 6	6.98 (2.14)	8.3 (0.7)	<0.0001
HBV DNA VL <6 $\log_{10}$ IU/mL at delivery, n (%)		74 (94.87)	51 (96.23)	0.6839
Reduction from baseline in HBV DNA VL, mean (SD), $\log_{10}$ IU/mL	At delivery	-3.87 (0.85)	-3.83 (0.83)	0.7883
	Postpartum Month 6	-0.89 (1.96)	0 (0.68)	0.0045
HBeAg+/HBeAg- at postpartum Month 6, n (%)		76 (98.7)/1 (1.3)	53 (100)/0	1

Maternal Efficacy Parameters		TAF Group (n=78)	TDF P2W Group (n=53)	*P*-Value
ALT, mean (SD), U/L	Baseline	24.03 (30.7)	16.74 (9.36)	0.0521
	Delivery	19.56 (20.15)	18.28 (9.67)	0.6285
	Postpartum Month 6	33.84 (29.61)	28.04 (16.24)	0.2616
ALT level >2 × ULN, n (%)	At least once	20 (25.64)	9 (16.98)	0.3658
	Lasting ≥3 months	7 (8.97)	1 (1.89)	0.1234
ALT level >5 × ULN, n (%)	At least once	9 (11.54)	3 (5.66)	0.3412
	Lasting ≥3 months	1 (1.28)	0	1

Note: Data were missing from 1 participant at 6 months in the TAF group and from no participants in the TDF P2W group.

The rates of delivery at a gestational age ≥37 weeks (*P*=0.6704) and body weight at birth (*P*=0.4282) were similar between groups (Table 10). One infant in the TAF group was HBsAg+ at Months 6 and 12; the infant's mother had a decrease in HBV DNA from 8.23 $\log_{10}$ IU/mL at baseline to 4.92 $\log_{10}$ IU/mL at delivery. Similarly, 1 infant in the TDF group was HBsAg+ at Months 6 and 12 (*P*=1 for each between-groups comparison per time point); this infant's mother also had a decrease in HBV DNA from 8.34 $\log_{10}$ IU/mL at baseline to 4.1 $\log_{10}$ IU/mL at delivery. In a univariate logistic regression analysis of risk factors associated with infant HBsAg+ status at postpartum Month 6 (overall, n=237; TAF group, n=75; TDF P2W or P4W groups, n=162), treatment type (TAF vs TDF) was not identified as a risk factor (odds ratio, 0.72; 95% CI: 0.07–7; *P*=0.7743).

Table 10. Infant Efficacy Results (Chen et al)[6]

Infant Efficacy Parameters		TAF Group (n=81)	TDF P2W Group (n=55)	*P*-Value
Gestational age, ≥37 weeks/<37 weeks, n (%)		67 (82.72)/14 (17.28)	47 (85.45)/8 (14.55)	0.6704
Type of delivery, vaginal/cesarean, n (%)		54 (66.67)/27 (33.33)	34 (61.82)/21 (38.18)	0.5615
Emergent cesarean delivery, n (%)		2 (2.47)	0	0.5147
Body weight at birth, mean (SD), g		2987.36 (482.56)	3051.58 (431.26)	0.4282
HBsAg+, n (%)	Delivery	6 (7.41)	8 (14.55)	0.1788
	Postpartum Month 6	1 (1.33)	1 (1.82)	1
	Postpartum Month 12	1 (1.28)	1 (1.82)	1
Anti-HBs+ at postpartum Month 12, n (%)		73 (94.81)	52 (94.55)	1
Anti-HBs titer at postpartum Month 12, mean (SD), mIU/mL		647.2 (378)	497.36 (390.54)	0.0285

Note: Of the 78 infants with 12 months of follow-up in the TAF group, 6 infants missed the postpartum Month 6 visit, and 3 missed the postpartum Month 12 visit; 1 did not have a sufficient sample for anti-HBs analysis. Due to the COVID-19 pandemic, 7 infants did not have data at Month 6 or 12, and 1 infant missed both of those assessments; all of these infants were HBsAg- at birth.

