רופא/ה ,רוקח/ת נכבד/ה,

הנדון: טרובדה טבליות מצופות
Truvada coated tablets

מרכיב פעיל: Emtricitabine 200 mg and Tenofovir Disoproxil (as Fumarate) 245 mg

התוויה המאושרת:

Truvada is indicated in combination with other anti-retroviral medicinal products for the treatment of HIV-1 infected adults over 18 years of age. Truvada is indicated in combination with safer sex practices for pre-exposure prophylaxis to reduce the risk of sexually acquired HIV-1 infection in adults at high risk.

חברת גיליאד סיאנסז ישראל בע"מ מבקשת ליידע על החמרות בעלון לרופא ולצרכן שהוגשו למשרד הבריאות באוקטובר 2018.
העדכונים מופיעים כטקסט אדום, הסימונים בצהוב הינם החמרות במידע הבטיחותי. ~~קו חוצה~~ מסמן טקסט שנמחק.
העדכונים המשמעותיים ביותר מופיעים בעמוד הבא במכתב זה, קיימים עדכונים מינוריים נוספים.

העלון לרופא ולצרכן בפורמט החדש נשלחו למשרד הבריאות לצורך פרסומם במאגר התרופות שבאתר משרד הבריאות:

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

כמו כן, ניתן לקבלם מודפסים על-ידי פניה לחברת 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

עדכונים מהותיים בעלון לרופא:

4.4 Special warnings and precautions for use

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Immune Reactivation Syndrome

In HIV infected patients with severe immune deficiency at the time of institution of CART, an inflammatory reaction to asymptomatic or residual opportunistic pathogens may arise and cause serious clinical conditions, or aggravation of symptoms. Typically, such reactions have been observed within the first few weeks or months of initiation of CART. Relevant examples are cytomegalovirus retinitis, generalised and/or focal mycobacterial infections, and *Pneumocystis jirovecii* pneumonia. Any inflammatory symptoms should be evaluated and treatment instituted when necessary. Autoimmune disorders (such as Graves' disease and autoimmune hepatitis) 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.

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Co-administration of other medicinal products

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Use with ledipasvir and sofosbuvir ~~or~~, sofosbuvir and velpatasvir or sofosbuvir, velpatasvir and voxilaprevir
Co-administration of tenofovir disoproxil ~~fumarate~~ with ledipasvir/sofosbuvir, sofosbuvir/velpatasvir or sofosbuvir/velpatasvir/voxilaprevir 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~~ when co-administered with ledipasvir/sofosbuvir, sofosbuvir/velpatasvir or sofosbuvir/velpatasvir/voxilaprevir and a pharmacokinetic enhancer has not been established. The potential risks and benefits associated with co-administration should be considered, particularly in patients at increased risk of renal dysfunction. Patients receiving ledipasvir/sofosbuvir~~-~~, sofosbuvir/velpatasvir or sofosbuvir/velpatasvir/voxilaprevir concomitantly with tenofovir disoproxil ~~fumarate~~ and a boosted HIV protease inhibitor should be monitored for adverse reactions related to tenofovir disoproxil ~~fumarate~~.

4.5 Interaction with other medicinal products and other forms of interaction

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Medicinal product by therapeutic areas	Effects on drug levels Mean percent change in AUC, C_{max}, C_{min} with 90% confidence intervals if available (mechanism)	Recommendation concerning co-administration with Truvada (emtricitabine 200 mg, tenofovir disoproxil ~~fumarate 300~~245 mg)
Sofosbuvir/Velpatasvir/ Voxilaprevir (400 mg/100 mg/ ~~100 mg+100 mg~~ q.d.) ~~+ Efavirenz/~~[3] + Darunavir (800 mg q.d.) + Ritonavir (100 mg q.d.) + Emtricitabine/Tenofovir disoproxil ~~fumarate~~ (600 mg/(200 mg /~~300~~245 mg q.d.)	Sofosbuvir: AUC: ↔ C_{max}: ↓ ~~19% (↓ 40 to ↑ 10)~~30% C_{min}: N/A GS-~~-~~331007[2]: AUC: ↔ C_{max}: ~~↓ 23% (↓ 30 to ↑ 16)~~:↔ EfavirenzC_{min}: N/A Velpatasvir: AUC: ↔ C_{max}: ↔ C_{min}: ↔ Voxilaprevir: AUC: ↑ 143% C_{max}:↑ 72% C_{min}: ↑ 300% Darunavir: AUC: ↔ C_{max}: ↔ C_{min}: ↓ 34% Ritonavir: AUC: ↑ 45% C_{max}: ↑ 60% C_{min}: ↔ Emtricitabine: AUC: ↔ C_{max}: ↔ C_{min}: ↔ Tenofovir: ~~AUC: ↔~~ AUC: ↑ 39% C_{max}: ↑ ~~25% (↑ 8 to ↑ 45)~~48% C_{min}: ~~↔~~↑ 47%	No dose adjustment is required.Increased plasma concentrations of tenofovir resulting from co-administration of tenofovir disoproxil, sofosbuvir/velpatasvir/voxilaprevir and darunavir/ritonavir may increase adverse reactions related to tenofovir disoproxil, including renal disorders. The safety of tenofovir disoproxil when used with sofosbuvir/velpatasvir/voxilaprevir and a pharmacokinetic enhancer (e.g. ritonavir or cobicistat) has not been established. The combination should be used with caution with frequent renal monitoring (see section 4.4).

4.8 Undesirable effects

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Immune Reactivation Syndrome: In HIV infected patients with severe immune deficiency at the time of initiation of CART, an inflammatory reaction to asymptomatic or residual opportunistic infections may arise. Autoimmune disorders (such as Graves' disease and autoimmune hepatitis) have also been reported; however, the reported time to onset is more variable and these events can occur many months after initiation of treatment (see section 4.4).

עדכונים מהותיים בעלון לצרכן:

2. לפני השימוש ~~בתרופה~~ בטרובדה

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חשוב גם שתספר לרופא אם הנך נוטל לדיפסוויר/סופוסבוביר~~,~~ ~~או~~ סופוסבוביר/ולפטסביר או סופוסבוביר/ולפטסביר/ווקסילפרביר לטיפול בזיהום בדלקת כבד **C**.