BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

TAVNEOS™ (avacopan) oral
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Tavneos (avacopan) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Rheumatologist, Nephrologist, Pulmonologist, or Otolaryngologist

2. Individual is 18 years of age or older

3. Individual has a confirmed diagnosis of severe active anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (granulomatosis with polyangiitis [GPA] and microscopic polyangiitis [MPA])

4. Will be used in combination with standard therapy (e.g., cyclophosphamide, azathioprine or mycophenolate mofetil if azathioprine is contraindicated, or rituximab), including glucocorticoids

5. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
    a. Liver function tests (serum alanine aminotransferase [ALT], aspartate aminotransferase [AST], alkaline phosphatase, and total bilirubin)
    b. Hepatitis B (HBV) testing with Hepatitis B surface antigen (HBsAg) and Hepatitis B core antibody (anti-HBc)
    c. Positive test for anti-myeloperoxidase (MPO) or anti-proteinase 3 (PR3) antibodies

7. Individual has an estimated glomerular filtration rate of at least 15 mL/min/1.73 m^2

8. Individual does not have active, serious infection, including localized infection

9. Individual does not have active, untreated and/or uncontrolled chronic liver disease (e.g., chronic active hepatitis B, untreated hepatitis C, uncontrolled autoimmune hepatitis) and cirrhosis

10. Individual does not have severe hepatic impairment (Child-Pugh Class C)

11. Individual is not currently taking any other drugs which cause severe adverse reactions or any drug interactions requiring discontinuation such as strong and moderate CYP3A4 inducers (e.g., carbamazepine, enzalutamide, phenobarbital, phenytoin, rifabutin, rifampin, St. John's wort, armodafinil, bexarotene, bosentan, dabrafenib, dexamethasone and others)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Tavneos (avacopan) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Rheumatologist, Nephrologist, Pulmonologist, or Otolaryngologist

2. Individual's condition has responded while on therapy with response defined as the following:
    a. Achieved and maintains absence of any clinical manifestations from ongoing active vasculitis
    b. Reduced number of relapses over baseline
    c. Documented evidence of efficacy, disease stability and/or improvement

3. Individual has been adherent with the medication

4. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any significant adverse drug effects that may exclude continued use such as:
    a. Hepatotoxicity
    b. Serious hypersensitivity reaction such as angioedema
    c. Hepatitis B reactivation
    d. Serious infection

6. Individual does not have active, serious infection, including localized infection

7. Individual does not have active, untreated and/or uncontrolled chronic liver disease (e.g., chronic active hepatitis B, untreated hepatitis C, uncontrolled autoimmune hepatitis) and cirrhosis

8. Individual has an estimated glomerular filtration rate of at least 15 mL/min/1.73 m^2

9. Individual does not have severe hepatic impairment (Child-Pugh Class C)

10. Individual is not currently taking any other drugs which cause severe adverse reactions or any significant drug interactions requiring discontinuation such as strong and moderate CYP3A4 inducers (e.g., carbamazepine, enzalutamide, phenobarbital, phenytoin, rifabutin, rifampin, St. John's wort, armodafinil, bexarotene, bosentan, dabrafenib, dexamethasone and others)

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:

Tavneos (avacopan) is a complement 5a receptor (C5aR, also known as CD88) antagonist indicated as an adjunctive treatment of adult patients with severe active anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (granulomatosis with polyangiitis [GPA] and microscopic polyangiitis [MPA]) in combination with standard therapy including glucocorticoids. Tavneos (avacopan) does not eliminate glucocorticoid use.

Avacopan inhibits the interaction between C5aR and the anaphylatoxin C5a. Avacopan blocks C5a-mediated neutrophil activation and migration and blocks the C5a-induced upregulation of CD11b (integrin alpha M) on neutrophils. The precise mechanism by which avacopan exerts a therapeutic effect in patients with ANCA-associated vasculitis has not been definitively established.

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ANCA–associated vasculitis is a serious and potentially life-threatening condition. The illness includes several related forms of small-vessel vasculitis: GPA (also known as Wegener's granulomatosis), MPA, renal-limited vasculitis, and eosinophilic granulomatosis with polyangiitis (known as Churg-Strauss). GPA and MPA have variable presentation in terms of organ manifestations and severity; however, the most commonly and severely affected organs include upper and lower respiratory tract and the kidneys.

