SUNLENCA® (lenacapavir)

Long-acting capsid inhibitor

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Important Information

These non-promotional slides are intended to be used as educational material only in response to an unsolicited question or request

The information in this presentation is intended for payers and healthcare decision makers only

The double-dagger (‡) symbol indicates that these slides may contain information that is not within FDA approved product labeling

Understanding Treatment-Experienced PLWH

Suppressed PLWH - May still be dealing with:

- Drug-drug or drug-food interactions
- Pill burden
- Pregnancy
- Cost
- Desire to simplify treatment
- Adverse events

PLWH experiencing virologic failure - Virologic failure may be associated with a variety of factors, including:

Adherence/patient related factors

- Unstable housing
- Missed appointments
- Intermittent access to ART
- Cost/ affordability
- Adverse events
- Pill burden/ frequency
- Comorbid conditions

HIV or ARV-related factors

- Prior treatment failure
- Resistance to prescribed ARVs
- Dispensing errors
- High pretreatment viral load
- Suboptimal PK, drug-drug or drug-food interactions
- Reduced efficacy due to suboptimal regimens
- Low barrier to resistance
- Transmitted drug resistance

PK, pharmacokinetics TE, treatment-experienced

DHHS. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV, Sep 2022. Available at: http://aidsinfo.nih.gov/guidelines (accessed January 2023)

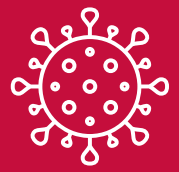
Challenges with Defining the HTE Population

FDA defines HTE PLWH as individuals with resistance to multiple drugs and drug classes and unable to construct a regimen that suppresses HIV-RNA to below assay quantification limits[1]

Literature	Triple-class virologic failure[2,3]	Patients with MDR virus after failure of an INSTI-based regimen[4]	≤ 2 available classes with limited number of active drugs in each class[5]	Have ≤ 2 fully active ARVs remaining from the 4 main classes that can be effectively combined to form a viable regimen[6]
Treatment Guidelines	**DHHS:** multiple or extensive drug resistance with few treatment options[7]			
Product Indications	**Rukobia:** Treatment of HTE adults with multidrug-resistant HIV-1 infection failing their current ARV regimen due to resistance, intolerance, or safety considerations[8]	**Trogarzo:** Treatment of HTE adults with multidrug resistant HIV-1 infection failing their current antiretroviral regimen[9]		

HTE, heavily treatment-experienced; MDR, Multi-drug resistant ; 1.Guidance for Industry: HIV-1 Infection: Developing ARV Drugs for Treatment. US DHHS, FDA, CDER. Revision 1. November 2015; 2.Costagliola D et al. Lancet Infec Dis 2012;12:119-127; 3.Lohse N et al.. AIDS 2005;19:815-822; 4. Santoro M et al. IJAA 2020;56(1):106027; 5. Bajema. K et al. AIDS 2020;34:2051-59; 6. Segal-Maurer S, et al. vCROI 2021. Oral #127 ; 7. DHHS. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV, Sep 2022. Available at: http://aidsinfo.nih.gov/guidelines. 8. VIIV Healthcare, Inc. Rukobia US Prescribing Information. July 2020; 9. Theratechnologies. Trogarzo US Prescribing Information. April 2020

SUNLENCA (lenacapavir) Indication



SUNLENCA (lenacapavir), a human immunodeficiency virus type 1 (HIV-1) capsid inhibitor, in combination with other antiretroviral(s), is indicated for the treatment of HIV-1 infection in heavily treatment-experienced adults with multidrug resistant HIV-1 infection failing their current antiretroviral regimen due to resistance, intolerance, or safety considerations

