VIFOR FRESENIUS MEDICAL CARE RENAL PHARMA

CSL Vifor

This promotional leavepiece is for UK Healthcare Professionals only

TARGETING IMPROVED CONTROL
IN ANCA-ASSOCIATED VASCULITIS (GPA/MPA)

An Avacopan Vifor▼-based regimen was non-inferior (p<0.001) but not superior vs GC-based regimen with respect to remission at Week 26, and superior with respect to sustained remission at Week 52 (p=0.007)[1,2]

Recommended for use by NICE*

A first-in-class treatment for GPA/MPA which selectively targets C5aR1[1,3,4]

*Avacopan Vifor, with a cyclophosphamide or rituximab regimen, is recommended by NICE, within its marketing authorisation, as an option for treating severe, active granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) in adults[1,5]

Adverse events should be reported. Reporting forms and information for the United Kingdom can be found at https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Vifor Fresenius Medical Care Renal Pharma, care of Vifor Pharma Ltd. Tel: +44 1276 853633. E-mail: MedicalInfo_UK@viforpharma.com

To access the prescribing information click here or scan the QR code overleaf

Avacopan Vifor ▼

UK-AVA-2500201 I Date of preparation: September 2025

AAV (GPA/MPA) is a rare, relapsing disease that can cause irreversible damage to vital organs[6–10]

AAV can impact a variety of organs, including the eyes, nose, ears and throat, skin, lungs and upper airways, the nervous system and the kidneys.[6–8]

Despite treatment, many AAV patients struggle to control their disease, and do not achieve or sustain remission[11,12*]

>1 in 3 patients are unable to sustain remission without continued use of GCs at Month 6 (n=82/197)[11,12†]

>1 in 2 patients are unable to sustain remission without continued use of GCs at Month 12 (n=112/197)[12†]

Risk of Relapse persists, further exacerbating organ damage[13]

A **7-year follow-up** in GPA/MPA patients showed that **every relapse is associated with an increase in damage**:[13]

44.6% of patients had relapsed (n=132/296)

Of patients that relapsed, **89.4%** had 1–3 relapses (n=118/132)

10.6% had ≥4 relapses (n=14/132)

~1 in 3 patients with severe damage‡

>2 in 3 patients with severe damage‡

Established therapies may add to the burden of disease[13–17]

Treatment of AAV has relied on non-specific immunosuppressants alongside high-dose/ or long-term GC, and may add to the burden of disease[9,13–18]

67% of GPA/MPA patients (n=198/296) experienced **potentially treatment-related damage 7 years post diagnosis[13]**

59% of **mortality** (n=33/56) in the first year after AAV diagnosis was due to treatment-related adverse events, **with half of mortality** (n=28/56) **due to infection[14]**

Patients with AAV may have reduced QoL[19–21]

Compared to population controls, patients receiving treatment for AAV have:[21]

7x Higher likelyhood of **poor physical QoL** (OR, 7.0; 95% CI, 4.4 to 11.1) (N=410)

2.5x Higher likelyhood of **poor mental QoL** (OR, 2.5; 95% CI, 1.7 to 3.6) (N=410)

*Study definition of full remission was BVAS 0 without continued use of GCs[11,12]
†Based on the RAVE no-inferiority trial of rituximab (RTX) vs cyclophosphamide (CYC) in GPA/MPA patients (N=197). In the six-month treatment period, patients received either RTX + placebo CYC + GC tapering (n=99) or CYC/AZA + placebo RTX + GC tapering (n=98). In the 12-month extension period, the RTX group in sustained remission received no further active treatment (n=99) and CYC/AZA was continued to Month 18 (n=98)[11,12]
‡35.9% of patients with 1–3 relapses and 71.4% of patients with ≥4 relapses experienced ≥5 items of damage at an average of 7.3 years from diagnosis[13]

ADVOCATE study design: evaluating the ability of an Avacopan Vifor-based regimen to achieve and sustain remission[2,22*]

ADVOCATE is an international, multicentre, active-comparator, randomised, double-blind, double-dummy, controlled, pivotal phase 3 trial of 52 weeks duration[2]

Avacopan Vifor-based regimen (n=166)

GC-based regimen (n=164)

