LifeWise
Health Plan of Washington

PHARMACY / MEDICAL POLICY – 5.01.588

Pharmacologic Prevention and Treatment of HIV/AIDS

Effective Date:	Mar. 1, 2025	RELATED MEDICAL POLICIES:
Last Revised:	Feb. 11, 2025	5.01.636 Chronic Hepatitis B Antiviral Therapy
Replaces:	N/A	

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Introduction

HIV and AIDS remain global problems due to difficulties preventing and treating these diseases. Resistance continues to make treatment challenging and may require complex medication regimens. HIV is a chronic disease without a cure. There are some US Food & Drug Administration (FDA) approved medications available that when taken as prescribed can prevent HIV. This is referred to as pre-exposure prophylaxis (or PrEP) and these medications can significantly reduce the chance of getting HIV. For treating HIV, current regimens begin with two drugs or three drugs to suppress the virus and act as a barrier against resistance. However, in some cases, individuals may have HIV with multiple drug resistances, which creates a difficult treatment situation. This policy describes when an add-on drug treatment may be considered medically necessary in these types of difficult treatment situations. This policy also describes when brand name drugs may be considered medically necessary for PrEP and HIV treatment.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Drug	Medical Necessity
Apretude (cabotegravir extended-release injectable suspension) intramuscular (IM)	**Apretude (cabotegravir extended-release injectable suspension) may be considered medically necessary when used for pre-exposure prophylaxis (PrEP) to reduce the risk of HIV-1 infection when the following criteria are met:** • The individual is aged 13 years or older and weighs greater than or equal to 35 kg **AND** • The maintenance dose prescribed is 600 mg every 2 months
Descovy (emtricitabine and tenofovir alafenamide) oral	**Descovy (emtricitabine and tenofovir alafenamide) may be considered medically necessary when used in combination with other antiretroviral agents for the treatment of HIV-1 infection when the following criteria are met:** • The individual has tried generic emtricitabine and tenofovir disoproxil fumarate first (two-drug combination) and had an inadequate response or intolerance to generic emtricitabine and tenofovir disoproxil fumarate (documentation required) **Descovy (emtricitabine and tenofovir alafenamide) may be considered medically necessary when used for pre-exposure prophylaxis (PrEP) to reduce the risk of HIV-1 infection**
Rukobia (fostemsavir) oral	**Rukobia (fostemsavir) may be considered medically necessary for the treatment of multidrug resistant HIV-1 when ALL the following criteria are met:** • The individual is aged 18 years or older **AND** • Viral load greater than 400 copies/mL **AND** • Documented failure or resistance to greater than or equal to 3 classes of antiretrovirals **AND** • Documentation that Rukobia (fostemsavir) will be used in combination with at least one other antiretroviral agent where resistance testing has demonstrated viral susceptibility **AND** • The dose is 600 mg taken twice daily

Drug	Medical Necessity

Sunlenca (lenacapavir) oral, SC	**Sunlenca (lenacapavir) may be considered medically necessary for the treatment of multidrug resistant HIV-1 when ALL the following criteria are met:**
	• The individual is aged 18 years or older
	AND
	• Viral load greater than or equal to 400 copies/mL
	AND
	• Documented failure or resistance to greater than or equal to 2 medications from each class of greater than or equal to 3 of these four classes of antiretrovirals:
	  ○ Nucleoside reverse-transcriptase inhibitors
	  ○ Non-nucleoside reverse-transcriptase inhibitors
	  ○ Protease inhibitors
	  ○ Integrase strand transfer inhibitors
	AND
	• The maintenance dose prescribed is 927 mg by SC injection every 6 months

