

Corporate Medical Policy

Ibalizumab-uiyk (Trogarzo™)

File Name:	ibalizumab_trogarzo
Origination:	10/2018
Last CAP Review:	2/2020
Next CAP Review:	2/2021
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Description of Procedure or Service

Ibalizumab-uiyk (Trogarzo™) is a recombinant humanized monoclonal antibody that is indicated in combination with other antiretroviral medications for the treatment of heavily treatment-experienced adults with multidrug resistant human immunodeficiency virus type 1 (HIV-1) infection who are failing their current antiretroviral regimen.

Human immunodeficiency virus (HIV) is the virus that causes acquired immunodeficiency syndrome (AIDS). HIV attacks and destroys CD4⁺ T-cells in the body that aid the immune system in fighting infection. The loss of CD4 cells prevents the body from fighting infection and without treatment, HIV can gradually destroy the immune system, advancing to AIDS, as defined by a CD4 count less than 200 cells/μl or the presence of any AIDS-defining condition. HIV-1 enters the CD4⁺ T-cell by binding to surface CD4 receptors and CCR5 or CXCR4 co-receptors, then fuses with the CD4 cell membrane allowing the virus to enter the host cell. Once inside the CD4 host cell, the virus releases HIV RNA and enzymes (reverse transcriptase and integrase) for replication and production of mature HIV out of the host cell to infect other CD4 cells.

There are currently six major classes of approved antiretroviral therapies categorized based on effect within the CD4 cell and interference of viral replication. There is no current cure for patients infected with HIV-1; however, advancements in combination antiretroviral therapy have allowed successful suppression of the virus, decreased transmission, and increased survival. Despite major advancements in HIV therapy, many patients encounter resistance to multiple antiretroviral drugs thus affecting level of viral suppression.

Ibalizumab-uiyk (Trogarzo), a CD4-directed post-attachment HIV-1 inhibitor, was approved by the U.S. Food and Drug Administration (FDA) in March 2018, 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. It works by binding to domain 2 of CD4 T-cells, blocking HIV-1 from entering and infecting the cell by interfering with post-attachment steps, and also prevents viral transmission that occurs through cell-to-cell fusion. There is no current evidence to indicate cross-resistance between ibalizumab-uiyk and any other approved classes of antiretroviral drugs.

*****Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Policy

BCBSNC will provide coverage for ibalizumab-uiyk (Trogarzo™) when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.

Ibalizumab-uiyk (Trogarzo™)

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When it is covered

Initial Therapy

Ibalizumab-uiyk (Trogarzo) is considered medically necessary for the treatment of adult patients (≥ 18 years old) with multidrug resistant human immunodeficiency virus type 1 (HIV-1) infection when the following criteria are met:

1. The patient has an HIV RNA viral load greater than 1,000 copies/mL; **AND**
2. The patient has a history of at least 6 months of antiretroviral treatment and has current or recent treatment failure; **AND**
3. The patient has documented resistance to at least one antiretroviral medication from each of the three classes of antiretroviral medications (protease inhibitors, nucleoside reverse transcriptase inhibitors, and non-nucleoside reverse transcriptase inhibitors) as measured by resistance testing; **AND**
4. The patient will be taking ibalizumab-uiyk (Trogarzo) in combination with an optimized background antiretroviral regimen, containing at least one agent that demonstrates full viral sensitivity/susceptibility.

Initial authorization: 6 months

Continuation Therapy

Continuation of treatment with ibalizumab-uiyk (Trogarzo) beyond 6 months after initiation of therapy, and every 12 months thereafter, is considered medically necessary for the treatment of multidrug resistant HIV-1 infection when patients meet the following criteria:

1. The patient has been receiving treatment with ibalizumab-uiyk (Trogarzo) and has demonstrated a clinically significant response without evidence of virologic failure (see Policy Guidelines); **AND**
2. The patient will continue taking an optimized background antiretroviral regimen in combination with ibalizumab-uiyk (Trogarzo).

When it is not covered

Ibalizumab-uiyk (Trogarzo) is considered **investigational** and therefore not covered when the above criteria are not met.

Policy Guidelines

Virologic failure may be defined as not achieving a viral load of < 200 copies/mL within 24 weeks of initiating antiretroviral therapy or as sustained recurrence of viremia to > 200 copies/mL (ie on two consecutive measurements) after initial viral suppression.

