BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

EVIDENCE-BASED CRITERIA	**ORIGINAL EFFECTIVE DATE: 10/14/24**
SECTION: SPECIALTY MEDICAL DRUGS	**LAST REVIEW DATE: 08/15/24**
	CURRENT EFFECTIVE DATE: 10/14/24
	LAST CRITERIA REVISION DATE:
NEXT ANNUAL REVIEW DATE: 3RD QTR 2025	**ARCHIVE DATE:**

CABENUVA® (cabotegravir and rilpivirine)
TROGARZO® (ibalizumab-uiyk)

Non-Discrimination Statement is located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Evidence-Based Criteria must be read in its entirety to determine coverage eligibility, if any.

This Evidence-Based Criteria provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Evidence-Based Criteria are subject to change as new information becomes available.

For purposes of this Evidence-Based Criteria, the terms "experimental" and "investigational" are considered to be interchangeable.

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CABENUVA® (cabotegravir and rilpivirine)
TROGARZO® (ibalizumab-uiyk)

Criteria:

Refer to FDA website for current indications and dosage.

- **Criteria for initial therapy:** Cabenuva (cabotegravir and rilpivirine) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an HIV Specialist or Infectious Disease Specialist

  2. Individual is 12 years of age or older and weighs at least 35 kilograms

  3. Individual has a confirmed diagnosis of human immunodeficiency virus type-1 (HIV-1) infection with **BOTH** of the following:

     - Has HIV-1 RNA less than 50 copies/mL (viral suppression)
     - Currently on a stable regimen (≥ 6 months) of antiretrovirals prior to request

  4. Individual meets **ONE** of the following:

     - Unable to maintain adherence to a daily oral antiretroviral regimen despite counseling
     - Documentation individual is unable to take oral medications due to gastrointestinal absorption or other physical limitations

  5. There are **NO** contraindications including:

     - Hypersensitivity to cabotegravir or rilpivirine
     - Coadministration with drugs where significant decreases in cabotegravir and/or rilpivirine plasma concentrations, which may result in loss of virologic response. Contraindicated drugs include:

       a. Anticonvulsants: carbamazepine, oxcarbazepine, phenobarbital, phenytoin
       b. Antimicrobials: rifabutin, rifampin, rifapentine
       c. Glucocorticoid (systemic): dexamethasone (more than a single-dose treatment)
       d. Herbal products: St John's wort

  Initial approval duration: 12 months

- **Criteria for continuation of coverage (renewal request):** Cabenuva (cabotegravir and rilpivirine) is considered medically necessary and will be approved when ALL of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an HIV Specialist or Infectious Disease Specialist

2. Individual's condition has not worsened while on therapy with worsening defined as individual maintains viral suppression with documentation of HIV-1 RNA less than 50 copies/mL

3. Individual has been adherent with the medication

4. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued such as:

   - Hypersensitivity to cabotegravir or rilpivirine
   - Coadministration with drugs where significant decreases in cabotegravir and/or rilpivirine plasma concentrations, which may result in loss of virologic response. Contraindicated drugs include:

     a. Anticonvulsants: carbamazepine, oxcarbazepine, phenobarbital, phenytoin
     b. Antimicrobials: rifabutin, rifampin, rifapentine
     c. Glucocorticoid (systemic): dexamethasone (more than a single-dose treatment)
     d. Herbal products: St John's wort

   - Hepatotoxicity
   - Suicidal ideation

Renewal duration: 12 months

- Cabenuva (cabotegravir and rilpivirine) for all other indications not previously listed is considered ***experimental or investigational*** and will not be covered when any **ONE** or more of the following criteria are met:

1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
3. Insufficient evidence to support improvement of the net health outcome; or
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but are not limited to:*

- Treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, or duration.

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CABENUVA® (cabotegravir and rilpivirine)
TROGARZO® (ibalizumab-uiyk)

TROGARZO (ibalizumab-uiyk)

- **Criteria for initial therapy:** Trogarzo (ibalizumab-uiyk) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an HIV Specialist or Infectious Disease Specialist

  2. Individual is 18 years of age or older

  3. Individual has a confirmed diagnosis of human immunodeficiency virus type 1 (HIV-1) infection with **BOTH** of the following:

     - Heavily treatment-experienced with multi-drug resistant HIV-1 infection
     - Failing current antiretroviral regimen with HIV-1 RNA greater than 1,000 copies/mL

  4. Individual has documented drug resistance to at least **ONE** antiretroviral from **EACH** of the following antiviral classes (See Definitions Section):

     - Nucleoside reverse transcriptase inhibitor (NRTI)
     - Non-nucleoside reverse transcriptase inhibitor (NNRTI)
     - Protease inhibitor (PI)

  5. Trogarzo will be used in combination with an optimized background regimen (OBR) with other antiretroviral(s)

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Trogarzo (ibalizumab-uiyk) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an HIV Specialist or Infectious Disease Specialist

  2. Individual's condition has responded while on therapy with response defined as **TWO** of the following:

     - Maintained and achieves a 70% reduction in viral load
     - Improved CD4+ cell count over baseline
     - There is no evidence of disease progression

  3. Individual has been adherent with the medication

4. Trogarzo will continue to be used in combination with an optimized background regimen (OBR) with other antiretroviral(s)

Renewal duration: 12 months

- Trogarzo (ibalizumab-uiyk) for all other indications not previously listed is considered ***experimental or investigational*** and will not be approved when any **ONE** or more of the following criteria are met:

1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
3. Insufficient evidence to support improvement of the net health outcome; or
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but are not limited to:*

- Treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, or duration.