Trogarzo (ibalizumab) IV	**Trogarzo (ibalizumab) infusions may be considered medically necessary for the treatment of multidrug resistant HIV-1 when ALL the following criteria are met:**
	• Viral load greater than 1,000 copies/mL
	AND
	• Documented failure or resistance to at least one medication from greater than or equal to 2 of these three classes of antiretrovirals
	  ○ Nucleoside reverse-transcriptase inhibitors
	  ○ Non-nucleoside reverse-transcriptase inhibitors
	  ○ Protease inhibitors
	AND
	• Treated with antiretrovirals for at least 6 months

Truvada (emtricitabine and tenofovir disoproxil fumarate) oral	**Truvada (emtricitabine and tenofovir disoproxil fumarate) may be considered medically necessary when used in combination with other antiretroviral agents for the treatment of HIV-1 infection when the following criteria are met:** • The individual has tried generic emtricitabine and tenofovir disoproxil fumarate first (two-drug combination) and had an

Drug	Medical Necessity
	inadequate response or intolerance to generic emtricitabine and tenofovir disoproxil fumarate (documentation required) **Truvada (emtricitabine and tenofovir disoproxil fumarate) may be considered medically necessary when used for pre-exposure prophylaxis (PrEP) to reduce the risk of HIV-1 infection when the following criteria are met:** • The individual has tried generic emtricitabine and tenofovir disoproxil fumarate first (two-drug combination) and had an inadequate response or intolerance to generic emtricitabine and tenofovir disoproxil fumarate (documentation required)

Drug	Investigational
As listed	**The medications listed in this policy are subject to the product's US Food and Drug Administration (FDA) dosage and administration prescribing information.** **All other uses of the drugs listed for conditions not outlined in this policy are considered investigational.**

Length of Approval	
Approval	**Criteria**
Initial authorization	**Non-formulary exception reviews and all other reviews for Rukobia (fostemsavir), Sunlenca (lenacapavir), and Trogarzo (ibalizumab) may be approved up to 12 months.** **Non-formulary exception reviews for Apretude (cabotegravir extended-release injectable suspension), Descovy (emtricitabine and tenofovir alafenamide), and Truvada (emtricitabine and tenofovir disoproxil fumarate) may be approved up to 12 months.** **All other reviews for Apretude (cabotegravir extended-release injectable suspension), Descovy (emtricitabine and tenofovir**

Length of Approval	
Approval	**Criteria**
	alafenamide), and Truvada (emtricitabine and tenofovir disoproxil fumarate) may be approved up to 3 years.
Re-authorization criteria	**Non-formulary exception reviews and all other reviews for Rukobia (fostemsavir), Sunlenca (lenacapavir), and Trogarzo (ibalizumab) will be approved up to 12 months when chart notes show a decreasing trend in viral load or continued viral load suppression.** **Non-formulary exception reviews for Apretude (cabotegravir extended-release injectable suspension), Descovy (emtricitabine and tenofovir alafenamide), and Truvada (emtricitabine and tenofovir disoproxil fumarate) will be approved up to 12 months when chart notes demonstrate that the individual continues to show a positive clinical response and is tolerating therapy.** **All other reviews for Apretude (cabotegravir extended-release injectable suspension), Descovy (emtricitabine and tenofovir alafenamide), and Truvada (emtricitabine and tenofovir disoproxil fumarate) will be approved up to 3 years when chart notes demonstrate that the individual continues to show a positive clinical response and is tolerating therapy.**

Documentation Requirements
The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following: • Office visit notes that contain the diagnosis, relevant history, physical evaluation, and medication history

Coding

Code	Description
HCPCS	
J0739	Injection, cabotegravir, (Apretude) 1 mg
J0750	Emtricitabine 200 mg and tenofovir disoproxil fumarate 300 mg, oral, FDA-approved prescription, only for use as HIV pre-exposure prophylaxis (not for use as treatment of HIV) (Truvada)
J0751	Emtricitabine 200 mg and tenofovir alafenamide 25 mg, oral, FDA-approved prescription, only for use as HIV pre-exposure prophylaxis (not for use as treatment of HIV) (Descovy)
J0799	FDA-approved prescription drug, only for use as HIV pre-exposure prophylaxis (not for use as treatment of HIV), not otherwise classified
J1746	Injection, ibalizumab-uiyk (Trogarzo), 10 mg
J1961	Injection, lenacapavir (Sunleca), 1 mg

Related Information

Benefit Application

Pharmacy Benefit

Descovy (emtricitabine and tenofovir alafenamide), Rukobia (fostemsavir), and Truvada (emtricitabine and tenofovir disoproxil fumarate) are managed through the pharmacy benefit.

