Tuesday, February 6, 2019

New York State Medicaid Drug Utilization Review Board
Submitted electronically: dur@health.ny.gov

Subject: Recommendations regarding lower cost HIV treatments Symfi, Symfi Lo, and Cimduo

To Whom It May Concern:

In the interest of potential cost savings to New York State (NYS) Medicaid, we are pleased to submit these recommendations to the Medicaid Drug Utilization Review Board (DURB) regarding three antiretroviral drug products with wholesale acquisition costs (WACs) that are significantly lower than comparable originator products.

New York State's Ending the HIV/AIDS Epidemic (EtE) plan has already dramatically reduced new HIV infections, expanded access to effective HIV care, and reduced AIDS mortality. The NYS Department of Health and members of the DURB are familiar with this track record of success and must continue to support the ongoing resource needs associated with the implementation of the NYS Blueprint to End the AIDS Epidemic.

As our recommendations on these antiretroviral drug products will lower cost to New York State's Medicaid Program, and will simultaneously reduce payments to NYS HIV/AIDS providers, it is imperative that the State share of these savings are reinvested in EtE activities and the State's HIV prevention, care and treatment infrastructure. As prices drug prices decrease, this has a potentially destabilizing impact on the care system. In the long term, the State Department of Health should work with the community to identify other strategies to maintain the HIV and community health care infrastructure so that it can continue to address health care disparities that exist in the populations we serve.

Our recommendations pertaining to Symfi™ (efavirenz 600 mg/tenofovir disoproxil 300 mg/lamivudine 300 mg), Symfi Lo™ (efavirenz 400 mg/tenofovir disoproxil 300 mg/lamivudine 300 mg), and Cimduo™ (tenofovir disoproxil 300 mg/lamivudine 300 mg) are proffered without conflicts of interest; none of the signers of this letter, all members of the End AIDS New York 2020 Community Coalition, have received in-kind or financial support from the manufacturer in 2018 or years prior.

In short, our recommendations are:

- The NYS DURB should fully evaluate the suitability of Symfi and/or Symfi Lo for inclusion on the Preferred Drug List (PDL), while leaving Atripla on the PDL, for all HIV-positive Medicaid clients currently receiving Atripla or opting to initiate ARV therapy with an efavirenz-inclusive single-tablet regimen (STR). This recommendation is contingent on voluntary rebates, beyond the Unit Rebate Amount (URA; 23.1%) that currently applies to Symfi or Symfi Lo as 505(b)(2) products approved by the U.S. Food and Drug Administration (FDA), that achieve cost savings that exceed those associated with Atripla's statutorily required URA and CPI penalties, plus any negotiated supplemental rebates. As these rebates will lower cost to NYS Medicaid Program, at least the state share of these savings should be reinvested in EtE activities.

- The NYS DURB should fully evaluate the suitability of Cimduo for inclusion on the PDL, while leaving Truvada on the PDL, for all HIV-positive Medicaid clients currently receiving Truvada or opting to initiate ARV therapy with a Truvada-inclusive regimen (STR). This recommendation is

contingent on voluntary rebates, beyond the 23.1% URA that currently applies to Cimduo, to achieve cost savings that exceed those associated with Truvada's statutorily required URA and CPI penalties, plus any negotiated supplemental rebates. As these rebates will lower cost to NYS's Medicaid Program, at least the state share of these savings should be reinvested in EtE activities.

- In close collaboration with the New York State Department of Health and Mental Hygiene's AIDS Institute Guidelines Program, the NYS DURB should evaluate the suitability of Cimduo and generic tenofovir disoproxil combined with generic lamivudine for inclusion on the PDL, with Truvada remaining on the PDL, for all HIV-negative Medicaid clients for whom pre-exposure prophylaxis (PrEP) is both indicated. This recommendation is contingent on voluntary rebates negotiated for Cimduo, beyond the URA that currently applies to Cimduo, that achieves cost savings beyond those currently associated with Truvada's statutorily required URA and CPI penalties, plus any negotiated supplemental rebates.

The signers of this letter note these list-price differentials are a notable advancement in fair HIV drug pricing. For some purchasers and payors, notably commercial plans and "Big 4" purchasers, the potential for cost savings is readily apparent. We also recognize that URAs, CPI penalties, and voluntary rebates on Atripla and Truvada likely render Cimduo and the Symfi products costlier Medicaid options, hence our stipulation that these be considered for the PDL contingent on the negotiation of voluntary rebates that ensure cost savings to NYS Medicaid.

**HIV Treatment Considerations**

On the basis of clinical trial safety and efficacy data, and long-term experience in clinical practice, the Department of Health and Human Services' Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV considers tenofovir disoproxil fumarate (TDF) plus emtricitabine (FTC) or lamivudine (3TC) a recommended nucleoside reverse transcriptase inhibitor combination for initial antiretroviral therapy in most persons with HIV when combined with dolutegravir (DTG), cobicistat-boosted elvitegravir (EVG), or raltegravir (RAL). [1] **We therefore support the inclusion of Cimduo on the NYS Medicaid PDL as a suitable option for people living with HIV initiating, or currently utilizing, treatment with a TDF-inclusive regimen.**

The signers of this letter also concur with the *Guidelines* regarding the suitability of efavirenz (EFV) as a component of first-line therapy. Given the availability of regimens with fewer treatment-limiting adverse events and also with non-inferior or superior efficacy, EFV-based regimens with TDF or TAF plus FTC or 3TC are only recommended in certain clinical situations.[1] Although many prescribers have moved toward TAF-based regimens based upon a purported improved safety profile compared to TDF, a recent systematic review and meta-analysis found that "In randomized clinical trials where TAF and TDF were used without pharmacokinetic enhances—ritonavir and cobicistat—there was no benefit of TAF versus TDF for HIV RNA suppression, clinical adverse events, discontinuation for renal adverse events, bone fractures, or discontinuation for bone-related adverse events."[2] **We therefore support the inclusion of Symfi on the NYS Medicaid PDL as a suitable option for people living with HIV who are currently utilizing Atripla**.

