TAVNEOS® (avacopan)

As their healthcare provider, you understand the unique needs of each patient with severe active GPA or MPA

Identify patients in your practice who could benefit from adding TAVNEOS®

Do your patients with severe active disease need more than standard therapy alone?

For severe active GPA and MPA, TAVNEOS® is an oral adjunctive therapy that can be used for new, relapsing, or persistent disease activity[1,2]

OVER 1,000 providers have prescribed TAVNEOS® for their patients with severe active GPA or MPA[3,*]

*Represents total number of unique prescribers with one or more new patient start forms submitted to AssistRx, Amber, or PANTHERx from October 2021 – March 2023.

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

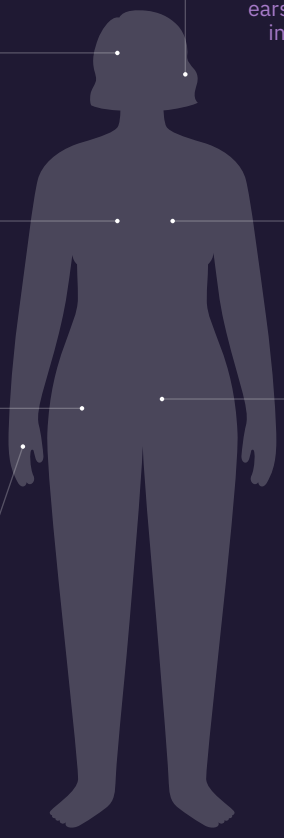
Serious hypersensitivity to avacopan or to any of the excipients.

Please see additional **Important Safety Information** throughout and click here for the **Full Prescribing Information** and **Medication Guide** for TAVNEOS.

Patients with severe active GPA or MPA might present with disease activity in one or more organs[2,4]

→ **Severe vasculitis** is defined by American College of Rheumatology (ACR) guidelines as having life-threatening or organ-threatening manifestations[2]

→ **Active vasculitis** is defined by ACR guidelines as new, persistent, or worsening signs and/or symptoms attributed to GPA or MPA, and not related to prior damage[2]



Eyes
Ocular redness, foreign body sensation, blurred vision, bloody tears[5]

ADVOCATE: 20%
eye involvement[6]

Ears
Otitis media, earache, hearing loss, otorrhea[7,9]

Nose/Throat
Sinusitis, nasal crusting, persistent rhinorrhea, nasal ulcers, stenotic lesion, airway inflammation[7,10]

ADVOCATE: 43.6%
ears, nose/throat involvement[6]

Chest
Dyspnea, haemoptysis, nodules, cavitations, pleuritic pain, alveolar opacities[7]

ADVOCATE: 43%
chest involvement[6]

Cardiovascular
Hyperlipidemia, elevated lipoprotein levels, hypertension[11]

ADVOCATE: 2.7%
cardiovascular involvement[6]

Renal
Hematuria, red cell casts, proteinuria[7]

ADVOCATE: 81.2%
renal involvement[6]

Gastrointestinal
Ulcers, bleeding, abdominal pain, ischemic bowel disease, peritonitis, ischemic hepatitis[12]

ADVOCATE: 1.5%
abdominal involvement[6]

Cutaneous
Livedo reticularis, leukocytoclastic angiitis, urticaria, tender nodules, purpura[7,8]

ADVOCATE: 14.2%
cutaneous involvement[6]

General
Headache, muscle pain, joint pain, coughing[7]

ADVOCATE: 68.2%
general involvement[6]

Nervous System
Neurological disorder: numbness, tingling sensation[13,14]

ADVOCATE: 20.9%
nerve involvement[6]

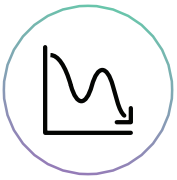
GPA and MPA impact the kidneys or another organ in about 80%-90% of cases, which can be considered active disease.[2,4]

→ Multiple minor manifestations of MPA or GPA, including localized disease, can also be considered severe, active disease.[2,3]

Patients in the ADVOCATE trial presented with a spectrum of clinical manifestations[6]

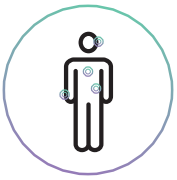
Please note these are just some of the signs and symptoms of GPA and MPA, which can present differently in each patient.

Careful monitoring may help detect obscure signs that your patients are experiencing severe active disease[15–20]



Disease worsening
New or re-emerging manifestations as well as deteriorating lab values (such as subtle elevations in creatinine or emergence of microscopic hematuria) may signal the need for clinical attention[15-17]

Immunosuppressant use
Strong or prolonged immunosuppression treatment could require close monitoring of disease activity[18]



Localized symptoms
Localized symptoms do not necessarily preclude the possibility that the disease activity is organ-threatening and may still require close monitoring[19,20]

Disease activity during the "maintenance" period
Subtle trends such as persistent or mild hematuria, subtle elevations in creatinine, or ENT symptoms may require a closer look in order to determine disease activity[19]

Common terms associated with GPA and MPA

ANCA-associated vasculitis (AAV)	A rare group of necrotizing vasculitis that predominantly affects small-to-medium blood vessels[10,21]
Granulomatosis with polyangiitis (GPA)	A subtype of AAV, previously called "**Wegener's granulomatosis**", that features necrotizing granulomatous inflammation and is commonly associated with PR3-ANCA[10,21]
Microscopic polyangiitis (MPA)	Another subtype of AAV where granulomatous inflammation is absent and is associated with MPO-ANCA[10,21]
Pauci-immune crescentic glomerulonephritis (PICGN)	A form of rapidly progressing glomerulonephritis (RPGN) that can lead to renal failure and is almost always a sign of ANCA-associated vasculitis[22]

The information contained in this resource should not replace your clinical decision-making regarding diagnoses and treatment. Healthcare providers are solely responsible for clinical decisions.

ANCA, antineutrophil cytoplasmic antibody; ENT, ear, nose, and throat; MPO-ANCA, anti-myeloperoxidase antineutrophil cytoplasmic antibody; PR3-ANCA, proteinase 3 antineutrophil cytoplasmic antibody.