Medical Benefit

Apretude (cabotegravir extended-release injectable suspension) and Trogarzo (ibalizumab) are managed through the medical benefit.

Medical / Pharmacy Benefit

Sunlenca (lenacapavir) is managed through both the medical and pharmacy benefit.

Evidence Review

Description

Medical Condition

HIV is a virus that attacks the body's immune system, specifically the CD4 T-cells, which results in increased vulnerability to infections and diseases. If left untreated, HIV may progress to AIDS (acquired immune deficiency syndrome), a late stage characterized by CD4 cell count <200 cells/mm or opportunistic illness. Individuals with AIDS have an increased risk of infections and viral-induced cancers, leading to a typical survival expectancy of three years without treatment. In 2019, 36,801 people were diagnosed with HIV in the United States and dependent areas (American Samoa, Guam, the Northern Mariana Islands, Puerto Rico, the Republic of Palau, and the US Virgin Islands). This statistic, combined with the fact that HIV does not have a cure, contributes to the estimate of 1,059,784 people in the US living with HIV.

Multidrug-resistant HIV continues to be a concern as a reason for treatment failure. A retrospective analysis published in 2017 looked at individuals in sub-Saharan Africa that failed first line tenofovir regimens and 16% of these 712 individuals had at least one TAM (thymidine analogue mutation), key players in resistance to NRTIs.

Four to five TAMs and M184V is one of the most common patterns of mutations associated with high-level resistance to NRTIs nucleoside reverse transcriptase inhibitors. Other MDR genes include Q151M and T69 insertions. As HIV-1 continues to multiply, the chances of mutation and multidrug resistance grows. If the virus develops multiple defensive genes, the individual may not adequately respond to typical drug regimens anymore. Currently, MDR is a blanket description due to the vast number of mutations that can confer resistance, making prevalence difficult to estimate. The World Health Organization (WHO) resistance report for 2017 examined resistance rates in low to middle income countries. Of these countries, resistance to two drug classes (NRTI and NNRTI) was measured ranging from not measured to 6.4%.

Rukobia (fostemsavir)

Fostemsavir is a prodrug for the active metabolite temsavir, a first-in-class HIV-1 attachment inhibitor developed for multidrug resistant individuals with few antiretroviral therapeutic alternatives. Temsavir works by binding to viral envelope glycoprotein 120 (gp120) close to the

CD4+ binding site. This locks gp120 into a closed state that does not allow the conformational change necessary for virus attachment to host CD4+ T cells.

Efficacy/Effectiveness

One pivotal phase 3 clinical trial (BRIGHTE) comprises the current evidence of efficacy in the target population at labeled dosing. This trial included two cohorts, one partially randomized, double blind, and placebo-controlled and the other open-label based on the number of fully active antiretroviral (ARV) classes available for optimized background therapy (OBT) (1-2 or none). The randomized cohort received fostemsavir 600 mg twice daily + OBT (n=203) or placebo twice daily + OBT (n=69) days 1-8 and then all received open-label fostemsavir 600 mg twice daily + OBT from day 9 onward. In the nonrandomized cohort, individuals received open-label fostemsavir 600 mg twice daily + OBT beginning day 1 (n=99). In the randomized cohort, fostemsavir 600 mg twice daily + OBT was significantly more effective than placebo + OBT from day 1-day 8 as measured by reduction from baseline in HIV-1 RNA viral load. At weeks 24, 48, and 96 in the randomized cohort, virologic response ranged from 53% to 60%, virologic failure ranged from 40% to 30%, CD4+ counts increased 90 cells/mm^3 to 205 cells/mm^3 from baseline, and CD4+ count response ranged from 48% to 76%.

