avacopan (Tavneos™)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO237

Description

Avacopan (Tavneos) is a complement C5a receptor antagonist for the treatment of antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (AAV).

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
avacopan (Tavneos)	10 mg capsules	Antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis	180 capsules/30 days

Initial Evaluation

I. **Avacopan (Tavneos)** may be considered medically necessary when the following criteria are met:
   A. Member is 12 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, a nephrologist, rheumatologist, pulmonologist, or a specialist in the treatment of vasculitis associated disorders; **AND**
   C. A diagnosis of **antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (AAV)** when the following are met:
      1. Diagnosis is classified as **granulomatosis with polyangiitis (GPA)** or **microscopic polyangiitis (MPA)**; **AND**
      2. Presence of organ-threatening manifestations (e.g., severe and progressive kidney involvement, severe lung or nervous system involvement); **AND**
      3. Treatment with high dose glucocorticoids in combination with standard of care agents (e.g., cyclophosphamide, rituximab) has been ineffective, contraindicated, or not tolerated; **AND**
      4. INDUCTION: Medication will be used in combination with cyclophosphamide or rituximab (e.g., Rituxan, Ruxience); **AND**
      5. MAINTENANCE: Medication will **NOT** be used in combination with rituximab (e.g., Rituxan, Ruxience)

II. Avacopan (Tavneos) is considered investigational when used for all other conditions, including but not limited to:

A. MPA or GPA in patients less than 12 years of age
B. Eosinophilic granulomatosis with polyangiitis (Churg-Strauss)
C. Systemic lupus erythematosus
D. IgA vasculitis
E. Rheumatoid vasculitis

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. For maintenance treatment, medication will **NOT** be used in combination with rituximab (e.g., Rituxan, Ruxience); **AND**
IV. Member has exhibited improvement or stability of disease symptoms (e.g., achievement of long-standing remission, decrease in rates of relapse); **OR**
V. Medication will be used for induction treatment in combination with cyclophosphamide or rituximab (e.g., Rituxan, Ruxience)

Supporting Evidence

I. ANCA-associated vasculitis (AAV) are a group of rare autoimmune disorders characterized by inflammation and destruction of small to medium-sized blood vessels and presence of circulating ANCA. Specific subtypes include GPA, MPA, renal-limited vasculitis, and eosinophilic granulomatosis with polyangiitis (EGPA). The presentation of AAV is highly variable and spectrum of disease may range from relatively mild and localized to the upper respiratory tract to life-threatening involvement of multiple organ systems. If left untreated AAV is a fatal disorder, with the main cause of death due to respiratory or renal failure.
II. Assessment of AAV requires expert guidance to differentiate activity from damage or infection and to consider differential diagnoses. Patients may require interventions by multiple different specialists depending on organ involvement and disease severity and may require services such as immunological monitoring, specialized radiography, assessment of eye involvement, and renal transplantation. The 2015 European League Against Rheumatism (EULAR) clinical guidelines recommend that all AAV patients should be managed in close collaboration with, or at, centers of expertise (Grade of recommendation: C).
III. The diagnosis of GPA or MPA is suspected in patients presenting with constitutional symptoms (e.g., fever, weight loss, arthralgias) with clinical evidence of renal or respiratory tract

involvement. Testing for ANCA should be performed using assays for proteins within neutrophils called proteinase 3 (PR3) and myeloperoxidase (MPO). Approximately 82 to 94 percent of patients with either GPA or MPA have a positive ANCA, depending on severity of disease. GPA is primarily associated with PR3-ANCA (65 to 75 percent of cases), while MPA is primarily associated with MPO-ANCA (55 to 65 percent of cases). A negative assay does not exclude the diagnosis of GPA or MPA and ANCA status may change over time. Tissue biopsies should be considered in cases of suspected AAV to confirm diagnosis. Tissue biopsy is particularly important in patients who are ANCA-negative or in whom there is a degree of diagnostic uncertainty. A negative or "nondiagnostic" biopsy does not exclude a diagnosis of AAV as diagnostic sensitivities vary depending on the organ biopsied.

IV. Disease severity is characterized as either organ or life threatening or non-organ threatening. Examples of non-organ threatening disease include skin involvement without ulceration, myositis, nasal, and paranasal disease without bony involvement or cartilage collapse. For non-organ threatening disease treatment with methotrexate or mycophenolate is preferred. For organ or life threatening disease, treatment with cyclophosphamide or rituximab is indicated.

V. Treatment of patients with AAV is comprised of two phases: induction and maintenance. Induction treatment typically lasts for three-to-six months with the goal of establishing remission. For some induction may extend for longer than 6 months, however this is not common. The optimal duration of maintenance is unknown. Therapy for induction and maintenance is chosen based on the severity of disease. The 2015 EULAR clinical guidelines recommend induction treatment based on severity of the disease:

<u>Induction/relapse</u>

- New onset organ-threatening or life threatening AAV – combination of high-dose glucocorticoids and either cyclophosphamide OR rituximab (Grade of recommendation: A)
- Non-organ threatening AAV – combination of high-dose glucocorticoids and either methotrexate or mycophenolate mofetil (Grade of recommendation: B for methotrexate, C for mycophenolate mofetil)