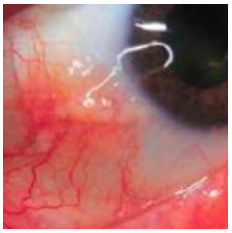
IMPORTANT SAFETY INFORMATION (CONT'D)
WARNINGS AND PRECAUTIONS
Hepatotoxicity: Serious cases of hepatic injury have been observed in patients taking TAVNEOS, including life-threatening events. Obtain liver test panel before initiating TAVNEOS, every 4 weeks after start of therapy for 6 months and as 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.

Please see additional **Important Safety Information** throughout and click here for the **Full Prescribing Information** and **Medication Guide** for TAVNEOS.

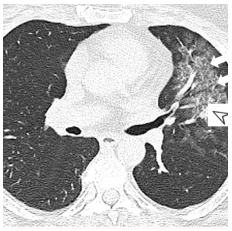
TAVNEOS® (avacopan)

3

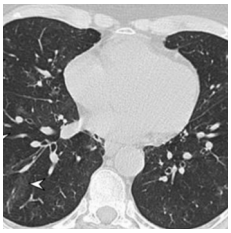
Successful identification and treatment of severe active GPA and MPA can be challenging and requires a careful assessment of heterogenous symptoms[15]



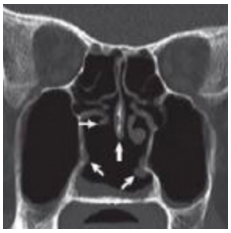
AAV with scleritis[23]



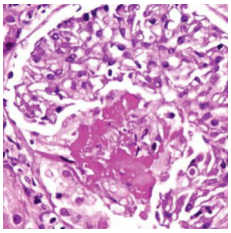
Chest computer tomography (CT) with ground-glass opacities in a patient with AAV with acute pulmonary hemorrhage[24]



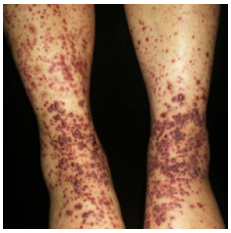
Chest CT with bilateral nodules and masses[24]



Sinonasal disease with coronal CT images showing destruction of the nasal cavity[15]



Kidney biopsy demonstrating necrotizing, pauci-immune glomerulonephritis[25]



Bilateral lower extremity purpura

Reproduced from Purpuric lesions in a patient with ANCA associated vasculitis, *BMJ*, Yang et al., 376,e065658, copyright notice 2023 with permission from BMJ Publishing Group Ltd.[26]

What are your goals for treatment?

The traditional goal in treatment is achieving remission. Remission of GPA and MPA is defined by the ACR guidelines as absence of clinical signs or symptoms attributed to GPA or MPA, on or off immunosuppressive therapy.[2]

→ ~1 in 2 patients still believe that "even in remission their vasculitis symptoms are debilitating"[27,*]

*According to an online, self-administered survey of 100 patients with GPA or MPA from July 21-August 25, 2022.

As part of the collaborative doctor-patient approach, it is important to set holistic goals when measuring each patient's progress towards remission.[15]

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

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 (avacopan) must not be readministered unless another cause has been established.

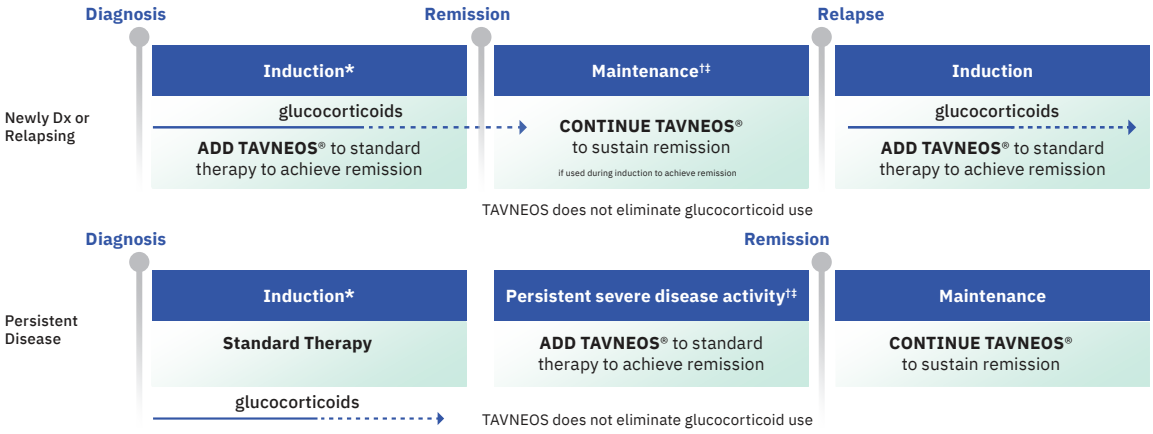
Hepatitis B Virus (HBV) Reactivation: Hepatitis B reactivation, including life-threatening hepatitis B, was observed in the clinical program. Screen patients for HBV. For patients with evidence of prior infection, consult with physicians with expertise in HBV and monitor during TAVNEOS therapy and for 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** throughout and click here for the **Full Prescribing Information** and **Medication Guide** for TAVNEOS.

