Written Testimony: AHCCCS – Updated Data, *Triumeq*

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 *Triumeq*® (abacavir/dolutegravir/lamivudine).

Updated Indication

Triumeq and *Triumeq PD,* are a combination of DTG (integrase transfer inhibitor [INSTI]), ABC, and lamivudine (both nucleoside analogue reverse transcriptase inhibitors) indicated for the treatment of HIV-1 in adults and pediatric patients weighing ≥ 10 kg.(PI, 3.1.1) *Triumeq* and *Triumeq PD* alone is not recommended in patients with resistance-associated integrase substitutions or clinically-suspected INSTI resistance, because the dose of DTG in *Triumeq* and *Triumeq PD* is insufficient in these subpopulations.

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

- Serious and sometimes fatal hypersensitivity reactions (HSRs) have occurred with ABC-containing products and is a multi-organ clinical syndrome.(PI, 2.1.1) Patients who carry the HLA-B*5701 allele are at a higher risk and all patients should be screened prior to first use.
- Severe acute exacerbations of hepatitis B virus (HBV) have been reported in patients co-infected with HBV who have discontinued 3TC.

Updated Dosing

The recommended dosage of *Triumeq* in adults is one tablet taken orally once daily, with or without food.(PI, 3.3.2)

Pediatric Population Body Weight	Number of Tablets (once daily)	Recommended Daily Dose
***Triumeq PD* Tablets (10 kg to <25 kg)**		
10 kg to <14 kg	4	240 mg ABC, 20 mg DTG, and 120 mg 3TC
14 kg to <20 kg	5	300 mg ABC, 25 mg DTG, and 150 mg 3TC
20 kg to <25 kg	6	360 mg ABC, 30 mg DTG, and 180 mg 3TC
***Triumeq* Tablets (≥25 kg)**		
≥25 kg	1	600 mg ABC, 50 mg DTG, and 300 mg 3TC

Do not interchange *Triumeq* and *Triumeq PD* on a milligram-per-milligram basis. In patients taking certain UGT1A or CYP3A inducers, an additional tablet of *Tivicay* should be taken, separated by 12 hours from *Triumeq*. Because *Triumeq* is an FDC and cannot be dose adjusted, it is not recommended in patients with creatinine clearance < 30 mL/min or patients with hepatic impairment.

Use in Pediatrics

- The clinical data supporting use of *Triumeq* and *Triumeq PD* in pediatric patients with HIV-1 infection weighing ≥10 kgs is derived from previously conducted pediatric trials using the individual components of *Triumeq* and *Triumeq PD*.(PI,29.1.1)

ARROW

- ARROW (NCT02028676) evaluated ABC and 3TC (as either single entities or a fixed dose combination) once daily, in combination with a third antiretroviral in HIV-1 infected pediatric patients who weighed ≥25 kg.(PI,48.3.1) At week 48 and 96, 72% and 67% of patients had an HIV-1 RNA <80 copies/mL.
- One event of Grade 4 hepatitis in the once-daily cohort was considered an uncertain causality by the investigator and no additional safety issues were identified in pediatric patients compared with historical data in adults.(PI,16.5.1)

IMPAACT P1093

- IMPAACT P1093 (NCT01302847) evaluated the pharmacokinetics, efficacy, safety, and tolerability of DTG, in HIV-1 infected infants, children, and adolescents ages ≥4 weeks to <18 years.(PI,48.3.1) Across all 3 cohorts, 67% (18/27) of patients weighing ≥10 kg achieved HIV-1 RNA <50 copies/mL at Week 48 (FDA Snapshot).
- Overall, the safety data in this pediatric study was similar to adults.(PI.16.6.1)

Treatment Guidelines

The United States Department of Health and Human Services Panel lists "Recommended Initial Regimens for Most People with HIV." (DHHS, G-3, Table 6) Included in these 4 regimens is *Triumeq* (dolutegravir [DTG] and abacavir/lamivudine [ABC/3TC]) in patients who are HLA-B*5701 negative). *Triumeq* is also listed as a preferred INSTI regimen as an "Initial Antiretroviral Regimens During Pregnancy for People Who Are Antiretroviral-Naïve."(DHHS,C-68, Table4) The use of Triumeq requires HLA-B*5701 testing before starting therapy. The use of DTG at conception has been associated with a small increase in the risk of NTDs, but this was not seen when DTG was started during pregnancy. However, in the most recent data from Botswana, there was no longer a significant difference in NTDs with the use of DTG-containing compared to non-DTG containing ARV regimens at conception.

Revisions to the Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection to address the recent FDA approval of Triumeq PD have not yet occurred. (DHHS Pediatric, vi.2.3) The Panel notes that this will be addressed in a future update.

References: **1.** ViiV Healthcare Local Label. **2.** DHHS Guidelines. Available at: clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf. Updated January 20, 2022. Accessed August 4, 2022. **3.** HIV Clinical Guidelines: Pediatric ARV. Available at: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/pediatric-arv/guidelines-pediatric-arv.pdf. Updated April 11, 2022. Accessed August 4, 2022.