יולי 2025

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:

- נרשם מינון חדש לתכשיר: **Biktarvy 30/120/15 mg**
- וכן חל עדכון בעלון לרופא ולצרכן של התכשיר בנדון.

ההתוויה הרשומה לתכשיר בישראל:

Biktarvy 30/120/15 mg is indicated for the treatment of human immunodeficiency virus-1 (HIV-1) infection in adults and paediatric patients at least 2 years of age and weighing at least 14 kg without present or past evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir (see section 5.1).

Biktarvy 50/200/25 mg is indicated for the treatment of ~~adults infected with~~ human immunodeficiency virus-1 (HIV-1) infection in adults and paediatric patients at least 6 years of age and weighing at least 25 kg without present or past evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir (see section 5.1).

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

גיליאד סיאנסז ישראל בע"מ

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טל: 09-8802050, פקס: 09-8802052

העדכונים המהותיים בעלון לרופא:

1. NAME OF THE MEDICINAL PRODUCT

Biktarvy® 30/120/15 mg
Biktarvy® 50/200/25 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Biktarvy® 30/120/15 mg
Each film-coated tablet of Biktarvy® 30/120/15 mg contains bictegravir sodium equivalent to 30 mg of bictegravir, 120 mg of emtricitabine, and tenofovir alafenamide fumarate equivalent to 15 mg of tenofovir alafenamide.

Biktarvy® 50/200/25 mg
Each film-coated tablet of Biktarvy® 50/200/25 mg contains bictegravir sodium equivalent to 50 mg of bictegravir, 200 mg of emtricitabine, and tenofovir alafenamide fumarate equivalent to 25 mg of tenofovir alafenamide.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet (tablet).

Biktarvy® 30/120/15 mg
Pink, capsule-shaped, film-coated tablet, debossed with "BVY" on one side and a score line on the other side of the tablet. Each tablet is approximately 14 mm x 6 mm. The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

Biktarvy® 50/200/25 mg
Purplish-brown, capsule-shaped, film-coated tablet debossed with "GSI" on one side and "9883" on the other side of the tablet. Each tablet is approximately 15 mm × 8 mm.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Biktarvy 30/120/15 mg is indicated for the treatment of human immunodeficiency virus-1 (HIV-1) infection in adults and paediatric patients at least 2 years of age and weighing at least 14 kg without present or past evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir (see section 5.1).

Biktarvy 50/200/25 mg is indicated for the treatment of ~~adults infected with~~ human immunodeficiency virus-1 (HIV-1) infection in adults and paediatric patients at least 6 years of age and weighing at least 25 kg without present or past evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir (see section 5.1).

4.2 Posology and method of administration

Therapy should be initiated by a physician experienced in the management of HIV infection.

Posology

Paediatric patients at least 2 years of age and weighing at least 14 kg to less than 25 kg
One 30/120/15 mg tablet to be taken once daily.

Adults and paediatric patients weighing at least 25 kg
One 50/200/25mg tablet to be taken once daily.

Missed doses
If the patient misses a dose of Biktarvy within 18 hours of the time it is usually taken, the patient should take Biktarvy as soon as possible and resume the normal dosing schedule. If a patient misses a dose of Biktarvy by more than 18 hours, the patient should not take the missed dose and simply resume the usual dosing schedule.

If the patient vomits within 1 hour of taking Biktarvy another tablet should be taken. If a patient vomits more than 1 hour after taking Biktarvy they do not need to take another dose of Biktarvy until the next regularly scheduled dose.

Special populations

Elderly
No dose adjustment of Biktarvy is required in 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).

Renal impairment
No dose adjustment of Biktarvy is required in ~~patients~~adults or adolescents (aged at least 12 years and of at least 35 kg body weight) 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 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).

No data are available to make dose recommendations in patients weighing < 35 kg with renal impairment or in paediatric patients less than 18 years with end stage renal disease.

