New Drug Fact Blast

Clinical Services

Drug/Manufacturer:	**Tavneos™ (avacopan) [ChemoCentryx, Inc.]**
Dosage Formulations:	10 mg capsules
FDA Approval Date: **FDB File Date:**	FDA: October 7, 2021 FDB: October 17, 2021
Indication:	Tavneos is indicated as 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.

Mechanism of Action:	• Tavneos is a complement 5a receptor (C5aR) antagonist that inhibits the interaction between C5aR and the anaphylatoxin C5a.
	• Tavneos blocks C5a-mediated neutrophil activation and migration.
	  ○ Activation of the alternative complement pathway is believed to play a role in the pathogenesis for ANCA-associated vasculitis through terminal C5a production.
	  ○ C5a primes and activates neutrophils, which then release C5a when stimulated by inflammatory cytokines such as tumor necrosis factor (TNF) alpha.
	  ○ When activated by C5a, the C5aR becomes a potent neutrophil chemoattractant and agonist, increasing neutrophil adhesion, inducing neutrophil degranulation, and producing reactive oxygen intermediates. C5aR activation also slows the neutrophils' ability to transverse small blood vessels, particularly in the presence of ANCA, by decreasing neutrophil deformability.
	  ○ C5a also activates vascular endothelial cells, promoting their retraction and increased vascular permeability.
	• Despite what is known above, the precise mechanism by which Tavneos exerts a therapeutic effect in patients with ANCA-associated vasculitis has not been definitively established.

Dose/ Administration:	• Tavneos is dosed 30 mg (3 capsules) twice daily with food • Reduce dose to 30 mg once daily when used concomitantly with strong CYP3A4 inhibitors • Capsules should not be crushed, chewed, or opened, but swallowed whole. • If a dose is missed, the patient should wait until the next usual scheduled time to take the next dose. Do not double the dose.
Disease State Clinical Highlights:	• ANCA-associated vasculitis (AAV) refers to a group of autoimmune disorders characterized by destruction and inflammation of small blood vessels; approximately 75% of patients have renal involvement (rapidly progressing glomerulonephritis). Diagnosis is frequently delayed as symptoms are not specific and multiple organ systems can be affected. • AAV is caused by antibodies called ANCAs (anti-neutrophil cytoplasmic autoantibodies) that target and attack neutrophils. When attached to neutrophils, ANCAs cause the neutrophil to attack small blood vessels in the body. There are 2 primary autoantibodies that can be involved in AAV: proteinase 3 (PR3)-ANCA and myeloperoxidase (MPO)-ANCA. These antibodies can be detected with an indirect immunofluorescence (IIF) utilizing alcohol-fixed buffy coat leukocytes or immunoassays such as enzyme-linked immunosorbent assay (ELISA). IIF is not antigen-specific, so use of immunoassays for screening is currently recommended. However, a small percentage of patients will not test positive for either autoantibody type; this is called "ANCA-negative" autoimmune vasculitis.

- Renal involvement in AAV is common. If renal vasculitis is suspected, a kidney biopsy is preferred when possible to confirm diagnosis; however, patients who are positive for ANCA should begin immunosuppressive therapy immediately while waiting for a biopsy. Despite a high rate of disease remission in AAV with therapy, the rate of end stage renal disease (ESRD) is around 8% at 6 months.
- As small blood vessels are present throughout the body, AAV can cause a variety of symptoms. Clinical symptoms and microscopic findings have been used to group AAV into 3 subtypes based on the organs involved, predominant autoantibody, rate of relapse, and clinical outcome:
  - **Microscopic polyangiitis (MPA):** Patients usually experience a range of symptoms such as kidney inflammation, skin lesions, and nerve damage, depending on which areas are affected. Weight loss and fevers frequently occur. Sometimes only the kidneys are affected, called "renal-limited ANCA vasculitis". Patients with MPA are more likely to develop ESRD.
  - **Granulomatosis with polyangiitis (GPA, previously called Wegener's):** Patients can experience blood vessel damage in various tissues, typically in the lungs, kidneys, and upper respiratory tract (nose, trachea, and ears). However, the inflammation is specifically caused by granulomas that form in the vasculature. GPA is the most common disease type.
  - **Eosinophilic granulomatosis with polyangiitis (EGPA, previously called Churg-Strauss):** This type of AAV is typically limited to the lungs and gastrointestinal tract, although other organs, like the heart and kidneys, may be affected. It is caused by granulomas primarily made up of eosinophils. Patients may experience asthma-like symptoms for many years before other symptoms of vasculitis appear. Only 40% of patients with EGPA produce detectable ANCA. Tavneos is not indicated for use in EGPA. Nucala® is currently the only FDA-approved agent for EGPA.