Whether your patient is experiencing new, relapsing, or persistent disease activity, TAVNEOS® (avacopan) can be a part of their journey

Treatment journey lexicon[1]



TAVNEOS® is an oral adjunctive therapy that can be added to standard therapy for severe active GPA or MPA[1,2]

The phase 3 ADVOCATE trial studied a TAVNEOS® regimen (TAVNEOS® + rituximab, or cyclophosphamide followed by azathioprine) vs Standard Therapy (prednisone taper + rituximab, or cyclophosphamide followed by azathioprine)[1,6,28]

→ 330 newly diagnosed or relapsed patients with GPA or MPA over 52 weeks in a randomized, double-blind, double-dummy, active-controlled fashion[1,6]

At Week 26, the TAVNEOS® arm was non-inferior to Standard Therapy in achieving remission[28,†]

→ 72.3% (120/166) of patients in the TAVNEOS® arm achieved remission vs 70.1% (115/164) on Standard Therapy

At Week 52, the TAVNEOS® arm was superior to Standard Therapy in sustaining remission[28,‡]

→ 65.7% (109/166) of patients in the TAVNEOS® arm achieved remission vs 54.9% (90/164) on Standard Therapy

*Induction therapies include, but are not limited to azathioprine, rituximab, mycophenolate mofetil, cyclophosphamide, and glucocorticoids.
†Remission was defined as achieving a Birmingham Vasculitis Activity Score (BVAS) of 0 and not taking glucocorticoids for treatment of GPA or MPA within 4 weeks prior to Week 26.
‡Sustained remission was defined as remission at Week 26 and at Week 52 and no use of glucocorticoids for 4 weeks before Week 52, without relapse between Week 26 and Week 52.

IMPORTANT SAFETY INFORMATION (CONT'D)
WARNINGS AND PRECAUTIONS (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.

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TAVNEOS® (avacopan)

See Induction - Severe Active GPA | Newly Diagnosed and Critical →

(Hypothetical Patient)

NEWLY DIAGNOSED, SEVERE ACTIVE MPA, INDUCTION PATIENT: START WITH TAVNEOS®

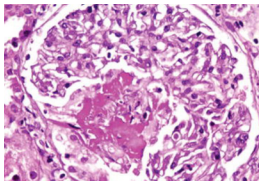
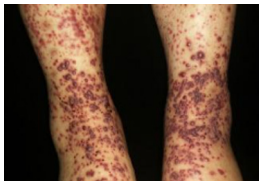
Patient characteristics

62 year-old female, School Administrator
Enjoys travel with husband and spending time with grandchildren

The following profile is hypothetical and provides some common patient characteristics you may see in patients who you may consider treating with TAVNEOS®. It is informational only and should not replace your clinical decision-making regarding diagnoses and treatment. Healthcare providers are solely responsible for clinical decisions.

History of Present Illness

→ Received inconclusive workup 30 days prior by her PCP based on complaint of fatigue
→ Found to have concomitant hypertension with hyperlipidemia and no other cardiovascular disease
- Baseline: BP: 145/85 mm Hg (ref: <120/80 mm Hg)[1]
- eGFR: 98 mL/min/1.73 m^2 (ref: >90 mL/min/1.73 m^2)[2]
- Serum creatinine: 0.8 mg/dL (ref: 0.59 – 1.04 mg/dL)[3]

Current presentation	Scans	Lab Values
Presents at the specialty clinic setting with extreme fatigue, hematuria and proteinuria on dipstick, fever, and new-onset lower extremity purpura	Kidney biopsy indicates necrotizing, pauci-immune glomerulonephritis[4]  Kidney biopsy demonstrating necrotizing, pauci-immune glomerulonephritis  Bilateral lower extremity purpura[5]	→ **eGFR:** 45 mL/min/1.73 m^2 (ref: >90 mL/min/1.73 m^2)[2] → **Serum creatinine:** 1.2 mg/dL (ref: 0.50–1.10 mg/dL)[3] → **Urinalysis:** hematuria and proteinuria[6] → **CRP:** 15 mg/L (ref: Low risk: <1.0 mg/L; Average risk: 1.0–3.0 mg/L; High risk: >3.0 mg/L)[3] → **ESR:** 84 mm/hr (ref: <20 mm/hr)[7] → **Serology:** +p-ANCA, High MPO-ANCA >8.0 AU/mL (ref: 0.0-0.9 AU/mL)[8]

Possible Diagnosis

→ Severe active MPA, with renal and cutaneous involvement

Potential treatment decision

→ **Induction:** Started rituximab; glucocorticoids as needed; **started TAVNEOS® 30 mg BID on Day 1**
→ **Maintenance:** Continue on rituximab + TAVNEOS® + glucocorticoids as needed

ANCA, antineutrophil cytoplasmic antibody; BID, twice daily; BP, blood pressure; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; ESR, erythrocyte sedimentation rate; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; MPO, anti-myeloperoxidase; p-ANCA, perinuclear antineutrophil cytoplasmic antibody; PCP, primary care provider.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Serious hypersensitivity to avacopan or to any of the excipients.

Please see additional **Important Safety Information** throughout and click here for the **Full Prescribing Information** and **Medication Guide** for TAVNEOS.

TAVNEOS® (avacopan)

See Induction - Severe Active MPA | Newly Diagnosed →

(Hypothetical Patient)

NEWLY DIAGNOSED AND CRITICAL, SEVERE ACTIVE GPA: START TAVNEOS®

Patient characteristics

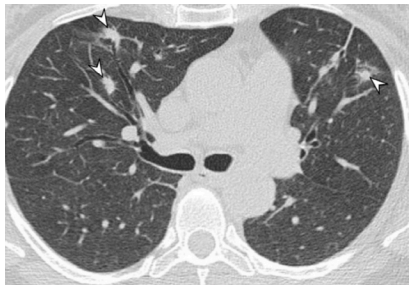
71 year-old male, Retired Banker

Enjoys golfing and attending grandchildren's sporting events

The following profile is hypothetical and provides some common patient characteristics you may see in patients who you may consider treating with TAVNEOS®. It is informational only and should not replace your clinical decision-making regarding diagnoses and treatment. Healthcare providers are solely responsible for clinical decisions.

