הודעה על החמרה (מידע בטיחות) בעלון לרופא ובעלון לצרכן

(מעודכן 05.2013)

תאריך 11.12.16

שם תכשיר באנגלית ומספר הרישום Viread 130-43-30944-23/24/25

שם בעל הרישום GILEAD SCIENCES ISRAEL LTD

טופס זה מיועד לפרוט ההחמרות בלבד !

עלון לרופא:

ההחמרות המבוקשות		
טקסט חדש	**טקסט נוכחי**	**פרק בעלון**
HIV-1 While effective viral suppression with antiretroviral therapy has been proven to substantially reduce the risk of sexual transmission, a residual risk cannot be excluded. Precautions to prevent transmission should be taken in accordance with national guidelines.		**4.4 Special warnings and precautions for use**
Co-administration of other medicinal products Viread should not be administered concomitantly with other medicinal products containing tenofovir disoproxil fumarate or tenofovir alafenamide.	Co-administration of other medicinal products Viread should not be administered concomitantly with other medicinal products containing tenofovir disoproxil fumarate.	**4.4 Special warnings and precautions for use**
Renal and bone effects in adult population	Renal *impairment:*	**4.4 Special warnings and precautions for use**

Renal monitoring It is recommended that creatinine clearance is calculated in all patients prior to initiating therapy with tenofovir disoproxil fumarate and renal function (creatinine clearance and serum phosphate) is also monitored after two to four weeks of treatment,	It is recommended that creatinine clearance is calculated in all patients prior to initiating therapy with tenofovir disoproxil fumarate and renal function (creatinine clearance and serum phosphate) is also monitored every four weeks during the first year	**4.4 Special warnings and precautions for use**
Interrupting treatment with tenofovir disoproxil fumarate should also be considered in case of progressive decline of renal function when no other cause has been identified.		**4.4 Special warnings and precautions for use**
Cases of acute renal failure after initiation of high dose or multiple non-steroidal anti-inflammatory drugs (NSAIDs) have been reported in patients treated with tenofovir disoproxil fumarate and with risk factors for renal dysfunction. If tenofovir disoproxil fumarate is co-administered with an NSAID, renal function should be monitored adequately. A higher risk of renal impairment has been reported in patients receiving tenofovir disoproxil fumarate in combination with a ritonavir or cobicistat boosted protease inhibitor. A close monitoring of renal function is required in these patients (see section 4.5). In patients with renal risk factors, the co-administration of tenofovir disoproxil fumarate with a boosted protease inhibitor should be carefully evaluated.	.	**4.4 Special warnings and precautions for use**

Renal impairment Renal safety with tenofovir disoproxil fumarate has only been studied to a very limited degree in adult patients with impaired renal function (creatinine clearance < 80 ml/min).		**4.4 Special warnings and precautions for use**
In other studies (prospective and cross-sectional), the most pronounced decreases in BMD were seen in patients treated with tenofovir disoproxil fumarate as part of a regimen containing a boosted protease inhibitor. Alternative treatment regimens should be considered for patients with osteoporosis that are at a high risk for fractures.		**4.4 Special warnings and precautions for use**

Renal and bone effects in paediatric population There are uncertainties associated with the long term effects of bone and renal toxicity. Moreover, the reversibility of renal toxicity cannot be fully ascertained. Therefore, a multidisciplinary approach is recommended to adequately weigh on a case by case basis the benefit/risk balance of treatment, decide the appropriate monitoring during treatment (including decision for treatment withdrawal) and consider the need for supplementation. *Renal monitoring* Renal function (creatinine clearance and serum phosphate) should be evaluated prior to treatment, and monitored during treatment as in adults (see above). *Renal management* If serum phosphate is confirmed to be < 3.0 mg/dl (0.96 mmol/l) in any paediatric patient receiving tenofovir disoproxil fumarate, renal function should be re-evaluated within one week, including measurements of blood glucose, blood potassium and urine glucose concentrations (see section 4.8, proximal tubulopathy). If renal abnormalities are suspected or detected then consultation with a nephrologist should be obtained to consider interruption of tenofovir disoproxil fumarate treatment. Interrupting treatment with tenofovir disoproxil fumarate should also be considered in case of progressive decline of renal function when no other cause has been identified. *Co-administration and risk of renal toxicity*		**4.4 Special warnings and precautions for use**

The same recommendations apply as in adults (see above). *Renal impairment* The use of tenofovir disoproxil fumarate is not recommended in paediatric patients with renal impairment (see section 4.2). Tenofovir disoproxil fumarate should not be initiated in paediatric patients with renal impairment and should be discontinued in paediatric patients who develop renal impairment during tenofovir disoproxil fumarate therapy.		