Gilead Sciences. SUNLENCA US Prescribing Information. 2022

Lenacapavir Targets Multiple Stages of the HIV Replication Cycle

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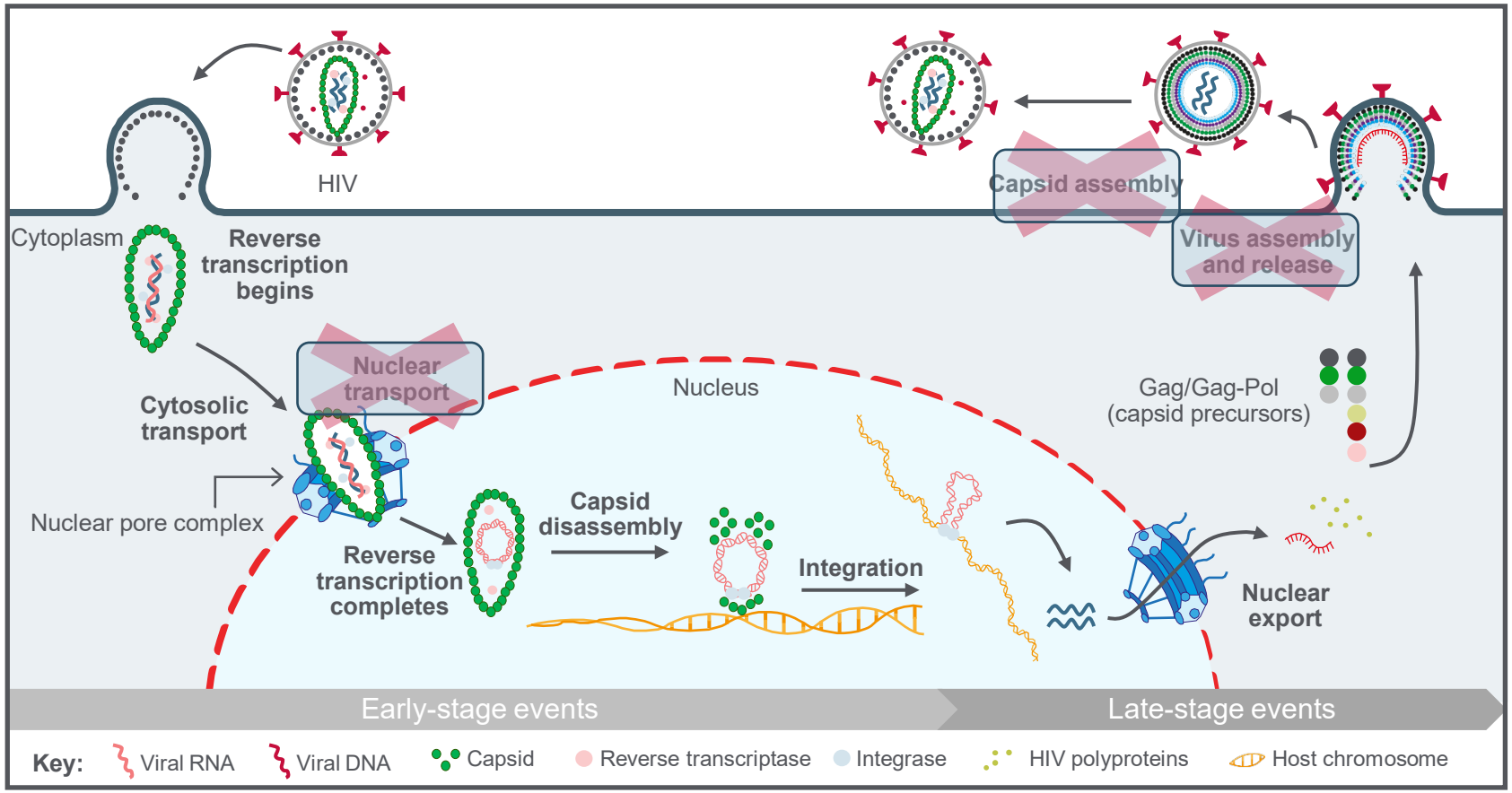
LEN

EC_{50}: 50 – 100 pM

Interrupts
multiple distinct stages
of the viral lifecycle



LEN binds directly between capsid protein subunits, modulating the stability and/or transport of capsid complexes, leading to inhibition of essential steps of the viral lifecycle

