BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
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FUZEON® (enfuvirtide) subcutaneous injection

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

This Pharmacy Coverage Guideline 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.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Fuzeon (enfuvirtide) 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/AIDS Specialist or Infectious Disease Specialist

  2. Individual is 5 years of age (weighing at least 11 kg or at least 24 pounds) or older

  3. A confirmed diagnosis of HIV-1 infection in a treatment experienced individual with ongoing HIV-1 replication despite antiretroviral therapy

  4. Documentation of **ONE** of the following:
     a. Viremia despite at least 3 months of antiretroviral therapy with a nucleoside reverse transcriptase inhibitor (NRTI) plus a non-nucleoside reverse transcriptase inhibitor (NNRTI) plus a protease inhibitor (PI) [See Definitions section]
     b. Viremia and documented resistance or intolerance to at least one agent in each of the NRTI, NNRTI, and PI classes

  5. Will be used with an individualized background regimen of 3-5 antiretroviral agents selected on the basis of prior treatment history and baseline genotypic and phenotypic viral resistance measurements

  6. Individual will not be used concurrently with Trogarzo (ibalizumab)

  7. There are no significant interacting drugs

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Fuzeon (enfuvirtide) 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/AIDS Specialist or Infectious Disease Specialist

  2. Individual's condition responded while on therapy
     a. Response is defined as **BOTH** of the following:
        i. Achieved and maintains reduced viral load or it is now undetectable
        ii. CD4 counts have improved

  3. Individual has been adherent with the medication

  4. Will be used with an individualized background regimen of 3-5 antiretroviral agents selected on the basis of prior treatment history and baseline viral resistance measurements

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5. Individual will not be used concurrently with Trogarzo (ibalizumab)

6. Individual has not developed any significant adverse drug effects that may exclude continued use
    a. Significant adverse effect such as:
        i. Injection site cellulitis or infection
        ii. Neuralgia and/or paresthesia
        iii. Pneumonia
        iv. Opportunistic infection due to immune reconstitution syndrome
        v. Autoimmune disorders (such as Graves' disease, polymyositis, and Guillain-Barré syndrome) due to immune reconstitution syndrome

7. There are no significant interacting drugs

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

    1. **Off-Label Use of Non-cancer Medications**

    2. **Off-Label Use of Cancer Medications**

Description:

Fuzeon (enfuvirtide) is an HIV-1 fusion inhibitor indicated for use in combination with other antiretroviral agents for the treatment of HIV-1 infection in treatment experienced individuals with HIV-1 replication despite ongoing antiretroviral therapy.

HIV-1 clinical isolates resistant to nucleoside analogue reverse transcriptase inhibitors (NRTI), nonnucleoside analogue reverse transcriptase inhibitors (NNRTI), and protease inhibitors (PI) were susceptible to enfuvirtide in cell culture. Enfuvirtide has no activity against HIV-2.

Enfuvirtide exhibited additive to synergistic effects in cell culture assays when combined with individual members of various antiretroviral classes, including lamivudine, zidovudine, indinavir, nelfinavir, and efavirenz.

Definitions:

Failure of antiretroviral therapy:
A confirmed HIV ribonucleic acid (RNA) level of > 50 copies/mL while on therapy or intolerance due to drug toxicity

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NNRTI: non-nucleoside reverse transcriptase inhibitors
- Rescriptor (delavirdine, DLV)
- Pifeltro (doravirine, DOR)
- Sustiva (efavirenz, EFV)
- Intelence (etravirine, ETR)
- Viramune, Viramune XR® (nevirapine, NVP)
- Edurant (rilpivirine, RPV)

NRTI: nucleoside reverse transcriptase inhibitors
- Ziagen (abacavir, ABC)
- Epzicom (abacavir + lamivudine)
- Trizivir (abacavir + lamivudine + zidovudine)
- Videx (didanosine [ddI])
- Emtriva (emtricitabine, FTC)
- Epivir (lamivudine, 3TC)
- Combivir (lamivudine+zidovudine)
- Zerit (stavudine, d4T)
- Hivid (zalcitabine, ddC)
- Retrovir (zidovudine, AZT or ZDV)

Protease inhibitors
- Reyataz (atazanavir, ATV)
- Prezista (darunavir, DRV)
- Lexiva (fosamprenavir, f-APV)
- Crixivan (indinavir)
- Viracept (nelfinavir, NFV)
- Norvir (ritonavir, RTV)
- Invirase (saquinavir, SQV)
- Aptivus (tipranavir, TPV)

Integrase inhibitors:
- Tivicay (dolutegravir, DTG)
- Vitekta (elvitegravir, EVG)
- Isentress, Isentress HD (raltegravir, RAL)

Cellular chemokine receptor (CCR5) antagonist:
- Selzentry (maraviroc, MVC)

Boosting agent:
- Tybost (cobicistat, COBI)

HIV combination products:
- Miscellaneous:
  - Triumeq (abacavir-dolutegravir-lamivudine) [NRTI+II+NRTI]?
  - Evotaz (atazanavir-cobicistat)
  - Biktarvy (bictegravir-emtricitabine-tenofovir alafenamide fumarate)

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Prezcobix (darunavir-cobicistat)
Juluca (dolutegravir-rilpivirine)
Genvoya (elvitegravir-cobicistat-emtricitabine-tenofovir alafenamide fumarate)
Stribild (elvitegravir-cobicistat-emtricitabine-tenofovir disoproxil fumarate)
Kaletra (lopinavir + ritonavir, LPV/r)

Reverse transcriptase Inhibitor combinations:

Epzicom (abacavir-lamivudine)
Trizivir (abacavir-lamivudine-zidovudine)
Atripla (efavirenz-emtricitabine-tenofovir disoproxil fumarate)
Symfi Lo (efavirenz-lamivudine-tenofovir disoproxil fumarate)
Odefsey (emtricitabine-rilpivirine-tenofovir alafenamide fumarate)
Complera (emtricitabine-rilpivirine-tenofovir disoproxil fumarate)
Descovy (emtricitabine-tenofovir alafenamide fumarate)
Truvada (emtricitabine-tenofovir disoproxil fumarate)
Combivir (lamivudine-zidovudine)

Resources:

Fuzeon (enfuvirtide) product information, revised by Genentech, Inc. 12-2019. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 15, 2021.

Fletcher CV. Overview of antiretroviral agents used to treat HIV. In: UpToDate, Sax PE, Mitty J (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Topic last updated March 03, 2021. Accessed December 15, 2021.

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. http://uptodate.com. Topic last updated October 15, 2020. Accessed January 08, 2021.