AHCCCS Pharmacy and Therapeutics Committee
Written Public Testimony
October 15, 2024

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Please check the box of the statement that best applies.:	I have a financial interest, affiliation or am employed by an organization that may have a direct interest in the business before the AHCCCS P&T Committee.
If yes, name organizations and roles::	ViiV Healthcare, Payer Medical Science Liaison
Summary of Testimony:	Written Testimony: Arizona Health Care Cost Containment System (AHCCCS) – Updated data, Cabenuva This document is a written testimony intended to summarize the key points below required for the Arizona Health Care Cost Containment System (AHCCCS) review of Cabenuva (cabotegravir extended-release injectable suspension [CAB LA]/rilpivirine extended-release injectable suspension [RPV LA]), co-packaged for intramuscular (IM) use. Indication Cabenuva, a 2-drug co-packaged product of cabotegravir, a human immunodeficiency virus type-1 (HIV-1) integrase strand transfer inhibitor (INSTI), and rilpivirine, an HIV-1 non-nucleoside reverse transcriptase (NNRTI), is indicated as a complete regimen for the treatment of HIV-1 infection in adults and adolescents 12 years of age and older weighing at least 35 kg to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to either CAB or RPV.(Cabenuva PI,2.1.1) Dosing Cabenuva is administered as 2 intramuscular injections either once-monthly or every-2-months. Please see the Full Prescribing Information for details.(Cabenuva PI,2.Section 2) ATLAS, FLAIR, and ATLAS-2M ATLAS was an

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	open-label, randomized, multicenter, non-inferiority study which evaluated switching to monthly Cabenuva vs. continuation of daily oral therapy in virologically suppressed participants.(Swindells,1112.2.2) FLAIR was a randomized, multicenter, active-controlled, open-label, non-inferiority study which evaluated monthly Cabenuva versus continuation of daily abacavir/dolutegravir/lamivudine in virologically suppressed participants.(Orkin,e670.4.1) ATLAS-2M was a randomized, multicenter, international, open-label non-inferiority study which evaluated maintenance treatment with Cabenuva every 8 weeks vs every 4 weeks.(Overton,1997.Figure 1) SOLAR SOLAR was a randomized, open-label, multi-center, phase 3b non-inferiority study that compared the rate maintaining virologic suppression after a switch to every-2-month Cabenuva vs. continuing bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) in adults with HIV-1.(Ramgopal,e569.Figure 1) Results: • Through Month 12, 1% (5) and
Drug/Product:	Cabenuva (cabotegravir extended-release injectable suspension [CAB LA]/rilpivirine extended-release injectable suspension [RPV LA])
Therapeutic Drug Class:	HIV
Testimony Format:	Written

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Summary of Testimony:

This document is a written testimony intended to summarize the key points below required for the Arizona Health Care Cost Containment System (AHCCCS) review of Dovato (dolutegravir 50 mg/lamivudine 300 mg [DTG/3TC]).

Indication

Dovato is indicated as a complete regimen for the treatment of HIV-1 infection in adults and adolescents 12 years of age and older and weighing at least 25 kg with no antiretroviral (ARV) treatment history or to replace the current ARV regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable ARV regimen with no history of treatment failure and no known substitutions associated with resistance to the individual components of Dovato.(PI, 2.3.1)

Boxed Warnings (see attached Prescribing Information, Section 5. for further information)

All patients with HIV-1 should be tested for the presence of hepatitis B virus (HBV) prior to or when initiating Dovato.(PI, 2.1.1) Severe acute exacerbations of hepatitis B have been reported in patients who are co-infected with HIV-1 and HBV and have discontinued 3TC, a component of Dovato.