History of Present Illness

→ Generally in good health but avoids scheduling an annual physical

Current presentation	Scans	Lab Values
Presents at the hospital emergency department with severe dyspnea, wheezing, progressive cough; stroke and myocardial infarction ruled out	Chest CT: Multiple bilateral nodules and masses, extensive at the bases[9] 	→ **Blood pressure:** 150/85 mm Hg (ref: <120/80 mm Hg)[1] → **Cardiac troponin I:** 0.05 ng/ml (ref: ≤0.04 ng/mL)[3] → **eGFR:** 98 mL/min/1.73 m^2 (ref: >90 mL/min/1.73 m^2)[2] → **Serum creatinine:** 0.8 mg/dL (ref: 0.70–1.30 mg/dL)[3] → **ESR:** 90 mm/hr (ref: <30 mm/hr)[7] → **SpO2:** 85% (ref: ≥95%)[10] → **Serology:** +c-ANCA, High PR3-ANCA >7.0 AU/mL (ref: 0.0-0.9 AU/mL)[8]

Possible Diagnosis

→ Severe active GPA, with respiratory involvement

Potential treatment decision

→ **At Hospital:** Glucocorticoids as needed; rituximab on day 1; **started on a 5-day supply of TAVNEOS® with direct hospital pharmacy** dispensing; treatment continuity maintained upon discharge to clinic

→ **After Discharge: Continued on TAVNEOS® 30 mg BID**, glucocorticoids as needed, rituximab maintenance

BID, twice daily; +c-ANCA and +PR3-ANCA, positive for antineutrophil cytoplasmic antibodies; ANCA, antineutrophil cytoplasmic antibody; BID, twice daily; CT, computed tomography; eGFR, estimated glomerular filtration rate; GPA, granulomatosis with polyangiitis; ESR, erythrocyte sedimentation rate; PR3, proteinase 3; SpO2, oxygen saturation rate.

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.

References: 1. Carey RM, Whelton PK; 2017 ACC/AHA Hypertension Guideline Writing Committee. *Ann Intern Med*. 2018;168(5):351-358. **2.** Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int Suppl*. 2013;3:1–150. **3.** American Board of Internal Medicine (ABIM) Laboratory Test Reference Ranges—January 2023. https://www.abim.org/Media/bfijryql/laboratory-reference-ranges.pdf. Accessed 05/19/2023. **4.** Lionaki S, Skalioti C, Marinaki S, and Boletus JN. Pauci-Immune Vasculitides with Kidney Involvement. In: Mohammed RHA (ed). *Vasculitis in Practice: An Update on Special Situations – Clinical and Therapeutic Considerations*. Hamilton, New Jersey: InTech Open; 2018;chap 2. **5.** Yang J, Li M. *BMJ* 2022;376:e065658 **6.** Hunter RW, Welsh N, Farrah TE, et al. *BMJ*. 2020;369:m1070. **7.** Tishkowski K, Gupta V. Erythrocyte Sedimentation Rate. In: StatPearls [Internet]. Treasure Island, Florida: StatPearls Publishing; 2023. **8.** Sinico RA, Guillevin L, eds. *Anti-Neutrophil Cytoplasmic Antibody (ANCA) Associated Vasculitis, Rare Diseases of the Immune System*, Berlin, Germany: Springer Nature; 2020. **9.** Palmucci S, Inì C, Cosentino S, et al. *Diagnostics (Basel)*. 2021; 11(12):2318. doi: 10.3390/diagnostics11122318 **10.** Hafen BB, Sharma S. Oxygen Saturation. In: StatPearls [Internet]. Treasure Island, Florida: StatPearls Publishing; 2023.

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TAVNEOS® (avacopan)

See Severe Active MPA | Relapsing Patient →

(Hypothetical Patient)

PERSISTENT DISEASE ACTIVITY, SEVERE ACTIVE GPA: ADD TAVNEOS®

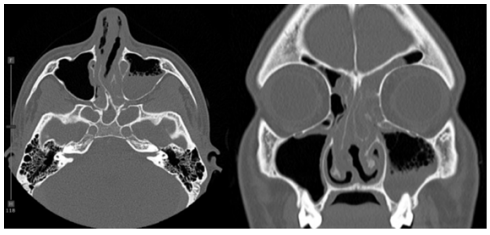
Patient characteristics

59 year-old male, Dental Technician
Proud of sustainable gardening and enjoys cooking "farm to table" for his family.
Planning a backyard greenhouse

The following profile is hypothetical and provides some common patient characteristics you may see in patients who you may consider treating with TAVNEOS®. It is informational only and should not replace your clinical decision-making regarding diagnoses and treatment. Healthcare providers are solely responsible for clinical decisions.

History of Present Illness

→ GPA diagnosis 12 months prior upon presenting to rheumatologist, based on presence of extreme fatigue, fever, unresolved cough, hearing loss, chest CT indicating bilateral infiltrate with ground-glass opacity, and ANCA-positive serology
→ **Previous induction therapy:** Rituximab (375 mg/m²/week for 4 weeks) + glucocorticoids with a standard dose taper + PJP prophylaxis.
→ **Maintenance** with rituximab + 7.5 mg of prednisone but unable to taper any further even at 12-month mark due to persistent symptoms.

Current presentation	Scans	Lab Values
Presents with lingering cough, chronic sinusitis, nasal crusting, and fatigue	→ CT reveals complete opacification of left front and left sphenoid sinus[1] 	→ **eGFR:** 76 mL/min/1.73 m² (ref: >90 mL/min/1.73 m²)[2] → **Serum creatinine:** 1.0 mg/dL (ref: 0.70–1.30 mg/dL)[3] → **ESR:** 84 mm/hr (ref: <30 mm/hr)[4] → **Serology:** +PR3-ANCA >2.0 AU/mL (ref: 0.0-0.9 AU/mL)[5]

Possible Diagnosis

→ Severe active GPA with persistent ENT involvement

Potential treatment decision

→ Added TAVNEOS® to maintenance regimen with goal of reducing prednisone dose

ANCA, antineutrophil cytoplasmic antibody; CT, computed tomography; eGFR, estimated glomerular filtration rate; ENT, ear, nose, and throat; ESR, erythrocyte sedimentation rate; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; MPO, anti-myeloperoxidase; PR3, proteinase 3; PJP, *Pneumocystis jiroveci* pneumonia; SpO2, oxygen saturation rate.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS

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.

