מאי 2025

הודעה על עדכון עלונים:

Sunlenca® film coated tablets

(lenacapavir 300 mg)

רופאים ורוקחים נכבדים,

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

ההתוויה הרשומה לתכשיר בישראל:

Sunlenca tablet, in combination with other antiretroviral(s), is indicated for the treatment of adults with multidrug resistant HIV-1 infection for whom it is otherwise not possible to construct a suppressive anti-viral regimen, for oral loading prior to administration of long-acting lenacapavir injection.

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 עדכוני עריכה נוספים.

העלונים לרופא ולצרכן נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות:

https://israeldrugs.health.gov.il/#!/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 סל"א.

בברכה,

מריה חורגין

רוקחת ממונה

גיליאד סיאנסז ישראל בע"מ

GILEAD
Creating Possible

העדכונים המהותיים בעלון לרופא:

4.8 Undesirable effects

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Summary of the safety profile

The most common adverse reaction in heavily treatment experienced adult participants ~~patients~~ with HIV was nausea (~~4~~6%).

5.1 Pharmacodynamic properties

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Resistance

In cell culture

HIV-1 variants with reduced susceptibility to lenacapavir have been selected in cell culture. In vitro resistance selections with lenacapavir identified 7 mutations in CA: L56I, M66I, Q67H, K70N, N74D/S, and T107N singly or in dual combination. Phenotypic susceptibility to lenacapavir was reduced 4- to >3,226-fold, relative to WT virus. HIV-1 variants with >10-fold reduction in susceptibility to lenacapavir compared to WT virus displayed diminished replication capacity in primary human CD4+ T lymphocytes and macrophages (0.03 – 28% and 1.9 – 72% of WT virus, respectively).

In GS-US-200-4625 ('CAPELLA'), ~~29~~39% (~~21~~28/72) of heavily treatment~~-~~-experienced ~~-~~participants ~~patients~~ met the criteria for resistance analyses through Week ~~52~~ 156 (HIV-1 RNA ≥50 copies/mL at confirmed virologic failure [suboptimal virologic response at Week 4, virologic rebound, or viremia at last visit]) and were analysed for lenacapavir-associated mutation emergence. Lenacapavir-associated capsid mutations were found in ~~11.1~~19.0% (n = ~~8~~14) of ~~these~~ participants~~patients~~. The M66I CA mutation was observed in 8.3% (n = 6) of participants~~patients~~, alone or in combination with other Sunlenca-associated capsid mutations including ~~N74D,~~ Q67Q/H/K/N, K70K/N/R/S, N74D/H, A105T ~~T107T/C,~~ and T107T/A/C~~. One patient had a K70H CA mutation emerging along with T107T/N, and one patient had emergence of both Q67H and K70R in CA~~. Four participants had emergence of Q67H + K70R in CA with or without A105T and/or T107N. One participant had emergence of K70N + N74K + T107T/N, one participant had emergence of N74D alone, one participant had emergence of Q67Q/H alone, and one participant had emergence of Q67K + K70H. Eight participants with virologic failure had emergent resistance substitutions to components of the OBR.

Phenotypic analyses indicated that the M66I and Q67K + K70H mutation~~s~~ patterns were associated with a~~n average~~ decrease in lenacapavir susceptibility of 234-fold (median) and ~~265~~167-fold, respectively, in comparison ~~when compared~~ to WT. The Q67H + K70R + A105T or T107N ~~CA~~ resistance pattern was associated with an average ~~15~~195-fold decrease in lenacapavir susceptibility compared to WT, and Q67H + K70R alone was associated with a 15-fold decrease in lenacapavir susceptibility compared to WT. The presence of mutations K70N + N74K was associated with a 289-fold decrease in lenacapavir susceptibility compared to WT, and the Q67Q/H mutation was associated with a 5.9-fold decrease in lenacapavir susceptibility compared to WT.

Clinical data

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The results at Weeks 26, ~~and~~ 52 and 156 are provided in Table 5 and Table 6.

Table 5: Virologic outcomes (HIV-1 RNA < 50 copies/mL and < 200 copies/mL) at weeks 26[a] ~~, and~~ 52[b] and 156[c] with Sunlenca plus OBR in the CAPELLA trial (Cohort 1)

