Worcestershire Acute Hospitals NHS Trust

Guideline for Avacopan treatment in patients with severe active granulomatosis with polyangiitis or microscopic polyangiitis

This guidance does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

Introduction

This guideline has been developed to support the use of Avacopan for adults with severe active granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA). It is based on NICE TA825 (Sept 2022) and the Midlands region NHSE approved usage from 9th June 2023. This guideline will be used alongside WAHT-REN-014 Guideline for Cyclophosphamide treatment in patients with vasculitis and other organ/life threatening autoimmune disorders. It outlines the procedures and pathways for prescribing and supplying Avacopan for this patient group.

This guideline is for use by the following staff groups:

Medical staff, nursing staff and pharmacy staff

Lead Clinician(s)

Dr Caroline Cardy	Consultant Rheumatologist
Dr Weng Oh	Consultant Nephrologist and Physician
Approved by *Rh*eumatology Governance on:	4th October 2023
Approved by Medicines Safety Committee on: *Where medicines included in guideline*	18th October 2023
Review Date: This is the most current document and should be used until a revised version is in place	4th October 2026

Key amendments to this guideline

Date	Amendment	Approved by:
October 2023	New document approved	Rheumatology Directorate Meeting Medicine Safety Committee
Sept 2024	Requested to be approved at this meeting, no changes to the content.	Renal Directorate Meeting

Background

Avacopan is an orally administered small-molecule C5a receptor antagonist that selectively blocks the effects of C5a through the C5a receptor, including blocking neutrophil chemoattraction and activation.

Avacopan together with a Cyclophosphamide or Rituximab regimen is recommended, within its marketing authorisation, as an option for treating severe active GPA or MPA in adults. It is recommended only if the company provides it according to the commercial arrangement (NICE TA825).

Specialised Commissioning Guidance (West Midlands)

- A decision to treat with Avacopan must be made by an appropriate specialist multi-disciplinary team experienced in treating severe vasculitis (minimum two clinicians, from different specialities nephrology, rheumatology, respiratory and/or neurology)
- All patients must be registered via Blueteq and meet the clinical criteria on the registration form
- The use of Avacopan requires ratification by the specialist MDT based at UHB
    - Within 5 working days of starting treatment, an email referral must have been made to the UHB Systemic Autoimmune Rheumatic Disease Inbox. uhb-tr.sardmdtrequests@nhs.net

Treatment pathway

New onset or relapsed organ-threatening GPA or MPA should be treated with Avacopan together with a Cyclophosphamide or Rituximab regimen

NOTE: *For patients with eGFR <15ml/min, or life threatening pulmonary haemorrhage requiring mechanical ventilation, Avacopan is NOT recommended and patients should receive a high dose glucocorticoid (GC) regimen*

1. Decision to treat following local multi-disciplinary discussion
2. Ensure satisfactory FBC and liver function

    Avacopan should be avoided in patients with
    - *Signs of liver disease*
    - *Leucopenia (wbc < 3.5 x 10^9/L)*
    - *Neutropenia (neutrophils < 1.5 x 10^9/L)*
    - *Lymphopenia (lymphocytes <0.5 x 10^9/L)*

3. Check blood borne virus screen (hepatitis B, hepatitis C, HIV)

    If there is evidence of past hepatitis B infection, discuss with ID team and consider commencing Lamivudine prophylaxis

4. Prescribe Avacopan 30mg twice a day (ensure one-month supply)

5. Register patient via Blueteq (prior to medication being requested via pharmacy team)

6. Enter patient on Avacopan database and inform rheumatology pharmacist (rheumatology patients only)

7. Prescribe Prednisolone 30mg once a day for one week followed by 20mg once a day for one week and no further steroid

   Note: *Intravenous Methylprednisolone pulses are not recommended. For patients that have received intravenous pulses of Methylprednisolone or higher doses of oral GC prior to referral, the 2-week oral GC regimen should consist of Prednisolone 20mg once a day for 1 week followed by 10mg once a day for 1 week*

8. Prescribe proton pump inhibitor therapy (e.g. lansoprazole 30mg daily) whilst on oral Prednisolone

9. Prescribe Cyclophosphamide or Rituximab regimen

   See WAHT-REN-014 Guideline for Cyclophosphamide treatment in patients with vasculitis and other organ/life threatening autoimmune disorders. See WR5539 for Cyclophosphamide prescription, WR4992 for Rituximab prescription

10. Email referral to the UHB Systemic Autoimmune Rheumatic Disease Inbox (rheumatology) (uhb-tr.sardmdtrequests@nhs.net)