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TAVNEOS® (avacopan)

See Persistent Disease Activity, Severe Active GPA: →

(Hypothetical Patient)

RELAPSING PATIENT, SEVERE ACTIVE MPA: ADD TAVNEOS®

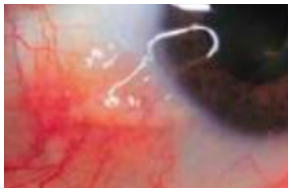
Patient characteristics

41 year-old female, Real Estate Agent
Owner/operator of commercial and residential real-estate franchise with ambitious growth goals

The following profile is hypothetical and provides some common patient characteristics you may see in patients who you may consider treating with TAVNEOS®. It is informational only and should not replace your clinical decision-making regarding diagnoses and treatment. Healthcare providers are solely responsible for clinical decisions.

History of Present Illness

→ Diagnosed with MPA 2 years prior
→ **Initial Induction:** Induced with rituximab; patient showed sensitivity, moved to cyclophosphamide; standard dose glucocorticoids
→ Current maintenance therapy: azathioprine + 5 mg glucocorticoids with monthly monitoring
→ Baseline lab values from last follow-up:
- **eGFR:** 70 mL/min/1.73 m^2 (ref: >90 mL/min/1.73 m^2)[2]
- **Serum creatinine:** 1.1 mg/dL (ref: 0.59 – 1.04 mg/dL)[3]
- **ESR:** 60 mm/hr (ref: 0-30 mm/hr)[6]
- **CRP:** 18 mg/L (ref: <3 mg/L)[3]
- **Urinalysis:** 4 red blood cell casts (ref: <2) and nephritic range proteinuria: 3 mg/24 hr (ref: <1 mg/24 hr)[7]
- **ANCA:** +p-ANCA, +MPO-ANCA (ref: 0.0-0.9 AU/mL)[5]

Current presentation	Scans	Lab Values
Presents at the clinic setting with slow hearing loss, coughing, wheezing, photophobia, blurred vision, and renal involvement indicating underlying severe disease	→ **Eye Examination:** reveals scleritis[8] 	→ **eGFR:** 51 mL/min/1.73 m^2 (ref: >90 mL/min/1.73 m^2)[2] → **Serum creatinine:** 1.4 mg/dL (ref: 0.50 -1.10 mg/dL)[3] → **ESR:** 60 mm/hr (ref: <20 mm/hr)[6] → **Urinalysis:** 3 red blood cell casts (ref: <2) and nephritic range proteinuria: 2.5 mg/24 hr (ref: <1 mg/24 hr)[8] → **CRP:** 25 mg/L (ref: Low risk: <1.0 mg/L; Average risk: 1.0–3.0 mg/L; High risk: >3.0 mg/L)[3] → **SpO2:** 90% (ref: ≥95%)[7] → **Serology:** +p-ANCA, High MPO-ANCA >3.0 AU/mL (ref: 0.0-0.9 AU/mL)[5]

Possible Diagnosis

→ Relapsing severe active MPA with minor ENT, ocular, and renal involvement

Potential treatment decision

→ Patient expressed reservations about increasing prednisone again. Added TAVNEOS® to maintenance instead of increasing glucocorticoids or starting on cyclophosphamide

ANCA, antineutrophil cytoplasmic antibody; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; ESR, erythrocyte sedimentation rate; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; MPO, anti-myeloperoxidase; p-ANCA, perinuclear antineutrophil cytoplasmic antibodies; SpO2, oxygen saturation rate.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

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.

References: 1. Lakhani DA, Balar AB, Adelanwa A, et al. *Radiol Case Rep.* 2021 Sep 5;16(11):3445-3450. **2.** Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int Suppl.* 2013;3:1–150. **3.** American Board of Internal Medicine (ABIM) Laboratory Test Reference Ranges—January 2023. https://www.abim.org/Media/bfijryql/laboratory-reference-ranges.pdf. Accessed 05/19/2023. **4.** Hafen BB, Sharma S. Oxygen Saturation. In: StatPearls [Internet]. Treasure Island, Florida: StatPearls Publishing; 2023. **5.** Sinico RA, Guillevin L, eds. *Anti-Neutrophil Cytoplasmic Antibody (ANCA) Associated Vasculitis, Rare Diseases of the Immune System*, Berlin, Germany: Springer Nature; 2020. **6.** Tishkowski K, Gupta V. Erythrocyte Sedimentation Rate. In: StatPearls [Internet]. Treasure Island, Florida: StatPearls Publishing; 2023. **7.** Hunter RW, Welsh N, Farrah TE, et al. *BMJ.* 2020;369:m1070. **8.** Macarie SS, Kadar A. *Rom J Ophthalmol.* 2020;64(1):3-7.

Please see additional **Important Safety Information** throughout and click here for the **Full Prescribing Information** and **Medication Guide** for TAVNEOS.

TAVNEOS® (avacopan)

See symptom ICD-10 coding →

Testing and diagnostic considerations in severe active GPA and MPA

ANCA Serology

→ c-ANCA/PR3 antibodies are most frequently seen in GPA, and p-ANCA/MPO antibodies are most often associated with MPA[1]

→ Although these antibodies are most frequently associated with respective diagnoses, ANCA positivity and specific antibodies vary by condition[1]

Frequency of ANCA types[2]

ANCA-Associated Vasculitis	PR3-ANCA (mostly c-ANCA)	MPO-ANCA (mostly p-ANCA)	Other
GPA	75%	20%	5% ANCA negative
MPA	30%	60%	10% ANCA negative

Example Lab Results for ANCA Profile[3]

A full ANCA profile can be utilized in diagnosing severe active GPA and MPA.

