מאי 2025

הודעה על עדכון עלונים:

Sunlenca® solution for injection

(lenacapavir 309 mg/ml)

רופאים ורוקחים נכבדים,

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

ההתוויה הרשומה לתכשיר בישראל:

Sunlenca solution for injection, 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.

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

העדכונים המהותיים בעלון לרופא:

4.2 Posology and method of administration

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Method of administration

For subcutaneous use only.

Sunlenca injections ~~should~~ must only be administered subcutaneously into the abdomen (two injections, each at a separate site) by a healthcare professional (see section 6.6). Sunlenca injections must NOT be administered intradermally (see section 4.4). For instructions on preparation and administration, see 'Instructions for Use' in the package leaflet. 'Instructions for Use' are also available as a card in the injection kit.

4.4 Special warnings and precautions for use

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Injection Site Reactions

Injection Site Reactions with Improper Administration

Improper administration (intradermal injection) has been associated with serious injection site reactions, including necrosis and ulcer. Sunlenca injections must only be administered subcutaneously (see section 4.2).

Slow or non-resolving injection site nodules and indurations
Administration of Sunlenca may result in local injection site reactions (ISRs), including nodules and indurations. The healthcare professional should inform patients that nodules and indurations at the injection site may take longer to resolve than other ISRs or may not resolve. In CAPELLA (see section 5.1), nodules associated with the first injections of Sunlenca had not resolved in 10% of participants after a median follow-up of 554 days, whereas all indurations had resolved (see section 4.8). The mechanism driving the persistence of injection site nodules in some participants is not fully understood but may be related to the presence of the subcutaneous drug depot and an associated foreign body response at the injection site. Non-resolving ISRs should be subject to clinical monitoring.

4.8 Undesirable effects

Summary of the safety profile

The most common adverse reactions in heavily treatment experienced adult participants ~~patients~~ with HIV were ~~injection site reactions (~~ISRs~~)~~ (~~63~~76%) and nausea (64%).

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Description of selected adverse reactions

Immune Reconstitution Inflammatory Syndrome
In ~~HIV infected~~ patients with HIV with severe immune deficiency at the time of initiation of CART, an inflammatory reaction to asymptomatic or residual opportunistic infections may arise. Autoimmune disorders (such as Graves' disease and autoimmune hepatitis) have also been reported; however, the

reported time to onset is more variable and these events can occur many months after initiation of treatment (see section 4.4).

Local injection site reactions
Through Week 156 of treatment, ~~M~~most participants ~~patients~~ had ~~ISRs that were~~ mild (Grade 1, 4254%) or moderate (Grade 2, 1~~8~~7%) ISRs. ~~Three~~ Six percent (4/72) of participants ~~patients~~ experienced a severe ~~(~~Grade 3~~)~~ ISR with a median time to resolution of 15 (range: 1 to 71) ~~that resolved within 1 to 8~~ days. No participants ~~patients~~ experienced a Grade 4 ISR. The median time to resolution ~~duration~~ of all ISRs, excluding nodules and indurations, was ~~6~~5 days. The median time to resolution of nodules and indurations associated with the first injections of Sunlenca was 191 (Q1, Q3: 71, 366) and 113 (Q1, Q3: 29, 224) days, respectively. After a median follow-up of 554 days, nodules associated with the first injections of Sunlenca had not resolved in 10% (7/72) of the participants. All indurations associated with the first injections of Sunlenca had resolved.~~The median duration of nodules and indurations was 180 and 118 days, respectively.~~

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'), ~~2~~39% (2~~8~~1/72) of heavily treatment~~-~~experienced ~~patients~~ participants 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 19.0~~11.1~~% (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~~ Four participants ~~patient~~ had emergence of Q67H + ~~a~~ K70~~H~~R in CA with or without A105T and/or ~~mutation emerging along with~~ T107~~T/~~N.~~,~~ ~~and o~~One participant ~~patient~~ had emergence of ~~both Q67H and K70R in CA~~ 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 195~~a 15~~-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

The efficacy and safety of Sunlenca in ~~HIV-1 infected,~~ heavily treatment-~~-~~experienced participants ~~patients~~ with multidrug resistant~~ce~~ HIV-1 is based on ~~52~~156-week data from a partially randomised, placebo-controlled, double-blind, multicentre study, GS-US-200-4625 ('CAPELLA').