Paediatric population
The safety and efficacy of Biktarvy in children less than 2 years of age or weighing less than 14 kg ~~under the age of 18 years~~ have not yet been established. No data are available.

Method of administration

Oral use.

Biktarvy can be taken with or without food (see section 5.2).
Due to the bitter taste, it is recommended that the film-coated tablets should not be chewed or crushed. For patients who are unable to swallow the tablet whole, the tablet may be split in half and both halves taken one after the other, ensuring that the full dose is taken immediately.
~~It is not recommended to chew, crush or split the tablet as it has a very bitter taste. No information available regarding tablet effectiveness after splitting, chewing or crushing it.~~

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4.4 Special warnings and precautions for use

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Biktarvy should not be co-administered with other antiretroviral medicinal products.

Paediatric population

Reductions in bone mineral density (BMD ≥ 4%) of the spine and total body less head (TBLH) have been reported in patients aged between 3 to < 12 years who received tenofovir alafenamide-containing products for 48 weeks (see section 4.8). The long-term effects of changes in BMD on the growing bone, including the risk of fracture, are uncertain. A multidisciplinary approach is recommended to decide the appropriate monitoring during treatment.

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4.8 Undesirable effects

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Paediatric population
The safety of Biktarvy was evaluated in 50 HIV-1 infected adolescents aged 12 to < 18 years and weighing ≥ 35 kg through Week 96 (48-week main phase and 48-week extension), in 50 children aged 6 to < 12 years and weighing ≥ 25 kg through Week 96 (48-week main phase and 48-week extension), and in 22 children ≥ 2 years of age and weighing ≥ 14 to < 25 kg through Week 24 in an open-label clinical study (GS-US-380-1474). In this study, no new adverse reactions have been observed in paediatric subjects aged 2 years and older living with HIV-1 as compared to adult subjects living with HIV-1. Bone mineral density data were not collected in this study. Reductions in BMD of the spine and of the TBLH ≥ 4% have been reported in paediatric patients receiving other tenofovir alafenamide containing products for 48 weeks (see section 4.4).

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5.1 Pharmacodynamic properties

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Paediatric population

In Study GS-US-380-1474, the pharmacokinetics, safety and efficacy of B/F/TAF in virologically-suppressed children and adolescents with HIV between the ages of 12 to < 18 years (≥ 35 kg) (n = 50), between the ages of 6 to < 12 years (≥ 25 kg) (n = 50), and ≥ 2 years of age (≥ 14 to < 25 kg) (n = 22) were evaluated.

Cohort 1: Virologically-suppressed adolescents (n = 50; 12 to < 18 years; ≥ 35 kg)

Patients in Cohort 1 had a mean age of 14 years (range: 12 to 17) and a mean baseline weight of 51.7 kg (range: 35 to 123), 64% were female, 27% were Asian, and 65% were Black. At baseline, median CD4+ cell count was 750 cells/mm^3 (range: 337 to 1207), and median CD4+% was 33% (range: 19% to 45%).

After switching to B/F/TAF, 98% (49/50) of patients in Cohort 1 remained suppressed (HIV-1 RNA < 50 copies/mL) at Week 48. The mean change from baseline in CD4+ cell count at Week 48 was -22 cells/mm^3. Two of 50 subjects met the criteria for inclusion in the resistance analysis population through Week 48. No emergent resistance to B/F/TAF was detected through Week 48.

Cohort 2: Virologically-suppressed children (n = 50; 6 to < 12 years; ≥ 25 kg)

Patients in Cohort 2 had a mean age of 10 years (range: 6 to 11) and a mean baseline weight of 31.9 kg (range: 25 to 69), 54% were female, 22% were Asian and 72% were Black. At baseline, median CD4+ cell count was 898 cells/mm^3 (range 390 to 1991) and median CD4+% was 37% (range: 19% to 53%).

After switching to B/F/TAF, 98% (49/50) of patients in Cohort 2 remained suppressed (HIV-1 RNA < 50 copies/mL) at Week 48. The mean change from baseline in CD4+ cell count at Week 48 was -40 cells/mm^3. No patient qualified for resistance analysis through Week 48.