General Comments & Additional Information
Clinical Info: ABNORMAL REPORT

Ordered Items
ANCA Profile

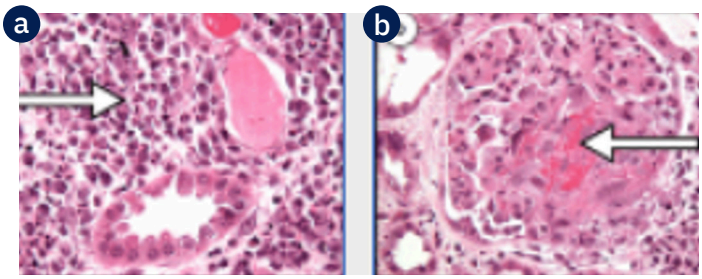
TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
ANCA Profile					
Anti-MPO Antibodies	**>8.0**	**High**	units	0.0-0.9	01
Anti-PR3 Antibodies	0.7		units	0.0-0.9	01
Cytoplasmic (C-ANCA)	**1:320**	**High**	titer	Neg:<1:20	01
Perinuclear (P-ANCA)	<1:20		titer	Neg:<1:20	01
The presence of positive fluorescence exhibiting P-ANCA or C-ANCA patterns alone is not specific for the diagnosis of Wegener's Granulomatosis (WG) or microscopic polyangiitis. Decisions about treatment should not be based solely on ANCA IFA results. The International ANCA Group Consensus recommends follow up testing of positive sera with both PR-3 and MPO-ANCA enzyme immunoassays. As many as 5% serum samples are positive only by EIA. Ref. AM J Clin Pathol 1999;111:507-513.					
Atypical pANCA	<1:20		titer	Neg:<1:20	01
The atypical pANCA pattern has been observed in a significant percentage of patients with ulcerative colitis, primary sclerosing cholangitis and autoimmune hepatitis.					

Biopsy

Biopsy is another supportive tool that can be confirmatory, particularly in cases with renal, pulmonary, or skin involvement, but treatment should not necessarily be delayed simply to get a biopsy.[4]

Pathology results from a real kidney biopsy with AAV[5]

Renal biopsy in a patient with severe active AAV showing (a) Severe interstitial inflammation (shown by the arrow) (b) segmental necrotizing and crescentic glomerulonephritis (shown by the arrow).



AAV, ANCA-associated vasculitis; ANCA, antineutrophil cytoplasmic antibody; c-ANCA, antineutrophil cytoplasmic antibodies; antibody; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; MPO, anti-myeloperoxidase; MPO-ANCA, anti-myeloperoxidase antineutrophil cytoplasmic antibody; pANCA, perinuclear antineutrophil cytoplasmic antibody; PR3-ANCA, proteinase 3 antineutrophil cytoplasmic antibody.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

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** throughout and click here for the **Full Prescribing Information** and **Medication Guide** for TAVNEOS.

TAVNEOS® (avacopan)

See clinical evaluation overview →

ICD-10 codes can help identify GPA or MPA patients with severe active disease who may be appropriate for TAVNEOS®[1–12]

This tool provides a few examples of queries on electronic medical records or practice management systems that may be helpful in identifying appropriate patients for TAVNEOS®.[1-12]

ICD-10 Codes associated with GPA or MPA[1]

M31.3 | Granulomatosis with Polyangiitis (GPA)*

M31.30 | Granulomatosis with Polyangiitis (GPA) without renal involvement

M31.31 | Granulomatosis with Polyangiitis (GPA) with renal involvement

M31.7 | Microscopic Polyangiitis (MPA)

177.6 | Unspecified Arteritis**

177.82 | Antineutrophil cytoplasmic antibody (ANCA) vasculitis

This tool should not be used for coding or reimbursement purposes. These examples are not intended to be instructive with respect to clinical decision-making or billing and coding. Healthcare providers are solely responsible for clinical decisions and ensuring the accuracy and validity of all billing and claims. This is not a guarantee of coverage or reimbursement for any product or service.

*GPA is formerly known as Wegener's granulomatosis.
**The diagnosis is related to ANCA-associated vasculitis or MPA/GPA, specifically, and confirmed or awaiting confirmation using one or more lab tests: ANCA serum/biopsy/urinalysis.

ANCA, antineutrophil cytoplasmic antibody; EMR, electronic medical record; ICD-10, International Classification of Diseases, Tenth Revision.

ICD-10 codes and EMR can also help identify patients who may have undiagnosed severe active GPA or MPA[13,14]

The following codes represent generalized symptoms that are common manifestations of GPA and MPA:[1]

ICD-10 Code	Manifestation
Vasculitic Rash with Systemic Features	
L98.9	Dermatosis
R23.3	Purpuric
R50.9	Fever
Respiratory Symptoms	
R04.2	Hemoptysis
R06.00	Dyspnea
R06.02	Shortness of Breath
R05.9	Cough
J45.909	Asthma
J44.9	Chronic
Ear, Nose, Throat/upper airway symptoms	
J32.9	Sinusitis
J01.81	Recurrent
H92.0	Earache
H90.2	Conductive hearing loss
M95.0	Saddle nose
J95.5	Subglottic stenosis
Eye Symptoms	
H15.00	Scleritis
H53.2	Diplopia
Nerve Symptoms	
R20.2	Paresthesia
G62.9	Neuropathy, neuropathic
Renal Disease	
N05.9	Glomerulonephritis

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.

References: 1. Pagnoux C. *Eur J Rheumatol*. 2016;3(3):122-133. **2.** Geetha D, Jefferson JA. *Am J Kidney Dis*. 2019;75(1):124-137. **3.** Data on file, Amgen Inc. **4.** Kitching AR, Anders HJ, Basu N. *Nat Rev Dis Primers*. 2020;6(1):71. **5.** Zagelbaum N, Shamim Z, Gilani A, et al. *Pulm Crit Care Med*. 2016;1(3):1-4. doi: 10.15761/PCCM.1000119 **6.** World Health Organization. (2019). *International statistical classification of diseases and related health problems* (11th ed.). https://icd.who.int/ Accessed May 19, 2023. **7.** Aitken M, Basu N. *Rheumatology (Oxford)*. 2020;59(Suppl 3):iii132-iii135. **8.** Al-Hussain T, Hussein MH, Conca W, et al. *Adv Anat Pathol*. 2017;24(4):226-234. **9.** Chung SA, Langford CA, Maz M, et al. *Arthritis Rheumatol*. 2021;73(8):1366-1383. **10.** Berden A, Göçeroğlu A, Jayne D, at al. *BMJ*. 2012;344:e26. **11.** Robson J, Doll H, Suppiah R, et al. *Rheumatology (Oxford)*. 2015;54(3):471-481. **12.** Neumann I. *Rheumatology (Oxford)*. 2020;59(Suppl 3):iii60-iii67. **13.** Kitching AR, Anders HJ, Basu N. *Nat Rev Dis Primers*. 2020;6(1):71. **14.** Sinico RA, Guillevin L, eds. *Anti-Neutrophil Cytoplasmic Antibody (ANCA) Associated Vasculitis, Rare Diseases of the Immune System*, Berlin, Germany: Springer Nature; 2020.

