ספטמבר 2023

הודעה על עדכון עלונים:

Biktarvy film coated tablets

(bictegravir / emtricitabine / tenofovir alafenamide fumarate)

רופאים ורוקחים נכבדים,

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

ההתוויה הרשומה לתכשיר בישראל:

Biktarvy is indicated for the treatment of adults infected with human immunodeficiency virus-1 (HIV-1) without present or past evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir.

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.

העלון לרופא נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות:

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

כמו כן ,ניתן לקבלו מודפס 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 סל"א.

בברכה,

מריה חורגין

רוקחת ממונה

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העדכונים המהותיים בעלון לרופא:

4.2 Posology and method of administration

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Posology

Special populations

Elderly

~~There are limited data on the use of Biktarvy in patients aged 65 years and over.~~ No dose adjustment of Biktarvy is required in ~~elderly~~ patients aged ≥ 65 years (see sections 4.8 and 5.2).

Hepatic impairment

No dose adjustment of Biktarvy is required in patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. Biktarvy has not been studied in patients with severe hepatic impairment (Child-Pugh Class C), therefore Biktarvy is not recommended for use in patients with severe hepatic impairment (see sections 4.4 and 5.2).

~~*Paediatric population*~~

~~The safety and efficacy of Biktarvy in children under the age of 18 years have not yet been established. No data are available.~~

Renal impairment

No dose adjustment of Biktarvy is required in patients with estimated creatinine clearance (CrCl) ≥ 30 mL/min.

No dose adjustment of Biktarvy is required in adult patients with end stage renal disease (estimated creatinine clearance < 15 mL/minute) who are receiving chronic haemodialysis. However, Biktarvy should generally be avoided and only be used in these patients if the potential benefits are considered to outweigh the potential risks (see sections 4.4 and 5.2). On days of haemodialysis, administer the daily dose of Biktarvy after completion of haemodialysis treatment.

~~Initiation of Biktarvy is not recommended in patients with estimated CrCl below 30 mL/min, as there are insufficient data available regarding the use of Biktarvy in this population (see section 5.2).~~

Initiation of Biktarvy should be avoided in patients with estimated creatinine clearance ≥15 mL/min and < 30 mL/min, or < 15 mL/min who are not receiving chronic haemodialysis, as the safety of Biktarvy has not been established in these populations (see section 5.2).

Paediatric population

The safety and efficacy of Biktarvy in children under the age of 18 years have not yet been established. No data are available.

~~*Hepatic impairment*~~

~~No dose adjustment of Biktarvy is required in patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. Biktarvy has not been studied in patients with severe hepatic impairment (Child-Pugh Class C), therefore Biktarvy is not recommended for use in patients with severe hepatic impairment (see sections 4.4 and 5.2).~~

~~*Paediatric population*~~

~~The safety and efficacy of Biktarvy in children under the age of 18 years have not yet been established. No data are available.~~

4.4 Special warnings and precautions for use

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Patients with end stage renal disease on chronic haemodialysis

Biktarvy should generally be avoided but may be used in adults with end stage renal disease (estimated CrCl < 15 mL/min) on chronic haemodialysis if the potential benefits outweigh the potential risks (see section 4.2). In a study of emtricitabine + tenofovir alafenamide in combination with elvitegravir + cobicistat as a fixed-dose combination tablet (E/C/F/TAF) in HIV-1 infected adults with end stage renal disease (estimated CrCl < 15 mL/min) on chronic haemodialysis, efficacy was maintained through 96 weeks but emtricitabine exposure was significantly higher than in patients with normal renal function. Efficacy was also maintained in the extension phase of the study in which 10 patients switched to Biktarvy for 48 weeks. Although no additional adverse reactions were identified, the implications of increased emtricitabine exposure remain uncertain (see sections 4.8 and 5.2).

4.8 Undesirable effects

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Other special populations

Patients co-infected with hepatitis B
In 16 HIV/HBV co-infected adults administered Biktarvy (8 HIV/HBV treatment-naïve adults in Study GS-US-380-1490; 8 HIV/HBV suppressed adults in Study GS-US-380-1878), the safety profile of Biktarvy was similar to that in patients with HIV-1 monoinfection (see section 5.1).

Elderly
Studies GS-US-380-1844, GS-US-380-1878 and the dedicated Study GS-US-380-4449 in patients ≥ 65 years old (evaluation of 86 HIV-1 infected, virologically-suppressed subjects ≥ 65 years old) included 111 patients aged ≥ 65 years who received Biktarvy. In these patients, no differences in the safety profile of Biktarvy were observed.