EC_{90}, 50% effective concentration; LEN, lenacapavir

Figure developed based on the following references: Link J, et al. Nature 2020;584:614-618; Bester SM, et al. Science 2020;370:360-364; Cihlar T, et al. vCROI, 2021, Oral 22; Muller B, et al. vCROI, 2021, Oral 19; Pathak VK, et al. vCROI, 2021, Oral 20; Ganser-Pornillos B, et al. vCROI, 2021, Oral 21

CAPELLA Study Design

Lenacapavir (LEN) in HTE PLWH

HTE PLWH with MDR, aged ≥12 years and weighing ≥35 kg
(N=72)

Outcomes (randomized cohort)

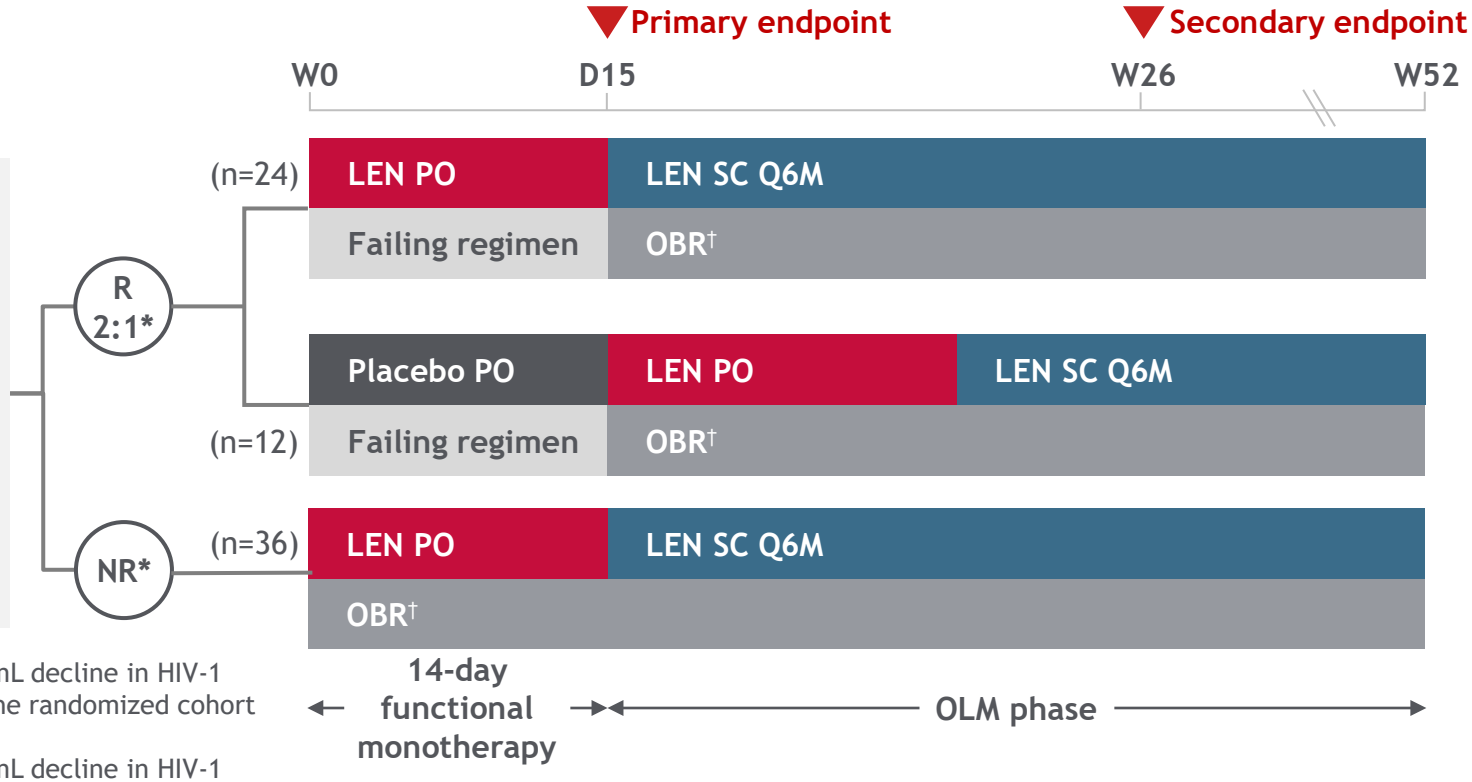
Primary: ≥0.5 $\log_{10}$ c/mL reduction in HIV-1 RNA from BL at Day 15
Secondary: HIV-1 RNA <50 c/mL and <200 c/mL at W26 and W52 (FDA snapshot)