Safety

One mother in the TAF group had an AE of nausea, and another had an AE of dry eyes. In the TDF group, AEs of mild gastrointestinal symptoms (n=3) and skin itching (n=1) occurred. No participants discontinued treatment due to intolerance. All AEs resolved without intervention.

ALT levels tended to peak 2 to 4 months postpartum and were similar between groups at delivery and at postpartum Month 6 (Table 9). No participants experienced decompensation. In a model that evaluated ALT levels in 332 participants from the TAF, TDF (P2W and P4W), and control groups, 87.2% of participants had generally stable ALT levels prepartum and postpartum. Additionally, 8% had moderate postpartum flares, 2.4% had marked postpartum flares, and 2.4% had flares during the third trimester; study investigators concluded these participants were candidates for antiviral treatment extension.

No major congenital abnormalities were noted in either group, and infant weights and heights (through Month 12) and laboratory values (eg, AST, ALT, Cr, and calcium levels) were generally similar between groups.

PK Data: TAF Use in Pregnancy and Lactation

TAF PK in Breastfeeding Women With CHB

Study design and demographics[8]

A phase 4, open-label, multicenter, single-arm study evaluated the PK of TAF and TFV in women with CHB who were breastfeeding and infant exposure. Treatment with TAF 25 mg once daily was initiated during the third trimester or postpartum. Samples were collected within 6 months postpartum once mothers had received ≥4 weeks of TAF, as follows: maternal blood, n=8; breast milk, n=8; and infant urine, n=7. Maternal plasma and breast milk samples were collected predose and several times through 24 hours postdose; infant urine samples were collected via urine bag at Hour 0 through Hour 8. Primary outcomes included TAF and TFV PK parameters in maternal plasma and breast milk. Infant drug exposure was assessed via TFV concentrations in urine, maternal breast milk to plasma ratio, and the RID.

In mothers, the median (range) of demographics at baseline was as follows: age, 34.5 (26.8–39.7) years; weight, 64.9 (44.9–130.8) kg; HBV VL, 2692 (<20–7720) IU/mL; duration of TAF at sample collection, 6.6 (5–11.1) weeks; and timing of sample collection, 11.3 (6–15.4) weeks postpartum. In infants, the median (range) weight at the time of sample collection was 3.49 (2.5–5.45) kg.

Results

Within 6 to 8 hours after a dose, TAF levels were below the LoQ in breast milk and maternal plasma in 7 of the 8 mothers (Figure 2),[8] and the TAF $t_{1/2}$ was 0.8 hours in breast milk and 0.9 hours in maternal plasma (Table 11).[11] TFV levels remained generally stable after a dose in both breast milk and maternal plasma, but higher levels were observed in breast milk than in maternal plasma.[8]

Figure 2. PKs of TAF and TFV in Maternal Plasma and Breast Milk (Kayes et al)[8]

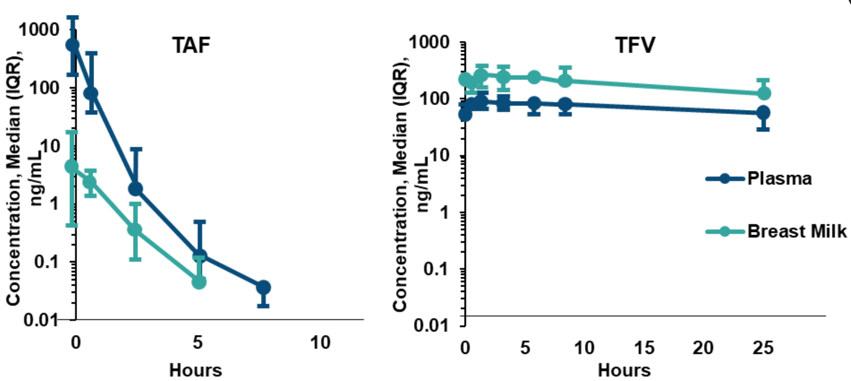


Table 11. PK Values (Non-Compartmental Analysis) of TAF and TFV in Maternal Plasma and Breast Milk (Kayes et al)[11]