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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 [~~h~~d]	0	0	3%
Discontinued study drug due to other reasons [~~i~~e] 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.
~~b~~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 or 156 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			

	Sunlenca plus OBR ~~(n = 36)~~		
	Week 26 **n = 36**	**Week 52** **n = 36**	**Week 156** **n = 34**
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~~Cohort 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~~ , 82~~83~~ 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 ~~of 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:

2.לפני השימוש בתרופה

אזהרות מיוחדות הנוגעות לשימוש בתרופה

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- **תגובות באתר הזרקת סאנלנקה**

גוש או בליטה קשיחה עלולים להופיע באתר ההזרקה. בחלק מהמקרים, גושים אלה נותרו למשך יותר משנה ובחלק מהמקרים לא נעלמו. אם הגוש לא נעלם עד מועד ההזרקה הבאה, הסב את תשומת לבו את הרופא. למידע נוסף, ראה סעיף 4, *תופעות לוואי*.

3.כיצד תשתמש בתרופה?

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אם פספסת זריקת סאנלנקה

- חשוב כי תקפיד על **קיום הפגישות הקבועות כל שישה חודשים** כדי לקבל זריקות של סאנלנקה. זה יסייע לשלוט בזיהום ה-HIV ולמנוע ממחלתך להתדרדר.
- אם אתה חושב שלא תוכל להגיע לפגישה לקבל את הזריקות, צור קשר עם הרופא שלך במהרה כדי לדון באפשרויות הטיפוליות שלך.

אם אתה מחמיץ נטילת טבליה או מקיא אותן, פנה לעלון לצרכן של סאנלנקה טבליות.

4.תופעות לוואי

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תופעות לוואי שכיחות מאוד

(*עלולות ~~מופיעות~~ להופיע ביותר ממשתמש אחד מעשרה)*

- **תגובות באתר בו הוזרקה סאנלנקה**

התסמינים כוללים:

- כאב וחוסר נוחות
- גוש או בליטה קשיחה אשר עלול לקחת זמן רב יותר להיעלמות מאשר תגובות אחרות באתר ההזרקה או אף לא להיעלם כלל
- תגובה דלקתית כגון אודם ,גירוד ונפיחות
- פצע פתוח בעור

תופעות לוואי שכיחות

(*~~שמופיעות~~עלולות להופיע בעד 1-10 משתמשים מתוך 100*)

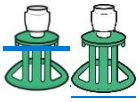
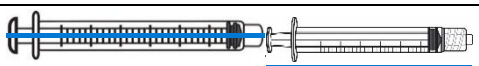
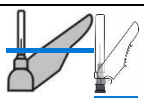
- בחילה

(שינויים בהנחיות ההזרקה מפורטות בעמוד הבא)

The following information is intended for healthcare professionals only:

Instructions for Use-Sunlenca solution for injection

Your pack contains

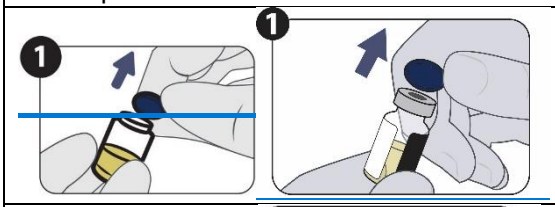
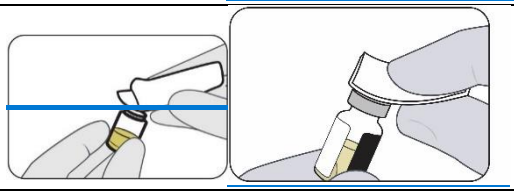
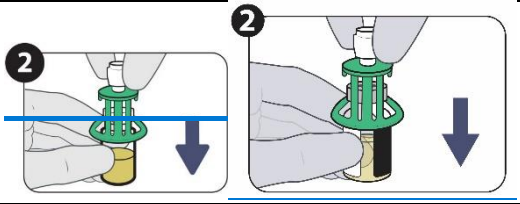
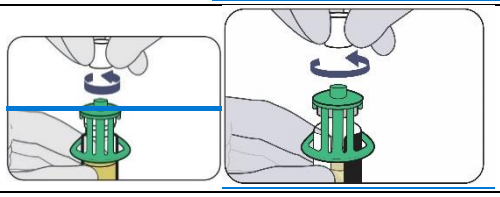
2 x vials	
2 x vial access devices	
2 x syringes	
2 x 22G, 13mm injection needles	

