INDICATION

TAVNEOS (avacopan) is 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 does not eliminate glucocorticoid use.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Serious hypersensitivity to avacopan or to any of the excipients.

ADVOCATE Data: Patients with Ear, Nose, and Throat (ENT) or Respiratory Manifestations at Baseline based on the Birmingham Vasculitis Activity Score (BVAS v3)

Have you considered prescribing TAVNEOS® for your adult patients with severe active GPA or MPA with ENT or respiratory involvement? Explore the relevant data below

Please see additional Important Safety Information on the next page.

Overall Study Results:

- The phase 3 ADVOCATE trial studied a TAVNEOS® regimen (TAVNEOS® + rituximab, or cyclophosphamide followed by azathioprine or mycophenolate mofetil*) vs Standard Therapy (prednisone taper† + rituximab, or cyclophosphamide followed by azathioprine or mycophenolate mofetil*)[1]

  *If azathioprine was not tolerated.

  - 330 newly diagnosed or relapsed‡ patients with GPA or MPA over 52 weeks in a randomized, double-blind, double-dummy, active-controlled fashion[1,2,3]
  - Glucocorticoids (GCs) were allowed in both treatment arms as pre-medication for rituximab to reduce hypersensitivity reactions, taper after GCs given during the Screening period, treatment of persistent vasculitis, worsening of vasculitis, or relapses, as well as for non-vasculitis reasons such as adrenal insufficiency[2]

- **At Week 26, the TAVNEOS® arm was non-inferior to the Standard Therapy arm in achieving remission[1,§]**
  - 72.3% (120/166) of patients in the TAVNEOS® arm achieved remission vs 70.1% (115/164) in the Standard Therapy arm
- **At Week 52, the TAVNEOS® arm was superior to the Standard Therapy arm in sustaining remission[1,**]**
  - 65.7% (109/166) of patients in the TAVNEOS® arm achieved sustained remission vs 54.9% (90/164) in the Standard Therapy arm

†Prednisone-taper: 60 mg/day tapered to 0 over 20 weeks.

‡Relapse was defined as the occurrence of at least 1 major item, at least 3 non-major items, or 1 or 2 non-major items for at least 2 consecutive visits based on the Birmingham Vasculitis Activity Score (BVAS v3) after a BVAS v3 of 0 had been achieved.[1,2]

§Remission was defined as achieving a BVAS v3 of 0 and not taking glucocorticoids for the treatment of GPA or MPA for 4 weeks before Week 26.[1]

**Sustained remission was defined as remission at Week 26 and at Week 52 and not taking glucocorticoids for the treatment of GPA or MPA for 4 weeks before Week 52, without relapse between Week 26 and Week 52.[1]

In a post hoc, exploratory analysis of the ADVOCATE trial, chest and ENT involvement in the two treatment groups was assessed. Chest and ENT involvement data were collected as part of the BVAS v3. Only patients with Chest or ENT manifestations at enrollment were included in the analysis.[4]

Tables 1 and 2 show overall data on the TAVNEOS® regimen and Standard Therapy across chest involvement and ENT involvement, respectively:

Table 1 - Patients With Chest Involvement (Overall)

	TAVNEOS® n = 166	Standard Therapy n = 164
Baseline	71 (42.8%)	71 (43.3%)
26 Weeks	**1 (0.6%)**	**4 (2.4%)**
52 Weeks	**0 (0.0%)**	**3 (1.8%)**

Table 2 - Patients With ENT Involvement (Overall)

	TAVNEOS® n = 166	Standard Therapy n = 164
Baseline	75 (45.2%)	69 (42.1%)
26 Weeks	**2 (1.2%)**	**6 (3.7%)**
52 Weeks	**2 (1.2%)**	**5 (3.0%)**

Analyses are exploratory and have not been adjusted for multiple comparisons. No conclusions of statistical or clinical significance can be drawn.

Data for Patients With Chest Involvement continued on next page

Table 3 shows data on the TAVNEOS® regimen and Standard Therapy across Chest involvement:

Table 3: Patients With Chest Involvement (By Sub-Organ)[2,4]

	Baseline		Week 26		Week 52	
	TAVNEOS® n = 166	Standard Therapy n = 164	TAVNEOS® n = 166	Standard Therapy n = 164	TAVNEOS® n = 166	Standard Therapy n = 164
Chest Overall	**71** (42.8%)	**71** (43.3%)	**1** (0.6%)	**4** (2.4%)	**0** (0.0%)	**3** (1.8%)
Infiltrate	31 (18.7%)	37 (22.6%)	0 (0.0%)	2 (1.2%)	0 (0.0%)	2 (1.2%)
Nodules or Cavities	37 (22.3%)	35 (21.3%)	1 (0.6%)	1 (0.6%)	0 (0.0%)	2 (1.2%)
Wheeze	11 (6.6%)	10 (6.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Massive Hemoptysis/ Alveolar Hemorrhage	5 (3.0%)	7 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pleural Effusion/ Pleurisy	10 (6.0%)	7 (4.3%)	0 (0.0%)	2 (1.2%)	0 (0.0%)	1 (0.6%)
Endobronchial Involvement	7 (4.2%)	9 (5.5%)	0 (0.0%)	1 (0.6%)	0 (0.0%)	0 (0.0%)
Respiratory Failure	1 (0.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other	1 (0.6%)	1 (0.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Analyses are exploratory and have not been adjusted for multiple comparisons. No conclusions of statistical or clinical significance can be drawn.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS

Hepatotoxicity: Serious cases of hepatic injury have been observed in patients taking TAVNEOS, including life-threatening events. Obtain liver test panel before initiating TAVNEOS, every 4 weeks after start of therapy for 6 months and as clinically indicated thereafter. Monitor patients closely for hepatic adverse reactions, and consider pausing or discontinuing treatment as clinically indicated (refer to section 5.1 of the Prescribing Information). TAVNEOS is not recommended for patients with active, untreated, and/or uncontrolled chronic liver disease (e.g., chronic active hepatitis B, untreated hepatitis C, uncontrolled autoimmune hepatitis) and cirrhosis. Consider the risks and benefits before administering this drug to a patient with liver disease.