If bone abnormalities are detected or suspected in paediatric patients, consultation with an endocrinologist and/or nephrologist should be obtained.	If bone abnormalities are suspected then appropriate consultation should be obtained.	**4.4 Special warnings and precautions for use**
Use with certain hepatitis C virus antiviral agents Co-administration of tenofovir disoproxil fumarate with ledipasvir/sofosbuvir has been shown to increase plasma concentrations of tenofovir, especially when used together with an HIV regimen containing tenofovir disoproxil fumarate and a pharmacokinetic enhancer (ritonavir or cobicistat). The safety of tenofovir disoproxil fumarate in the setting of ledipasvir/sofosbuvir and a pharmacokinetic enhancer has not been established. The potential risks and benefits associated with co-administration of ledipasvir/sofosbuvir with tenofovir disoproxil fumarate given in conjunction with a boosted HIV protease inhibitor (e.g. atazanavir or darunavir) should be considered, particularly in patients at increased risk of renal dysfunction. Patients receiving ledipasvir/sofosbuvir concomitantly with tenofovir disoproxil fumarate and a boosted HIV protease inhibitor should be monitored for adverse reactions related to tenofovir disoproxil fumarate.		**4.4 Special warnings and precautions for use**
Weight and metabolic parameters An increase in weight and in levels of blood lipids and glucose may occur during antiretroviral therapy. Such changes may in part be linked to disease control and life style. For lipids, there is in some cases evidence for a treatment effect, while for weight gain there is no strong evidence relating this to any particular treatment. For monitoring of blood lipids and		**4.4 Special warnings and precautions for use**

glucose reference is made to established HIV treatment guidelines. Lipid disorders should be managed as clinically appropriate.		
Autoimmune disorders (such as Graves' disease) have also been reported to occur in the setting of immune reactivation; however, the reported time to onset is more variable and these events can occur many months after initiation of treatment.		**4.4 Special warnings and precautions for use**
Concomitant use not recommended Viread should not be administered concomitantly with other medicinal products containing tenofovir disoproxil fumarate or tenofovir alafenamide.	Concomitant use not recommended Viread should not be administered concomitantly with other medicinal products containing tenofovir disoproxil fumarate	**4.5 Interaction with other medicinal products and other forms of interaction**
Hepatitis C virus antiviral agents Ledipasvir/Sofosbuvir (90 mg/400 mg q.d.) + Atazanavir/Ritonavir (300 mg q.d./100 mg q.d.) + Emtricitabine/Tenofovir disoproxil fumarate (200 mg/300 mg q.d.)[1] Increased plasma concentrations of tenofovir resulting from co-administration of tenofovir disoproxil fumarate, ledipasvir/sofosbuvir and atazanavir/ritonavir may increase adverse reactions related to tenofovir disoproxil fumarate, including renal disorders. The safety of tenofovir disoproxil fumarate when used with ledipasvir/sofosbuvir and a pharmacokinetic enhancer (e.g. ritonavir or cobicistat) has not been established. The combination should be used with caution with frequent renal monitoring, if other alternatives are not available (see section 4.4).		**4.5 Interaction with other medicinal products and other forms of interaction**

Ledipasvir/Sofosbuvir (90 mg/400 mg q.d.) + Darunavir/Ritonavir (800 mg q.d./100 mg q.d.) + Emtricitabine/Tenofovir disoproxil fumarate (200 mg/300 mg q.d.)1 Increased plasma concentrations of tenofovir resulting from co-administration of tenofovir disoproxil fumarate, ledipasvir/sofosbuvir and darunavir/ritonavir may increase adverse reactions related to tenofovir disoproxil fumarate, including renal disorders. The safety of tenofovir disoproxil fumarate when used with ledipasvir/sofosbuvir and a pharmacokinetic enhancer (e.g. ritonavir or cobicistat) has not been established. The combination should be used with caution with frequent renal monitoring, if other alternatives are not available (see section 4.4).		**4.5 Interaction with other medicinal products and other forms of interaction**

Ledipasvir/Sofosbuvir (90 mg/400 mg q.d.) + Efavirenz/Emtricitabine/Tenofovir disoproxil fumarate (600 mg/200 mg/300 mg q.d.) No dose adjustment is recommended. The increased exposure of tenofovir could potentiate adverse reactions associated with tenofovir disoproxil fumarate, including renal disorders. Renal function should be closely monitored (see section 4.4).		**4.5 Interaction with other medicinal products and other forms of interaction**
Ledipasvir/Sofosbuvir (90 mg/400 mg q.d.) + Emtricitabine/Rilpivirine/Tenofovir disoproxil fumarate (200 mg/25 mg/300 mg q.d.) No dose adjustment is recommended. The increased exposure of tenofovir could potentiate adverse reactions associated with tenofovir disoproxil fumarate, including renal disorders. Renal function should be closely monitored (see section 4.4).		**4.5 Interaction with other medicinal products and other forms of interaction**
After 168 weeks, 16% (7/45) of the tenofovir disoproxil fumarate group, 4% (2/45) of the emtricitabine plus tenofovir disoproxil fumarate group, and 14% (3/22) of the entecavir group experienced tolerability failure. Thirteen percent (6/45) of the tenofovir disoproxil fumarate group, 13% (6/45) of the emtricitabine plus tenofovir disoproxil fumarate group, and 9% (2/22) of the entecavir group had a confirmed increase in serum creatinine ≥ 0.5 mg/dl or confirmed serum phosphate of < 2 mg/dl. At week 168, in this population of patients with decompensated liver disease, the rate of death was of 13% (6/45) in the tenofovir disoproxil fumarate group, 11% (5/45) in the emtricitabine plus tenofovir disoproxil fumarate group		**4.8 Undesirable effects**

