VENTURA COUNTY HEALTH CARE PLAN

Utilization Review Policy

POLICY: Human Immunodeficiency Virus – Trogarzo™ (ibalizumab-uiyk injection for intravenous use – Theratechnologies)

TAC APPROVAL DATE: 04/08/2020

OVERVIEW

Trogarzo is a long-acting humanized immunoglobulin G4 monoclonal antibody indicated in combination with other antiretroviral(s) [ARV{s}] for the treatment of human immunodeficiency virus type-1 (HIV-1) infection in heavily treatment-experienced adults with multidrug resistant (MDR) HIV-1 infection failing their current ARV regimen.[1] It is a chronic therapy administered by a trained healthcare professional intravenously (IV), after diluting the appropriate number of vials in 250 mL of 0.9% Sodium Chloride Injection, USP. Patients should receive a single loading dose of 2,000 mg followed by a maintenance dose of 800 mg once every 2 weeks (Q2W). Trogarzo is available in a single-dose, 2 mL vial containing 150 mg/mL of ibalizumab-uiyk. Each vial delivers approximately 1.33 mL containing 200 mg of ibalizumab-uiyk.

Disease Overview

Multiclass or three-class drug resistant HIV-1 infection is usually defined as the presence of phenotypic or genotypic resistance to resistance to at least one drug in each of the following three classes: the nucleoside reverse transcriptase inhibitors (NRTIs)-, non-nucleoside reverse transcriptase inhibitors (NNRTIs)-, and protease inhibitors (PIs)-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 ARVs.

In the pivotal trial for Trogarzo, all patients had documented resistance to at least one ARV from the NRTI, NNRTI, and PI classes. The Table below provides examples of drugs from each class. NOTE: This is not all inclusive.

Table 1. Examples of HIV ARVs by Class.

Drug Class	Examples
NRTIs	Ziagen® (abacavir), Videx EC® (didanosine delayed-release), Videx® Pediatric (didanosine), Emtriva® (emtricitabine), Epivir®, (lamivudine), Zerit®, (stavudine), Viread®, (tenofovir disoproxil fumarate), Retrovir® (zidovudine), Combivir® (lamivudine/zidovudine), Epzicom® (abacavir/lamivudine), Trizivir® (abacavir/lamivudine/zidovudine), Truvada® (emtricitabine/tenofovir disoproxil fumarate), Descovy® (emtricitabine/tenofovir alafenamide)
NNRTIs	Rescriptor® (delavirdine), Sustiva® (efavirenz), Intelence® (etravirine), Viramune® (nevirapine), Viramune® XR™ (nevirapine XR), Edurant® (rilpivirine)
PIs	Reyataz® (atazanavir), Prezista® (darunavir), Lexiva® (fosamprenavir), Crixivan® (indinavir), Viracept® (nelfinavir), Norvir® (ritonavir), Invirase® (saquinavir), Aptivus® (tipranavir), Kaletra® (lopinavir/ritonavir), Prezcobix® (darunavir/cobicistat), and Evotaz® (atazanavir/cobicistat)
INSTIs	Isentress® (raltegravir), Isentress® HD (raltegravir), Tivicay® (dolutegravir), and Vitekta® (elvitegravir)

Table 1 (continued). Examples of HIV ARVs by Class.

Drug Class	Examples
Fusion Inhibitor	Fuzeon® (enfuviritide)
CCR5-Antagonist	Selzentry® (maraviroc tablets)
Combination Products	Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide tablets), Dutrebis™ (lamivudine/raltegravir potassium), Complera® (emtricitabine/rilpivirine/tenofovir disoproxil fumarate), Odefsey® (emtricitabine/rilpivirine/tenofovir alafenamide), Atripla® (efavirenz/ emtricitabine/tenofovir disoproxil fumarate), Stribild® (cobicistat/elvitegravir/emtricitabine/tenofovir disoproxil fumarate), Triumeq® (abacavir/dolutegravir/lamivudine), and Genvoya® (cobicistat/elvitegravir/emtricitabine/tenofovir alafenamide), Symtuza® (darunavir/cobicistat/emtricitabine/tenofovir alafenamide)

HIV – Human immunodeficiency virus; ARVs – Antiretrovirals; NRTIs – Nucleoside reverse transcriptase inhibitors; NNRTIs – Non-nucleoside reverse transcriptase inhibitors; PIs – Protease inhibitor; INSTIs – Integrase strand-transfer inhibitor.