Safety/Tolerability

A total of 370 subjects (271 randomized and 99 nonrandomized) received at least 1 dose of fostemsavir 600 mg twice daily in the BRIGHTE trial. Overall, most (81%) of the adverse reactions reported with fostemsavir were mild or moderate in severity. The proportion of subjects who discontinued treatment with fostemsavir due to an adverse event was 7% at Week 96 (randomized: 5% and nonrandomized: 12%). The most common adverse events leading to discontinuation were related to infections (3% of subjects receiving fostemsavir). Serious drug reactions occurred in 3% of subjects and included 3 cases of severe immune reconstitution inflammatory syndrome. Adverse reactions reported in ≥ 2% of subjects receiving fostemsavir plus OBT in the BRIGHTE trial, randomized cohort (week 96 analysis) are nausea (10%), diarrhea (4%), headache (4%), abdominal pain (3%), dyspepsia (3%), fatigue (3%), rash (3%), sleep disturbance (3%), immune reconstitution inflammatory syndrome (2%), somnolence (2%), and vomiting (2%).

Sunlenca (lenacapavir)

Lenacapavir is a multistage, selective inhibitor of HIV-1 capsid function that directly binds to the interface between capsid protein (p24) subunits in hexamers. Lenacapavir inhibits HIV-1 replication by interfering with multiple essential steps of the viral lifecycle, including capsid-mediated nuclear uptake of HIV-1 proviral DNA (by blocking nuclear import proteins binding to capsid), virus assembly and release (by interfering with Gag/Gag-Pol functioning, reducing production of capsid protein subunits), and capsid core formation (by disrupting the rate of capsid subunit association, leading to malformed capsids).

Efficacy/Effectiveness

In clinical studies, lenacapavir has demonstrated successful antiviral activity for up to 6 months after a single subcutaneous injection. The primary data for evaluating lenacapavir came from the CAPELLA (phase II/III) and CALIBRATE (phase II) studies. CAPELLA is a Phase II/III, double-blinded, placebo-controlled global multicenter study designed to evaluate the antiviral activity of lenacapavir administered every six months as a subcutaneous injection in heavily treatment-experienced men and women with multi-drug resistant HIV-1 infection. CALIBRATE is an on-going, Phase II, open-label, active-controlled study in treatment-naïve men and women with HIV-1 infection designed to evaluate the efficacy and safety profile of lenacapavir containing regimens.

CALIBRATE is a Phase 2, active-controlled, induction-maintenance study of treatment-naive people with HIV with CD4+ cell counts at least 200 cells/µl. Participants were randomized (2:2:2:1) to one of four treatment groups. The first and second groups received lenacapavir (given initially orally for loading/lead-in, then subcutaneously) with oral daily emtricitabine/tenofovir alafenamide, prior to switching from emtricitabine/tenofovir alafenamide to oral daily tenofovir alafenamide (Group 1) or bictegravir (Group 2). The third group received oral daily lenacapavir with emtricitabine/tenofovir alafenamide throughout the study. The fourth group, a control arm, received oral daily bictegravir/emtricitabine/tenofovir alafenamide. Lenacapavir, administered subcutaneously or orally, in combination with emtricitabine/tenofovir alafenamide led to high rates of viral suppression by Week 28 (94%; n = 147/157). Lenacapavir, given subcutaneously or orally, in combination with oral daily emtricitabine/tenofovir alafenamide (F/TAF) led to high rates of viral suppression by Week 28 (94%; n=147/157). Specifically, in the pooled subcutaneous lenacapavir + F/TAF arms, 93% (n=98/105) achieved an undetectable viral load (<50 copies/mL). In the oral lenacapavir + F/TAF arm, 94% (n=49/52) achieved an undetectable viral load (<50 copies/mL).\