Dosing and Administration

Prior to or when initiating Dovato, test patients for HBV infection. The recommended dosage of Dovato in adults and adolescents 12 years of age and older and weighing at least 25 kg is one tablet taken orally once daily with or without food.(PI, 2.5.2) In patients taking Dovato and carbamazepine or rifampin, an additional tablet of Tivicay (DTG) 50 mg should be taken, separated by 12 hours from Dovato(PI, 3, Table 1). Because Dovato is an FDC and dosage adjustments cannot be made to 3TC, Dovato is not recommended in patients with CrCl < 30 mL/min. Clinical Update • The efficacy of Dovato is supported by data from two phase 3, randomized, double-blind, controlled trials (GEMINI-1 and GEMINI-2) in adults with no ARV treatment history, and data from two phase 3, randomized, open-label, controlled trials (TANGO and SALSA) in virologically suppressed adults.(PI. 27.2.1, Llibre, 5.5.1). Additional clinical data is provided below: PASO DOBLE • Ongoing phase 4, randomized, open-label study across 30 sites in Spain comparing Dovato vs Biktarvy (bictegravir/ emtricitabine/ tenofovir alafenamide, BIC/FTC/TAF) as maintenance therapy in virologically suppressed participants.(Ryan, 4) Participants had no prior history of exposure to DTG or BIC prior to switching to either Dovato or Biktarvy. • Proportion of participants with HIV-1 RNA ≥ 50 copies/mL at Week 48, ITT-E (primary endpoint) was 2.2% for Dovato (N=277) and 0.7% for Biktarvy (N=276); treatment difference (95% CI): 1.4% (-0.5% to 3.4%).(Ryan, 7) Non-inferiority (4% margin) was established. • Confirmed virological failure (HIV-1 RNA ≥ 50 copies/mL followed by a second consecutive HIV-1 RNA assessment ≥ 200 copies/mL) was met in one participant in the Biktarvy arm and zero participants in the Dovato arm. (Ryan, 9) No cases of treatment emergent resistance occurred in either arm. • Fewer participants experienced a drug-related AE with Dovato compared to Biktarvy (19 vs 27 participants). (Ryan, 11) • Participants on Dovato had statistically significantly less weight gain compared to Biktarvy (1.81 kg vs 0.89 kg; mean adjusted difference 0.92 kg, P = 0.16). (Ryan, 12) The proportion of participants with weight gain >5% from baseline was 20.0% for Dovato vs 29.9% for Biktarvy; adjusted odds ratio (95% CI)

1.81 (1.19-2.76), P = 0.006. (Ryan, 14)
DYAD
• Ongoing phase 4, randomized, open-label, single-center study evaluating the efficacy and safety of switching participants from Biktarvy (virologically suppressed for ≥ 3 months) to Dovato. Participants were randomized 2:1 to switch to Dovato (N=149) or continue Biktarvy (N=73).(Rolle)
• Proportion of participants with HIV-1 RNA ≥ 50 copies/mL at Week 48, ITT-E (primary endpoint) was 4% for Dovato and 7% for Biktarvy; adjusted treatment difference (95% CI): -2.8% (-11.4% to 3.1%).(Rolle) Non-inferiority (6% margin) was established.
• There were 12 (8.1%) participants in the Dovato arm and 6 (8.2%) participants in the Biktarvy arm with confirmed virologic withdrawal. (Rolle) Nine of 12 participants in the Dovato arm had no NRTI or INSTI resistance at CVW and all 9 continued Dovato. Three of 6 participants in the Biktarvy arm had no NRTI/INSTI resistance at CVW and all 3 continued Biktarvy. There were no cases of INSTI resistance in the Dovato arm with one case in the Biktarvy arm.
• A higher proportion of participants experienced a drug-related AE with Dovato compared to Biktarvy (21% vs 3%).(Rolle)
• The mean change in weight from baseline at Week 48 was -1.0 kg in the Dovato arm vs 0.2 kg in the Biktarvy arm (no statistically significant difference between arms). (Rolle)
SOLAR-3D
• Prospective, open-label, 96-week study (w/ 144-week extension) in virologically suppressed participants on a stable ARV regimen for ≥ 6 months and switching to Dovato, comparing those with and without a history of prior M184V/I.(Blick, 3)
• Proportion of participants with HIV-1 RNA ≥ 50 copies/mL at Weeks 48, 96, and 144, ITT-E (Weeks 48 and 96 were primary endpoints) were 2%, 4%, and 4%, respectively, for those with historical M184V/I (N=50) and 6%, 2%, and 2% for those with no historical M184V/I (N=50). (Blick, 8)
• No cases of confirmed virologic failure occurred in the historical M184V/I arm and 1 case occurred in the no historical M184V/I arm. (Blick, 13) No cases of treatment-emergent resistance occurred in either arm through Week 144.
• The occurrence of viral load blips through Week 144 was consistent across both treatment arms. (Blick, 14) The overall safety profiles were similar through Week 144 for both treatment arms. (Blick, 16)
SOUND
• Prospective, open-label, pilot study to evaluate virologically suppressed participants on Biktarvy who were switched to Dovato on Day 1 and followed for 96 weeks.(Blick) Participants had an unknown resistance history to DTG or 3TC.
• At Week 96, 37/40 participants (92.5%) remained suppressed on Dovato.(Blick) There were no discontinuations due to AEs.
References: 1. ViiV Healthcare Local Label. 2. Llibre J, et al. Clin Infect Dis. 2022. 3. Ryan P, et al. AIDS 2024. 4. Rolle CP, et al. AIDS 2024. 5. Blick G, et al. AIDS 2024. 6. Slim J, et al. AIDS 2024.