2019 – present (ongoing)

HIV-1 RNA ≥400 c/mL

Resistance to ≥2 ARVs from ≥3 of 4 main ARV classes (NRTI, NNRTI, PI, INSTI)

≤2 fully active ARV options remaining



LEN dosing

Oral tablets:
D1: 600 mg (2 × 300 mg)
D2: 600 mg (2 × 300 mg)
D8: 1 × 300 mg

SC injections:
D15: 927 mg (2 × 1.5 mL SC into the abdomen) and then Q6M/26 weeks

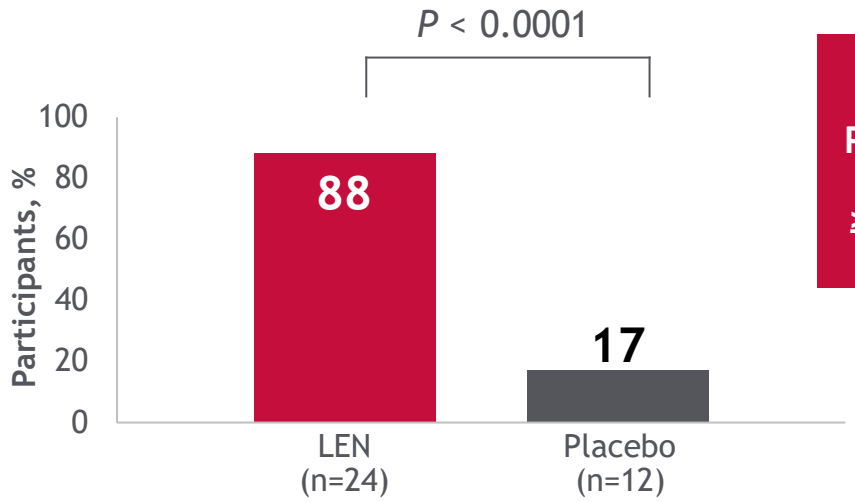
Participants with <0.5 log10 c/mL decline in HIV-1 RNA during screening entered the randomized cohort

Participants with ≥0.5 log10 c/mL decline in HIV-1 RNA during screening entered the nonrandomized cohort

†Investigational agents (eg, fostemsavir) permitted, atazanavir, atazanavir/cobicistat, atazanavir/ritonavir, efavirenz, entecavir, nevirapine, tipranavir not permitted. *BL, baseline; D, day; HTE, heavily treatment-experienced; INSTI, integrase strand transfer inhibitor; LEN, lenacapavir; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; MDR, multidrug resistance; NR, nonrandomized; OBR, optimized background regimen; OLM, open-label maintenance; PI, protease inhibitor; PLWH, people living with HIV; PO, by mouth; Q6M, every 6 months; R, randomized; RNA, ribonucleic acid; SC, subcutaneous(ly); W, week.

