AVACOPAN IN ANCA VASCULITIS

TARGET AUDIENCE	Secondary Care
PATIENT GROUP	ANCA vasculitis patients

Clinical Guidelines Summary

Avacopan is available for use in Scotland in combination with rituximab or cyclophosphamide based regimens for treatment of ANCA vasculitis.

It is a C5a complement inhibitor and may have a significant role in reducing harms associated with steroid therapy in this condition.

Its use should be directed by specialist services.

AVACOPAN IN ANCA VASCULITIS

Avacopan is a complement C5a receptor inhibitor. It may be used as an adjunctive agent with standard induction therapy in treatment of ANCA associated vasculitis.

Avacopan likely offers a safe steroid avoidance strategy in non-severe disease, and when combined with PEXIVAS low dose oral steroid in severe disease is likely to offer improved outcomes with scope for earlier steroid withdrawal.

Avacopan has been accepted for use in Scotland (SMC 2578) in combination with a rituximab or cyclophosphamide regimen, for the treatment of adult patients with severe, active granulomatosis with polyangiitis (GPA) or microscopic polyangiits (MPA).

The SMC approval is based on results from the ADVOCATE clinical trial. Here, 331 newly diagnosed AAV patients were randomised to receive Avacopan 30mg twice daily or prednisolone on a reducing regimen. All patients received standard induction treatment with cyclophosphamide (followed by azathioprine) or rituximab. At 26 weeks, the rates of disease remission were similar between the two groups. At 52 weeks, sustained remission was higher in the Avacopan group. Both regimens had similar rates of serious adverse events.
The ADVOCATE study excluded people with severe disease (eGFR <15 ml/min and diffuse alveolar haemorrhage).

The drug manufacturer for Avacopan (Vifor Pharma) has shared clinical protocols from UK units – Preston, Birmingham, and Imperial College London. These had been reviewed in preparation of this guidance, along with local West of Scotland guidance (NHS Ayrshire and Arran) and discussion.

It should be noted that these units typically include intravenous cyclophosphamide as part of their remission-induction regimen, which differs from local NHSL nephrology practice, typically using oral cyclophosphamide. Other aspects of their protocols differ, too.

Avacopan use should be directed and closely monitored by specialists (e.g. renal and rheumatology), with MDT input. It should be prescribed and supplied initially by hospital pharmacies. Once the patient is considered stable by the specialist team, supply may be continued via homecare. Specialist pharmacists for individualities should be consulted to arrange this.

This is an evolving and “high-stakes” therapeutic area. Clinicians should discuss Avacopan use with the MDT and should appraise themselves of the latest evidence base and guidance available.

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Eligibility criteria

De novo or relapsed organ-threatening or life-threatening GPA, MPA or RLV (renal limited vasculitis) (not Eosinophilic Granulomatosis with Polyangiitis or dual-antibody (i.e. ANCA plus anti-GBM) disease)

Exclusion criteria and contra-indications

Pre-treatment Total WBC < 3.5 / neutrophil count <1.5 x$10^{3/}$mL; or lymphocytes < 0.5 x 10^{9}/L.

Severe hepatic impairment (Child-Pugh Class C)

Transaminases >x3 ULN

Blood borne virus screen (hepatitis B core antibody, hepatitis B surface antibody, hepatitis B surface antigen, hepatitis C, HIV). If there is evidence of past hepatitis B infection, consider commencing lamivudine prophylaxis (and discussion with ID).

Pregnant or breast-feeding patients should not be treated with Avacopan.

Prescribing

Avacopan should be used in combination with an induction regimen including steroids **t**ogether with rituximab and/or cyclophosphamide. This should only be done by specialist acute teams.

Dosing

Dose is 30mg twice daily
No dose adjustment is required during Plasma Exchange (PEX) therapy or in severe renal disease.
Avacopan should be taken with food.

