GILEAD

רופא/ה ,רוקח/ת נכבד/ה,

STRIBILD®
elvitegravir 150mg/ cobicistat 150mg/ emtricitabine 200mg/ tenofovir disoproxil fumarate 300mg tablets

הנדון: סטריבילד טבליות מצופות
Stribild coated tablets

מרכיבים פעילים:

150 mg elvitegravir/ 150 mg cobicistat/ 200 mg emtricitabine/ 245 mg of tenofovir disoproxil (equivalent to 300 mg of tenofovir disoproxil fumarate).

התוויה מאושרת:

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.

חברת גיליאד סיאנסז ישראל בע"מ מבקשת ליידע על החמרות בעלון לרופא ועידכונים בעלון לצרכן שהוגשו למשרד הבריאות במרץ 2018.

<u>עדכונים מהותיים בעלון לרופא:</u>
החמרות שהוספו מופיעות כטקסט אדום. קו חוצה מסמן ~~טקסט שנמחק~~.
בפירוט שלהלן מופיעות רק ההחמרות שהתעדכנו מתוך הפרק.

4.3 Contraindications

Co administration is contraindicated with ~~the following~~ medicinal products that are highly dependent on CYP3A ~~due to the potential~~ for clearance and for which elevated plasma concentrations are associated with serious or life threatening adverse reactions. Therefore ~~or loss of virologic response and possible resistance to~~ Stribild should not be co-administered with medicinal products that include, but are not limited to, the following (see section 4.5):

Co-administration is contraindicated with medicinal products that are strong inducers of CYP3A due to the potential for loss of virologic response and possible resistance to Stribild. Therefore, Stribild should not be co-administered with medicinal products that include, but are not limited to, the following (see section 4.5):

- anticonvulsants: carbamazepine, phenobarbital, phenytoin
- antimycobacterials: rifampicin
- herbal products: St. John's wort (*Hypericum perforatum*)

4.4 Special warnings and precautions for use

Stribild should not be administered concomitantly with medicinal products containing tenofovir disoproxil, lamivudine or adefovir dipivoxil used for the treatment of hepatitis B infection, or with other medicinal products containing tenofovir alafenamide.

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Contraception requirements
Female patients of childbearing potential should use either a hormonal contraceptive containing at least 30 µg ethinyloestradiol and containing drospirenone or norgestimate as the progestogen or should use an alternative reliable method of contraception (see sections 4.5 and 4.6). The use of Stribild with oral contraceptives containing other progestogens should be avoided (see section 4.5). Plasma concentrations of drospirenone are expected to be increased following co-administration with Stribild and clinical monitoring is recommended due to the potential for hyperkalaemia (see section 4.5).

4.5 Interaction with other medicinal products and other forms of interaction

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
ORAL CONTRACEPTIVES		
Drospirenone/Ethinyloestradiol (3 mg/~~Norgestimate~~ (0.~~18~~002~~/0.215 mg once daily)/Ethinylestradiol (0.025~~ mg once daily)/ Elvitegravir (150 mg once daily~~single dose)/Cobicistat (150 mg once daily)[4]	Interaction not studied with Stribild. *Expected* DrospirenoneNorgestimate: AUC: ↑ ~~126%~~ ~~C_{min}: ↑ 167%~~ ~~C_{max}: ↑ 108%~~ ~~Ethinylestradiol:~~ ~~AUC: ↓ 25%~~ ~~C_{min}: ↓ 44%~~ ~~C_{max}: ↔~~ ~~Elvitegravir:~~ ~~AUC: ↔~~ ~~C_{min}: ↔~~ ~~C_{max}: ↔~~	Plasma concentrations of drospirenone may be increased when co-administered with cobicistat-containing products. Clinical monitoring is recommended due to the potential for hyperkalemia. Caution should be exercised when co-administering Stribild and a hormonal contraceptive. The hormonal contraceptive should contain at least 30 µg ethinyloestradiol~~ethinylestradiol~~ and contain drospirenone or norgestimate as the progestogen~~progestagen~~ or patients should use an alternative reliable method of contraception (see sections 4.4 and 4.6). The long-term effects of substantial increases in progestogen exposure are unknown.~~ in progesterone exposure are unknown. Co-administration of Stribild with oral contraceptives containing progestagens other than norgestimate has not been studied and therefore should be avoided.~~
Atorvastatin (10 mg single dose)/ Elvitegravir (150 mg once daily)/ Cobicistat (150 mg once daily)/ Emtricitabine (200 mg once daily)/ Tenofovir alafenamide (10 mg once daily)	Atorvastatin: AUC: ↑160% C_{min}: NC C_{max}: ↑132% Elvitegravir: AUC: ↔ C_{min}: ↔ C_{max}: ↔	Concentrations of atorvastatin are increased when co-administered with elvitegravir and cobicistat. Start with the lowest possible dose of atorvastatin with careful monitoring upon co-administration with Stribild.

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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
~~Atorvastatin~~ Pitavastatin	Interaction not studied with any of the components of Stribild. Concentrations of ~~atorvastatin and~~ pitavastatin may be increased when administered with elvitegravir and cobicistat.	~~Co-administration of atorvastatin with Stribild is not recommended. If the use of atorvastatin is considered strictly necessary, the lowest possible dose of atorvastatin should be administered with careful safety monitoring.~~ Caution should be exercised when co-administering Stribild with pitavastatin.

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

https://www.old.health.gov.il/units/pharmacy/trufot/index.asp?safa=h

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,

ענת גולדבוים
רוקחת ממונה

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