SCREENING AND RANDOMISATION

GC treatment during the screening period had to be tapered to 20 mg or less of prednisone equivalent before the patient began the trial, and this open-label GC treatment was further tapered to discontinuation by the end of Week 4 of the trial

Avacopan Vifor, 30 mg twice daily
Placebo prednisone taper over 20 weeks

Prednisone, 60 mg/day with tapering to zero over 20 weeks
Placebo Avacopan Vifor, twice daily

Both study arms received

RTX
CYC
AZA

Non-study GCs supplied for: i) AAV worsening; ii) non-AAV related reasons

0 — 26 Weeks — 52

ADVOCATE phase 3 endpoints

PRIMARY ENDPOINTS[2]

% of patients in clinical remission (BVAS of 0 and no GC use in previous 4 weeks) at Week 26
% of patients in sustained remission at Week 52, defined as clinical remission at Week 26 through to Week 52

SECONDARY ENDPOINTS[2]

Change in glucocorticoid-induced toxicity as measured by change from baseline over the first 26 weeks in the GTI
Early remission, defined as BVAS 0 at Week 4
Change from baseline over 52 weeks in health-related QoL as measured by the domains and component scores of the SF-36 v2 and EQ-5D-5L VAS and index
Proportion of patients and time to experiencing a relapse†
In patients with renal disease at baseline (based in the BVAS renal component), the % change in eGFR, UACR and MCP-1:creatinine ratio from baseline over 52 weeks
Change in the VDI from baseline over 52 weeks

There was no pre-specified plan for adjustment of confidence intervals for multiplicity of the secondary endpoints; point estimates and 95% confidence intervals only are presented, and no definite conclusions can be drawn from these data[2]

*All the patients received one of three regimens: CYC IV at a dose of 15 mg/kg of body weight up to 1.2 g on Day 1 and at Weeks 2, 4, 7, 10, and 13; CYC orally at a dose of 2 mg/kg up to 200 mg/day for 14 weeks; or IV RTX at a dose of 375 mg/m² body-surface area/week for 4 weeks. From Week 15 onward, CYC was followed by oral AZA at a target dose of 2 mg/kg/day. No RTX was given beyond the first 4 weeks[2]
†Relapse was defined as occurrence of at least one major item in the BVAS, or three or more minor items in the BVAS, or one or two minor items in the BVAS at two consecutive visits, after having previously achieved remission at Week 26 (BVAS 0 and having received no GCs for treatment of vasculitis for 4 weeks)[2,22]

Target improved disease control vs GC-based regimen

PRIMARY ENDPOINT

An Avacopan Vifor-based regimen was non-inferior but not superior vs GC-based regimen with respect to remission at Week 26 and superior with respect to sustained remission at Week 52[2]

Week 26: non-inferiority in achieving clinical remission

72.3% **Avacopan Vifor-based regimen** (n=120/166) vs **70.1%** **GC-based regimen** (n=115/164)

P<0.001 for non-inferiority (Difference, 3.4, 95% CI, -6 to 12.8)

Week 52: superior sustained clinical remission

65.7% **Avacopan Vifor-based regimen** (n=109/166) vs **54.9%** **GC-based regimen** (n=90/164)

P<0.007 for superiority (Difference, 12.5, 95% CI, 2.6 to 22.3)

SECONDARY ENDPOINT

Lower absolute risk of relapse over 52 weeks with an Avacopan Vifor-based regimen vs a GC-based regimen[2*]

10.1% of Avacopan Vifor-based regimen patients (n=16/158) vs **21%** of GC-based regimen patients (n=33/157)

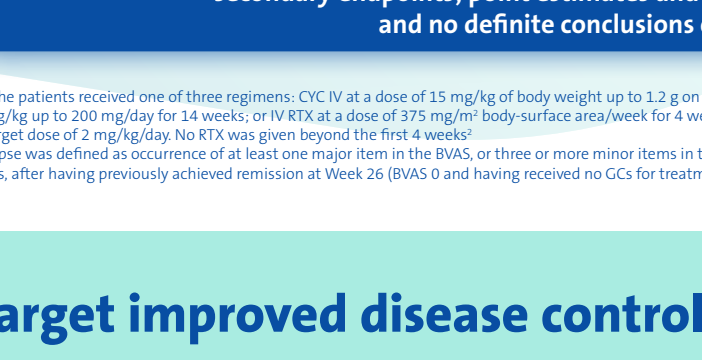
2x **as many patients relapsed in the GC-based** regimen vs the Avacopan Vifor-based regimen