Cohort 3: Virologically-suppressed children (n = 22; ≥ 2 years; ≥ 14 kg to < 25 kg)
Patients in Cohort 3 had a mean age of 5 years (range: 3 to 9) and a mean baseline weight of 18.8 kg (range: 14 to 24), 50% were female, 23% were Asian and 73% were Black. At baseline, median CD4+ cell count was 962 cells/mm^3 (range 365 to 1986) and median CD4+% was 32% (range: 24% to 46%).

After switching to B/F/TAF, 91% (20/22) of patients in Cohort 3 remained suppressed (HIV-1 RNA < 50 copies/mL) at Week 24. The mean change from baseline in CD4+ cell count at Week 24 was −126 cells/mm^3, and the mean change in CD4+% from baseline to Week 24 was 0.2% (range: -7.7% to 7.5%). No patient qualified for resistance analysis through Week 24.

5.2 Pharmacokinetic properties

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Paediatric population
Mean bictegravir C_{max}, and exposures of emtricitabine and tenofovir alafenamide (AUC and/or C_{max}), achieved in 50 children between the ages of 6 to < 12 years (≥ 25 kg) who received the 50 mg/200 mg/25 mg dose of B/F/TAF and in 22 children ≥ 2 years of age (≥ 14 to < 25 kg) who received the 30 mg/120 mg/15 mg dose of B/F/TAF, in Study GS-US-380-1474 were generally higher than exposures in adults. The exposures of bictegravir, emtricitabine, tenofovir alafenamide and tenofovir in children, adolescents, and adults are presented in Table 5.

Table 5: Exposures of Bictegravir, Emtricitabine, Tenofovir Alafenamide and Tenofovir in Children, Adolescents and Adults

	Children aged ≥ 2 years ≥ 14 to < 25 kg[a]	Children aged 6 to < 12 years ≥ 25 kg[a]	Adolescents aged 12 to < 18 years ≥ 35 kg[a]	Adults[ba]
	B/F/TAF (30 mg/120 mg/15 mg)	B/F/TAF (50 mg/200 mg/25 mg)		
	n = 12	n = 25	n = 24	n = 77
BIC				
AUC_{tau} (ng•h/mL)	108 364.5 (22.9)	121 034.2 (36.4)	109 668.1 (30.6)	94 227.1 (34.7)
C_{max} (ng/mL)	10 040.0 (19.9)	10 988.8 (28.3)	8 087.1 (29.9)	6 801.6 (30.1)
C_{tau} (ng/mL)	1 924.5 (78.3)[c]	2 366.6 (78.8)[d]	2 327.4 (48.6)	2 256.7 (47.3)[gb]
FTC				
AUC_{tau} (ng•h/mL)	14 991.2 (21.9)	17 565.1 (36.9)	13 579.1 (21.7)	12 293.6 (29.2)
C_{max} (ng/mL)	3 849.2 (34.7)	3 888.4 (31.0)	2 689.2 (34.0)	2 127.0 (34.7)
C_{tau} (ng/mL)	210.3 (242.9)[c]	226.7 (322.8)[d]	64.4 (25.0)	96.0 (37.4)[he]
TAF				
AUC_{tau} (ng•h/mL)	305.4 (42.6)	434.5 (94.9)[e]	347.9 (113.2)[f]	229.3 (63.0)
C_{max} (ng/mL)	413.8 (31.0)	581.8 (99.9)[d]	333.9 (110.6)	276.5 (62.4)
C_{tau} (ng/mL)	N/A	N/A	N/A	N/A
TFV				
AUC_{tau} (ng•h/mL)	326.6 (23.8)	427.7 (28.5)	333.5 (31.5)	292.6 (27.4)[di]
C_{max} (ng/mL)	21.9 (29.2)	35.5 (89.0)	24.0 (64.2)	15.2 (26.1)[di]
C_{tau} (ng/mL)	10.3 (30.5)[c]	14.0 (30.2)[d]	11.1 (32.4)	10.6 (28.5)[di]