Drug/Product: Dovato (Dolutegravir/lamivudine)

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Summary of Testimony:	Product Summary for Apretude This information is provided in response to your request for information about Apretude® (cabotegravir extended-release injectable suspension [CAB LA]) for intramuscular (IM) use. Indication Apretude is indicated in at-risk adults and adolescents weighing at least 35 kg for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection. (PI, 1) Individuals must have a negative HIV-1 test prior to initiating Apretude (with or without an oral lead-in with oral cabotegravir) for HIV-1 PrEP. Dosing (see attached Prescribing Information, Section 2, for further information) Screen all individuals for HIV-1 infection immediately prior to initiating Apretude for HIV-1 PrEP and prior to each injection while taking Apretude. (PI, 2.1) Prior to initiating Apretude, an oral lead-in therapy may be used for ~1 month to assess the tolerability of Apretude. Apretude is for IM gluteal injection only. Initiate Apretude with a two 600 mg (3 mL) injections given 1 month apart on the last day of the oral lead-in (if used), or within 3 days, and continue with the injections every 2 months thereafter. Contraindications Apretude is contraindicated in patients: unknown or positive HIV-1 status; with previous hypersensitivity reaction (HSR) to CAB; coadministration with drugs where significant

decreases in CAB plasma concentrations may occur. (PI, 4)

Updated Efficacy Data

• The efficacy of Apretude to reduce the risk of acquiring HIV-1 infection is supported by data from two Phase 3 randomized, multinational, double-blinded, double-dummy trials: HPTN 083 [NCT02720094] and HPTN 084 [NCT03164564]. (PI, 14.1, Landovitz, Delaney-Moretlwe)

• Patients were randomized to one of the following arms:

• Arm 1: daily oral CAB 30 mg + daily oral tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) placebo for up to 5 weeks, followed by CAB LA 600 mg IM every 4 weeks x2 doses followed by CAB LA 600 mg IM every 8 weeks thereafter + daily oral TDF/FTC placebo, OR, Arm 2: daily oral TDF/FTC 300 mg/200 mg or oral CAB placebo for 5 weeks, followed by daily oral TDF/FTC + CAB LA placebo IM every 4 weeks x2 doses then every 8 weeks thereafter.