ENCORE 1, a multinational randomized placebo-controlled trial, compared two once-daily doses of EFV (combined with TDF/FTC): EFV 600 mg (standard dose) versus EFV 400 mg (reduced dose).[3] At 96 weeks, EFV 400 mg was noninferior to EFV 600 mg for rate of viral suppression. Study drug-related adverse events were less frequent in the EFV 400 mg group than in the 600 mg group. Although there were fewer self-reported CNS events in the 400 mg group, the groups had similar rates of psychiatric events. **Though EFV at a reduced dose has not been studied in the U.S. population, in pregnant women, or in patients**

**with TB/HIV coinfection, we support the inclusion of Symfi Lo on the NYS Medicaid PDL as a suitable option for people living with HIV who are currently utilizing Atripla.**

**Primary HIV Prevention Considerations**

The totality of evidence to date, from pharmacological data to observational studies to direct and indirect comparisons in randomized trials, suggests that 3TC and FTC can be considered to be interchangeable and that if there are any differences, these are likely to be very small and not of major clinical importance when used as a component of antiretroviral therapy.[4],[5] The use of 3TC for PrEP has not been studied in clinical trials, with the exception of one Phase I study with results that have not been published in the medical literature,[6] hence its use for primary HIV prevention in either Cimduo or as a stand-alone generic product in combination with stand-alone generic TDF is not fully supported by Housing Works and TAG. **We do, however, encourage the DURB to consider inclusion of these products on the NYS Medicaid PDL, either in close collaboration with the New York State Department of Health and Mental Hygiene's AIDS Institute Guidelines Program or in response to any affirmative recommendations following an extensive review of TDF/3TC's potential safety, efficacy, and risks conducted by Medical Care Criteria Committee.**

As per NYS Guidelines maintained by the Medical Care Criteria Committee, the preferred non-occupational post-exposure prophyalxis (nPEP) regimen is tenofovir plus either FTC or 3TC plus either raltegravir or dolutegravir.[7] **We therefore recommend, without reservation, the inclusion of Cimduo on the NYS Medical PDL as an option for nPEP.**

We thank you for the opportunity to submit these recommendations in the interest of potential cost savings to the NYS Medicaid program and the critical resource needs associated with the State's efforts to end AIDS as an epidemic. Please email Reed Vreeland at r.vreeland@housingworks.org to confirm receipt of this letter and do not hesitate to be in touch with any questions, comments, or concerns.

Respectfully submitted,

Apicha Community Health Center

End AIDS Now

Finger Lakes Community Health

Harlem United

Hispanic Health Network

Housing Works

Latino Commission on AIDS

New York Transgender Advocacy Group (NYTAG)

Saint Ann's Corner of Harm Reduction

Southern Tier AIDS Program

The LGBT Community Center, NYC

Treatment Action Group (TAG)

VOCAL New York

[1] HHS Panel on Antiretroviral Guidelines for Adults and Adolescents. What to Start: Initial Combination Regimens for the Antiretroviral-Naive Patient. In: Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. 2017 Oct 17. https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/11/what-to-start

[2] Hill A, Hughes SL, Gotham D, Pozniak AL. Tenofovir alafenamide versus tenofovir disoproxil fumarate: is there a true difference in efficacy and safety? J Virus Erad. 2018 Apr 1;4(2):72–79.

[3] Group ES. Efficacy of 400 mg efavirenz versus standard 600 mg dose in HIV-infected, antiretroviral-naive adults (ENCORE1): a randomised, double-blind, placebo-controlled, non-inferiority trial. *Lancet*. 2014. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24522178.

[4] Ford N, Hill A, Vitoria M, Mills EJ. Editorial commentary: Comparative efficacy of lamivudine and emtricitabine: comparing the results of randomized trials and cohorts. Clin Infect Dis. 2015 Jan 1;60(1):154-6. doi: 10.1093/cid/ciu767.

[5] Ford N, Vitoria M, Doherty M, Gray A. Candidates for inclusion in a universal antiretroviral regimen: are lamivudine and emtricitabine interchangeable? Curr Opin HIV AIDS. 2017 Jul;12(4):334-338. doi: 10.1097/COH.0000000000000377. [6] Mancuzo, A.V. Avaliação da Profilaxia Oral Pre-Exposição em homens que fazem sexo com homens: estudo clínico de fase 1 (Evaluation of oral pre-exposure prophylaxis in a cohort of MSM: a phase 1 clinical trial). MSc Dissertation, School of Medicine, Federal University of Minas Gerais, Brazil. 2017.

[7] Medicare Care Criteria Committee. PEP for Non-Occupational Exposure to HIV (nPEP). 2018 May. https://www.hivguidelines.org/pep-for-hiv-prevention/non-occupational/#tab_5