	MPA	GPA	EGPA
Incidence per million person-years	1.5 - 16	1.9 - 13	0.8 - 4
ANCA-Positivity	~ 90%	~ 90%	~ 40%
PR3-ANCA	~ 25%	~ 75%	< 10%
MPO-ANCA	~ 60%	~ 20%	30-40%
Predominant Organ Involvement	Kidneys	Nose, sinuses, lungs, kidneys, joints, eyes	Lungs, upper airways, peripheral nerves, heart, skin
Rate of Renal Involvement	> 90%	~ 70 %	~ 25%
Rapidly progressive glomerulonephritis (RPGN)	~ 65%	~ 50%	< 15%

- AAV has an incidence of 200 to 400 cases per million people. An estimated 60,000 people in the United States have AAV. It is diagnosed most commonly in late middle age (50 to 60 years old).
- AAV is classified according to severity (nonsevere or severe) and extent (limited or systemic) of the disease.
  - Guidelines typically define severe disease as vasculitis with life- or organ-threatening conditions, such as alveolar hemorrhage, rapidly progressing glomerulonephritis, central nervous system vasculitis, mononeuritis multiplex, cardiac involvement, mesenteric ischemia, or limb/digit ischemia.
  - Clinical studies typically use the Birmingham Vasculitis Activity Score (BVAS) to determine disease activity and identify items representing severe disease. Presence of at least 1 major item, 3 non-major items, or 2 renal items of proteinuria and hematuria on BVAS are typically used to define severe disease.
- Prior to the use of high-dose glucocorticoids and cyclophosphamide, the mortality rate for patients with severe AAV was about 80% one year after diagnosis. The mortality rate has decreased substantially in recent years with the use of immunosuppressive

	therapies. The current estimated 5-year survival rate is 74-91% for GPA and 45-76% for MPA.
	• Infections associated with immunosuppressive therapy are now the leading cause of death for patients with severe AAV in the first year of diagnosis, accounting for 34 - 48% of the mortality reported in some studies. Glucocorticoid therapy is also frequently cited as a major contributor to impaired quality of life for patients with AAV.
	• Current treatment of GPA and MPA includes induction of remission, followed by maintenance of remission to prevent disease relapse.
	  ○ Induction of Remission
	  ▪ Severe GPA and MPA: First-line agents include cyclophosphamide or rituximab, along with glucocorticoids. Rituximab may be preferred over cyclophosphamide as it is less toxic and generally better tolerated.
	  ▪ Nonsevere GPA and MPA (no organ- or life-threatening manifestations): First-line agents include glucocorticoids in combination with either methotrexate or mycophenolate mofetil.
	  ▪ Therapy is initiated upon initial diagnosis or relapse of disease
	  ▪ Duration of induction is usually 3-6 months
	  ▪ Goals of therapy: preventing mortality, achieving clinical remission, and limiting permanent organ damage
	  ○ Maintenance of Remission
	  ▪ Rituximab is first-line, typically given for 18 months after remission. However, in patients with a higher risk of relapse (GPA, previous history of relapse, or PR3-ANCA positive), rituximab should be continued for 4 years after remission.
	  ▪ Azathioprine and methotrexate may be used if rituximab is unavailable or contraindicated
	  ▪ Leflunomide and mycophenolate mofetil may be used if rituximab, azathioprine, and methotrexate are contraindicated or not tolerated
	  ▪ Low-dose prednisone therapy in maintenance of remission is currently being studied

