STEP THERAPY CRITERIA

BRAND NAME	**Truvada**
(Generic)	**(emtricitabine/tenofovir disoproxil fumarate)**

Status: CVS Caremark Criteria
Type: Initial Step Therapy, Post Step Therapy Prior Authorization ***Ref #2664-D***

FDA-APPROVED INDICATIONS[1]

Treatment of Human Immunodeficiency Virus-1 (HIV-1) Infection
Truvada is indicated in combination with other antiretroviral agents for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults and pediatric patients weighing at least 17 kg.

Pre-Exposure Prophylaxis
Truvada is indicated in combination with safer sex practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in at-risk adults and adolescents weighting at least 35 kg. Individuals must have a negative HIV-1 test immediately prior to initiating Truvada for HIV-1 PrEP.

If clinical symptoms consistent with acute viral infection are present and recent (<1 month) exposures are suspected, delay starting PrEP for at least one month and reconfirm HIV-1 status or use a test cleared by the FDA as an aid in the diagnosis of HIV-1 infection, including acute or primary HIV-1 infection.

When considering Truvada for pre-exposure prophylaxis the following factors may help to identify individuals at high risk:
- Has partner(s) known to be HIV-1 infected, or
- Engages in sexual activity within a high prevalence area or social network and one or more of the following:
  - inconsistent or no condom use
  - diagnosis of sexually transmitted infections
  - exchange of sex for commodities (such as money, food, shelter, or drugs)
  - use of illicit drugs or alcohol dependence
  - incarceration
  - partner(s) of unknown HIV-1 status with any of the factors listed above

When prescribing Truvada for pre-exposure prophylaxis, healthcare providers must:
- Prescribe Truvada as part of a comprehensive prevention strategy because Truvada is not always effective in preventing the acquisition of HIV-1 infection
- Counsel all uninfected individuals to strictly adhere to the recommended Truvada dosing schedule because the effectiveness of Truvada in reducing the risk of acquiring HIV-1 was strongly correlated with adherence as demonstrated by measurable drug levels in clinical trials
- Confirm a negative HIV-1 test immediately prior to initiating Truvada for a PrEP indication. If clinical symptoms consistent with acute viral infection are present and recent (< 1 month) exposures are suspected, delay starting PrEP for at least one month and reconfirm HIV-1 status or use a test approved by the FDA as an aid in the diagnosis of HIV-1 infection, including acute or primary HIV-1 infection
- Screen for HIV-1 infection at least once every 3 months while taking Truvada for PrEP

COMPENDIAL USES

- Postexposure prophylaxis (PEP) following occupational or non-occupational exposure to HIV[2,3]
- Pre-exposure prophylaxis of HIV in adult injection drug users at substantial risk of HIV acquisition (e.g., HIV-positive injecting partner, sharing injecting equipment, recent methadone or other medication-based treatment program)[4]

INITIAL SCREEN-OUT CRITERIA

1. If the request for Truvada is for less than a 30 day supply, then the request for Truvada will be approved without requiring PA criteria review.

2. If the request for Truvada is for a patient who has not filled Truvada in the previous 120 days, then the request for Truvada will be approved without requiring PA criteria review.
3. If the request for Truvada is for a patient who has filled Truvada previously but has not filled any other antiretroviral medication in the past 120 days, then the request for Truvada will be approved without requiring PA criteria review.
4. If the patient does not meet any of the above criteria (1, 2, or 3), then the system will reject with a message indicating that prior authorization (PA) is required. The request will then be subject to the PA criteria below for approval.

CRITERIA FOR APPROVAL

1	Is the requested medication prescribed in combination with other antiretroviral agents for **postexposure prophylaxis** of human immunodeficiency virus (HIV) infection? [If yes, no further questions.]	Yes	No
2	Is the requested medication prescribed as monotherapy for **pre-exposure prophylaxis** of human immunodeficiency virus (HIV) infection? [If yes, no further questions.]	Yes	No
3	Is the requested medication prescribed in combination with other antiretroviral agents for the treatment of human immunodeficiency virus (HIV) infection? [If no, no further questions.]	Yes	No
4	The preferred medication on your patient's plan is Cimduo. Is the patient able to be switched to Cimduo? [If yes, no further questions.]	Yes	No
5	Does the patient have a contraindication to lamivudine? [If yes, no further questions.]	Yes	No
6	Has the patient had an intolerable adverse effect with lamivudine? [If yes, no further questions.]	Yes	No
7	Is the patient's weight less than 35 kilograms?	Yes	No

RATIONALE

To ensure the safe, clinically appropriate, and cost-effective use of Truvada for pre-exposure prophylaxis (PrEP) of human immunodeficiency virus (HIV) infection.