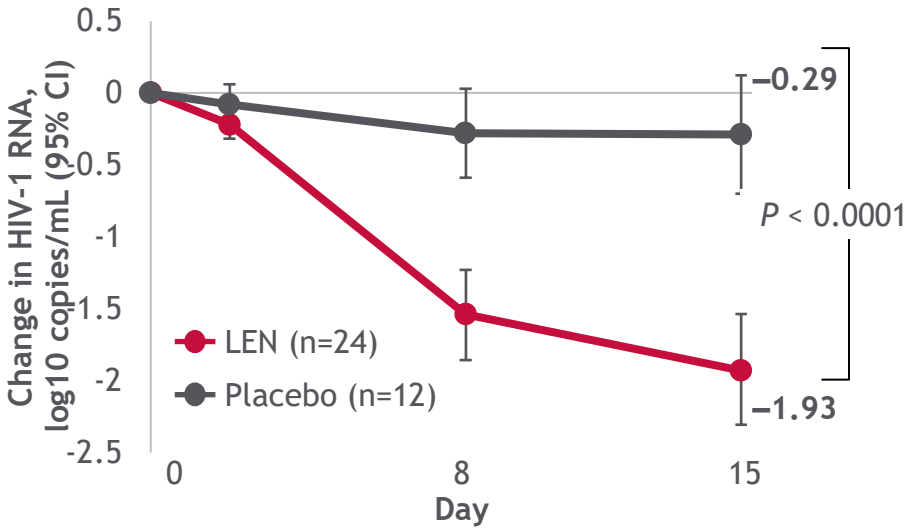
Segal-Maurer S, et al. N Engl J Med 2022;386:1793-803. Ogbuagu O, et al. CROI 2022. Poster 491.

Outcomes for Primary & Secondary Endpoints (n = 36)



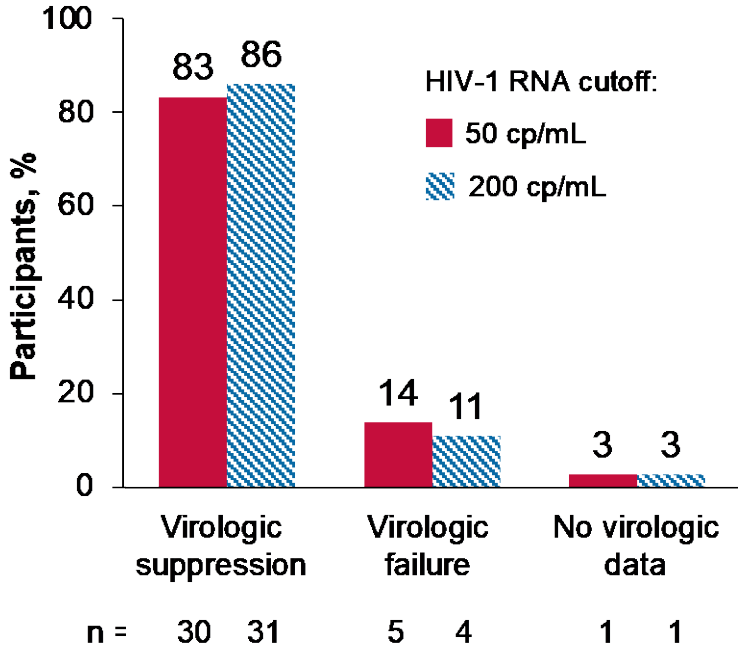
Primary Endpoint

Proportion Achieving HIV-1 RNA Decline ≥0.5 log_{10} copies/mL at Day 15



Mean Change in HIV-1 RNA (95% CI)

Virologic Outcomes at Week 52



LEN led to a decline in viral load at day 15

LEN, in combination with OBR, achieved and maintained high rates of virologic suppression at W52

