דצמבר 2020

# הודעה על עדכון עלונים:

# Vemlidy film coated tablets

**(tenofovir alafenamide 25 mg)**

רופאים ורוקחים נכבדים,

חברת גיליאד סיאנסז ישראל בע"מ מבקשת להודיעכם על עדכון בעלון לרופא של התכשיר בנדון.

**ההתוויה הרשומה לתכשיר בישראל:**

| |
|---|
| Vemlidy is indicated for the treatment of chronic hepatitis B in adults and adolescents (aged 12 years and older with body weight at least 35 kg) |

השינויים מסומנים בעלון המצורף כאשר הטקסט המודגש באדום הוסף לעלון ואילו הטקסט המחוק ~~בקו~~ ~~חוצה~~ נגרע ממנו. העלונים לרופא ולצרכן נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות:

https://data.health.gov.il/drugs/index.html#/byDrug

כמו כן ,ניתן לקבלם מודפסים על ידי פנייה לבעל הרישום: גיליאד סיאנסז ישראל בע"מ, רחוב החרש 4 ,ת.ד. 6090, פארק העסקים הוד השרון 4524075, ישראל.

בברכה,

מריה חורגין

רוקחת ממונה

גיליאד סיאנסז ישראל בע"מ

**העדכונים המהותיים בעלון לרופא:**

**4.4 Special warnings and precautions for use**

Renal impairment

*Patients with creatinine clearance < 30 mL/min*

The use of Vemlidy once daily in patients with CrCl ≥ 15 mL/min ~~but~~and < 30 mL/min ~~and in patients with CrCl < 15 mL/min who are receiving haemodialysis~~ is based on Week 24 interim data on the efficacy and safety of switching from another antiviral regimen to tenofovir alafenamide in an ongoing open-label clinical study of virologically suppressed chronic HBV-infected patients (see sections 4.8 and 5.1).~~very limited pharmacokinetic data and on modelling and simulation. There are no safety data on the use of Vemlidy to treat HBV-infected patients with CrCl < 30 mL/min.~~ There are very limited data on the safety and efficacy of Vemlidy in HBV-infected patients with CrCl < 15 mL/min on chronic haemodialysis (see sections 4.8, 5.1 and 5.2).

The use of Vemlidy is not recommended in patients with CrCl < 15 mL/min who are not receiving haemodialysis (see section 4.2).

**4.8 Undesirable effects**

Other Special Populations

In an ongoing open-label Phase 2 study (GS-US-320-4035; "*Study 4035*") in virologically suppressed patients with moderate to severe renal impairment (eGFR by Cockcroft-Gault method 15 to 59 mL/min; Part A, Cohort 1, N = 78), end stage renal disease (ESRD) (eGFR < 15 mL/min) on haemodialysis (Part A, Cohort 2, N = 15), and/or moderate to severe hepatic impairment (Child-Pugh Class B or C at screening or by history; Part B, N = 31) who switched from another antiviral regimen to tenofovir alafenamide, no additional adverse reactions to tenofovir alafenamide were identified through Week 24.

## 5.1 Pharmacodynamic properties

*Renal and/or hepatic impairment Study 4035*

*Study 4035* is an ongoing open-label clinical study to evaluate the efficacy and safety of switching from another antiviral regimen to tenofovir alafenamide in virologically suppressed chronic HBV-infected patients. Part A of the study includes patients with moderate to severe renal impairment (eGFR by Cockcroft-Gault method between 15 and 59 mL/min; Cohort 1, N = 78) or ESRD (eGFR by Cockcroft-Gault method < 15 mL/min) on hemodialysis (Cohort 2, N = 15). Part B of the study includes patients (N = 31) with moderate to severe hepatic impairment (Child-Pugh Class B or C at screening or a history of CPT score ≥ 7 with any CPT score ≤ 12 at screening). The final clinical and laboratory outcomes will be reported following study completion at Week 96.

## 5.2 Pharmacokinetic properties

*Renal impairment*

No clinically relevant differences in tenofovir alafenamide or tenofovir pharmacokinetics were observed between healthy subjects and patients with severe renal impairment (estimated CrCl > 15 but < 30 mL/min) in studies of tenofovir alafenamide (Table 10).

Exposures of tenofovir in subjects with ESRD (estimated creatinine clearance < 15 mL/min) on chronic haemodialysis who received tenofovir alafenamide (N = 5) were substantially higher than in subjects with normal renal function (Table 10). No clinically relevant differences in tenofovir alafenamide pharmacokinetics were observed in patients with ESRD on chronic haemodialysis as compared to those with normal renal function.

**Table 10: Pharmacokinetics of tenofovir alafenamide and its metabolite tenofovir in subjects with renal impairment as compared to subjects with normal renal function**

| | AUC (mcg•hour per mL) Mean (CV%) | | |
|---|---|---|---|
| **Estimated Creatinine Clearance[a]** | **Normal renal function ≥ 90 mL per minute (N = 13)[b]** | **Severe renal impairment 15–29 mL per minute (N = 14)[b]** | **ESRD on haemodialysis < 15 mL per minute (N = 5)[c]** |
| Tenofovir alafenamide | 0.27 (49.2)[d] | 0.51 (47.3)[d] | 0.30 (26.7)[e] |
| Tenofovir | 0.34 (27.2)[d] | 2.07 (47.1)[d] | 18.8 (30.4)[f] |

CV = coefficient of variation

a. By Cockcroft-Gault method.

b. PK assessed on a single dose of TAF 25 mg in subjects with normal renal function and in subjects with severe renal impairment in Study GS-US-120-0108.

c. PK assessed prior to haemodialysis following multiple-dose administration of TAF 25 mg in 5 HBV-infected subjects in Study GS-US-320-4035. These subjects had a median baseline eGFR by Cockcroft-Gault of 7.2 mL/min (range, 4.8 to 12.0).

d. $AUC_{inf}$.

e. $AUC_{last}$.

f. $AUC_{tau}$