• HPTN 083, a non-inferiority study, evaluated CAB LA vs. daily oral TDF/FTC for PrEP in HIV-1 uninfected cisgender men and transgender women who have sex with men.(PI, 14.1, Landovitz)The primary endpoint was the rate of incident HIV-1 infections. CAB LA was statistically superior to TDF/FTC at preventing HIV acquisition (HR=0.34, 95% CI 0.18-0.62). There were a total of 52 incident HIV infections with 13 incident infections in the CAB LA arm vs 39 incident infections in the TDF/FTC arm. Further testing revealed 1 of the infections in the CAB LA arm to be prevalent then yielding a 69% reduction in the risk of HIV-1 incident infection relative to TDF/FTC (HR=0.31, 95% CI 0.16-0.58, P=0.0003)

• CAB LA was chosen by 96% of participants overall at the start of the open-label extension phase of HPTN 084. The most common reason cited was “prefer injection and/or don’t like pills”. (Clement)

• HPTN 084, a superiority study, evaluated CAB LA vs. daily oral TDF/FTC for PrEP in HIV-1 uninfected cisgender women. The primary endpoint was the rate of incident HIV-1 infections.(PI, 14.1, Delaney-Moretlwe) CAB LA was statistically superior to TDF/FTC at preventing HIV acquisition (HR=0.12, 95% CI 0.05-0.31). There were a total of 40 incident HIV infections with 4 incident infections in the CAB LA arm and 36 in the TDF/FTC arm. Further testing revealed 1 of the infections in the CAB LA arm to be prevalent then yielding a 90% reduction in the risk of HIV-1 incident infection relative to TDF/FTC (HR=0.10, 95% 0.04-0.27; P4x the protein-adjusted (PA)-IC90 (>0.664 µg/mL) within 1 day. (Han, 2) Plasma concentrations of CAB (without the administration of the OLI) are predicted to be >4x the PA-IC90 in 90% of patients by approximately 3 days after injection and in 95% of patients by approximately 1 week. The correlate of protection for CAB LA is not known.

Pregnancy outcomes

• In the randomized and open-label extension phase of HPTN084 no maternal deaths or HIV infections were reported. (Delaney-Moretlwe, 8)

PK during pregnancy

• A nested sub-study from HPTN 084 evaluated the PK of CAB LA among a subset of participants (n=75) who continued to receive CAB LA injections during pregnancy (who had received ≥4 CAB LA injections. A preliminary analysis was presented with the first 50 participants. (Marzinke, 15)

• CAB LA concentrations decrease throughout pregnancy but mostly remain above PA-IC90 targets.

Treatment Guidelines

• Apretude is recommended (IA rating) for HIV prevention in adults reporting sexual behaviors that place them at substantial ongoing risk of HIV exposure and acquisition in the CDC guidelines.(CDC, 2)

• Apretude is recommended (AIa rating) as PrEP for cisgender men and transgender women who have sex with men in the IAS-USA guidelines.(Saag, 1661)

• Apretude may be offered as an additional prevention choice for people at substantial risk of HIV infection, as part of combination prevention approaches (conditional recommendation; moderate certainty of evidence). (WHO, 10)

This information is provided as a professional service in response to your unsolicited request. ViiV Healthcare requests that the recipient of this information only share the contents with the Pharmacy and Therapeutics Committee members for the purposes of making evidence-based decisions regarding formulary inclusion.

References: 1.ViiV Healthcare Local Label; 2. Landovitz R, et al. N Engl J Med 2021;385(7):595-609; 3. Delany-Moretlwe S, et al. Lancet 2022;399:1779-89. 4. Clement M, et al. AIDS 2024. 5.Delany-Moretlwe S, et al. AIDS 2023. 6. Han K, et al. AAC. 2024:e0147523. 7.Delany-Moretlwe S, et al. AIDS 2024. 8. Marzinke MA, et al. AIDS 2024.9. CDC. https://www.cdc.gov/hiv.pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf; 10. Saag MS, et al. JAMA. 2020;324:1651-1669 11. WHO.https://www.who.int/publications/i/item/9789240054097

Drug/Product:	Apretude (cabotegravir extended-release injectable suspension [CAB LA])
Therapeutic Drug Class:	HIV
Testimony Format:	Written