Drug Coverage Policy

Effective Date.....9/15/2024
Coverage Policy Number IP0171
Policy Title.....Trogarzo

Human Immunodeficiency Virus – Trogarzo

- Trogarzo® (ibalizumab-uiyk intravenous infusion – Theratechnologies)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna HealthCare Coverage Policy

Trogarzo is a long-acting humanized immunoglobulin G4 monoclonal antibody indicated in combination with other antiretroviral(s) for the treatment of **human immunodeficiency virus type-1 (HIV-1) infection** in heavily treatment-experienced adults with multidrug resistant HIV-1 infection failing their current antiretroviral regimen.[1] Patients should receive a single intravenous loading dose of 2,000 mg followed by a maintenance dose of 800 mg once every 2 weeks. The loading dose and maintenance doses of Trogarzo can be administered as a diluted intravenous (IV) infusion or undiluted IV push.

Disease Overview
Multiclass or three-class drug resistant HIV-1 infection is usually defined as the presence of phenotypic or genotypic resistance to at least one drug in each of the following three classes: the nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and

protease inhibitors classes.[2] Trogarzo blocks HIV-1 from infecting CD4+ T cells by binding to domain 2 of CD4.[1] This interferes with post-attachment steps required for the entry of HIV-1 virus particles into host cells and prevents the viral transmission that occurs via cell-cell fusion. The binding specificity to domain 2 of CD4 allows Trogarzo to block viral entry into host cells without causing immunosuppression. There is no antagonism with other antiretrovirals. In the pivotal trial for Trogarzo, all patients had documented resistance to at least one antiretroviral from the nucleoside reverse transcriptase inhibitor, non-nucleoside reverse transcriptase inhibitor, and protease inhibitor classes.

Guidelines
According to the Department of Health and Human Services Guidelines for the use of antiretrovirals in adults and adolescents with HIV (February 27, 2024), in patients with multidrug resistance without fully active antiretroviral options, consensus on optimal management is lacking.[4] Maximal virologic suppression remains the goal of treatment; however, if it cannot be achieved, the goals are to preserve immune function, prevention clinical progression, and minimize the development of further resistance that may compromise future regimens. The Guidelines note that that even partial virologic suppression of HIV-1 RNA to > 0.5 $\log_{10}$ copies/mL from baseline correlates with clinical benefit. There is evidence that continuing antiretroviral therapy even in the presence of viremia and the absence of CD4+ count increases, reduces the risk of disease progression. Additional data suggest that even modest reductions in HIV-1 RNA levels continue to confer immunologic and clinical benefits. In general, adding a single, fully active antiretroviral to the regimen is not recommended because of the risk of rapid development of resistance. Patients with ongoing detectable viremia who lack sufficient treatment options to construct a fully suppressive regimen are noted to be candidates for Rukobia™ (fostemsavir extended-release tablets), Sunlenca® (lenacapavir subcutaneous [SC] injection) and/or Trogarzo. For people with multidrug-resistant HIV-2, Trogarzo and Sunlenca may be considered based on *in vitro* data. Optimal treatment strategies for individuals with HIV-2 are not defined.

The International Antiviral Society-USA (December 2022) provides some guidance on patients with viral failure.[4] The regimen should also include at least one, and preferably two other fully active drugs, optimally from drug classes not previously used. Therapies may include Rukobia, Sunlenca (currently under FDA review), Selzentry® (maraviroc tablets, generic and oral solution), Trogarzo, or Fuzeon® (enfuviritide SC injection).

Medical Necessity Criteria

Trogarzo is considered medically necessary when the following is met

Human Immunodeficiency Virus (HIV)-1. Approve for the duration outlined below if the patient meets ONE of the following (A or B):

- **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, and v):
  - **i.** Patient is ≥ 18 years of age; AND
  - **ii.** According to the prescriber, the patient is failing a current antiretroviral regimen for HIV; AND
  - **iii.** Patient has multiple antiretroviral drug resistance as demonstrated by resistance to at least one antiretroviral from at least THREE of the following antiviral classes (a, b, c, d, e, f):
    - **a)** Nucleoside reverse transcriptase inhibitor;
      Note: Examples of nucleoside reverse transcriptase inhibitors include but are not limited to abacavir, didanosine, emtricitabine, lamivudine, stavudine, tenofovir disoproxil fumarate, tenofovir alafenamide, zidovudine.