Guidelines

The Department of Health and Human Services (DHHS) guidelines for the treatment of adults and adolescents with HIV-1 recognize the difficulty in treating patients with extensive resistance.[3] . Managing patients with extensive resistance is complex and usually requires consultation with an HIV expert. Patients with ongoing detectable viremia who lack sufficient treatment options to construct a fully suppressive regimen may be candidates for Trogarzo.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Trogarzo. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the of the specialized skills required for evaluation and diagnosis of patients treated with Trogarzo as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Trogarzo to be prescribed by or in consultation with a physician who specializes in the condition being treated.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Trogarzo is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Human Immunodeficiency Virus (HIV) Infection.** Approve for the duration outlined below if the patients meets ONE of the following conditions (A or B):
   - **A)** Initial Therapy: Approve for 6 months if the patient meets ALL of the following conditions (i, ii, iii, iv, v, and vi):
     - **i.** The patient is greater than or equal to 18 years of age; AND
     - **ii.** The patient has an HIV type 1 infection; AND
     - **iii.** According to the prescribing physician, the patient is failing a current antiretroviral regimen for HIV; AND
     - **iv.** The 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) nucleoside reverse transcriptase inhibitor (NRTI) [e.g., abacavir, didanosine, emtricitabine, lamivudine, stavudine, tenofovir disoproxil fumarate, tenofovir alafenamide, zidovudine]; OR
b) non-nucleoside reverse transcriptase inhibitor (NNRTI)[e.g., delaviridine, efavirenz, etravirine, nevirapine, nevirapine XR, rilpivirine]; OR
c) protease inhibitor (PI) [e.g., atazanavir, darunavir), fosamprenavir, indinavir, nelfinavir, ritonavir, saquinavir, tipranavir]; OR
d) fusion inhibitor [e.g., Fuzeon® (enfuviritide for injection)]; OR
e) integrase strand transfer inhibitor (INSTI) [e.g., raltegravir, raltegravir, dolutegravir, and elvitegravir]; OR
f) CCR5-antagonist [e.g., Selzentry® (maraviroc tablets)]. AND

v. The requested agent will be taken in combination with an optimized antiviral background regimen including one or more other antiretroviral agents; AND
vi. The requested agent is prescribed by or in consultation with a physician who specializes in the treatment of human immunodeficiency virus (HIV) infection.

B) Patients Currently Receiving Trogarzo: Approve for 1 year if the patient meets ALL of the following conditions (i, ii, and iii):
i. The patient has an HIV type 1 infection; AND
ii. The requested agent will continue to be taken in combination with an optimized antiviral background regimen including one or more other antiretroviral agents; AND
iii. The patient has responded (e.g., HIV-1 RNA $\geq$ 0.5 $\log_{10}$ reduction from baseline in viral load) to a Trogarzo-containing regimen, as determined by the prescribing physician.

Dosing. Approve the following dosing regimens (A, B, and C):
A) Loading dose of 2,000 mg as an IV infusion; AND
B) Maintenance dose of 800 mg IV every 2 weeks (Q2W); AND
C) If an 800-mg maintenance dose is missed by $\geq$ 3 days of the scheduled dosing day, a loading dose (2,000 mg) should be administered as early as possible. Resume maintenance dosing (800 mg) Q2W thereafter.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Trogarzo has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Human Immunodeficiency Virus (HIV), Type 2.** Trogarzo has only been evaluated in HIV-1 infection. The Department of Health and Human Services (DHHS) guidelines for the treatment of adults and adolescents with HIV-1 state that there are no data on the activity of Trogarzo against HIV-2.[3]

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Trogarzo™ injection [prescribing information]. Montreal, Quebec, Canada: Theratechnologies, Inc; May 2018.
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.

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. Available at http://www.aidsinfo.nih.gov/ContentFiles/ AdultandAdolescentGL.pdf. Accessed March 30, 2020. Updated December 18, 2019.

OTHER REFERENCES UTILIZED

- Emu B, Fessel J, Schrader S, et al. Phase III study of ibalizumab for multidrug-resistant HIV-1. *N Engl J Med.* 2018;379:645-654.
- Emu B, Lalezari J, Kumar P, et al. Ibalizumab: 96-week data and efficacy in patients resistant to common antiretrovirals [poster]. Presented at: the Conference on Retroviruses and Opportunistic Infections; Seattle, WA; March 4-7. 2019.

HISTORY

Type of Revision	Summary of Changes	TAC Approval Date
New Policy	--	04/04/2018
Annual Revision	Removal of Labs/Diagnostics, Waste Management, and Duration of Therapy sections. Removal of the note asking the prescriber to list the components of an antiviral regimen/class the patient is resistant to.	04/03/2019
Annual Revision	No criteria changes	04/08/2020