



Indian Health Service
National Pharmacy and Therapeutics Committee
Formulary Brief: HIV Guidelines & PrEP Updates
- July 2020 -



Background:

During the Summer 2020 meeting, the National Pharmacy and Therapeutics Committee (NPTC) reviewed current clinical practice guidelines and medication updates for HIV infection. Specific drugs, including dolutegravir or raltegravir, are used along with the combination product, tenofovir disoproxil fumarate (TDF) plus emtricitabine, to make a complete antiretroviral regimen. This review resulted in the **addition of dolutegravir for use in HIV treatment during pregnancy** to the National Core Formulary (NCF). This modification aligns the NCF with current recommendations from recent HHS treatment guidelines for HIV.

Discussion:

Dolutegravir, an integrase strand transfer inhibitor, was added as the “preferred” backbone for HIV treatment during pregnancy in the April 2020 update to the guidelines formally titled, *Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States: The Perinatal Guidelines*.¹ The decision utilized new data on neural tube defects in children born to women treated with dolutegravir. The adherence benefits of once-daily dolutegravir and its higher barrier to resistance was weighed against the neural tube defect (NTD) risk. Also, women starting dolutegravir during pregnancy are likely to be past the time of neural tube development by the time pregnancy is realized. The expert panel decided that the greater likelihood of virologic suppression and subsequent decreased risk of vertical HIV transmission outweighed the risk of NTD. The risk of NTD was previously thought to be as high as 0.9% with dolutegravir however additional, updated information downgraded the risk to approximately 0.3%. The background risk is estimated to be 0.1%.¹ The HHS guidelines include a [guide for counseling women](#) on the risk of NTD, thereby aiding providers in discussions regarding decision making for dolutegravir use in pregnant women, women wishing to conceive, or any women of child-bearing age. The risk of NTD would be greatest in women wishing to conceive or those of child-bearing age with an unplanned pregnancy.

The previous medication named to the NCF for pregnant women with HIV was raltegravir. Raltegravir remains as acceptable alternative in the HHS Perinatal guidelines and on the NCF. Raltegravir-based antiretroviral therapy remains the treatment of choice for HIV post-exposure prophylaxis in the context of occupational and non-occupational exposure cases.

Raltegravir is dosed twice daily while dolutegravir is given once-daily. As such, dolutegravir results in improved adherence over raltegravir. Dolutegravir is also more effective and reliable at lowering viral load due to a higher barrier to development of drug resistance. Its advantages are thus twofold comparatively to raltegravir use.

The HHS Perinatal Guidelines also recommend dolutegravir as an “alternative” for women wishing to conceive or those women not using contraception.

It is important to note that dolutegravir or raltegravir in pregnancy or pre-conception must be combined with an appropriate nucleoside reverse transcriptase inhibitor backbone to provide effective antiretroviral therapy. The combination of emtricitabine 200 mg and tenofovir disoproxil fumarate 300 mg (brand name, Truvada®) plus dolutegravir or raltegravir are the two IHS National Core Formulary choices:

1. *dolutegravir 50 mg QD + (emtricitabine 200 mg / TDF 300 mg) QD*
2. *raltegravir 400 mg BID + (emtricitabine 200 mg / TDF 300 mg); taken once daily.*

A newer formulation of tenofovir is available in combination with emtricitabine for the treatment of HIV (emtricitabine 200 mg / tenofovir alafenamide 25 mg, brand name Descovy®) but is not approved in pregnancy and should be avoided in women wishing to conceive as well as during pregnancy.

Other recent changes to the HHS HIV treatment guidelines were discussed in the meeting but did not result in formulary changes. A summary review of the HHS guideline changes can be found in the [“What’s New”](#) section.² The other guideline change of significance was the FDA approval of two-drug HIV

treatment regimens. Two different 2-drug treatment regimens have received FDA approval to date including (1) dolutegravir + rilpivirine and (2) dolutegravir + lamivudine. While these regimens have FDA approval, use of two-drug antiretroviral therapy within the IHS has been limited to date. Although individual practitioners may find them useful, the current NCF choices are considered safe and effective. No additional changes were deemed necessary by the committee at this time.

Details about ongoing [HIV Elimination](#) efforts and epidemiology in Native People living with HIV were reviewed and are summarized in the July 2019 [NPTC brief](#) and have not changed since.

HIV Pre-Exposure Prophylaxis (PrEP):

No changes were ultimately made to the NCF for HIV PrEP. There was careful consideration of the current PrEP formulary option. The only other FDA-approved alternative for PrEP (emtricitabine 200 mg / tenofovir alafenamide 25 mg) utilizes the same two active ingredients but with a different tenofovir formulation, and has data suggesting it may be safer in patients with pre-existing renal or bone density issues.⁵ The alternative product however is not approved for PrEP in cis-gender women and is not approved for PrEP for people sharing injection equipment to administer drugs. The pharmacodynamics of emtricitabine 200 mg / tenofovir alafenamide 25 mg make it effective for preventing HIV within 20 days after starting, while the current NCF choice is effective within 10 days.⁶ These practical limitations, combined with potential generic availability in the near future made changes to HIV PrEP management unadvisable.

The NPTC also reviewed the topic of “on demand” PrEP as an alternative to daily PrEP.⁷ While the practice of utilizing PrEP on an “as needed” basis has encouraging initial data, there are no FDA-approved medications with this indication or guidance. Educating providers on the topic of “on demand” PrEP is important so that informed discussions can occur with inquiring patients. It should be restated that “on demand” PrEP is not an endorsed practice for IHS providers. Daily PrEP administration is superior and adherence with PrEP medications is the key to its effectiveness. Decreasing PrEP utilization to “as needed” is not consistent with medication adherence messaging necessary to maximize PrEP effectiveness.

The branded name of emtricitabine / TDF was removed from the NCF to reflect the expected patent expiration and arrival of generic equivalents.

Findings:

Based on findings from the review of current HIV guidelines and therapies, the NPTC voted to add dolutegravir to the NCF as the preferred anchor drug for treatment of women with HIV during pregnancy and as an alternative for women attempting to conceive. The NPTC considered changes to PrEP but made minor changes (i.e., brand name removal) of the drug combination currently on the formulary.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the [NPTC website](#).

References:

1. U.S. Department of Health & Human Services. HIV Perinatal Guidelines: [Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States](#). Accessed 8/3/2020.
2. U.S. Department of Health & Human Services. HIV Perinatal Guidelines: [What's New in Guidelines for the Use of Antiviral Agents in Adults and Adolescents](#). Accessed 8/3/2020.
3. U.S. Department of Health & Human Services. [What is Ending the HIV Epidemic: A Plan for America?](#) Accessed 8/3/2020.
4. Indian Health Service. National Pharmacy & Therapeutics Committee. Formulary Brief: [HIV Treatment](#). Accessed 8/3/2020.
5. Schwarze-Zander C, Piduhn H, Boesecke C, et al. [Switching tenofovir disoproxil fumarate to tenofovir alafenamide in a real life setting: what are the implications?](#) *HIV Medicine*. 2020; 21(6): 378-385.
6. Gilead Sciences, Inc. (2019). [DESCOYVY® \(emtricitabine and tenofovir alafenamide\) Product Insert](#). Foster City, CA.
7. Roux P, Fessard L, Suzan-Monti M, et al. [Is On Demand HIV Pre-exposure Prophylaxis a Suitable Tool for Men Who Have Sex With Men Who Practice Chemsex? Results from a Substudy of the ANRS-IPERGAY Trial](#). *J Acquir Immune Defic Syndr*. 2018; 79(2):69-75.