SECONDARY ENDPOINT

Avacopan Vifor-based regimen demonstrated a larger reduction in GC-toxicity vs a GC-based regimen[2*]

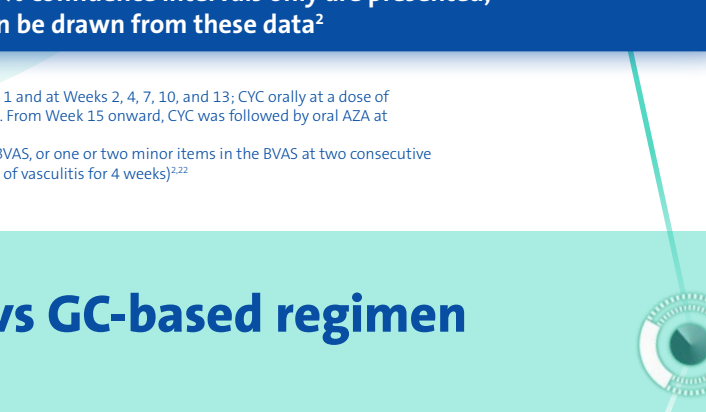
16.8 reduction in GTI Cumulative Worsening Score (CWS) in Avacopan Vifor-based regimen vs GC-based regimen at Week 26[2]

12.1 reduction in GTI Aggregate Improvement Score (AIS) in Avacopan Vifor-based regimen vs GC-based regimen at Week 26[2]



Difference at Week 13: -11.0 (95% CI, -19.7 to -2.2)
Difference at Week 26: -16.8 (95% CI, -25.6 to -8.0)

Graph adapted from Jayne D, et al. *N Engl J Med* 2021



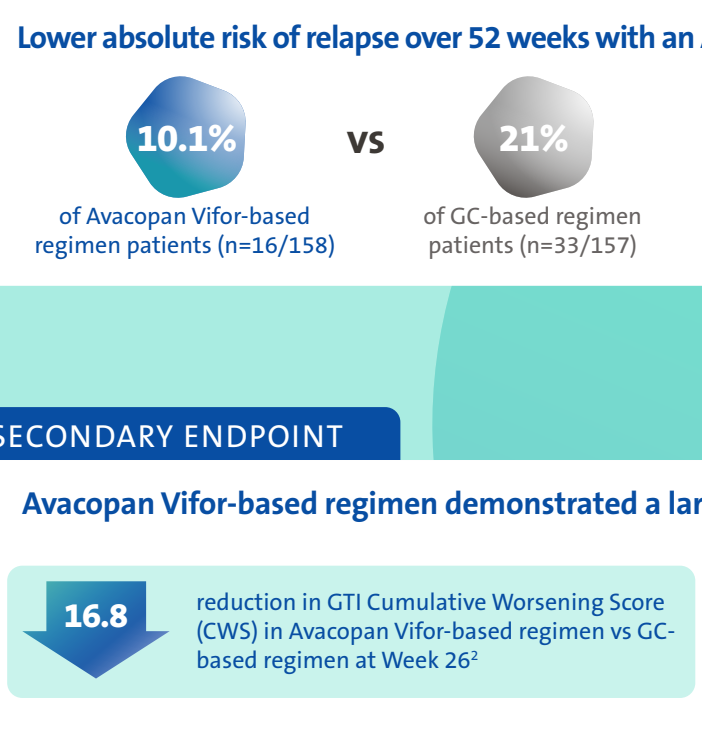
Difference at Week 13: -13.3 (95% CI, -22.2 to -4.4)
Difference at Week 26: -12.1 (95% CI, -21.1 to -3.2)

Graph adapted from Jayne D, et al. *N Engl J Med* 2021

SECONDARY ENDPOINT

Avacopan Vifor-based regimen demonstrated numerical improvements in physical and mental QoL vs GC-based regimen at both Week 26 and 52[2,22*]