BIC = bictegravir; FTC = emtricitabine; TAF = tenofovir alafenamide fumarate; TFV = tenofovir
N/A = not applicable; %CV = percentage coefficient of variation
Data are presented as mean (%CV).

a Intensive PK data from Study GS-US-380-1474
b Intensive PK data from Studies GS-US-380-1489, GS-US-380-1490, GS-US-380-1844, GS-US-380-1878 for BIC, FTC and TAF PK exposures and population PK data from Studies GS-US-292-0104 and GS-US-292-0111 for TFV PK exposures
c n = 11
d n = 24
e n = 22
f n = 23
g n = 75
h n = 74
i n = 841

~~a Intensive PK data from Studies GS-US-380-1489, GS-US-380-1490, GS-US-380-1844, GS-US-380-1878 for BIC, FTC and TAF PK exposures and population PK data from Studies GS-US-292-0104 and GS-US-292-0111 for TFV PK exposures~~
~~b n = 75~~
~~c n = 74~~
~~d n = 841~~

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6.4 Special precautions for storage

Biktarvy 50/200/25 mg:
No special storage conditions are required. Storage at room temperature is recommended.

Bottle
Store in the original package in order to protect from moisture. Keep the bottle tightly closed. Do not use if seal over bottle opening is broken or missing.

Blister
Store in the original package in order to protect from moisture. Do not use if foil over blister is broken or pierced.

Biktarvy 30/120/15 mg:
Store below 30°C. Store in the original package in order to protect from moisture. Keep the bottle tightly closed. Do not use if seal over bottle opening is broken or missing.

The medicine can be used for up to 30 days after first opening of the bottle but not after the expiry date. After opening, store below 30°C.

6.5 Nature and contents of container

The following pack configurations are available:

Biktarvy 50/200/25 mg:
Bottle
White, high density polyethylene (HDPE) bottle with a polypropylene continuous-thread, child-resistant cap, lined with an induction activated aluminium foil liner containing 30 film-coated tablets. Each bottle contains silica gel desiccant and polyester coil.

Blister
Outer carton containing 1 bottle of 30 film-coated tablets.
Blister packs consisting of polyvinyl chloride/polyethylene/polychlorotrifluoroethylene (PVC/PE/PCTFE) film, sealed to aluminium foil lidding material fitted with a molecular sieve desiccant within each blister cavity.

- Outer carton containing 30 film-coated tablets (4 x blister strips containing 7 film-coated tablets and 1 x blister strip containing 2 film-coated tablets).
- Outer carton containing 90 (3 blister packs of 30) film-coated tablets.

Biktarvy 30/120/15 mg:
Bottle
White, high density polyethylene (HDPE) bottle with a polypropylene continuous-thread, child-resistant cap, lined with an induction activated aluminium foil liner containing 30 film-coated tablets. Each bottle contains silica gel desiccant and polyester coil.

Not all pack sizes may be marketed.

העדכונים המהותיים בעלון לצרכן:

ביקטארווי® 30/120/15 מ"ג
ביקטארווי® 50/200/25 מ"ג
טבליות מצופות

ביקטארווי® 30/120/15 מ"ג	ביקטארווי® 50/200/25 מ"ג
חומרים פעילים: כל טבליה מכילה – ביקטגרביר (סודיום) 30 (bictegravir as sodium) מ"ג אמטריציטאבין(emtricitabine) 120מ"ג טנופוביר אלאפנאמיד (פומראט) (as fumarate tenofovir alafenamide) 15 מ"ג	**חומרים פעילים:** כל טבליה מכילה – ביקטגרביר (סודיום) 50 (bictegravir as sodium) מ"ג אמטריציטאבין (emtricitabine) 200 מ"ג טנופוביר אלאפנאמיד (פומראט) (as fumarate tenofovir alafenamide) 25 מ"ג