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TAVNEOS® (avacopan)

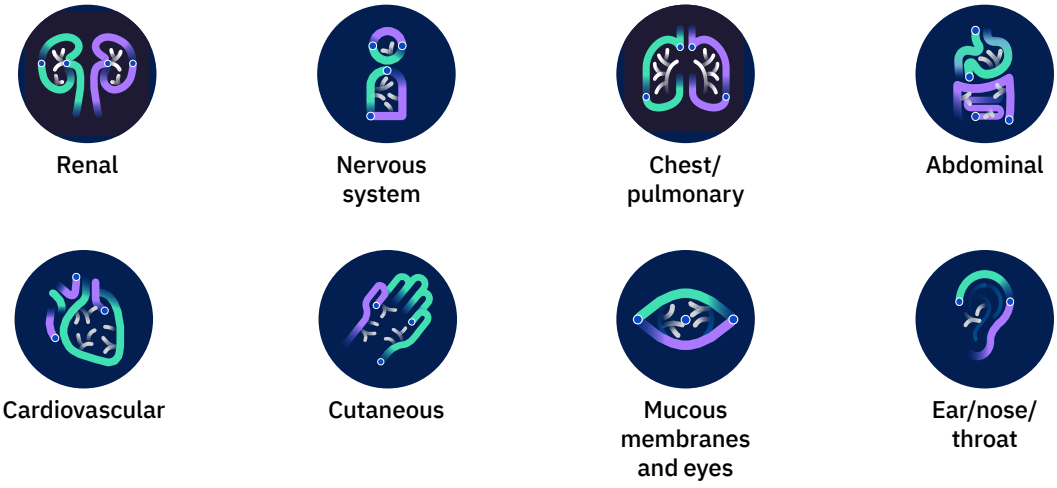
See BVAS manifestations →

Birmingham Vasculitis Activity Score (BVAS) is a composite score that provides a standardized measure of current disease activity in clinical trials such as ADVOCATE[1,2]

There are 56 clinical features, grouped into 9 organ systems plus an "Other" category, each of which is given a numerical value according to its perceived clinical relevance as decided by expert consensus.[1,3,4] Additionally, BVAS:

→ Was developed by consensus expert opinion
→ Has been in use for over 25 years
→ Is considered the most reliable instrument for measuring vasculitic disease activity

BVAS evaluates clinical items in the following organ systems:[1,3]



The 9th clinical item is "general" which includes myalgia, arthralgia/arthritis, fever, weight loss.

A higher total BVAS score equates to a more active vasculitic disease at the time of evaluation.[1]

BVAS is a validated endpoint with demonstrated high reliability. It is efficient in terms of time and effort and is recommended for use in clinical trials.[2]

IMPORTANT SAFETY INFORMATION (CONT'D)
DRUG INTERACTIONS
Avoid coadministration of TAVNEOS with strong and moderate CYP3A4 enzyme inducers. Reduce TAVNEOS dose when coadministered with strong CYP3A4 enzyme inhibitors to 30 mg once daily. Monitor for adverse reactions and consider dose reduction of certain sensitive CYP3A4 substrates.

Please see additional **Important Safety Information** throughout and click here for the **Full Prescribing Information** and **Medication Guide** for TAVNEOS.

TAVNEOS® (avacopan)

See BVAS clinical overview →

While BVAS is primarily used in clinical trials, it may be helpful to understand the spectrum of manifestations that could indicate severe active GPA and MPA[1,2]

The below information is adapted from BVAS Version 3.0. Below are the manifestations listed in BVAS organized by organ system. Major manifestations are bolded.[4]

Abdominal

- → Peritonitis
- → Bloody diarrhea
- → **Ischemic abdominal pain**

Cutaneous

- → Infarct
- → Purpura
- → Ulcer
- → **Gangrene**
- → Other skin vasculitis

Nervous system

- → Headache
- → **Meningitis**
- → Organic confusion
- → Seizures (not hypertensive)
- → **Cerebrovascular accident**
- → Organic confusion
- → **Spinal cord lesion**
- → **Cranial nerve palsy**
- → Sensory peripheral neuropathy
- → **Mononeuritis multiplex**

Cardiovascular

- → Loss of pulses
- → Valvular heart disease
- → Pericarditis
- → **Ischemic cardiac pain**
- → **Cardiomyopathy**
- → **Congestive cardiac failure**

ENT

- → Bloody nasal discharge/crusts/ulcers/granulomata
- → Paranasal sinus involvement
- → Subglottic stenosis
- → Conductive hearing loss
- → **Sensorineural hearing loss**

Renal

- → Hypertension
- → Proteinuria >1+
- → **Hematuria ≥10 RBCs/HPF**
- → Serum creatinine 125-249 µmol/L
- → Serum creatinine 250-499 µmol/L
- → **Serum creatinine ≥500 µmol/L**
- → **Rise in serum creatinine >30% or fall in creatinine clearance >25%**

Chest

- → Wheeze
- → Nodules or cavities
- → Pleural effusion / pleurisy
- → Infiltrate
- → Endobronchial involvement
- → **Massive hemoptysis/alveolar hemorrhage**
- → **Respiratory failure**

Mucous membranes/Eyes

- → Mouth ulcers
- → Genital ulcers
- → Adnexal inflammation
- → Significant proptosis
- → Scleritis/Episcleritis
- → Conjunctivitis/Blepharitis/Keratitis
- → Blurred vision
- → Sudden visual loss
- → Uveitis
- → **Retinal changes (vasculitis/thrombosis/exudate/hemorrhage)**

General

- → Myalgia
- → Arthralgia / arthritis
- → Fever ≥100.4° F
- → Weight loss ≥2 kg

BVAS, Birmingham Vasculitis Activity Score; GPA, granulomatosis with polyangiitis; HPF, high-power field; MPA, microscopic polyangiitis; RBC, red blood count.