Drug Clinical Highlights:	• Tavneos is the first FDA-approved, orally administered inhibitor of the complement C5a receptor and represents the first new drug for AAV in the past decade.
	• Contraindications: serious hypersensitivity to avacopan or any of the excipients
	• Warnings and Precautions:
	  ○ Hepatoxicity
	  ▪ A high incidence of transaminase elevations and hepatobiliary events, including serious and life-threatening events, occurred in clinical trials
	  ▪ Obtain liver function tests (serum alanine aminotransferase [ALT], aspartate aminotransferase [AST], alkaline phosphatase, and total bilirubin) before initiation of therapy, every 4 weeks for the first 6 months of therapy, and as clinically indicated thereafter
	  ○ Serious Hypersensitivity Reactions
	  ▪ In clinical trials, two cases of angioedema occurred, including one serious event requiring hospitalization
	  ▪ Observe for signs and symptoms of angioedema and manage accordingly
	  ○ Hepatitis B Virus (HBV) Reactivation
	  ▪ Cases of HBV reactivation, including life-threatening hepatitis B, occurred in clinical trials. Before initiating therapy, screen for HBV infection by measuring HBsAg (Hepatitis B surface antigen) and anti-HBc (Hepatitis B core antibodies).
	  ▪ Monitor patients with evidence of current or prior HBV infection for clinical and laboratory signs of hepatitis or HBV reactivation during and for six months following Tavneos therapy.
	  ▪ For patients who develop reactivation of HBV, withhold Tavneos and begin appropriate anti-infective therapy.
	  ○ Serious Infections

- Serious, including fatal, infections occurred in clinical trials. The most common were pneumonia and urinary tract infections.
- Avoid use in patients with active, serious infections, including localized infections.
- Consider the risks and benefits of therapy prior to initiation of Tavneos therapy in patients:
  - With chronic or recurrent infection
  - Who have been exposed to tuberculosis
  - With a history of serious or opportunistic infection
  - Who have resided or traveled in areas of endemic tuberculosis or endemic mycoses
  - With underlying conditions that predispose them to infection

- Drug Interactions
  - Strong and moderate CYP3A4 inducers (i.e., rifampin): avoid use
  - Strong CYP3A4 inhibitors (i.e., itraconazole): reduce dose to 30 mg once daily
  - Sensitive CYP3A4 substrates: monitor for adverse reactions and consider dose reduction of sensitive substrates with narrow therapeutic windows
- Adverse Reactions (≥ 5%): nausea, headache, hypertension, diarrhea, vomiting, rash, fatigue, upper abdominal pain, dizziness, blood creatinine increased, and paresthesia
- Clinical Studies
  - **CLEAR (NCT01363388)**
    - Randomized, double-blind, placebo-controlled Phase 2 study on the safety and efficacy of avacopan in subjects with AAV on background cyclophosphamide or rituximab therapy
    - Primary End Point: Proportion of subjects achieving ≥ 50% reduction in Birmingham Vasculitis Activity Score (BVAS) by Week 12 and no worsening in any body system (Vasculitis Damage Index [VDI])
      - BVAS version 3 was used to capture vasculitis disease severity. Scoring ranges from 0 to 63, with higher scores meaning more severe disease activity. BVAS is used to score conditions that are directly attributable to vasculitis within the last 3 months and refers to current disease activity.
      - VDI is used to record any condition that has occurred and lasted for at least 3 months since the start of vasculitis and refers to chronic damage whether or not it has anything to do with vasculitis. Scoring ranges from 0 to 64. VDI is a cumulative measure of damage, so the score never improves but either remains the same or gets worse. A total VDI score of > 4 significantly increases the risk of mortality at 2 years.
    - Three subjects received rescue glucocorticoids during the treatment period: 1 in the control group and 2 in the avacopan without prednisone group.
    - Lower incidence of glucocorticoid-related adverse events in the treatment groups was primarily driven by a lower incidence of psychiatric disorders and new onset or worsening diabetes.
    - At 12 weeks of follow-up, avacopan alone or with prednisone was shown to be noninferior to the control