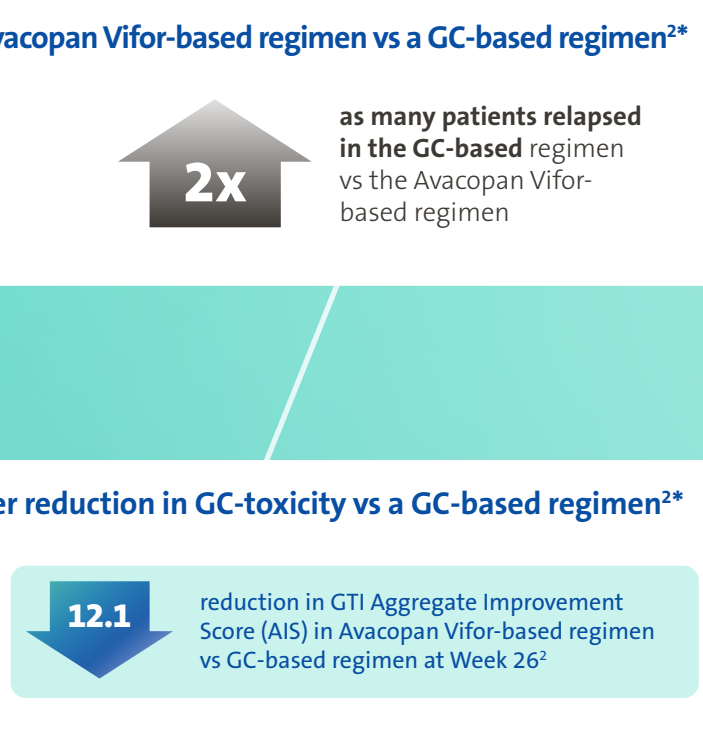
Physical component score[2]



Difference at Week 26: 3.10 (95% CI, 1.17 to 5.03)
Difference at Week 52: 2.35 (95% CI, 0.40 to 4.31)

Graph adapted from Jayne D, et al. *N Engl J Med* 2021

Mental component score[22]



Difference at Week 26: 1.58 (95% CI, –0.61 to 3.77)
Difference at Week 52: 1.70 (95% CI, –0.52 to 3.92)

Graph adapted from Jayne D, et al. *N Engl J Med* 2021 [Suppl Appendix]

Target improved disease control with Avacopan Vifor, a first-in-class targeted treatment for GPA/MPA[1,2,4]

*There was no pre-specified plan for adjustment of confidence intervals for multiplicity of the secondary end points; point estimates and 95% confidence intervals only are presented, and no definite conclusions can be drawn from these data[2]

Avacopan Vifor

Inclusion and Exclusion Criteria[22]

INCLUSION CRITERIA

- ≥12 years old*
- Newly-diagnosed or relapsing GPA or MPA according to Chapel Hill Consensus Conference definitions
- Indicated for RTX or CYC treatment
- Either MPO+ or PR3+
- Estimated eGFR of ≥15 mL/min/1.73 m^2
- At least one major or three non-major items, or at least two renal items of haematuria and proteinuria on BVAS

EXCLUSION CRITERIA

- Alveolar haemorrhage requiring invasive pulmonary ventilation anticipated to last beyond screening
- Any other multisystem autoimmune disease
- Coagulopathy or bleeding disorder
- Required dialysis or plasma exchange within 12 weeks prior to screening
- A kidney transplant
- Had received CYC within 12 weeks prior to screening, RTX within 12 months prior to screening (or 6 months with B cell reconstitution, CD19 count > $0.01x10^9$/L), cumulative dose of IV GCs > 3 g within 4 weeks, or oral GCs of >10 mg per day prednisone (or equivalent) for >6 weeks continuously prior to screening

*Adult GPA/MPA patients participated in this study. For additional details, visit clinicaltrials.gov, study code: NCT02994927

Safety Profile[1]

Most common adverse reactions:[1]

Nausea 23.5%	**Headache** 20.5%	**Decreased white blood cell count** 18.7%	**Nasopharyngitis** 15.1%
Diarrhoea 15.1%	**Vomiting** 15.1%	**Upper respiratory tract infection** 14.5%	