References: 1. Kermani TA, Cuthbertson D, Carette S, et al. *J Rheumatol*. 2016;43(6):1078-1084. **2.** Merkel PA, Aydin SZ, Boers M, et al. *J Rheumatol*. 2011;38(7):1480-1486. **3.** Data on file, Amgen Inc. **4.** Mukhtyar C, Lee R, Brown D, et al. *Ann Rheum Dis*. 2009;68(12):1827-1832.

TAVNEOS® is the first and only oral targeted therapy designed for patients with severe active GPA and MPA[1,29]

The recommended dose of TAVNEOS® is 30 mg (three 10 mg capsules) **twice daily**, with food[1]

Advise patients that TAVNEOS® capsules should not be crushed, chewed, or opened[1]

If a dose is missed, instruct the patient to wait until the usual scheduled time to take the next regular dose. Instruct the patient not to double the next dose[1]

Reduce the dosage of TAVNEOS® to 30 mg once daily when used concomitantly with strong CYP3A4 inhibitors[1]

Now TAVNEOS® patients have the comprehensive support of AMGEN behind them

Visit TAVNEOS® Connect and download the start form

TAVNEOS® connect

→ **For any questions** throughout the process, please contact the TAVNEOS® Connect team at 1-833-TAVNEOS (833-828-6367) Option 2, M-F, 8 AM-8 PM ET

→ **If requesting Quick Start,** fax completed start form, including prescription, to the TAVNEOS® Connect Hub, 1-833-200-7366
- Pay close attention to highlighted areas to ensure complete referral submission

To learn more about TAVNEOS® visit TAVNEOSPRO.com

As an adjunctive therapy, TAVNEOS® can be initiated with or added to standard therapy for severe active GPA and MPA[1,2]

IMPORTANT SAFETY INFORMATION (CONT'D)

DRUG INTERACTIONS

Avoid coadministration of TAVNEOS with strong and moderate CYP3A4 enzyme inducers. Reduce TAVNEOS dose when coadministered with strong CYP3A4 enzyme inhibitors to 30 mg once daily. Monitor for adverse reactions and consider dose reduction of certain sensitive CYP3A4 substrates.

TAVNEOS is available as a 10 mg capsule. To report a suspected adverse event, call 1-833-828-6367. You may report to the FDA directly by visiting www.fda.gov/medwatch or calling 1-800-332-1088.

CYP3A4, cytochrome P450 3A4.

References: 1. TAVNEOS [package insert]. Cincinnati, OH: Amgen Inc. **2.** Chung SA, Langford CA, Maz M, et al. *Arthritis Rheumatol*. 2021;73(8):1366-1383. **3.** Data on file, Amgen; [1]; 2023. **4.** Lamprecht P, Kerstein A, Klapa S, et al. *Front Immunol*. 2018;9:680. **5.** Tekin MI, Özdal MPC. *Acta Medica*. 2021;52(4):257-263. **6.** Data on file, Amgen; [2]; 2023. **7.** Berden A, Göçeroğlu A, Jayne D, at al. *BMJ*. 2012;344:e26. **8.** Abdel-Halim M, Mahmoud A, Ragab G. *Vessel Plus*. 2022;6(8):1-14. **9.** Padoan R, Campaniello D, Felicetti M, et al. *Vessel Plus*. 2021;5(41):1-18. **10.** Yates M, Watts R. *Clin Med*. 2017;17(1)60-64. **11.** Kronbichler A, Leierer J, Gauckler P, et al. *Rheumatology*. 2020;59:iii79-iii83. **12.** Ledó N, Pethö AG. *BMC Gastroenterol*. 2021;21(158):1-7. **13.** Wludarczyk A, Szczeklik W. *Ex Rev Neuro*. 2016;16(8):861-863. **14.** Koike H, Nishi R, Ohyama K, et al. *Neurol Ther*. 2022;11:21-38. **15.** Kitching AR, Anders HJ, Basu N. *Nat Rev Dis Primers*. 2020;6(1):71. **16.** Hunter RW, Welsh N, Farrah TE, et al. *BMJ*. 2020;369:m1070. **17.** Jariwala MP, Laxer RM. *Front Pediatr*. 2018;6:226. **18.** Geetha D, Jefferson JA. *Am J Kidney Dis*. 2019;75(1):124-137. **19.** Salama AD. *Kidney Int Rep*. 2020;5(1):7-12. **20.** Hellmich B, Sanchez-Alamo B, Schirmer JH, et al. *Ann Rheum Dis*. 2023; 2023 Mar 16;ard-2022-223764. doi: 10.1136/ard-2022-223764. **21.** Al-Hussain T, Hussein MH, Conca W, et al. *Adv Anat Pathol*. 2017;24(4):226-234. **22.** Syed R, Rehman A, Valecha G, et al. *Biomed Res Int*. 2015;2015:402826. doi: 10.1155/2015/402826 **23.** Macarie SS, Kadar A. *Rom J Ophthalmol*. 2020;64(1):3-7. **24.** Palmucci S, Inì C, Cosentino S, et al. *Diagnostics (Basel)*. 2021; 11(12):2318. doi: 10.3390/diagnostics11122318 **25.** Lionaki S, Skalioti C, Marinaki S, and Boletus JN. Pauci-Immune Vasculitides with Kidney Involvement. In: Mohammed RHA (ed). *Vasculitis in Practice: An Update on Special Situations – Clinical and Therapeutic Considerations*. Hamilton, New Jersey: InTech Open; 2018;chap 2. **26.** Yang J, Li M. *BMJ* 2022;376:e065658 **27.** Data on file, Amgen; [3] 2022. **28.** Jayne DRW, Merkel PA, Schall TJ, Bekker P; ADVOCATE Study Group. *N Engl J Med*. 2021;384(7):599-609. **29.** Roccatello D, Fenoglio R, Oddone V, et al. *Kidney Blood Press Res*. 2022;47(8):506-513.

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