CAPELLA enrolled 36 heavily treatment-experienced people with HIV who were failing their existing regimen were randomly assigned (2:1) to lenacapavir or placebo in a double-blind manner. Participants had HIV-1 RNA at least 400 copies/ml and were resistant to at least two agents from at least three of the four major antiretroviral classes. For the first 2 weeks, in addition to receiving their existing antiretroviral regimen, 24 participants received oral lenacapavir (600 mg on Days 1 and 2 and 300 mg on Day 8), and 12 received placebo. Thus, these first 14 days were considered a period of functional monotherapy. At Day 15, all participants initiated an investigator-selected optimized background regimen. Those initially assigned to oral lenacapavir started subcutaneous lenacapavir (927 mg) every 6 months, while those on placebo started a lenacapavir 2-week oral lead-in, followed by subcutaneous, 6-month dosing. Subsequently, an additional nonrandomized cohort of 36 participants received 14 weeks of oral lenacapavir followed by subcutaneous lenacapavir every 6 months. Following initiation of lenacapavir, rapid reductions in HIV-1 RNA were observed among the 36 randomized individuals; at the end of the first 14 days (functional monotherapy), 88% (21/24) receiving lenacapavir had a reduction in HIV-1 RNA of at least 0.5 log10 copies/ml compared with 17% (2/12) receiving placebo. At Week 26, 81% of randomized participants (29/36) had HIV-1 RNA less than 50 copies/ml.

Safety/Tolerability

In CALIBRATE lenacapavir was well tolerated. No serious adverse events or Grade 4 adverse events were reported as related to study drugs. Two participants discontinued due to adverse events (both due to Grade 1 injection site induration). There were no deaths in the trial and no participants experienced a study drug-related serious adverse event (AE), and no Grade 3 or 4 AEs were considered study-drug related. Most frequent AEs were injection site erythema, injection site pain (12% each), injection site swelling (11%) and headache (10%). All injection site reactions were mild or moderate.

In the CAPELLA trial, there were no study drug-related serious AEs leading to discontinuations. lenacapavir related injection site reactions occurred in 56% (40/72) and were mostly mild or moderate (38/40). Most common injection site reactions (>20%) were swelling (26%) and erythema (24%); both resolved within days.

Trogarzo (ibalizumab)

Trogarzo (ibalizumab) is an HIV-1 entry inhibitor that binds to CD4 receptors on T-cells. This binding creates a conformational change that prevents HIV from attaching and entering the cell. CD4-mediated immune functions are not affected due to the specificity of binding location.

Efficacy/Effectiveness

The efficacy for ibalizumab was evaluated from one phase II study and two phase III studies. In all trials, ibalizumab showed efficacy in reducing HIV-1 viral load and increasing CD4 cell count in individuals who have failed multiple anti-retroviral regimens. In the primary trial, 17 of the 40 individuals (43%) had a HIV-1 RNA < 50 copies/mL after 24 weeks of treatment.

The studies were limited to multi-drug resistant HIV-1 infection, and thus only examined a limited sample of individuals with no comparator arms. Additionally, the studies have not yet been published and thus unavailable for further assessment. There is no data on differences between how well the drug worked among sex, race, and age.

Safety/Tolerability

Safety data is limited, but ibalizumab has currently shown a mild side effect profile. Most common (>5%) were diarrhea (8%), dizziness (8%), nausea (5%), and rash (5%). One individual experienced a case of immune reconstitution inflammatory syndrome (IRIS). Current data extends to approximately 48 weeks. In April 2021 the prescribing information was updated to include a warning that based on animal data, Trogarzo may cause reversible immunosuppression (CD4+ T cell and B cell lymphocytopenia) in infants born to mothers exposed to Trogarzo during pregnancy.

