Tavneos (avacopan)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Tavneos (avacopan) drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines, and clinical studies. The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

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 does not eliminate glucocorticoid use.

POLICY

Required Documentation

A. Initial requests:
    1. Chart notes or medical records showing a history of positive serum assay for anti-proteinase-3 (anti-PR3) or anti-myeloperoxidase (anti-MPO) antibody
    2. Chart notes or medical records of pre-treatment objective assessment of the most impactful aspects of the member's ANCA-associated vasculitis (e.g., renal, pulmonary, neurologic)
B. Continuation requests: Chart notes or medical records showing stabilization or improvement in the most impactful aspects of the member's ANCA-associated vasculitis (e.g., renal, pulmonary, neurologic)

Criteria for Initial Approval

Anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (granulomatosis with polyangiitis [GPA] and microscopic polyangiitis [MPA])

Authorization of 12 months may be granted for treatment of severe active ANCA-associated vasculitis (GPA and MPA) when all of the following criteria are met:

A. Tavneos will be used in combination with standard therapy (e.g. rituximab, cyclophosphamide, methotrexate, azathioprine, mycophenolate mofetil)
B. The member has a history of testing positive for anti-PR3 or anti-MPO antibody
C. Documentation of pre-treatment objective assessment of the most impactful aspects of the member's ANCA-associated vasculitis (e.g., renal, pulmonary, neurologic)

Continuation of Therapy

Authorization of 12 months may be granted for continued treatment for severe active ANCA-associated vasculitis (GPA and MPA) in members who achieve or maintain a positive clinical response as evidenced by stabilization or improvement in the most impactful aspects of the member's ANCA-associated vasculitis (e.g., renal, pulmonary, neurologic).

Tavneos is considered **not medically necessary** for members who do not meet the criteria set forth above.

Dosage and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Quantity Limits:

Medication	Standard Limit	FDA-recommended dosing
Tavneos (avacopan) 10 mg capsule	180 per 30 days	30 mg twice daily

CLINICAL RATIONALE

Background

ANCA-associated vasculitis (AAV) is a group of autoimmune diseases in which autoantibodies cause small vessel vasculitis and organ dysfunction that can lead to severe, life-threatening disease. AAV includes three subtypes: most commonly GPA or MPA, and less commonly eosinophilic GPA and is defined by necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels associated with myeloperoxidase (MPO) ANCA or proteinase 3 (PR3) ANCA. Globally, the incidence of GPA is 0.4 cases to 11.9 cases per 1 million person-years, and the incidence of MPA is 0.5 cases to 24.0 cases per 1 million persons-years. The typical age of onset is 45 years to 65 years for GPA and 55 years to 75 years for MPA.

ANCAs are most commonly autoantibodies directed against the neutrophil granule proteins MPO and PR3, which play an essential role in the inflammatory process. The AAV subtype GPA is most often characterized with ANCAs directed against PR3, whereas subtype MPA is primarily associated with ANCAs directed against MPO. Neutrophil activation from ANCAs contributes to the inflammatory response seen in AAV as ANCA-activated neutrophils attack cell walls, inducing further injury. Complement component 5a (C5a), a complement fragment, binds to the complement 5a receptor (C5aR) expressed on neutrophils, which leads to an amplification of the inflammatory process. The manifestations and organ dysfunction seen in AAV are secondary to this inflammatory process and common complications include renal disease and pulmonary fibrosis. Other complications include nerve issues and muscle weakness, ear pain and infection, and gastrointestinal problems. Patients with AAV are also at an increased risk of cardiovascular events such as death, stroke, and myocardial infarction as well as venous thromboembolic events.

The 2021 American College of Rheumatology/Vasculitis Foundation Guidelines for remission induction therapies for patients with active, severe GPA or MPA prefer rituximab over cyclophosphamide, each in combination with a steroid taper (Chung, 2021). Reduced-dose glucocorticoids has been shown to be non-inferior to standard dosing with no significant difference in sustained remission, death, or end-stage kidney disease but an improvement in rate of serious infections at one year. Currently, only Rituxan (rituximab) and its biosimilars are FDA approved for AAV subtypes GPA and MPA. Tavneos is a recently approved C5aR antagonist that blocks C5a-mediated neutrophil activation and migration. The precise mechanism by which Tavneos exerts a therapeutic effect in patients with AAV has not been definitively established. It is available as 10 mg capsules with a recommended dosage of 30 mg twice daily.

Efficacy

The efficacy of Tavneos was evaluated in a multinational, double-blind, double-dummy, phase III, randomized controlled trial (ADVOCATE) of 330 patients with newly diagnosed or relapsing GPA or MPA AAV. Patients were eligible if they tested positive for PR3 or MPO antibodies and had 1 major or ≥ 3 nonmajor items or ≥ 2 renal items of hematuria and proteinuria on the BVAS. Patients were excluded if they had received > 3 g of IV glucocorticoids within 4 weeks, or > 10 mg per day of oral prednisone (or equivalent) for > 6 weeks continuously. Patients in both arms of the study received standard therapy with rituximab or cyclophosphamide and a prednisone taper. The results are summarized in the table below:

ADVOCATE 2021 RESULTS

Endpoints*	Tavneos (n = 166)	Prednisone (n = 164)	Difference (95% CI)	p-value
Remission at week 26	72.30%	70.10%	3.4 (-6.0 to 12.8)	Noninferiority: < 0.001; Superiority: NS
Sustained remission at week 52	65.70%	54.90%	12.5 (2.6 to 22.3)	Noninferiority: < 0.001; Superiority: 0.007
GTI at week 26	39.7 ± 3.4	56.6 ± 3.4	-16.8 (-25.6 to -8.0)	NA
Relapse	10.10%	21.00%	0.25 to 0.84	0.49
Change in eGFR at week 52	7.3 ± 1.0	4.1 ± 1.0	3.2 (0.3 to 6.1)	NA
BVAS of 0 at week 4	68.90%	62.70%	-5.6 (-15.4 to 4.2)	NA
Mean total prednisone equivalent through week 52	1,349 mg	3,655 mg	NA	NA

*Data is presented as least square means ± standard error unless otherwise noted

GTI = Glucocorticoid Toxicity Index

Safety

In ADVOCATE, the incidence of serious adverse events was 23.5% with Tavneos and 25% in the prednisone arm. Serious infections and serious opportunistic infections occurred in 13.3% vs 15.2%, and 3.6% vs 6.7%, in the Tavneos vs. prednisone groups, respectively. Abnormal liver function tests were more frequent in the Tavneos group (9 vs 6) than in the prednisone group. There were 2 patient deaths in the Tavneos arm and 4 deaths in the prednisone arm. Tavneos carries warnings for hepatotoxicity, hepatitis B reactivation and serious infection.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- Not applicable (N/A)

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POLICY HISTORY

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