	Sunlenca plus OBR ~~(n= 36)~~		
	Week 26 (n= 36)	**Week 52 (n= 36)**	**Week 156 n = 34[d]**
HIV-1 RNA < 50 copies/mL	81%	83%	65%[e]
HIV-1 RNA < 200 copies/mL	89%	86%	68%[f]
HIV-1 RNA ≥ 50 copies/mL[~~e~~g]	19%	14%	18%
HIV-1 RNA ≥ 200 copies/mL[~~e~~g]	11%	11%	15%
No virologic data in week 26, ~~or week~~ 52 or 156 Window	0	3%	18%
Discontinued study drug due to AE or death [~~d~~h]	0	0	3%
Discontinued study drug due to other reasons [~~e~~i] and last available HIV-1 RNA < 50 copies/mL or < 200 copies/mL	0	3%	9%
Missing data during window but on study drug	0	0	6%

a Week 26 window was between Days 184 and 232 (inclusive).
b Week 52 window was between Days 324 and 414 (inclusive).
c Week 156 window was between Days 1052 and 1142 (inclusive).
d Two participants who completed the CAPELLA trial before Week 156 were excluded from the analysis.
e Based on missing = excluded analysis to impute missing values, 82% (23/28) of participants had HIV-1 RNA < 50 copies/mL at Week 156.
f Based on missing = excluded analysis to impute missing values, 86% (24/28) of participants had HIV-1 RNA < 200 copies/mL at Week 156.
~~e~~g Includes participants ~~patients~~ who had ≥ 50 copies/mL or ≥ 200 copies/mL, respectively, in the Week 26 or 52 window; participants ~~patients~~ who discontinued early due to lack or loss of efficacy; participants ~~patients~~ who discontinued for reasons other than an adverse event (AE), death or lack or loss of efficacy and at the time of discontinuation had a viral value of ≥ 50 copies/mL or ≥ 200 copies/mL, respectively.
~~d~~h Includes participants ~~patients~~ who discontinued due to AE or death at any time point from Day 1 through the time window if this resulted in no virologic data on treatment during the specified window.
~~e~~i Includes participants ~~patients~~ who discontinued for reasons other than an AE, death or lack or loss of efficacy, e.g., withdrew consent, loss to follow-up, etc.

Table 6: Virologic outcomes (HIV-1 RNA < 50 copies/mL) by baseline covariates at weeks 26[a] ~~, and~~ 52[b] and 156[c] with Sunlenca plus OBR in the CAPELLA trial (Cohort 1)

	Sunlenca plus OBR ~~(n = 36)~~		
	Week 26 n = 36	**Week 52 n = 36**	**Week 156 n = 34**
Baseline plasma viral load (copies/mL)			
≤ 100,000	86% (25/29)	86% (25/29)	67% (18/27)
> 100,000	57% (4/7)	71% (5/7)	57% (4/7)
Baseline CD4+ (cells/mm^3)			
< 200	78% (21/27)	78% (21/27)	58% (15/26)
≥ 200	89% (8/9)	100% (9/9)	88% (7/8)
Baseline INSTI resistance profile			
With INSTI resistance	85% (23/27)	81% (22/27)	62% (16/26)
Without INSTI resistance	63% (5/8)	88% (7/8)	71% (5/7)
Number of fully active ARV agents in the OBR			
0	67% (4/6)	67% (4/6)	67% (4/6)
1	86% (12/14)	79% (11/14)	58% (7/12)
≥ 2	81% (13/16)	94% (15/16)	69% (11/16)
Use of DTG and/or DRV in the OBR			
With DTG and DRV	83% (10/12)	83% (10/12)	58% (7/12)
With DTG, without DRV	83% (5/6)	83% (5/6)	60% (3/5)
Without DTG, with DRV	78% (7/9)	89% (8/9)	67% (6/9)
Without DTG or DRV	78% (7/9)	78% (7/9)	75% (6/8)

ARV = antiretroviral; DRV = darunavir; DTG = dolutegravir; INSTI = integrase strand-transfer inhibitor; OBR = optimised background regimen

a Week 26 window was between Days 184 and 232 (inclusive).

b Week 52 window was between Day 324 and 414 (inclusive).

~~b~~c Week 156 window was between Days 1052 and 1142 (inclusive).

In C~~c~~ohort 1, at Weeks 26, ~~and~~ 52~~,~~ and 156, the mean change from baseline in CD4+ cell count was 81 cells/mm^3 (range: -101 to 522), ~~and 83~~82 cells/mm^3 (range: -194 to 467), and 157 cells/mm^3 (range: - 93 to 659), respectively.

In ~~c~~Cohort 2, at Weeks 26, 52 and 156, 81% (29/36), 72% (26/36), and 58% (21/36) of participants ~~patients~~ achieved HIV-1 RNA < 50 copies/mL, respectively, and the mean change from baseline in CD4+ cell count was 98 cells/mm^3 (range: -103 to 459), 113 cells/mm^3 (range: -124 to 405), and 173 cells/mm^3 (range: -168 to 455), respectively.

העדכונים המהותיים בעלון לצרכן:

שינויי עריכה בלבד - N/A