Ibalizumab-uiyk (Trogarzo™)

Trogarzo is given as an intravenous (IV) infusion in the cephalic vein of the patient's right or left arm if accessible, and should be administered by a trained medical professional. Trogarzo should not be given as an IV push or bolus.

The recommended dosing regimen for Trogarzo is 2,000 mg administered intravenously as a single loading dose, followed by a maintenance dose of 800 mg every 2 weeks. Dose modification is not required upon administration with any other antiretroviral or treatment.

According to the manufacturer's safety information for Trogarzo, the most common adverse reactions (incidence $\geq 5\%$) include diarrhea, dizziness, nausea, and rash. Additionally, Immune Reconstitution Inflammatory Syndrome (IRIS) has been reported in patients treated with Trogarzo in combination with other antiretroviral therapies.

The safety and effectiveness of Trogarzo have not been established in pediatric patients.

The efficacy and safety of ibalizumab-uiyk plus an optimized background regimen was evaluated in a single-arm, open-label, multicenter phase 3 study of 40 adult patients with multidrug-resistant HIV-1 infection who had failed multiple antiretroviral therapies. Patients included in the study had a viral load of greater than 1,000 copies of HIV-1 RNA per milliliter and documented resistance to at least one antiretroviral medication from each of three classes of antiretrovirals as measured by resistance testing. Patients must also have been treated with antiretrovirals for at least 6 months with current or recent therapy failure (i.e. within the last 8 weeks). Patients enrolled in the study had received a median of 10 antiretroviral drugs, and at baseline, mean viral load was 4.5 \log_{10} copies/ml and mean CD4 count was 150 cells/ μ l. Patients underwent a 7-day control period of continued treatment with their current antiretroviral regimen to establish baseline HIV viral load, followed by intravenous infusion of a 2,000 mg loading dose of ibalizumab on day 7. Viral load was assessed 7 days after administration of the loading dose. Patients received 800 mg of ibalizumab every 14 days in combination with individually optimized background regimens, including at least one fully active agent, for a total of 25 weeks. The primary end point was the proportion of patients with a decrease in viral load of at least 0.5 \log_{10} copies/ml from baseline (day 7) to day 14, which was 83% (N=40; 95% CI, 67 to 93; P<0.001). Secondary end points included mean change from baseline in viral load and in CD4 count, which were measured at week 25. At study completion, 43% of patients achieved a viral load less than 50 copies/ml and 50% of patients achieved less than 200 copies/ml. There was a mean reduction in viral load of 1.6 \log_{10} copies/ml from baseline and mean increase in CD4 count of 62 cells/ μ l from baseline.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: J1746

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

Theratechnologies Inc. Trogarzo (ibalizumab-uiyk). Highlights of prescribing information. May 2018. Available at: <http://www.trogarzo.com/PrescribingInformation/>. Accessed September 2018.

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U.S. Food and Drug Administration. FDA approves new HIV treatment for patients who have limited treatment options. Available at: <https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm599657.htm>. Accessed September 2018.

Emu B, Fessel, J, Schrader S, et al. Phase 3 study of ibalizumab for multidrug-resistant HIV-1. *N Engl J Med*. 2018 Aug 16;379(7):645-654.

U.S. Department of Health and Human Services. HIV Overview: The HIV Life Cycle. Last reviewed July 27, 2018. <https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/19/73/the-hiv-life-cycle>. Accessed October 2018.

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at: <http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf>. Accessed October 2017.

Medical Director review 10/2018

Specialty Matched Consultant Advisory Panel – 2/2019

Specialty Matched Consultant Advisory Panel – 2/2020

Policy Implementation/Update Information

- 10/12/18 New policy developed. Trogarzo is considered medically necessary for the treatment of adult patients with multidrug resistant human immunodeficiency virus type 1 (HIV-1) infection. Added HCPCS codes C9399, J3490, and J3590 to “Billing/Coding” section. References added. Medical Director review 10/2018. (krc)
- 12/31/18 Added code J1746 to Billing/Coding section and deleted codes C9399, J3490, J3590 effective 1/1/19. (krc)
- 3/12/19 Specialty Matched Consultant Advisory Panel review 2/20/2019. (krc)
- 3/10/20 Specialty Matched Consultant Advisory Panel review 2/19/2020. No change to policy statements. (krc)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.