Apretude (cabotegravir extended-release injectable suspension)

Apretude (cabotegravir extended-release injectable suspension) is an HIV integrase strand transfer inhibitor (INSTI). Cabotegravir inhibits HIV integrase by binding to the integrase active site and blocking the strand transfer step of retroviral deoxyribonucleic acid (DNA) integration that is essential for the HIV replication cycle.

Efficacy/Effectiveness

The safety and efficacy of cabotegravir long-acting (CAB-LA) to reduce the risk of acquiring HIV-1 infection were evaluated in 2 randomized, double-blind, controlled, multinational trials, HPTN 083 in HIV-1 uninfected men and transgender women who have sex with men and have evidence of high-risk behavior for HIV-1 infection and HPTN 084 in HIV-1 uninfected cisgender women at risk of acquiring HIV-1. Participants randomized to receive CAB-LA initiated oral lead-in dosing with 1 oral cabotegravir 30-mg tablet and a placebo daily for up to 5 weeks, followed by CAB-LA 600-mg (3-mL) intramuscular injection at months 1 and 2 and every 2 months thereafter and a daily placebo tablet. Participants randomized to receive emtricitabine/disoproxil fumarate (FTC/TDF) initiated oral FTC/TDF and placebo daily for up to 5 weeks, followed by oral FTC/TDF daily and placebo intramuscular injection at months 1 and 2 and every 2 months thereafter.

In HPTN 083, a non-inferiority study, 4,566 cisgender men and transgender women who have sex with men were randomized 1:1 and received either CAB-LA (n = 2,281) or FTC/TDF (n = 2,285) as blinded study medication up to Week 153. At baseline, the median age of participants was 26 years, 12% were transgender women, 72% were non-White, and 67% were younger than 30 years. The primary endpoint was the rate of incident HIV-1 infections among participants randomized to daily oral cabotegravir and intramuscular injections of CAB-LA every 2 months compared with daily oral FTC/TDF. The primary analysis demonstrated the superiority of CAB-LA compared with FTC/TDF with a 69% reduction in the risk of acquiring HIV-1 infection, hazard ratio (95% CI) 0.31 (0.16, 0.58). Results from all subgroup analyses were consistent with the overall protective effect. A lower rate of incident HIV-1 infections was observed for participants randomized to ACAB-LA compared with participants randomized to FTC/TDF.

In HPTN 084, a superiority study, 3,224 cisgender women were randomized 1:1 and received either CAB-LA (n = 1,614) or FTC/TDF (n = 1,610) as blinded study medication up to Week 153. At baseline, the median age of participants was 25 years, >99% were non-White, >99% were cisgender women, and 49% were <25 years of age. The primary endpoint was the rate of incident HIV-1 infection among participants randomized to oral cabotegravir and CAB-LA compared with oral FTC/TDF. The primary analysis demonstrated the superiority of CAB-LA compared with FTC/TDF with an 90% reduction in the risk of acquiring incident HIV infection (HR 0.10 [95% CI 0.04, 0.27]). Results from pre-planned subgroup analyses were consistent with the overall protective effect. A lower rate of incident HIV-1 infection was observed for participants randomized to CAB-LA compared with participants randomized to FTC/TDF.

There were 12 incident infections and 4 prevalent infections among subjects in the CAB-LA arm of HPTN 083. Genotypic data were generated for viruses from 13 of these 16 subjects (4 subjects with prevalent infections and 9 subjects with incident infections) and phenotypic data were generated for 3 of these viruses. INSTI resistance-associated substitutions were detected in 5 viruses from subjects who achieved target plasma concentrations of cabotegravir and included R263K (2-fold less susceptible to cabotegravir), E138A+Q148R (6-fold less susceptible to cabotegravir), E138K+Q148K, G140A+Q148R (13-fold less susceptible to cabotegravir), and L74I+E138E/K+G140G/S+Q148R+E157Q. There were 3 incident infections and 1 prevalent infection among subjects in the CAB-LA arm of HPTN 084. All 3 incident infections occurred during periods with cabotegravir exposures below the target concentration. No variants expressing INSTI resistance-associated substitutions were detected.