The most common serious adverse reactions are **liver function abnormalities (5.4%)** and **pneumonia (4.8%)[1]**

In the post-marketing setting, **drug-induced liver injury** and **vanishing bile duct syndrome** (VBDS), including cases with fatal outcome, have been reported (frequency unknown)[1]

Avacopan Vifor is a substrate of CYP3A4. The use of strong CYP3A4 enzyme inducers with Avacopan Vifor is to be avoided. Strong CYP3A4 enzyme inhibitors should be used with caution in patients who are being treated with Avacopan Vifor[1]

Grapefruit and grapefruit juice can increase the concentration of Avacopan Vifor; therefore, grapefruit and grapefruit juice are to be avoided in patients treated with Avacopan Vifor[1]

Avacopan Vifor is contraindicated for use in patients hypersensitive to the active substance or any of the excipients[1]

See the SmPC for further details on adverse events and interactions

Avacopan Vifor is taken as a fixed oral dose with required monitoring[1]

Avacopan Vifor is taken as part of a treatment regimen in combination with immunosuppressants (RTX or CYC followed by oral AZA or mycophenolate mofetil, and glucocorticoids as clinically indicated)[1]

30 MG Avacopan Vifor
(3 X 10 MG CAPSULES)

TAKEN TWICE DAILY

TAKEN WITH FOOD AND SWALLOWED WHOLE WITH WATER
(MUST NOT BE CRUSHED, CHEWED, OR OPENED)

If a patient misses a dose, the missed dose is to be taken as soon as possible, unless within three hours of the next scheduled dose. If within three hours, then the missed dose is not to be taken[1]

Patients must be monitored for:

Hepatic transaminases and total bilirubin at least every 4 weeks after the start of therapy for the first 6 months of treatment, and as clinically indicated thereafter[1]*

White blood cell count as clinically indicated and as part of the routine follow-up of the patient's underlying condition[1†]

*Treatment must be re-assessed clinically and temporarily stopped if ALT or AST is >3x ULN. Treatment must be temporarily stopped if ALT or AST is >5× ULN. Please consult Summary of Product Characteristics for information about permanent discontinuation[1]

†Treatment must be temporarily stopped if a patient develops leukopenia (WBC count <$2×10^9$/L) or neutropenia (neutrophils <$1×10^9$/L) or lymphopenia (lymphocytes <$0.2×10^9$/L)[1]

Special Warnings and Precautions[1]

CONTRAINDICATIONS: Hypersensitivity to the active substance or to any of the excipients

- Hepatic transaminases, total bilirubin and WBC count must be obtained prior to initiation of therapy and monitored as clinically indicated and as part of the routine follow-up of the patients underlying condition
- Treatment with Avacopan Vifor must not be initiated if WBC count is less than 3500/µL, or neutrophil count less than 1500/µL, or lymphocyte count less than 500/µL
- The safety of immunisation with live vaccines, following Avacopan Vifor therapy has not been studied. Administer vaccinations preferably prior to initiation of treatment with Avacopan Vifor or during quiescent phase of the disease
- Patients must be assessed for any serious infection, treatment must be temporarily stopped if a patient has an active, serious infection (i.e. requiring hospitalisation or prolonged hospitalisation)
- Caution must be taken when treating patients with a history of hepatitis B, hepatitis C, HIV or tuberculosis
- Monitor patients treated for ANCA-associated vasculitis according to standard practice for clinical signs and symptoms of *Neisseria* infections
- *Pneumocystis jirovecii* pneumonia prophylaxis is recommended for adult GPA/MPA patients during Avacopan Vifor treatment, according to local clinical practice guidelines
- Angioedema has been reported in patients receiving Avacopan Vifor and Avacopan Vifor must be withheld in cases of angioedema
- Avacopan Vifor is not recommended for use during pregnancy or in women of childbearing potential not using contraception.
- Patients with GPA or MPA are at risk of cardiac disorders such as myocardial infarction, cardiac failure, and cardiac vasculitis. Serious adverse events of cardiac disorder have been reported in patients treated with Avacopan Vifor
- Immunomodulatory medicinal products may increase the risk for malignancies. The clinical data are currently limited
- Avacopan Vifor contains macrogolglycerol hydroxystearate, which may cause stomach upset and diarrhoea