HTE, heavily treatment-experienced; OBR, optimized background regimen

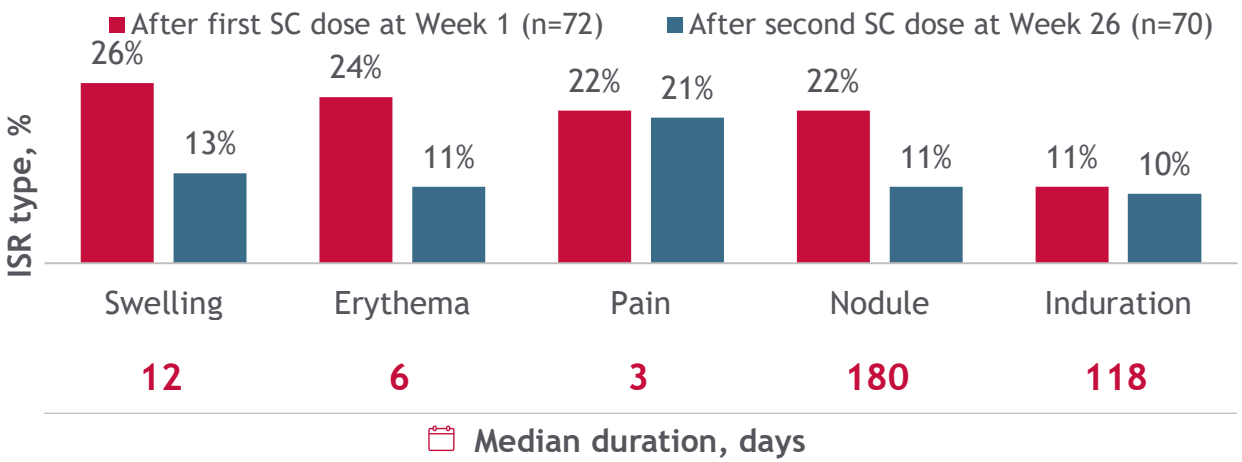
1. Molina JM, et al. vIAS 2021, OALX01LB02; 2. Ogbuagu O, et al. CROI 2022, Poster 491

AEs at Week 52 & Incidence of ISRs Related to SC LEN

CAPELLA: Lenacapavir (LEN) in HTE PLWH

Any grade AEs ≥ 3%	LEN + OBR (N = 72)
Injection Site Reactions (ISRs)	65%
Nausea	4%

Incidence of ISRs Related To SC LEN[1,2]



After a median follow up of 553 days, 30% of nodules and 13% of indurations (in 10% and 1% of subjects, respectively) associated with the first injections of SUNLENCA had not fully resolved

ISRs

- All nodules were Grade 1, except in 1 participant
  - Grade 2 nodules in 1 participant after the 2nd and 3rd injections both resolved after 3 days
- Most ISRs were Grade 1 or 2 in severity (no Grade 4)
  - Grade 3 ISRs in 2 participants:
    - (n=1) swelling and erythema, resolved in 4 and 8 days, respectively
    - (n=1) pain, resolved in 1 day
- One participant discontinued at Week 52 due to ISR – Grade 1 nodule

- No SAEs related to study drug
- No discontinuations due to non-ISR AEs

LEN was generally well tolerated with one discontinuation (n=1/72) due to ISR

*Only includes AEs related to LEN and excludes AEs unrelated to LEN.
AE, adverse event; HTE, heavily treatment-experienced; ISR, injection site reaction; LEN, lenacapavir; PLWH, people living with HIV; SAE, serious adverse event; SC, subcutaneous.
1. Gilead Sciences. SUNLENCA US Prescribing Information. 2022; 2. Molina J-M, et al. vIAS 2021. OALX01LB02; 3. Ogbuagu O, et al. CROI 2022. Poster 491.

SUNLENCA Dosing & Administration

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Dosing Initiation	Maintenance

Option 1

Week	
1	Day 1 (GS, GSI) Day 2 (GSI)
2	Day 8
3	Day 15

OR

Option 2*

Week		
1	Day 1 (GS, GSI)	Day 2 (GSI)
2	Day 8 (GS)	
3	Day 15	

927-mg subcutaneous injection (2 x 1.5-mL vials)

927-mg subcutaneous injection (2 x 1.5-mL vials)

1 2 3 4 5 **MONTH 6 (±2w)** 7 8 9 10 11 **MONTH 12 (±2w)**

Optimized Background Regimen (OBR)