Cabotegravir had reduced susceptibility (>5-fold change) to recombinant HIV-1 strain NL432 viruses harboring the following integrase amino acid substitutions: G118R, Q148K, Q148R, T66K+L74M, E92Q+N155H, E138A+Q148R, E138K+Q148K/R, G140C+Q148R, G140S+Q148H/K/R, Y143H+N155H, and Q148R+N155H (range: 5.1-fold to 81-fold). The substitutions E138K+Q148K and Q148R+N155H conferred the greatest reductions in susceptibility of 81-fold and 61-fold, respectively. Viruses harboring E138A+Q148R or G140A+Q148R with reduced susceptibility to cabotegravir were isolated from subjects using CAB-LA in HPTN 083. These viruses remained susceptible to bictegravir and dolutegravir but had cross-resistance to elvitegravir and raltegravir.

Safety/Tolerability

The safety assessment of CAB-LA is based on the analysis of data from 2 international, multicenter, double-blind trials, HPTN 083 and HPTN 084. Adverse reactions were reported while on blinded study product following exposure to CAB-LA and oral cabotegravir tablets as oral lead-in. The median time on blinded study product in HPTN 083 was 65 weeks and 2 days (range: 1 day to 156 weeks and 1 day), with a total exposure on cabotegravir of 3,231 person-years. The median time on blinded study product in HPTN 084 was 64 weeks and 1 day (range: 1 day to 153 weeks and 1 day), with a total exposure on cabotegravir of 2,009 person-years. In HPTN 083, 6% of participants in the group receiving CAB-LA every 2 months and 4% of participants receiving FTC/TDF once daily discontinued due to adverse events (all causality). Non-injection-site–associated adverse events leading to discontinuation and occurring in at least 1% of participants was alanine aminotransferase with CAB-LA and FTC/TDF. In HPTN 084, 1% of participants receiving CAB-LA and 1% of participants receiving FTC/TDF discontinued due

to adverse events. The most commonly reported adverse event (all causality) leading to discontinuation was increased alanine aminotransferase (<1%) with CAB-LA and FTC/TDF.

The most frequent adverse reactions associated with the intramuscular administration of CAB-LA in HPTN 083 were injection site reactions (ISR). After 20,286 injections, 8,900 ISRs were reported. Of the 2,117 participants who received at least one injection of CAB-LA, 1,740 (82%) participants experienced at least one ISR, of which a total of 3% of participants discontinued CAB-LA because of ISRs. Among the participants who received CAB-LA and experienced at least one ISR, the maximum severity of reactions was mild (Grade 1) in 41% of participants, moderate (Grade 2) in 56% of participants, and severe (Grade 3) in 3% of participants. The median duration of overall ISR events was 4 days. The proportion of participants reporting ISRs at each visit and the severity of the ISRs decreased over time.

The most frequent adverse reactions associated with the intramuscular administration of CAB-LA in HPTN 084 were ISRs. After 13,068 injections, 1,171 ISRs were reported. Of the 1,519 participants who received at least one injection of CAB-LA, 578 (38%) participants experienced at least one ISR. No participants discontinued CAB-LA because of ISRs. Among the participants who received CAB-LA and experienced at least one ISR, the maximum severity of reactions was mild (Grade 1) in 66% of participants, moderate (Grade 2) in 34% of participants, and severe (Grade 3) in less than 1% of participants. The median duration of overall ISR events was 8 days. The proportion of participants reporting ISRs at each visit and the severity of the ISRs generally decreased over time.

2019 Update

Reviewed Trogarzo (ibalizumab) prescribing information and conducted a literature search from July 1, 2018, through July 31, 2019. No new evidence found that would change this policy.