Supply

Initial supply via acute hospital dispensary
Ongoing supplies can be arranged via homecare

Monitoring

Liver function and full blood count should be closely monitored (pre-treatment and at least monthly for the first 3 months then every 3 months)

Stop treatment if

- active serious infection (i.e. requiring hospitalisation or prolonged hospitalisation)
- ALT or AST rises to > 5 x ULN
- leucopaenia (white blood cell count < 2 x 10^9/L)
- neutropaenia (neutrophils < 1 x 10^9/L)
- lymphopaenia (lymphocytes < 0.2 x 10^9/L)

Treatment can be resumed again upon normalisation of values based on risk / benefit assessment (severe LFT abnormalities should be discussed with clinical pharmacy colleagues before resuming)

Adverse events should be reported with MHRA Yellow Card scheme.

Cautions

Active untreated infection including TB, HBV, HCV, HIV

Drug interactions

Avacopan is a substrate of CYP3A4.

The use of strong CYP3A4 enzyme inducers (e.g., carbamazepine, enzalutamide, phenytoin, rifampicin, St. John's Wort) may reduce the reduce the efficacy of avacopan; these patients should be considered for 'standard' steroid taper.

The use of strong CYP3A4 inhibitors (e.g. itraconazole, clarithromycin, ketoconazole, lopinavir/ritonavir, ritonavir, saquinavir, telaprevir, voriconazole) may increase the risk of side effects due to the increased exposure of avacopan; these patients should be monitored regularly for the development of leucopenia and/or transaminitis. Grapefruit and grapefruit juice should be avoided.

Duration of therapy

Review duration of treatment at 3 months: in those with renal-limited disease and non-recovery of kidney function from dialysis-dependence at 3 months, ongoing treatment may not be justified Otherwise, aim to continue for one year.

Additional treatment for PCP prophylaxis (e.g. co-trimoxazole) will be required as usual.

Lives vaccines should be avoided during treatment. Specific encapsulated organism vaccination (e.g. meningococcal) is not required.

Estimated impact

The SMC predict 123 patients are eligible for treatment in Scotland per year, and NHS Lanarkshire (NHSL) normally accounts for roughly 10% of this. However, estimated patient numbers between renal and rheumatology are ~20/year.

It is anticipated that all new presentations and relapses requiring treatment would be considered eligible for Avacopan treatment, notwithstanding all of the caveats included in this guideline.

SMC assessed the potential cost and have deemed it cost effective when provided through an NHS Scotland Patient Access Scheme (PAS).

Side Effects

Diarrhoea (15.1%)

Headache (20.5%)

Abnormal liver function tests (5.4%) - all serious hepatic abnormalities resolved when avacopan was stopped, avoid with other drugs with potential hepatotoxicity

Increased risk of infection (23.5%), upper respiratory tract infection (14.5%), pneumonia (4.8%)

Nausea (23.5%)

Nasopharyngitis (15.1%)

WCC reduced (18.7%)

Vomiting (15.1%)

References/Evidence

Avacopan for the Treatment of ANCA-Associated Vasculitis.
Jayne DRW et al N Engl J Med. 2021;384(7):599.

SMC 2578 – SMC approval Avacopan
https://www.scottishmedicines.org.uk/medicines-advice/avacopan-tavneos-full-smc2578/

Ajay Dhaygude, Managing ANCA-associated vasculitis: a guide; NHS Lancashire Teaching Hospitals NHS Foundation Trust

Steve McAdoo; ICHNT Renal and Transplant Centre ANCA Associated Vasculitis (AAV) Immunosuppression Guidelines; Glomerulonephritis (GN) Clinical Research Group (Imperial College London)

Induction of remission for ANCA associated vasculitis
University Hospitals Birmingham Guideline

NHS Ayrshire and Arran Area Drug & Therapeutics Committee
Guideline for the use of Avacopan (Tavneos®) in ANCA-associated vasculitis

Appendices

1. **Governance information for Guidance document**

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Responsible Person (if different from lead author)	

CONSULTATION AND DISTRIBUTION RECORD

AVACOPAN IN ANCA VASCULITIS

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Distribution	

CHANGE RECORD

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Feb 2024	Jack Fairweather		1.2
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