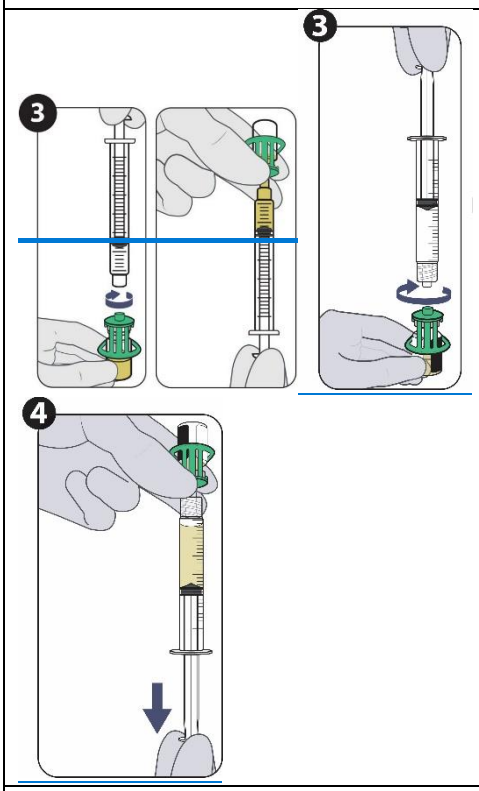
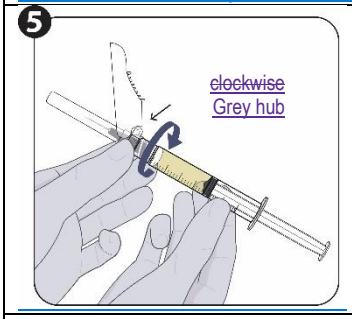
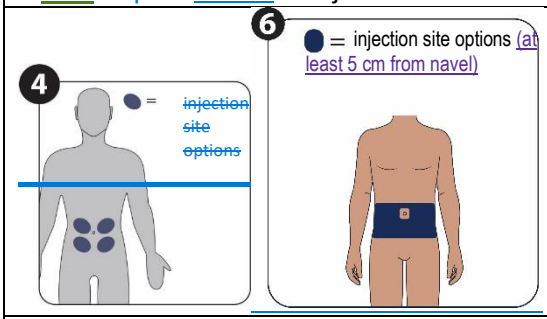
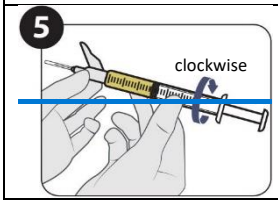
All the components are for single use.

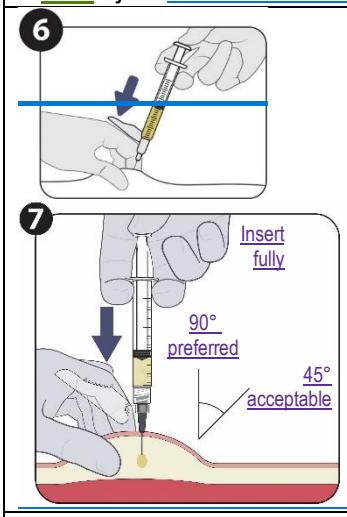
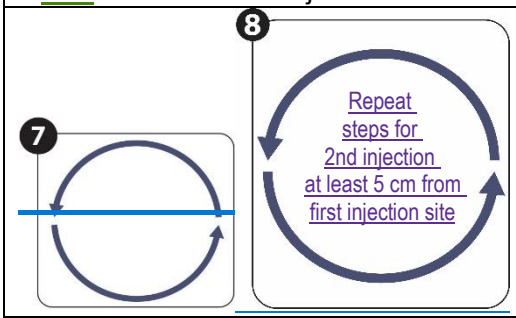
A complete dose requires two 1.5 mL injections. The use of the vial access device is required.

Make sure that:

- Vial and prepared syringe contains a yellow-to-brown solution with no particles
- Contents are not damaged
- Product is not expired

1. Prepare Vial	
	Remove cap.
	Clean vial stopper with alcohol wipe.
2. Prepare Vial Access Device	
	Push Down.
	Twist off.

<table>
<tr><td colspan="2">3., 4. Attach and Fill Syringe</td></tr>
<tr><td> 
</td><td>• Attach syringe and inject 1.5 mL of air into vial.
• Flip upside down and withdraw all contents.</td></tr>
<tr><td colspan="2">5. Attach 22G Injection Needle to Syringe, Expel Air Bubbles, and Prime to 1.5 mL</td></tr>
<tr><td> 
</td><td></td></tr>
<tr><td colspan="2">~~5.~~6. ~~Prepare~~ Clean an Injection Site on Patient’s Abdomen</td></tr>
<tr><td> 
</td><td>Injection site options (at least 5 cm from navel)</td></tr>
<tr><td colspan="2">~~3. Assemble needle and Syringe~~</td></tr>
<tr><td> 
</td><td>~~Attach Injection Needle and Prime to 1.5 mL~~</td></tr>
</table>

~~6.~~7. Inject 1.5 mL of Sunlenca Subcutaneously ~~Dose~~	
	~~Inject 1.5 mL of Sunlenca Subcutaneously~~
~~7.~~8. Administer 2nd Injection	
	~~Repeat steps for 2nd injection at new injection site.~~