Patients with renal impairment
The safety of emtricitabine + tenofovir alafenamide was evaluated in a single arm, open-label clinical study (GS-US-292-1825), in which 55 virologically-suppressed HIV-1 infected patients with end stage renal disease ($eGFR_{CG}$ < 15 mL/min) on chronic haemodialysis received emtricitabine + tenofovir alafenamide in combination with elvitegravir + cobicistat as a fixed-dose combination tablet for 96 weeks. In an extension phase of Study GS-US-292-1825, 10 patients switched to Biktarvy for 48 weeks. No additional adverse reactions were identified in patients with end stage renal disease on chronic haemodialysis in this study (see sections 4.4 and 5.2).

5.2 Pharmacokinetic properties

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Other special populations

Hepatic impairment
Clinically relevant changes in the pharmacokinetics of bictegravir were not observed in subjects with moderate hepatic impairment. The pharmacokinetics of emtricitabine have not been studied in subjects with hepatic impairment; however, emtricitabine is not significantly metabolised by liver enzymes, so the impact of liver impairment should be limited. Clinically relevant changes in the pharmacokinetics of tenofovir alafenamide or its metabolite tenofovir were not observed in patients with mild, moderate, or severe hepatic impairment.

Renal impairment
Severe Renal Impairment (estimated creatinine clearance ≥ 15 and < 30 mL/minute)
No clinically relevant differences in bictegravir, tenofovir alafenamide, or tenofovir pharmacokinetics were observed between healthy subjects and subjects with severe renal impairment (estimated CrCl ≥ 15 mL/min and < 30 mL/min) in Phase 1 Studies. In a separate Phase 1 study of emtricitabine

alone.~~. There are no pharmacokinetic data on bictegravir or tenofovir alafenamide in patients with creatinine clearance less than 15 mL/min. M~~mean systemic emtricitabine exposure was higher in patients with severe renal impairment (CrCl < 30 mL/min) (33.7 µg•h/mL) than in subjects with normal renal function (11.8 µg•h/mL). The safety of Biktarvy has not been established in subjects with estimated creatinine clearance ≥ 15 mL/min and < 30 mL/min.

End Stage Renal Disease (estimated creatinine clearance < 15 mL/minute)
Exposures of emtricitabine and tenofovir in 12 patients with end stage renal disease (estimated CrCl < 15 mL/min) on chronic haemodialysis who received emtricitabine + tenofovir alafenamide in combination with elvitegravir + cobicistat as a fixed dose combination tablet in Study GS-US-292-1825 were significantly higher than in patients with normal renal function. No clinically relevant differences in tenofovir alafenamide pharmacokinetics were observed in patients with end stage renal disease on chronic haemodialysis as compared to those with normal renal function. In the extension phase of Study GS-US-292-1825, lower bictegravir C_{trough} was observed in patients with end stage renal disease who received Biktarvy compared to patients with normal renal function, but this difference was not considered clinically relevant. No additional adverse reactions were identified in patients with end stage renal disease on chronic haemodialysis in this study (see section 4.8).

There are no pharmacokinetic data on bictegravir, emtricitabine or tenofovir alafenamide in patients with end stage renal disease (estimated CrCl < 15 mL/min) not on chronic haemodialysis. The safety of Biktarvy has not been established in these patients.

~~*Hepatic impairment*~~
~~**Clinically relevant changes in the pharmacokinetics of bictegravir were not observed in subjects with moderate hepatic impairment. The pharmacokinetics of emtricitabine have not been studied in subjects with hepatic impairment; however, emtricitabine is not significantly metabolised by liver enzymes, so the impact of liver impairment should be limited. Clinically relevant changes in the pharmacokinetics of tenofovir alafenamide or its metabolite tenofovir were not observed in patients with mild, moderate, or severe hepatic impairment.**~~

העדכונים המהותיים בעלון לצרכן:

3. כיצד תשתמש בתרופה?

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➔ **היוועץ ברופא או ברוקח אם אתה נוטל:**
- **סותרי חומצה** לטיפול בכיבי קיבה, צרבת או ריפלוקס חומצי המכילים אלומיניום ו/או מגנזיום הידרוקסיד
- **תוספי מינרלים** או **ויטמינים** המכילים מגנזיום או ברזל

➔ **ראה סעיף 2 למידע נוסף** על נטילת תרופות אלו במקביל לביקטארווי.

אם הנך עובר טיפולי דיאליזה, קח את המנה היומית של ביקטארווי לאחר השלמת טיפול הדיאליזה.

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6. מידע נוסף

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מגשית (בליסטר)
ביקטארווי זמינה באריזות מגשית חודשיות של 30 טבליות ובאריזות רב-חודשיות של 3 קרטונים המכילים 30 טבליות כל אחד. כל אריזה בודדת מכילה ארבע מגשיות המכילות שבע טבליות כל אחת ובנוסף מגשית המכילה שתי טבליות. בכל חלל במגשית נמצא סופח לחות אשר אסור לבליעה או להסרה.