אוגוסט 2020

הודעה על עדכון עלונים:

Stribild film coated tablets

(elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil (as fumarate)

רופאים ורוקחים נכבדים,

חברת גיליאד סיאנסז ישראל בע"מ מבקשת להודיעכם כי חל עדכון בעלון לרופא ובעלון לצרכן של התכשיר בנדון.

ההתוויה הרשומה לתכשיר בישראל:

Stribild is indicated for the treatment of human immunodeficiency virus-1 (HIV-1) infection in adults aged 18 years and over who are antiretroviral treatment-naïve or are infected with HIV-1 without known mutations associated with resistance to any of the three antiretroviral agents in Stribild.

השינויים מסומנים בעלון המצורף כאשר הטקסט המודגש באדום הוסף לעלון ואילו הטקסט המחוק ~~בקו חוצה~~ נגרע ממנו. הסימונים בצהוב הינם החמרות במידע הבטיחותי.

העדכונים המשמעותיים ביותר מופיעים במכתב זה, קיימים עדכונים מינוריים נוספים.

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 .

התכשיר משווק ע"י חברת סל"א.

בברכה,

מריה חורגין

רוקחת ממונה

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העדכונים המהותיים בעלון לרופא:

4.5 Interaction with other medicinal products and other forms of interaction

Co-administration of Stribild with medicinal products that are primarily metabolised by CYP3A or CYP2D6, or are substrates of P-gp, BCRP, OATP1B1 or OATP1B3 may result in increased plasma concentrations of those products, which could increase or prolong their therapeutic effect and adverse reactions (see Concomitant use contraindicated and section 4.3). Co-administration of Stribild with medicinal products that have active metabolite(s) formed by CYP3A may result in reduced plasma concentrations of these active metabolite(s).…

Table 1: Interactions between the individual components of Stribild and other medicinal products

Medicinal product by therapeutic areas	Effects on drug levels Mean percent change in AUC, C_{max}, C_{min}[1]	Recommendation concerning co-administration with Stribild
Nucleoside reverse transcriptase inhibitors (NRTIs)		
Didanosine	Co-administration of tenofovir disoproxil and didanosine results in a 40-60% increase in systemic exposure to didanosine.	Co-administration of Stribild and didanosine is not recommended. Increased systemic exposure to didanosine may increase didanosine related adverse reactions. Rarely, pancreatitis and lactic acidosis, sometimes fatal, have been reported. Co-administration of tenofovir disoproxil and didanosine at a dose of 400 mg daily has been associated with a significant decrease in CD4 cell count, possibly due to an intracellular interaction increasing phosphorylated (i.e. active) didanosine. A decreased dosage of 250 mg didanosine co-administered with tenofovir disoproxil therapy has been associated with reports of high rates of virological failure within several tested combinations for the treatment of HIV-1 infection. However, in case of initiation of Stribild in patients previously taking didanosine or discontinuation of Stribild and change to a regimen including didanosine there could be a short period when measurable plasma levels of didanosine and tenofovir occur.
MEDICINAL PRODUCTS or ORAL SUPPLEMENTS CONTAINING POLYVALENT CATIONS (e.g. Mg, Al, Ca, Fe, Zn)~~ANTACIDS~~ ~~ANTACIDS~~		
Magnesium/aluminium-containing antacid suspension (20 mL single dose)/Elvitegravir (50 mg single dose)/Ritonavir (100 mg single dose)	Elvitegravir (antacid suspension after ± 2 hours): AUC: ↔ C_{min}: ↔ C_{max}: ↔ Elvitegravir (simultaneous administration): AUC: ↓ 45% C_{min}: ↓ 41% C_{max}: ↓ 47% Elvitegravir plasma concentrations are lower with antacids due to local complexation in the gastrointestinal tract and not to changes in gastric pH.	~~Elvitegravir plasma concentrations are lower with antacids due to local complexation in the gastrointestinal tract and not to changes in gastric pH.~~ It is recommended to separate Stribild and ~~antacid~~ administration of antacids, medicinal products or oral supplements containing polyvalent cations by at least 4 hours. For information on other acid reducing agents (e.g. H_2-receptor antagonists and proton pump inhibitors), see Studies conducted with other medicinal products.

Medicinal product by therapeutic areas	Effects on drug levels Mean percent change in AUC, C_{max}, C_{min}[1]	Recommendation concerning co-administration with Stribild
Calcium or iron supplements (including multivitamins) Other cation-containing antacids Cation-containing laxatives Sucralfate Buffered medicinal products	Interaction not studied with any of the components of Stribild. Elvitegravir plasma concentrations are expected to be lower with antacids, medicinal products or oral supplements containing polyvalent cations, due to local complexation in the gastrointestinal tract and not to changes in gastric pH.	
~~***FOOD SUPPLEMENTS***~~		
~~Multivitamin supplements~~	~~Interaction not studied with any of the components of Stribild.~~	~~As the effect of cationic complexation of elvitegravir cannot be excluded when Stribild is co-administered with multivitamin supplements, it is recommended to separate Stribild and multivitamin supplements dosing by at least 4 hours.~~
ANTIPLATELETS		
Clopidogrel	Interaction not studied with any of the components of Stribild. Co-administration of clopidogrel with cobicistat is expected to decrease clopidogrel active metabolite plasma concentrations, which may reduce the antiplatelet activity of clopidogrel.	Co-administration of clopidogrel with Stribild is not recommended.
Prasugrel	Interaction not studied with any of the components of Stribild. Stribild is not expected to have a clinically relevant effect on plasma concentrations of the active metabolite of prasugrel.	No dose adjustment of prasugrel is required.

4.8 Undesirable effects

Lactic acidosis
Cases of lactic acidosis have been reported with tenofovir disoproxil alone or in combination with other antiretrovirals. Patients with predisposing factors such as patients with decompensated liver disease, or patients receiving concomitant medications known to induce lactic acidosis are at increased risk of experiencing severe lactic acidosis during tenofovir disoproxil treatment, including fatal outcomes.

העדכונים המהותיים בעלון לצרכן:

2. לפני השימוש בסטריבילד

בנוסף, חשוב ליידע את הרופא במידה והנך נוטל תרופה המשתייכת לאחת מהמשפחות הבאות:

- **נוגדי טסיות**, להפחתת הסיכון לקרישי דם, כגון:
  - קלופידוגרל

תרופות או תוספי תזונה המכילים מינרלים (כגון מגנזיום, אלומיניום, סידן, ברזל, אבץ), כגון:

- תוספי מינרלים, ויטמינים (כולל מולטי-ויטמינים), סותרי חומצה ומשלשלים

במידה והנך נוטל תרופות, תוספי תזונה סותרי חומצה או משלשלים המכילים מינרלים (כגון מגנזיום, אלומיניום, סידן, ברזל או אבץ), יש ליטול אותם לפחות ארבע שעות לפני או ארבע שעות אחרי נטילת סטריבילד.