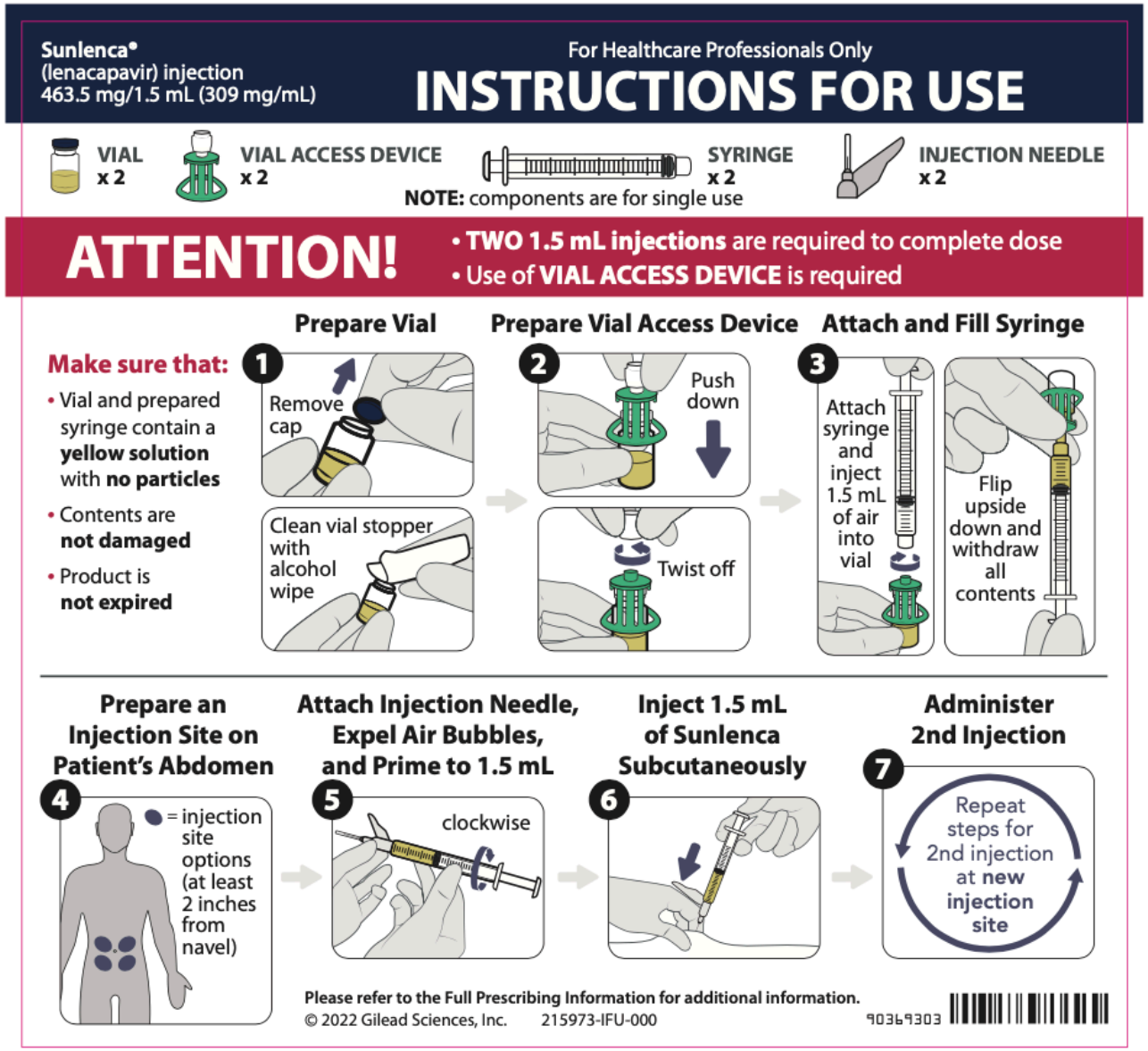
Following dosing initiation using 1 of 2 regimens, patients receive SC lenacapavir from their HCP every 6 months while continuing their OBR

- 600 mg orally (2 x 300-mg tablets)
- 300 mg orally
- 927-mg subcutaneous injection (2 x 1.5-mL vials)

*EU dosing only. US dosing uses both options; SC, subcutaneous

1. Gilead Sciences. SUNLENCA US Prescribing Information. 2022. 2. EMA Summary of Product Characteristics for SUNLENLCA

Lenacapavir Administration Instructions



Gilead Sciences. SUNLENCA US Prescribing Information. 2022

SUNLENCA Access