PK Parameters, Median (IQR)	Maternal Plasma		Breast Milk	
	TAF	TFV	TAF	TFV
$t_{1/2}$, h	0.9 (0.7–1.1)	40.5 (18.5–65.1)	0.8 (0.8–2.2)	26.4 (18.5–33)
C_{max}, ng/mL	166.5 (84.5–354.8)	16.7 (11.3–19.9)	2.3 (0.9–11.6)	49.2 (30–58.5)
T_{max}, h	0.5 (0.5–1.1)	1.3 (0.7–2.6)	0.5 (0.5–1.3)	4.3 (3–8)
AUC_{all}, ng·h/mL	149.9 (70.9–214.3)	207.4 (146.4–305.6)	2.9 (2.4–3.4)	602.6 (517–1015.6)

Abbreviations: AUC_{all}=area under the concentration-time curve for all time points; C_{max}=peak concentration; T_{max}=time needed to achieve peak concentration.

The median (IQR) breast milk to plasma ratio of TFV was greater than that of TAF: TFV, 2.81 (2.04–3.98) and TAF, 0.03 (0.026–0.04), indicating that TFV was more concentrated in breast milk than plasma and TAF was diluted in breast milk. The RID of TAF (18.75 ng/kg/day) was 0.005% of the maternal dose and was below the accepted standard of safe exposure (<10%). Three infant urine samples had TFV levels above the LoQ: 12, 24, and 25 ng/mL. There was no clear correlation between TFV levels in infant urine and maternal plasma and breast milk levels.[8] The median urine TFV level at steady state in infants (5 ng/mL) was lower than the median levels of TFV in another study that was conducted in adults (1480 ng/mL).[8,12]

No safety data were provided.[8]

References

1. Enclosed. Gilead Sciences Inc, VEMLIDY® (tenofovir alafenamide) tablets, for oral use. U.S. Prescribing Information. Foster City, CA.
2. Antiretroviral Pregnancy Registry Steering Committee. *The Antiretroviral Pregnancy Registry Interim Report: 01 January 1989 Through 31 July 2025. Morrisville, NC.* July 2025.
3. Pan CQ, Zhu L, Yu AS, Zhao Y, Zhu B, Dai E. Tenofovir Alafenamide Versus Tenofovir Disoproxil Fumarate for Preventing Vertical Transmission in Chronic Hepatitis B Mothers: A Systematic Review and Meta-Analysis. *Clin Infect Dis.* 2024;79(4):953-964.
4. Liu Z, Zhao Y, Wang W, et al. Preventing mother-to-child transmission of hepatitis B virus with a new antiviral nucleotide analogue - tenofovir alafenamide fumarate: a nationwide multi-center cohort study (Interim analysis) [Poster PC026]. Paper presented at: 32th Annual Meeting of APASL 2023; February 15-19, 2023; Taipei, Taiwan.
5. Han G, Zhou G, Sun T, et al. Tenofovir alafenamide in blocking mother-to-child transmission of hepatitis B virus: a multi-center, prospective study. *J Matern Fetal Neonatal Med.* 2022:1-8.
6. Chen HL, Lee CN, Chang CH, et al. Tenofovir alafenamide or tenofovir disoproxil fumarate in pregnancy to prevent HBV transmission: Maternal ALT trajectory and infant outcomes. *Liver Int.* 2024:1-13.
7. Zeng QL, Zhou YH, Dong XP, et al. Expected 8-Week Prenatal vs 12-Week Perinatal Tenofovir Alafenamide Prophylaxis to Prevent Mother-to-Child Transmission of Hepatitis B Virus: A Multicenter, Prospective, Open-Label, Randomized Controlled Trial. *Am J Gastroenterol.* 2024.
8. Kayes T, Crane H, Symonds A, et al. Plasma and breast milk pharmacokinetics of tenofovir alafenamide in mothers with chronic hepatitis B infection. *Alimentary Pharmacology & Therapeutics.* 2022;56(3):510-518.
9. Pan CQ, Zhu L, Yu AS, Zhao Y, Zhu B, Dai E. Tenofovir Alafenamide Versus Tenofovir Disoproxil Fumarate for Preventing Vertical Transmission in Chronic Hepatitis B Mothers: A Systematic Review and Meta-Analysis [Supplement]. *Clin Infect Dis.* 2024;79(4):953-964.
10. Clinical Trials. Preventing Mother-to-child Transmission of Hepatitis B Virus With Tenofovir Alafenamide (TAF) Available at: https://clinicaltrials.gov/ct2/show/NCT05177926. Accessed: 17 April 2023. Last Update: 05 January. 2022.