CLEAR (NCT01363388)	Placebo BID Plus 60 mg Prednisone (n=20)	Avacopan 30mg BID Plus 20 mg Prednisone (n=22)	Avacopan 30 mg BID Without Prednisone (n=21)
BVAS Baseline			
Mean ± SEM	13.6 ± 1.4	14.3 ± 1.3	13.6 ± 1.4
BVAS Week 4			
Mean ± SEM	6.6 ± 1.2	4.9 ± 0.7	5.3 ± 1.3
% Change	-40 ± 12	-64 ± 5	-61 ± 9
P value	-	P=0.04	P=0.04
BVAS Week 12			
Mean ± SEM	5.0 ± 1.6	2.6 ± 0.7	3.6 ± 1.1
% Change	-56 ± 14	-79 ± 5	-73 ± 7
P value	-	P=0.09	P=0.09

VDI Baseline Mean ± SEM	1.2 ± 0.3	0.9 ± 0.3	0.5 ± 0.3
VDI Week 12 Mean ± SEM Change	1.8 ± 0.4 0.7 ± 0.2	1.2 ± 0.3 0.3 ± 0.1	0.8 ± 0.3 0.2 ± 0.1
Remission (BVAS 0) at week 4 sustained through week 12 no. (%) P value	1 (5%) -	3 (14%) P=0.10	6 (29%) P=0.04
Primary End Point: treatment response at week 12 no. (%) P value – noninferiority	14 (70%) -	19 (86.4%) P=0.002	17 (81%) P=0.01
Patients with adverse effect potentially related to glucocorticoids no. (%)	15 (65%)	4 (18%)	11 (50%)

SEM=Standard Error of the Mean
BID=twice daily

- **CLASSIC (NCT02222155)**
  - Randomized, double-blind, placebo-controlled Phase 2 study on safety and efficacy of 2 different dosage regimens of avacopan plus Standard of Care (SOC) vs SOC only
  - Standard of Care = combination of high-dose glucocorticoids (60 mg/day prednisone steadily tapering to 10 mg/day by week 11 and 0 mg/day by week 20) and either cyclophosphamide or rituximab
  - 3 arms:
    - Avacopan 10 mg BID for 12 weeks plus SOC (n=13)
    - Avacopan 30 mg BID for 12 weeks plus SOC (n=16)
    - Placebo BID for 12 weeks plus SOC (n=13)
  - Primary End Points:
    - Incidence of adverse events
    - Proportion of subjects achieving ≥ 50% reduction in BVAS by week 12 and no worsening in any body system (VDI) - same primary end point as the CLEAR study
  - Main findings:
    - The addition of avacopan to SOC was well tolerated, with similar rates of adverse events across all arms
    - The mean percentage decrease in BVAS from baseline was also similar across all groups
    - Cumulative vasculitis damage, as measured by VDI, appeared to be lower in both avacopan groups
    - There may be a potential clinical benefit with the addition of avacopan 30 mg to SOC. Early disease remission, renal response in patients with hematuria and albuminuria, renal function (estimated glomerular filtration rate [eGFR]), and patient quality of life assessments were all higher in the avacopan 30 mg arm.

CLASSIC (NCT02222155)	**Placebo BID Plus SOC (n=13)**	**Avacopan 10mg BID Plus SOC (n=13)**	**Avacopan 30mg BID Plus SOC (n=16)**
BVAS Baseline Mean (SD)	15.0 (4.5)	15.8 (2.5)	15.1 (1.6)
VDI Baseline Mean (SD)	1.2 (1.8)	0.8 (2.5)	0.6 (1.2)
Any Adverse Event occurring in > 10% of patients no. (%)	13 (100)	11(85)	15 (94)
Intent to Treat Population	**n=13**	**n=12**	**n=15**