Serious Hypersensitivity Reactions: Cases of angioedema occurred in a clinical trial, including 1 serious event requiring hospitalization. Discontinue immediately if angioedema occurs and manage accordingly. TAVNEOS must not be readministered unless another cause has been established.

Hepatitis B Virus (HBV) Reactivation: Hepatitis B reactivation, including life-threatening hepatitis B, was observed in the clinical program. Screen patients for HBV. For patients with evidence of prior infection, consult with physicians with expertise in HBV and monitor during TAVNEOS therapy and for 6 months following. If patients develop HBV reactivation, immediately discontinue TAVNEOS and concomitant therapies associated with HBV reactivation, and consult with experts before resuming.

Serious Infections: Serious infections, including fatal infections, have been reported in patients receiving TAVNEOS. The most common serious infections reported in the TAVNEOS group were pneumonia and urinary tract infections. Avoid use of TAVNEOS in patients with active, serious infection, including localized infections. Consider the risks and benefits before initiating TAVNEOS in patients with chronic infection, at increased risk of infection, or who have been to places where certain infections are common.

Please see additional Important Safety Information on the next page.

Data for Patients With ENT Involvement continued on next page

Table 4 shows data on the TAVNEOS® regimen and Standard Therapy across ENT involvement:

Table 4: Patients With ENT Involvement (By Sub-Organ)[2,4]

	Baseline		Week 26		Week 52	
	TAVNEOS® n = 166	Standard Therapy n = 164	TAVNEOS® n = 166	Standard Therapy n = 164	TAVNEOS® n = 166	Standard Therapy n = 164
ENT Overall	**75** (45.2%)	**69** (42.1%)	**2** (1.2%)	**6** (3.7%)	**2** (1.2%)	**5** (3.0%)
Blood Nasal Disc/ Crust/Ulcer/ Granulomata	51 (30.7%)	47 (28.7%)	1 (0.6%)	5 (3.0%)	1 (0.6%)	4 (2.4%)
Paranasal Sinus Involvement	36 (21.7%)	30 (18.3%)	1 (0.6%)	1 (0.6%)	0 (0.0%)	1 (0.6%)
Conductive Hearing Loss	21 (12.7%)	23 (14.0%)	0 (0.0%)	0 (0.0%)	1 (0.6%)	0 (0.0%)
Sensorineural Hearing Loss	10 (6.0%)	9 (5.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.6%)
Subglottic Stenosis	1 (0.6%)	6 (3.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other	2 (1.2%)	1 (0.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Analyses are exploratory and have not been adjusted for multiple comparisons. No conclusions of statistical or clinical significance can be drawn.

If you have an adult patient with severe active GPA or MPA experiencing new, relapsing, or persistent disease activity, you can prescribe TAVNEOS® using the TAVNEOS® Start Form here.

Start your patients on TAVNEOS® today to achieve and sustain remission.

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS

The most common adverse reactions (≥5% of patients and higher in the TAVNEOS group vs. prednisone group) were nausea, headache, hypertension, diarrhea, vomiting, rash, fatigue, upper abdominal pain, dizziness, blood creatinine increased, and paresthesia.

DRUG INTERACTIONS

Avoid co-administration of TAVNEOS with strong and moderate CYP3A4 enzyme inducers. Reduce TAVNEOS dose when co-administered with strong CYP3A4 enzyme inhibitors to 30 mg once daily. Consider dose reduction of CYP3A4 substrates when co-administering TAVNEOS. Co-administration of avacopan and 40 mg simvastatin increases the systemic exposure of simvastatin. While taking TAVNEOS, limit simvastatin dosage to 10 mg daily (or 20 mg daily for patients who have previously tolerated simvastatin 80 mg daily for at least one year without evidence of muscle toxicity). Consult the concomitant CYP3A4 substrate product information when considering administration of such products together with TAVNEOS.

TAVNEOS is available as a 10 mg capsule.

Please see Full Prescribing Information and Medication Guide for TAVNEOS.

To report a suspected adverse event, call 1-833-828-6367. You may report to the FDA directly by visiting http://www.fda.gov/medwatch or calling 1-800-332-1088.

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.

2. TAVNEOS® [package insert]. Cincinnati, OH: Amgen Inc.

3. Data on file, Amgen Inc; 2023.

4. Specks, U., Jayne DRW., & Merkel PA. Insights from the advocate study: Respiratory tract involvement in patients with ANCA-associated vasculitis in a randomized, double-blind, placebo-controlled, phase 3 trial of Avacopan. Paper presented at: American Thoracic Society 2022 International Conference, May 13-18, 2022 - San Francisco, CA.

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