11. Kayes T, Crane H, Symonds A, Dumond J, Cottrell M, Di Girolamo J. Corrigendum to ‘‘Plasma and breast milk pharmacokinetics of tenofovir alafenamide in mothers with chronic hepatitis B infection". *Aliment Pharmacol Ther.* 2023;57.
12. Haaland RE, Martin A, Livermont T, et al. Brief Report: Urine Emtricitabine and Tenofovir Concentrations Provide Markers of Recent Antiretroviral Drug Exposure Among HIV-Negative Men Who Have Sex With Men. *J Acquir Immune Defic Syndr.* 2019;82(3):252-256.

Abbreviations

β2M=β-2 microglobulin
AE=adverse event
APR=Antiretroviral Pregnancy Registry
ARV=antiretroviral
BMD=bone mineral density
CHB=chronic hepatitis B
CK=creatine kinase
HAV=hepatitis A virus
HBeAg=hepatitis B envelope antigen
HBs=hepatitis B surface
HBsAg=hepatitis B surface antigen
HEV=hepatitis E virus
LoQ=level of quantification
LTFU=lost to follow-up
MTCT=mother-to-child transmission
P2W/P4W=stopping medication 2/4 weeks postpartum
PEIU/mL=Paul Ehrlich Institute units per mL
PK=pharmacokinetic(s)
PP=per protocol
PROM=premature rupture of membranes
RID=relative infant dose
RR=risk ratio
$t_{1/2}$=half-life
TAF=tenofovir alafenamide
TB=total bilirubin
TDF=tenofovir disoproxil fumarate
TFV=tenofovir
ULN=upper limit of normal
VL=viral load

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Vemlidy US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/liver-disease/vemlidy/vemlidy_pi.

Follow-Up

For any additional questions, please contact Gilead Medical Information at:

☎1-866-MEDI-GSI (1-866-633-4474) or 🖰 www.askgileadmedical.com

Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or
🖰 www.gilead.com/utility/contact/report-an-adverse-event

FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖰 www.accessdata.fda.gov/scripts/medwatch

Data Privacy

The Medical Information service at Gilead Sciences may collect, store, and use your personal information to provide a response to your medical request. We may share your information with other Gilead Sciences colleagues to ensure that your request is addressed appropriately. If you report an adverse event or concern about the quality of a Gilead or Kite product, we will need to use the information you have given us in order to meet our regulatory requirements in relation to the safety of our medicines.

It may be necessary for us to share your information with Gilead's affiliates, business partners, service providers, and regulatory authorities located in countries besides your own. Gilead Sciences has implemented measures to protect the personal information you provide. Please see the Gilead Privacy Statement (www.gilead.com/privacy-statements) for more information about how Gilead handles your personal information and your rights. If you have any further questions about the use of your personal information, please contact gilead.privacy@gilead.com.