BVAS in ITT population			
Response at Week 12*, no. (%)	11 (85)	11 (92)	12 (80)
Mean decrease from baseline, %	82	96	82
Early disease remission**	2 (15)	1 (8)	3 (20)
Remission at week 12***	7 (54)	8 (67)	7 (47)
VDI in ITT population			
Day 85	1.46	1.0	0.86
Mean increase from baseline	0.31	0.09	0.14

* Defined as BVAS decrease of at least 50% from baseline and no worsening in any body system component at day 85
** Defined as BVAS = 0 at day 29 and sustained at day 85
*** Defined as BVAS = 0 at day 85

- **ADVOCATE (NCT02994927)**
  - Double-blind, active-controlled, Phase 3 trial
  - 330 patients with newly diagnosed or relapsed AAV were randomized 1:1 to one of the following groups:
    - Avacopan group (N=166): patients received 30 mg twice daily for 52 weeks plus prednisone-matching placebo for 20 weeks
    - Prednisone group (N=164): patients received avacopan-matched placebo twice daily for 52 weeks plus prednisone (tapered from 60 mg/day to 0 mg/day over 20 weeks)
  - All patients received standard immunosuppressive regimens of IV cyclophosphamide (31%), oral cyclophosphamide (4%), or IV rituximab (65%) with follow up therapy of oral azathioprine or mycophenolate mofetil.
  - Glucocorticoid therapy during the screening period had to be tapered to 20 mg or less of prednisone equivalent before beginning the trial, then further tapered to discontinuation by the end of week 4.
  - Patients with worsening disease that involved a major item in the BVAS could be treated with rescue glucocorticoid therapy.
  - Patient Demographics:
    - Mean patient age = 60.9 years
    - GPA = 54.8%, MPA = 45.2%
    - PR3-ANCA = 43.0%, MPO-ANCA = 57.0%
    - Mean baseline BVAS = 16.2
    - Disease manifestations:
      - Renal component = 81.2%
      - General component = 68.2%
      - Ear/nose/throat component = 43.6%
      - Chest component = 43.0%
  - Primary Efficacy End Points
    - Clinical remission at week 26 defined as a BVAS of 0 and no receipt of glucocorticoids for 4 weeks before week 26
    - Sustained remission defined as remission at week 26 and at week 52 with no receipt of glucocorticoids for 4 weeks before week 52
      - Patients were not considered in sustained remission if they had remission at week 26 but a relapse thereafter
  - Key Secondary End Points
    - Glucocorticoid-induced toxic effects according to the Glucocorticoid Toxicity Index (GTI) during the first 26 weeks as measured by the Cumulative Worsening Score (GTI-CWS) and the Aggregate Improvement Score (GTI-AIS)
      - Cumulative Worsening Score (GTI-CWS) – ranges from 0 to 410
      - Aggregate Improvement Score (GTI-AIS) – ranges from -317 to 410
      - For both scales, higher scores indicate greater severity of toxic effects
    - Change from baseline in health-related quality of life
      - 36-Item Short Form Survey (SF-36), version 2
      - EuroQol Group 5-Dimensions 5-Level Questionnaire (ED-5D-5L)

- Range 0-100 for both, with higher scores indicating better quality of life
- Change from baseline in eGFR and urinary albumin:creatinine ratio

- Study results:
  - Avacopan was noninferior, but not superior, to tapered prednisone for remission at week 26
  - Avacopan was superior to tapered prednisone for sustained remission at week 52
  - There was a greater incidence of glucocorticoid-induced toxic effects in the prednisone group
  - Positive effects of avacopan on eGFR and albuminuria were seen; this may be due to blockade in the glomeruli of the C5a-C5aR axis, arresting the potent chemoattraction and activation of neutrophils that damage the glomeruli
  - Quality of life improved in both treatment groups
- Notes:
  - Glucocorticoids were used by patients in the avacopan group. Mean total prednisone-equivalent dose of oral and IV glucocorticoids:
    - Avacopan group: 1,349 mg (4 mg per patient per day)
    - Prednisone group: 3,655 mg (12 mg per patient per day)
  - Nine patients in the avacopan group and 6 in the prednisone group experienced an abnormal liver function test. All events resolved with the withdrawal of trial and other potentially hepatotoxic medications.
  - Incidence of glucocorticoid-related adverse events (based on European League against Rheumatism criteria)
    - Avacopan group: 66.3%
    - Prednisone group: 80.5%
  - Findings on all secondary end points were not included in the final package insert