Patients with both GPA and MPA typically present with nonspecific symptoms including fever, malaise, anorexia, weight loss, myalgias, and arthralgias. Specific organ involvement can include ear, nose, and throat; trachea and lungs; kidney; skin; ophthalmic and orbital; and neurologic. Other organ systems less commonly involved include the gastrointestinal tract, heart (pericarditis, myocarditis, conduction system abnormalities), lower genitourinary tract (including the ureters and prostate), parotid glands, thyroid, liver, or breast.

The diagnosis of GPA or MPA should be suspected in any patient who presents with constitutional symptoms and clinical evidence of glomerulonephritis or upper or lower respiratory tract involvement. The diagnosis is based upon the combination of characteristic clinical findings, laboratory tests, and imaging studies. A positive ANCA test strongly supports but does not confirm the diagnosis. Histologic examination of tissue obtained by biopsy of an affected organ (generally, kidney, skin, or lung) remains the most definitive method to establish a diagnosis and is still often required.

GPA and MPA are thought to be triggered by the production of circulating autoantibodies against the neutrophil-expressed antigens myeloperoxidase (MPO) or proteinase 3 (PR3). The current treatment for GPA and MPA includes induction of and maintenance of remission using glucocorticoids combined with either rituximab or cyclophosphamide followed by oral azathioprine, methotrexate, mycophenolate, or rituximab.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Definitions for vasculitides adopted by the 2012 International Chapel Hill Consensus Conference on the Nomenclature of Vasculitides (CHCC2012)

- Small-vessel vasculitis
  - Vasculitis predominantly affecting small vessels, defined as small intraparenchymal arteries, arterioles, capillaries, and venules. Medium arteries and veins may be affected.
- ANCA-associated vasculitis (AAV)
  - Necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels (ie, capillaries, venules, arterioles, and small arteries), associated with myeloperoxidase (MPO) ANCA or proteinase 3 (PR3) ANCA. Not all patients have ANCA. Add a prefix indicating ANCA reactivity, e.g., MPO-ANCA, PR3-ANCA, ANCA-negative.
- Microscopic polyangiitis (MPA)
  - Necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels (ie, capillaries, venules, or arterioles). Necrotizing arteritis involving small and medium arteries may be present. Necrotizing glomerulonephritis is very common. Pulmonary capillaritis often occurs. Granulomatous inflammation is absent.

- Granulomatosis with polyangiitis (Wegener's)(GPA)
  - Necrotizing granulomatous inflammation usually involving the upper and lower respiratory tract, and necrotizing vasculitis affecting predominantly small to medium vessels (e.g., capillaries, venules, arterioles, arteries and veins). Necrotizing glomerulonephritis is common.

Resources:

Tavneos (avacopan) product information, revised by ChemoCentryx, Inc. 06-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 23, 2024.

Falk RJ, Merkel PA, King TE. Granulomatosis with polyangiitis and microscopic polyangiitis: Clinical manifestations and diagnosis. In: UpToDate, Glassock RJ, Appel GB, Lam AQ, Seo P (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through August 2024. Topic last updated June 26, 2023. Accessed October 01, 2024.

Merkel PA, Kaplan AA, Falk RJ. Granulomatosis with polyangiitis and microscopic polyangiitis: Induction and maintenance therapy. In: UpToDate, Appel GB, Fervenza FC, Lam AQ, Seo P (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through August 2024. Topic last updated July 09, 2024. Accessed October 01, 2024.

Falk RJ, Merkel PA. Granulomatosis with polyangiitis and microscopic polyangiitis: Management of relapsing disease. In: UpToDate, Glassock RJ, Appel GB, Lam AQ, Seo P (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through August 2024. Topic last updated March 16, 2023. Accessed October 01, 2024.

Jayne DRW, Merkel PA, Schall TJ, Bekker P. Avacopan for the treatment of ANCA-associated vasculitis. NEJM 2021 Feb 18; 384 (7):599-609. Accessed October 27, 2021. Re-evaluated October 01, 2024.