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~~ביקטארווי 30/120/15 מ"ג מיועדת למבוגרים, מתבגרים וילדים מגיל שנתיים ומעלה השוקלים לפחות 14 קילוגרם.~~
~~ביקטארווי 50/200/25 מ"ג התרופה מיועדת למבוגרים , מתבגרים וילדים בני 6 שנים ומעלה, השוקלים לפחות 25 ק"ג.בני 18 ומעלה.~~

1. למה מיועדת התרופה?
ביקטארווי 30/120/15 מ"ג מיועדת לטיפול בזיהום בנגיף הכשל החיסוני האנושי מסוג 1 (HIV-1) במבוגרים, מתבגרים וילדים מגיל שנתיים ומעלה השוקלים לפחות 14 ק"ג.
ביקטארווי 50/200/25 מ"ג מיועדת לטיפול ~~במבוגרים עם~~בזיהום בנגיף הכשל החיסוני האנושי מסוג 1 (HIV-1) ללא עדות קיימת או בעבר לעמידות ויראלית לתרופות מקבוצת מעכבי אינטגרז, אמטריציטאבין או טנופוביר. במבוגרים, מתבגרים וילדים בני 6 שנים ומעלה, השוקלים לפחות 25 ק"ג.

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! אזהרות מיוחדות הנוגעות לשימוש בתרופה
...
בעת נטילת ביקטארווי
אחרי שהתחלת ליטול ביקטארווי, שים לב לסימנים הבאים:

- סימני דלקת או זיהום
- כאבי מפרקים, נוקשות ~~מפרקים~~ או בעיות בעצמות

-> אם הנך מבחין באחד מהתסמינים האלו, ספר מיד לרופא שלך. למידע נוסף, ראה סעיף 4, תופעות לוואי**.**

קיימת אפשרות כי תחווה בעיות בכליות ~~בגלל נטילת~~ אם תיטול ביקטארווי למשך תקופה ארוכה (ראה "אזהרות מיוחדות הנוגעות לשימוש בתרופה זו") **.**

תרופה זו אינה מהווה ריפוי לזיהום ב-HIV. בזמן שאתה נוטל ביקטארווי, אתה עדיין עלול לפתח זיהומים או מחלות אחרות אשר קשורות לזיהום ב-HIV.
...
ילדים ומתבגרים

ביקטארווי 30/120/15 מ"ג מיועדת למבוגרים, מתבגרים וילדים מגיל שנתיים ומעלה השוקלים לפחות 14 קילוגרם.
אין לתת ביקטארווי 30/120/15 מ"ג לילדים מתחת לגיל שנתיים או השוקלים מתחת ל-14 ק"ג ללא קשר -לגיל. אין מידע על יעילות ובטיחות השימוש בביקטארווי בילדים מתחת לגיל שנתיים או השוקלים פחות מ

ק"ג. בילדים ומתבגרים אשר שוקלים 25 ק"ג או יותר, ניתן להשתמש בטבליות ביקטארווי 50/200/25 מ"ג. ביקטארווי 50/200/25 מ"ג מיועדת למובגרים, מתבגרים וילדים בני 6 שנים ומעלה, השוקלים לפחות 25 ק"ג. ~~ביקטארווי 50/200/25 מ"ג מיועדת למבוגרים, מתבגרים וילדים בני 6 שנים ומעלה, השוקלים לפחות 25 ק"ג.~~

אבדן מסת עצם דווח עבור חלק מהילדים מגילאי 3 ועד 12 שנים אשר קיבלו את אחד החומרים הפעילים (טנופוביר אלפנמיד) הכלול בביקטארווי. ההשפעות ארוכות הטווח על בריאות העצם וסיכון עתידי לשברים בילדים אינם ידועות. הרופא שלך יבחן את בריאות העצמות של ילדך ככל שייידרש.
~~אין לתת תרופה זו לילדים ומתבגרים מתחת לגיל 18. השימוש בביקטארווי בילדים ומתבגרים מתחת לגיל 18 טרם נחקר.~~