and 14% (3/22) in the entecavir group. The rate of hepatocellular carcinoma was 18% (8/45) in the tenofovir disoproxil fumarate group, 7% (3/45) in the emtricitabine plus tenofovir disoproxil fumarate group and 9% (2/22) in the entecavir group.		
Renal and urinary disorders: Uncommon: increased creatinine, proximal renal tubulopathy (including Fanconi syndrome)	*Renal and urinary disorders:* Uncommon: increased creatinine	**4.8 Undesirable effects**
However, in some patients, declines in creatinine clearance did not completely resolve despite tenofovir disoproxil fumarate discontinuation. Patients at risk of renal impairment (such as patients with baseline renal risk factors, advanced HIV disease, or patients receiving concomitant nephrotoxic medications) are at increased risk of experiencing incomplete recovery of renal function despite tenofovir disoproxil fumarate discontinuation (see section 4.4).		**4.8 Undesirable effects**
Metabolic parameters: Weight and levels of blood lipids and glucose may increase during antiretroviral therapy	*Lipids, lipodystrophy* and *metabolic abnormalities:* Combination antiretroviral therapy has been associated with metabolic abnormalities	**4.8 Undesirable effects**
Autoimmune disorders (such as Graves' disease) have also been reported; however, the reported time to onset is more variable and these events can occur many months after initiation of treatment		**4.8 Undesirable effects**
Reductions in BMD have been reported in paediatric patients. In HIV-1 infected adolescents, the BMD Z-scores observed in subjects who received tenofovir disoproxil fumarate were lower than those observed in subjects who received placebo.		**4.8 Undesirable effects**
Reductions in BMD have been observed in HBV infected adolescents. The BMD Z-scores		**4.8 Undesirable effects**

observed in subjects who received tenofovir disoproxil fumarate were lower than those observed in subjects who received placebo (see sections 4.4 and 5.1).		
The use of tenofovir disoproxil fumarate is not recommended in paediatric patients with renal impairment (see sections 4.2 and 4.4).		**4.8 Undesirable effects**
In addition, a K70E substitution in HIV-1 reverse transcriptase has been selected by tenofovir and results in low-level reduced susceptibility to tenofovir.		**5.1 Pharmacodynamic properties**
One patient in the tenofovir disoproxil (as fumarate) arm developed the K70E substitution in the virus.		**5.1 Pharmacodynamic properties**

עלון לצרכן:

ההחמרות המבוקשות		
פרק בעלון	**טקסט נוכחי**	**טקסט חדש**
אזהרות מיוחדות הנוגעות לשימוש בתרופה:		**אין לתת ויראד למתבגרים שקיימות אצלם בעיות כליות**
אזהרות מיוחדות הנוגעות לשימוש בתרופה:		לאחר התחלת נטילה של תרופות לטיפול בזיהום ב-HIV, בנוסף לזיהומים מזדמנים, עלולות להופיע גם מחלות אוטואימוניות (מצב שבו מערכת החיסון תוקפת רקמות בריאות בגוף). מחלות אוטואימוניות עלולות להתפתח חודשים רבים לאחר תחילת הטיפול. אם תבחין בתסמינים כלשהם של זיהום או בתסמינים אחרים כגון חולשת שרירים, חולשה המתחילה בכפות הידיים והרגליים ומתפשטת מעלה לכיוון הגו, דפיקות לב, רעד או פעילות-יתר (היפראקטיביות), הודע על כך מיד לרופא כדי לקבל את הטיפול הנחוץ.

אזהרות מיוחדות הנוגעות לשימוש בתרופה:		**אל תיטול ויראד** אם אתה כבר נוטל תרופות אחרות המכילות טנופוביר דיסופרוקסיל פומאראט. אל תיטול ויראד ביחד עם תרופות המכילות אדפוביר דיפיבוקסיל
אין להשתמש בתרופה מבלי להיוועץ ברופא לפני התחלת הטיפול:		• תרופות נוגדות דלקת לא סטרואידיות (NSAIDs, לשיכוך כאבי עצמות או כאבי שרירים).
נהיגה ושימוש במכונות		ויראד עלולה לגרום סחרחורות. אם אתה חש סחרחורת בעת נטילת ויראד, **אין לנהוג או לרכוב על אופניים** ואין להפעיל כלים או מכונות מסוכנים.
תגובות בין תרופתיות:		
הריון והנקה:		
כיצד תשתמש בתרופה:		
תופעות לוואי:		• נזק לתאי אבובית הכליה

מצ"ב העלון, שבו מסומנות ההחמרות המבוקשות על רקע צהוב .

שינויים שאינם בגדר החמרות סומנו (בעלון) בצבע שונה. יש לסמו רק תוכן מהותי ולא שינויים במיקום הטקסט.

הועבר בדואר אלקטרוני בתאריך _____