ADVOCATE (NCT02994927)	Avacopan (N=166)	Prednisone (N=164)	Difference (95% CI)
Primary End Points			
Remission at week 26, no. (%)	120 (72.3)	115 (70.1)	3.4 (-6.0 to 12.8) Noninferiority P value < 0.001 Superiority P value = 0.24
Sustained remission at week 52, no. (%)	109 (65.7)	90 (54.9)	12.5 (2.6 to 22.3) Noninferiority P value < 0.001 Superiority P value = 0.007
Secondary End Points			
GTI-CWS			
Week 13			
Patients Evaluated	160	161	
Least-squares mean	25.7 ± 3.4	36.6 ± 3.4	-11.0 (-19.7 to -2.2)
Week 26			
Patients Evaluated	154	153	
Least-squares mean	39.7 ± 3.4	56.6 ± 3.4	-16.8 (-25.6 to -8.0)
GTI-AIS			
Week 13			
Patients Evaluated	160	161	
Least-squares mean	9.9 ± 3.4	23.2 ± 3.5	-13.3 (-22.2 to -4.4)
Week 26			
Patients Evaluated	154	153	
Least-squares mean	11.2 ± 3.5	23.4 ± 3.5	-12.1 (-21.1 to -3.2)
eGFR – ml/min/1.73 m^2*			
Baseline			
Patients Evaluated	131	134	
Mean	44.6 ± 2.4	45.6 ± 2.4	

Change from baseline to week 26			
Patients Evaluated	121	127	
Least-squares mean	5.8 ± 1.0	2.9 ± 1.0	2.9 (0.1 to 5.8)
Change from baseline to week 52			
Patients Evaluated	119	125	
Least-squares mean	7.3 ± 1.0	4.1 ± 1.0	3.2 (0.3 to 6.1)
SF-36 physical component score			
Baseline			
Patients Evaluated	165	160	
Mean	39.2 ± 0.8	40.1 ± 0.8	
Change from baseline to week 26			
Patients Evaluated	153	147	
Least-squares mean	4.45 ± 0.73	1.34 ± 0.74	3.10 (1.17 to 5.03)
Change from baseline to week 52			
Patients Evaluated	147	144	
Least-squares mean	4.98 ± 0.74	2.63 ± 0.75	2.35 (0.40 to 4.31)
Score on EQ-5D-5L visual-analogue scale			
Baseline			
Patients Evaluated	166	162	
Mean	65.8 ± 1.5	63.4 ± 1.8	
Change from baseline to week 26			
Patients Evaluated	153	150	
Least-squares mean	9.1 ± 1.4	5.5 ± 1.4	3.6 (-0.1 to 7.2)
Change from baseline to week 52			
Patients Evaluated	149	146	
Least-squares mean	13.0 ± 1.4	7.1 ± 1.4	5.9 (2.3 to 9.6)
Urinary albumin:creatinine ratio **			
Baseline			
Patients Evaluated	125	128	
Geometric mean (range)	433 (20-6461)	312 (11-5367)	
Percent change from baseline to week 4			
Patients Evaluated	121	124	
Least-squares mean ± SE	-40 ± 10	0 ± 9	-40 (-53 to -22)
Percent change from baseline to week 13			
Patients Evaluated	116	121	
Least-squares mean ± SE	-55 ± 10	-49 ± 9	-12 (-32 to 13)
Percent change from baseline to week 26			
Patients Evaluated	113	118	
Least-squares mean ± SE	-63 ± 10	-70 ± 10	25 (-3 to 61)
Percent change from baseline to week 52			
Patients Evaluated	109	114	
Least-squares mean ± SE	-74 ± 10	-77 ± 10	12 (-14 to 45)

* in patients with renal disease at baseline based on the BVAS

** in patients with renal disease at baseline based on the BVAS and a urinary albumin:creatinine ratio of at least 10 at baseline. Percent changes from baseline are based on ratios of geometric means of visit over baseline.