2020 Update

Reviewed Trogarzo (ibalizumab) prescribing information and conducted a literature search on the management of HIV individuals who are failing therapy. No new evidence found that would change this policy. Added an “Investigational” table and a “Documentation Requirements” table to policy.

2021 Update

Reviewed Trogarzo (ibalizumab) and Rukobia (fostemsavir) prescribing information and conducted a literature search on the management of HIV individuals who are failing therapy. Included a new Trogarzo warning regarding the risk of embryo-fetal toxicity and updated the HIV statistics referenced within policy. No new evidence found that would change this policy.

2022 Update

Reviewed prescribing information for all drugs in policy and conducted a literature search on PrEP. Added coverage criteria for Apretude (cabotegravir extended-release injectable suspension) for use in at-risk adults and adolescents weighing at least 35 kg for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection.

2023 Update

Reviewed prescribing information for all drugs in policy. Added coverage for Sunlenca (lenacapavir) for the treatment of multidrug resistant HIV-1 in adult individuals.

2024 Update

Reviewed prescribing information for all drugs in policy. No changes to policy statements.

2025 Update

Reviewed prescribing information for all drugs in policy. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information. Removed step therapy requirement from Apretude (cabotegravir extended-release injectable suspension) coverage criteria. Removed step therapy requirement from Descovy (emtricitabine and tenofovir alafenamide) HIV pre-exposure prophylaxis (PrEP) coverage criteria.

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History

Date	Comments
11/01/18	New policy, approved October 9, 2018, effective February 1, 2019. Add to Prescription Drug section. Trogarzo (ibalizumab) may be considered medically necessary when criteria are met. Added HCPCS codes J3490, J3590.
01/01/19	Coding update, added new HCPCS code J1746 (new code effective 1/1/19).
09/01/19	Annual Review, approved August 22, 2019. Policy updated with literature review; no changes to policy statements. Removed HCPCS codes J3490 and J3590.
10/01/20	Annual Review, approved September 1, 2020. No changes to policy statements.
12/01/20	Interim Review, approved November 10, 2020. Changed policy name from Trogarzo (ibalizumab) to Pharmacologic Treatment of HIV/AIDS. Added Rukobia (fostemsavir) to policy for the treatment of multidrug resistant HIV-1.
11/01/21	Annual Review, approved October 21, 2021. No changes to policy statements.
01/01/22	Interim Review, approved December 14, 2021. Added criteria for both Descovy (emtricitabine and tenofovir alafenamide) and Truvada (emtricitabine and tenofovir disoproxil fumarate) for the treatment of HIV-1 infection and PrEP when the patient has tried generic emtricitabine and tenofovir disoproxil fumarate first.
07/01/22	Annual Review, approved June 14, 2022. Changed title from Pharmacologic Treatment of HIV/AIDS to Pharmacologic Prevention and Treatment of HIV/AIDS. Added criteria for Apretude (cabotegravir extended-release injectable suspension) for PrEP to reduce the risk of HIV-1 infection. Added HCPCS code J0739.

Date	Comments
02/01/23	Annual Review, approved January 10, 2023. Added coverage for Sunlenca (lenacapavir) for the treatment of multidrug resistant HIV-1 in adult individuals. Changed the wording from "patient" to "individual" throughout the policy for standardization. Added HCPC code J3490 for Sunlenca.
07/01/23	Coding update. Added new HCPCS code J1961
01/01/24	Coding update. Added new HCPCS codes J0750, J0751 & J0799.
08/01/24	Annual Review, approved July 8, 2024. No changes to policy statements.
03/01/25	Annual Review, approved February 11, 2025. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information. Removed step therapy requirement from Apretude (cabotegravir extended-release injectable suspension) coverage criteria. Removed step therapy requirement from Descovy (emtricitabine and tenofovir alafenamide) HIV pre-exposure prophylaxis (PrEP) coverage criteria. Removed HCPCS code J3490, since HCPC J1961 now represents Sunleca.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.