Scan the QR code or click here to view the Avacopan Vifor prescribing information and adverse event reporting

References and Abbreviations

AAV, ANCA-associated vasculitis; **AIS,** aggregate improvement score; **ALP,** alkaline phosphatase; **ALT,** alanine aminotransferase; **ANCA,** anti-neutrophil cytoplasmic antibody; **AST,** aspartate aminotransferase; **AZA,** azathioprine; **BVAS,** Birmingham Vasculitis Activity Score; **C5aR1,** complement component 5a receptor 1; **CD19,** cluster of differentiation 19; **CI,** confidence interval; **CWS,** Cumulative Worsening Score; **CYC,** cyclophosphamide; **CYP3A4,** Cytochrome P450 3A4; **eGFR,** estimated glomerular filtration rate; **EQ-5D-5L,** EuroQoL 5-dimension 5-level; **GC,** glucocorticoids; **GPA,** granulomatosis with polyangiitis; **GTI,** Glucocorticoid toxicity index; **HIV,** Human Immunodeficiency Virus; **IV,** intravenous; **MCP-1,** monocyte chemoattractant protein-1; **MPA,** microscopic polyangiitis; **MPO,** myeloperoxidase; **NICE,** National Institute for Health and Care Research; **OR,** odds ratio; **PR3,** proteinase 3; **QoL,** quality of life; **RAVE,** Ritximab in ANCA-Associated Vasculitis; **RTX,** rituximab; **SF-36,** Medical Outcomes Survey Short-Form 36; **SmPC,** Summary of Product Characteristics; **UACR,** urine albumin-to-creatinine ratio; **ULN,** upper limit of normal; **VAS,** Visual Analogue Scale; **VBDS,** vanishing bile duct syndrome; **VDI,** Vasculitis Damage Index; **WBC,** white blood cell.

1. Avacopan Vifor UK SmPC. **2.** Jayne D, et al. *N Engl J Med* 2021;384(7):599–609. **3.** Bekker P, et al. *PLoS One* 2016;11(10):e0164646. **4.** European Medicines Agency (2021). First-in-class medicine recommended for treatment of rare blood vessel inflammation. Available at: https://www.ema.europa.eu/en/news/first-class-medicine-recommended-treatment-rare-blood-vessel-inflammation. Date accessed: September 2025. **5.** NICE (2022). Avacopan for treating severe active granulomatosis with polyangiitis or microscopic polyangiitis. Available at: https://www.nice.org.uk/guidance/TA825. Date accessed: September 2025. **6.** Wallace ZS, Miloslavsky EM. *BMJ* 2020;368:m421. **7.** Pagnoux C. *Eur J Rheumatol* 2016;3(3):122–33. **8.** Al Hussain T, et al. *Adv Anat Pathol* 2017;24(4):226–34. **9.** Yates M, et al. *Ann Rheum Dis* 2016;75(9):1583–94. **10**. European Medicines Agency (2018). Development of medicines for rare diseases. Available at: https://www.ema.europa.eu/en/news/development-medicines-rare-diseases. Date accessed: September 2025. **11.** Stone JH, et al. *N Engl J Med* 2010;363(3):221–32. **12.** Specks U, et al. *N Engl J Med* 2013;369(5):417–27. **13.** Robson J, et al. *Rheumatology (Oxford)* 2015;54(3):471–81. **14.** Little MA, et al. *Ann Rheum Dis* 2010;69(6):1036–43. **15.** Hoffman GS, et al. *Ann Intern Med* 1992;116(6):488–98. **16.** Wei L, et al. *Ann Intern Med* 2004;141(10):764–70. **17.** van Staa TP, et al. *J Bone Miner Res* 2000;15(6):993–1000. **18.** Lamprecht P, et al. *EMJ Rheumatol* 2021;8(1):36–42. **19.** Walsh M, et al. *Arthritis Care Res* (Hoboken) 2011;63(7):1055–61. **20.** Robson JC, et al. *Rheumatol Int* 2018;38(4):675–82. **21.** Basu N, et al. *Ann Rheum Dis* 2014;73(1):207–11. **22.** Jayne D, et al. *N Engl J Med* 2021;384(7):599–609. [Supp Appendix].