- The FDA's Arthritis Advisory Committee reviewed avacopan on May 6, 2021. The committee voted 9 to 9 that the efficacy data support approval and 10 to 8 that the safety data support its approval. The final vote on whether the overall benefit-risk profile supported avacopan approval was 10 to 8 in favor.
  - Concerns were raised that ADVOCATE was attempting to demonstrate efficacy of both remission induction and remission maintenance, which many believed should have been split into 2 separate studies.
  - No patients received rituximab maintenance therapy in ADVOCATE; however, the indication was not approved at study design. Concerns were raised that the study no longer reflected the addition of avacopan to standard of care.
  - Concerns were raised on the potential confounding effects of the use of non-study supplied glucocorticoids in both treatment arms as well as potential differences in the cyclophosphamide and rituximab standard treatment groups.
  - Concerns were also raised about the safety of avacopan, especially with respect to liver toxicity.

Price Per Unit (WAC):

- $80.27 per capsule
- $14,448.60 per month

	• $175,791.30 per year
Therapeutic Alternatives:	• Rituxan® (rituximab) was FDA-approved for AAV in 2011, with an additional approval for maintenance therapy in AAV in 2018. • Current therapies for induction of remission utilize high-dose glucocorticoids with either cyclophosphamide or rituximab. • Rituximab is considered first-line therapy for maintenance of remission. Azathioprine and methotrexate are second-line therapies, with leflunomide and mycophenolate as third line. • Tavneos is currently only indicated for use in combination with standard therapy including glucocorticoids. Its likely place in therapy is during induction of remission to reduce the high dose of glucocorticoids typically needed to achieve remission.
Prior Authorization Approval Criteria:	**Must meet the following criteria:** <u>Initial Therapy:</u> • Prescribed by or in consultation with a rheumatologist, nephrologist, or other specialist in the treated disease state **AND** • Participant is aged 18 years or older **AND** • Documented diagnosis of GPA or MPA types AAV (ICD10 M31.30, M31.31, or M31.7) **AND** • Documentation of positive test for PR3-ANCA or MPO-ANCA **AND** • Documentation of baseline clinical criteria (e.g., LFTs, eGFR, BVAS, VDI) **AND** • Lack of severe hepatic impairment (Child Pugh C) **AND** • Participant is currently receiving or beginning standard therapy including glucocorticoids for induction of remission • Initial approval for 6 months <u>Continuation of Therapy:</u> • Continued approval for 12 months may be given following documentation of clinical benefit of therapy (e.g., decreased glucocorticoid dose, improved or sustained renal function, improved BVAS score, sustained VDI score) and demonstrated evidence of continued need in maintenance of remission while on standard therapy (e.g., rituximab, azathioprine, or methotrexate) **Additional Provider Diagnostic/Monitoring Criteria, if desired:** • Monitor LFTs every 4 weeks for the first 6 months of therapy and as clinically indicated thereafter • Screen for HBV prior to initiating therapy • Screen for signs/symptoms of infection before and during therapy
Implication to State Medicaid Program:	• LOE: 2035 • Tavneos represents ChemoCentryx's first approval in its 24-year history. Estimated peak sales of $708 million are expected by 2026. • ChemoCentryx has developed TAVNEOS Connect, a patient support program designed to assist patients who are prescribed Tavneos and has partnered with specialty pharmacies Amber Specialty Pharmacy and PANTHERx Rare. • ChemoCentryx is also studying Tavneos for the treatment of patients with C3 glomerulopathy (Phase 2, ACCOLADE, NCT03301467), hidradenitis suppurativa (Phase 2, AURORA, NCT03852472) and lupus nephritis. The FDA granted orphan drug designation for ANCA-associated vasculitis and C3G.

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