Written Testimony: Arizona Health Care Cost Containment System (AHCCS) – 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 (AHCCS) review of *Cabenuva*® (cabotegravir extended-release injectable suspension [CAB LA]/rilpivirine extended-release injectable suspension [RPV LA]), co-packaged for intramuscular (IM) use.

Updated 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.(PI,2.1.1)

Updated Dosing

Prior to initiating treatment, oral lead-in therapy may be considered to assess the tolerability of CAB and RPV with the recommended dosage used for approximately 1 month.(PI,2.3.1). *Cabenuva* is for IM gluteal injection only. *Cabenuva* (600 mg CAB LA and 900 mg RPV LA) should be initiated on the last day of current antiretroviral therapy or oral lead-in and continue with injections of *Cabenuva* (400 mg CAB LA and 600 mg RPV LA) every month thereafter. *Cabenuva* (600 mg CAB LA and 900 mg RPV LA) should be initiated on the last day of current antiretroviral therapy or oral lead-in for 2 consecutive months and continue with injections of *Cabenuva* (600 mg CAB LA and 900 mg RPV LA) every 2 months thereafter.

If oral lead-in is used, the recommended oral lead-in daily dose is one 30-mg tablet of *Vocabria* (cabotegravir) and one 25-mg tablet of *Edurant* (rilpivirine) taken with a meal for approximately 1 month (at least 28 days), followed by IM injections of *Cabenuva*.

Efficacy Data (FLAIR Week 124 Data only)

FLAIR was a randomized, multicenter, active-controlled, open-label, non-inferiority study which evaluated *Cabenuva* in virologically suppressed participants.(Orkin, e670.4.1)

- Patients were randomized to continue abacavir/dolutegravir/lamivudine (ABC/DTG/3TC) or switch to *Cabenuva*.(Orkin, e670.5.12) At Week 96 participants on ABC/DTG/3TC had the option to transition to *Cabenuva* either as a direct to injection (DTI) group (n=111) or with an oral lead-in (OLI, n=121).
- ATLAS and FLAIR Week 48 data has been previously reviewed by AHCCS Committee on 5/19/21.
- ATLAS and FLAIR Week 96 data has been previously reviewed by AHCCS Committee on 10/18/21.

Results – Week 124:

- Virologic outcomes at Week 124 (after 24 weeks of *Cabenuva*) during the extension phase of FLAIR were similar between participants who received OLI or DTI. One participant (<1%) in each group had an HIV-1 RNA ≥50 copies/mL.(Orkin, e672.6.1)
- Most participants maintained virologic suppression: 110(99%) in the DTI group and 113 (93%) in the OLI group.(Orkin, e672.6.11)
- There was 1 additional participant with CVF since the 96 week analysis, totaling 4 participants over 124 weeks.(Orkin, e673.4.8)

Safety Overview

- The overall safety profile was consistent with that observed at Week 48 and when injection therapy with *Cabenuva* was initiated directly without the oral lead-in phase.(PI,12.4.1)
- Injection site reactions (ISRs) were the most common AE, occurring after 914 (21%) of 4422 injection in the extension phase.(Orkin,e668.3.15) ISRs were numerically less common in the OLI arm (338/2128) than the DTI arm (576/2314).(Orkin,e674.3.1)

Efficacy Data (ATLAS-2M Week 48 & 96 Data only)

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,1996.2.1)

- Virologically suppressed adults, either already receiving *Cabenuva* every 4 weeks from the ATLAS study or oral standard of care, were randomized to either *Cabenuva* (600 mg CAB LA and 900 RPV LA) every 8 weeks or *Cabenuva* (400 CAB LA and 600 mg RPV LA) every 4 weeks.

Results:

- Week 48 data established non-inferiority of *Cabenuva* every 8-weeks vs. every 4-weeks (HIV-1 RNA ≥50 copies; 2% vs 1%) and remained through Week 96.(Overton,1999.5.1) (Jaeger,e683.4.1)
- There were 8 (1.5%) confirmed virologic failures in the every 8-week arm and 2 (0.4%) in the every 4-week arm at Week 48.(Overton,2000.2.1) One additional patient in the every 8-week dosing group met confirmed virologic failure.(Jaeger,e684.2.1)

Safety Overview

- 21% and 24% of patients in the every 8-week arm and every 4-week arms experienced a drug-related, non-ISR AE.(Overton,2001.Table3)
- ISRs were the most common AE reported. In both arms, 86% of ISRs had a duration of 1 to 7 days.(Overton,2002.2.1)
- In the every 8-week arm and the every 4-week arm, 1% (n=6) and 2%(n-11) of patients, respectively, withdrew from the study for injection-related reasons.(Overton,2001.Table3)
- The occurrence of AEs through 96 weeks were generally similar between the treatment arms and consistent with what was reported at Week 48. ISRs were the most common AEs reported and injection site pain was the most common ISR reported.(Jaeger,e684.4.1)

Use in Pediatrics

The safety and effectiveness of *Cabenuva* have been established in adolescents aged 12 to younger than 18 years weighing at least 35 kg, which is supported by the trials in adults and the MOCHA (NCT03497676) trial in adolescents.(PI,23.1.1) Please see the full Prescribing Information for additional information.

Treatment Guidelines

- *Cabenuva* is strongly recommended for virologically suppressed patients with HIV-1 in both DHHS (AI rating) and IAS-USA (AIa rating) guidelines.(Saag,1657.Box 3)(DHHS,I-33.5.1)

References: **1.**ViiV Healthcare Local Label; **2.** Orkin C, et al. Lancet HIV 2021;8:e668-6678; **3.** Overton E, et al. Lancet 2020;396:1994-2005; **4.** Jaeger H, et al. Lancet HIV. 2021;8(11):e679-89; **5.** Saag MS, et al. *JAMA*. 2020;324(16):1651-1669; **6.** DHHS Guidelines. Available at: clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf. Updated Jun. 3, 2021. Accessed April 25, 2022.