b) Non-nucleoside reverse transcriptase inhibitor;
Note: Examples of non-nucleoside reverse transcriptase inhibitors include but are not limited to delavirdine, efavirenz, etravirine, nevirapine, nevirapine XR, rilpivirine.

c) Protease inhibitor;
Note: Examples of protease inhibitors include but are not limited to atazanavir, darunavir, fosamprenavir, indinavir, nelfinavir, ritonavir, saquinavir, tipranavir.

d) Fusion inhibitor;
Note: An example of a fusion inhibitor includes but is not limited to Fuzeon (enfuviritide subcutaneous injection).

e) Integrase strand transfer inhibitor;
Note: Examples of integrase strand transfer inhibitors include but are not limited to raltegravir, dolutegravir, elvitegravir.

f) CCR5-antagonist; AND
Note: An example of a CCR5-antagonist includes but is not limited to Selzentry (maraviroc tablets).

iv. The medication will be taken in combination with an optimized antiviral background regimen including one or more other antiretroviral agents; AND

v. The medication is prescribed by or in consultation with a physician who specializes in the treatment of HIV infection.

B) Patient is Currently Receiving Trogarzo. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. The medication will continue to be taken in combination with an optimized antiviral background regimen including one or more other antiretroviral agents; AND

ii. Patient has responded to a Trogarzo-containing regimen, as determined by the prescriber.
Note: Examples of a response are HIV RNA < 50 cells/mm^3, HIV-1 RNA ≥ 0.5 $\log_{10}$ reduction from baseline in viral load, improvement or stabilization of CD4 T-cell count.

Dosing. Approve the following dosing regimens (A and B):

A. Loading dose of 2,000 mg as an intravenous infusion or intravenous push, given one time; AND
Note: Approve an additional 2,000 mg loading dose if an 800-mg maintenance dose is missed by ≥ 3 days of the scheduled dosing day, with maintenance dosing (800 mg intravenously every 2 weeks) resumed thereafter.

B. Maintenance dose of 800 mg, as an intravenous infusion or intravenous push, given every 2 weeks

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (criteria will be updated as new published data are available).

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J1746	Injection, ibalizumab-uiyk, 10 mg

References

1. Trogarzo® injection [prescribing information]. Montreal, Quebec, Canada: Theratechnologies; December 2023.
2. Imaz, A, Falco V, Ribera E, et al. Antiretroviral salvage therapy for multiclass drug-resistant HIV-1-infected patients: from clinical trials to daily clinical practice. *AIDS*. 2011;13:180-193.
3. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents with HIV. Department of Health and Human Services. Last Updated: February 27, 2024. Available at: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/whats-new-adult-adolescent-arv.pdf. Accessed on March 7, 2024.
4. Gandhi RT, Bedimo R, Hoy JF, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults 2022 recommendations of the International Antiviral Society–USA Panel. *JAMA.* 2023;329(1):63-84.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Review	**Human Immunodeficiency Virus (HIV)-1 Infection.** **Updated** 'Documentation of multidrug-resistant HIV-1 infection' TO 'Patient has multiple antiretroviral drug resistance as demonstrated by resistance to at least one antiretroviral from at least THREE of the following antiviral classes' **Added** age, specialist requirement **Added** 'patient is currently receiving Trogarzo' criteria **Condition Not Covered.** **Removed** 'Human Immunodeficiency Virus (HIV)-2'	8/1/2024
Selected Revision	**Human Immunodeficiency Virus-1 Infection.** Patient is Currently Receiving Trogarzo: The criterion that the patient has responded to a Trogarzo-containing regimen (e.g., HIV-1 RNA ≥ 0.5 log10 reduction from baseline in viral load), as determined by the prescriber was modified by removing the example of a treatment response to a note, and to add HIV RNA < 50 cells/mm3 and	9/15/2024

	improvement or stabilization in CD4 T-cell count as examples of a treatment response.	

The policy effective date is in force until updated or retired.