<u>Maintenance:</u> Combination of low-dose glucocorticoids initially and either azathioprine, rituximab, methotrexate or mycophenolate mofetil for at least 24 months following sustained remission (Grade of recommendation: A)

VI. Avacopan (Tavneos) was studied in one 52-week, randomized, double-blind, double-dummy, Phase 3 clinical trial in 331 patients with newly diagnosed or relapsed GPA or MPA, in whom treatment with cyclophosphamide or rituximab was indicated. Enrolled patients were 12 years of age or older, with median patient age of 61 years. Avacopan (Tavneos) was studied at an oral dose of 30 mg twice daily against oral prednisone taper over a 21-week period (6 0mg, 45 mg for patients <55 kg and 30 mg for patients <37 kg per day starting dose). All patients received cyclophosphamide followed by azathioprine (or mycophenolate mofetil) or rituximab. Patients were allowed to receive glucocorticoid rescue therapy and to continue glucocorticoids for non-vasculitis reasons. The primary efficacy outcomes were clinical remission at week 26 and sustained remission at week 52 and no receipt of glucocorticoids for 4 weeks before evaluation of efficacy endpoints.

Primary Endpoints	Avacopan (n=166)	Prednisone (n=164)	Difference (95% CI)	p-value
Remission at wk 26, no %	120 (72.3)	115 (70.1)	3.4 (-6.0-12.8)	**Noninferiority: p<0.001** Superiority: p=0.24
Sustained remission at wk 52, no %	109 (65.7)	90 (54.9)	12.5 (2.6-22.3)	**Noninferiority: p<0.001 Superiority: p=0.007**

VII. Safety profile of avacopan (Tavneos) is still developing and is limited to a small population, 166 patients who received at least one dose of avacopan (Tavneos) and 134 who received it for more than six months. Overall a similar proportion of patients in both treatment arms experienced adverse events (AEs), including serious adverse events (SAEs) and AEs leading to discontinuation. SAEs occurred in 42.2% vs 45.1% of the avacopan (Tavneos) and prednisone arms, respectively. Common SAEs included ANCA-positive vasculitis, 7.2% vs 12.2%; pneumonia, 4.8% vs 3.7%; GPA, 3% vs 0.6%; acute kidney injury 1.2% vs 0.6%; and urinary tract infection 1.8% vs 1.2% in the avacopan (Tavneos) and prednisone arms, respectively. There were more patients in the avacopan (Tavneos) group than in the prednisone group that experienced SAEs of abnormality on liver-function testing, 5.4% vs 3.7%, respectively. More patients experienced AEs related to glucocorticoids in the prednisone group than in the avacopan (Tavneos) group, 80.5% vs 66.3%, respectively.

VIII. The place in therapy for avacopan's (Tavneos) is evolving; however, it is currently limited by evidence gathered from one Phase 3 clinical trial with a small safety database. High dose glucocorticoids have a known safety profile and remain highly effective when used in combination with the standard of care (e.g., cyclophosphamide, rituximab) to induce remission. This coupled with absence of significant differences in the observed adverse events seen in patients treated with avacopan (Tavneos), makes high dose glucocorticoids an appropriate first-line treatment option. Though there were fewer steroid related adverse events noted in the avacopan (Tavneos) arm during the pivotal clinical trial, the majority of adverse events expected with a prednisone taper when starting with a high dose are predictable, manageable, and transient. At this time, insight to the safety profile and cost-effectiveness of glucocorticoids are favorable to avacopan (Tavneos).

IX. Maintenance therapy is initiated after successful induction of remission. Avacopan (Tavneos) has not been studied in combination with rituximab as maintenance therapy. Further studies are needed to establish safety and efficacy of this combination therapy. At this time it is unknown whether efficacy may be additive if these therapies are used in combination, and safety of this combination is unknown.

Investigational or Not Medically Necessary Uses

I. Avacopan (Tavneos) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. MPA or GPA in patients less than 12 years of age
   B. Eosinophilic granulomatosis with polyangiitis (Churg-Strauss)
   C. Systemic lupus erythematosus

D. IgA vasculitis
E. Rheumatoid vasculitis

References

1. Jayne DRW, Merkel PA, Schall TJ, Bekker P; ADVOCATE Study Group. Avacopan for the Treatment of ANCA-Associated Vasculitis. N Engl J Med. 2021;384(7):599-609. doi:10.1056/NEJMoa2023386
2. Yates M, Watts RA, Bajema IM, et al. EULAR/ERA-EDTA recommendations for the management of ANCA-associated vasculitisAnnals of the Rheumatic Diseases 2016;75:1583-1594.
3. McGeoch L, Twilt M, Famorca L, et al. CanVasc Recommendations for the Management of Antineutrophil Cytoplasm Antibody-associated Vasculitides. J Rheumatol. 2016;43(1):97-120. doi:10.3899/jrheum.150376
4. U.S. Food and Drug Administration. Office of Immunology and Inflammation. (2021). *FDA Briefing Document.* Available at: https://www.fda.gov/media/148176/download.

Policy Implementation/Update:

Action and Summary of Changes	Date
Added criteria in the renewal section which ensures medication will not be used in combination with rituximab for maintenance and if used for induction treatment, medication will be used in combination with cyclophosphamide or rituximab and does not require attestation of achieved remission.	01/2022
Policy created	08/2021