Description:

Cabenuva, a 2-drug co-packaged product of cabotegravir, an HIV-1 integrase strand transfer inhibitor (INSTI), and rilpivirine, an HIV-1 non-nucleoside reverse transcriptase inhibitor (NNRTI), is indicated as a complete regimen for the treatment of HIV-1 infection in adults and adolescents 12 years of age and older and weighing at least 35 kg to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine.

Trogarzo, a CD4-directed post-attachment HIV-1 inhibitor, in combination with other antiretroviral(s), is indicated 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.

Definitions:

Classification of antiretroviral drugs (agents listed alphabetically):

Drug (abbreviations)	US Brand Name

CABENUVA® (cabotegravir and rilpivirine)
TROGARZO® (ibalizumab-uiyk)

Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs)	
Abacavir (ABC)	Ziagen
Emtricitabine (FTC)	Emtriva
Lamivudine (3TC)	Epivir
Stavudine (d4T)	Zerit
Tenofovir alafenamide (TAF)	Vemlidy
Tenofovir disoproxil fumarate (TDF)	Viread
Zidovudine (ZDV, AZT)	Retrovir
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	
Delavirdine (DLV)	Rescriptor
Doravirine (DOR)	Pifeltro
Efavirenz (EFV)	Sustiva
Etravirine (ETR)	Intelence
Nevirapine (NVP)	Viramune, Viramune XR
Rilpivirine (RPV)	Edurant
Protease inhibitors (PIs)	
Atazanavir (ATV)	Reyataz
Atazanavir-cobicistat (ATV/COBI)	Evotaz
Darunavir (DRV)	Prezista
Darunavir-cobicistat (DRV/COBI)	Prezcobix
Fosamprenavir (FPV)	Lexiva
Indinavir (IDV)	Crixivan
Lopinavir/ritonavir boosting (LPV/r)	Kaletra
Nelfinavir (NFV)	Viracept
Ritonavir (RTV) (used as a pharmacokinetic boosting agent)	Norvir
Saquinavir (SQV)	Invirase
Tipranavir (TPV)	Aptivus

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Fusion inhibitor	
Enfuvirtide (T-20)	Fuzeon
Integrase strand transfer inhibitors (INSTIs)	
Cabotegravir (CAB; oral formulation)	Vocabria
Dolutegravir (DTG)	Tivicay
Elvitegravir (EVG)	Vitekta
Raltegravir (RAL)	Isentress, Isentress HD
CCR5 antagonist	
Maraviroc (MVC)	Selzentry
Attachment inhibitor	
Fostemsavir	Rukobia
Post-attachment inhibitor	
Ibalizumab-uijk	Trogarzo
Capsid Inhibitor	
Lenacapavir	Sunlenca
Fixed-dose combinations	
Abacavir-lamivudine (ABC/3TC)	Epzicom
Abacavir-lamivudine-zidovudine (ABC/3TC/ZDV)	Trizivir
Bictegravir-emtricitabine-tenofovir alafenamide (BIC/FTC/TAF)	Biktarvy
Darunavir-cobicistat-emtricitabine-tenofovir alafenamide (DRV/COBI/FTC/TAF)	Symtuza
Dolutegravir-abacavir-lamivudine (DTG/ABC/3TC)	Triumeq
Dolutegravir-lamivudine (DTG/3TC)	Dovato
Dolutegravir-rilpivirine (DTG/RPV)	Juluca
Doravirine-lamivudine-tenofovir disoproxil fumarate (DOR/3TC/TDF)	Delstrigo

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Efavirenz-emtricitabine-tenofovir disoproxil fumarate (EFV/FTC/TDF)	Atripla
Efavirenz- lamivudine -tenofovir disoproxil fumarate (EFV/FTC/TDF)	Symfi, Symfi Lo
Elvitegravir-cobicistat-emtricitabine-tenofovir alafenamide (ECF/TAF or EVG/COBI/FTC/TAF)	Genvoya
Elvitegravir-cobicistat-emtricitabine-tenofovir disoproxil fumarate (ECF/TDF or EVG/COBI/FTC/TDF)	Stribild
Rilpivirine-emtricitabine-tenofovir alafenamide (RPV/FTC/TAF)	Odefsey
Rilpivirine-emtricitabine-tenofovir disoproxil fumarate (RPV/FTC/TDF)	Complera
Tenofovir alafenamide-emtricitabine (TAF/FTC)	Descovy
Tenofovir disoproxil fumarate-emtricitabine (TDF/FTC)	Truvada
Zidovudine-lamivudine (ZDV/3TC)	Combivir
Injectable combination	
Cabotegravir plus rilpivirine (CAB/RPV; extended-release injectable formulation)	Cabenuva

History:	**Date**:	**Activity**:
Pharmacy and Therapeutics Committee	08/15/24	Approved guideline (effective 10/14/24)
Clinical Pharmacist	05/17/24	Development

Coding:

HCPCS: J0741, J1746

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Resources:

Literature reviewed 08/15/2024. We do not include marketing materials, poster boards and non-published literature in our review.

1. Cabenuva (cabotegravir and rilpivirine) product information, revised by ViiV Healthcare Company 12/2023, at DailyMed http://dailymed.nlm.nih.gov. Accessed June 27, 2024.

2. Daar ES. Selecting an antiretroviral regimen for treatment-experienced patients with HIV who are failing therapy. In: UpToDate, Sax PE, Mitty J (Eds), UpToDate, Waltham, MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated May 31, 2024. Accessed June 27, 2024.

3. Trogarzo (ibalizumab) product information, revised by Theratechnologies Inc. 12/2023, at DailyMed http://dailymed.nlm.nih.gov. Accessed June 27, 2024.

4. Wood BR. Use of long-acting cabotegravir-rilpivirine in people with HIV. In: UpToDate, Sax PE, Mitty J (Eds), UpToDate, Waltham, MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated March 27, 2024. Accessed June 27, 2024.

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Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html