Truvada, a combination product containing emtricitabine and tenofovir (nucleoside reverse transcriptase inhibitors), is FDA-approved for the following: 1) in combination with other antiretroviral agents for the treatment of HIV-1 infection, and 2) in combination with safer sex practices for PrEP to reduce the risk of sexually acquired HIV-1 in high-risk adults.[1] Truvada in combination with other antiretroviral agents may also be used off-label for postexposure prophylaxis (PEP) of HIV.[2,3] For both occupational and non-occupational PEP, an initial 28-day course of therapy is recommended.[2,3]

The US Public Health Service has issued guidelines on the use of PrEP for individuals at high risk for HIV.[4] A summary is shown in the table below.

US Public Health Service Guidelines on HIV PrEP[4]

Clinically Eligible	Starting PrEP Medication	Follow-Up On PrEP Medication
▪ Patient is at substantial risk for HIV acquisition ▪ Documented negative HIV test result immediately (at least one week) before starting PrEP ▪ No signs/symptoms of acute HIV infection	▪ Prescribe Truvada once daily, continuously, for no more than a 90-day supply	▪ Follow up visits at least every 3 months with ○ HIV testing ○ Pregnancy testing if applicable ○ Medication adherence counseling ○ Behavioral risk reduction support

▪ Baseline pregnancy test for women who may become pregnant ▪ Normal renal function (CrCl is ≥ 60 mL/min) and no contraindicated medications ▪ Documented HBV infection status and HBV vaccine status		○ Side effect assessment ▪ Renal function at 3 months and then at least every 6 months

Abbreviations: CrCl = creatinine clearance, HIV = human immunodeficiency virus, PrEP = pre-exposure prophylaxis, HBV = hepatitis B virus.

SAFETY

WARNING: POSTTREATMENT ACUTE EXACERBATION OF HEPATITIS B and RISK OF DRUG RESISTANCE WITH USE OF TRUVADA FOR PrEP IN UNDIAGNOSED EARLY HIV-1 INFECTION[1]

Severe acute exacerbations of hepatitis B virus (HBV) have been reported in HBV-infected patients who have discontinued Truvada. Hepatic function should be monitored closely in HBV-infected patients who discontinue Truvada. If appropriate, initiation of anti-hepatitis B therapy may be warranted. Truvada used for a PrEP indication must only be prescribed to individuals confirmed to be HIV-negative immediately prior to initial use and periodically (at least every 3 months) during use.[1] Drug-resistant HIV-1 variants have been identified with use of Truvada for a PrEP indication following undetected acute HIV-1 infection. Do not initiate Truvada for a PrEP indication if signs or symptoms of acute HIV-1 infection are present unless negative infection status is confirmed.

Do not use Truvada for a PrEP indication in HIV-1 uninfected individuals with estimated creatinine clearance below 60 mL/min. Renal impairment, including cases of acute renal failure and Fanconi syndrome (renal tubular injury with severe hypophosphatemia), has been reported with the use of tenofovir. It is recommended that estimated creatinine clearance (CrCl) be assessed in all individuals prior to initiating therapy and as clinically appropriate during therapy with Truvada.

REFERENCES

1. Truvada [package insert]. Foster City, CA: Gilead Sciences, Inc.; May 2018.
2. Kuhar DT, Henderson DK, Stuble KA, et al. Updated US Public Health Service Guidelines for the Management of Occupational Exposures to Human Immunodeficiency Virus and Recommendations for Postexposure Prophylaxis. *Infect Control Hosp Epidemiol.* 2013;34(9):875-892.
3. US Department of Health and Human Services. Updated guidelines for antiretroviral postexposure prophylaxis after sexual, injection drug use, or other nonoccupational exposure to HIV-United States 2016. https://www.cdc.gov/hiv/pdf/programresources/cdc-hiv-npep-guidelines.pdf Accessed April 16, 2018.
4. US Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the Unites States – 2017 Update. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf. Accessed April 16, 2018.

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