Monitoring

The monitoring and prescribing of Avacopan will remain the responsibility of the lead clinician/designated team for the full duration of treatment

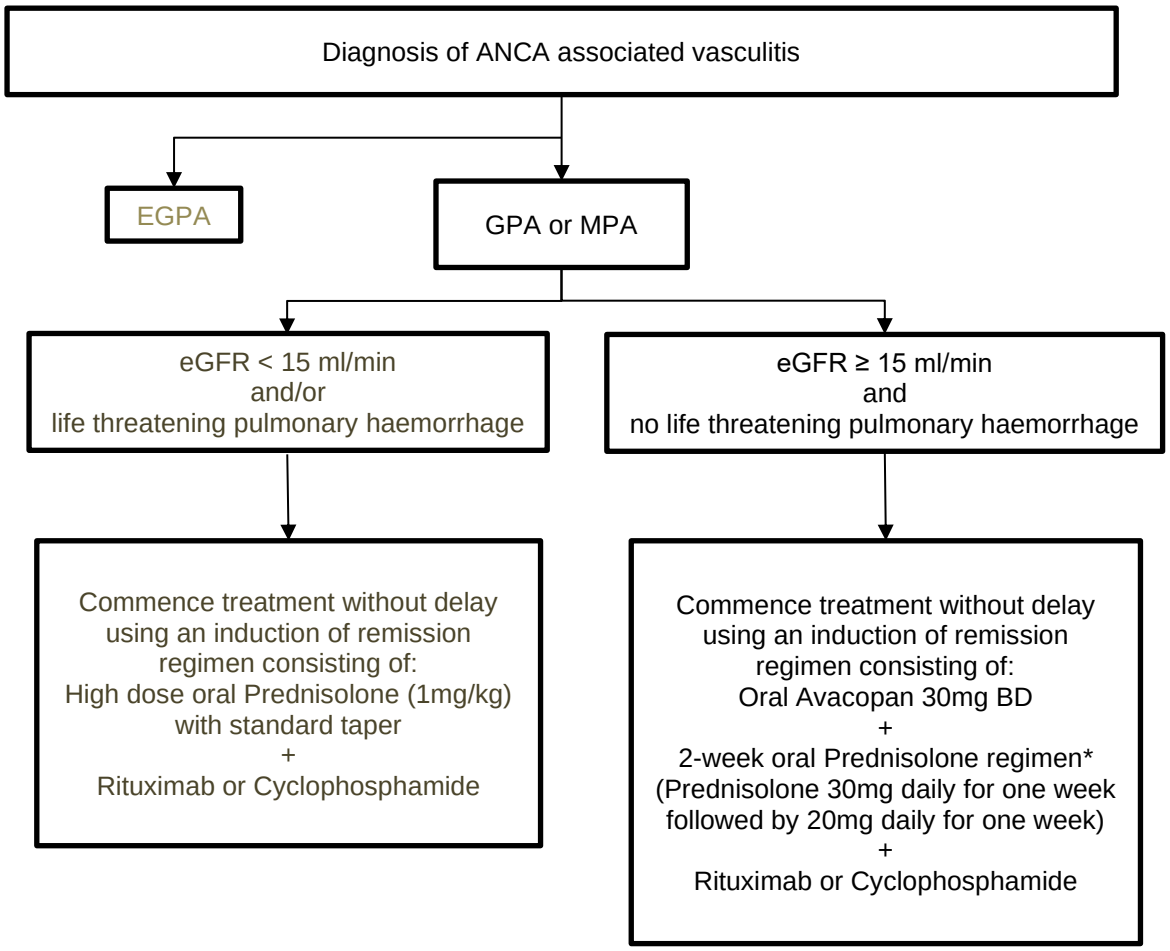
Monitoring requirements

- Monitor liver function and full blood count fortnightly for 6 weeks, monthly for 3 months, and 3 monthly or according to clinical need thereafter

Stop treatment temporarily if:
- patient has an active serious infection (i.e. requiring hospitalisation)
- ALT or AST rises to > 5 x ULN
- leucopenia (wbc < 2 x 10^9/L)
- neutropenia (neutrophils < 1 x 10^9/L)
- lymphopenia (lymphocytes < 0.2 x 10^9/L)

Note: Avacopan is a substrate of CYP3A4. Co-administration of inducers or inhibitors of this enzyme may affect the pharmacokinetics of Avacopan (consult SmPC for further detail).

Flow chart for use of Avacopan in ANCA associated vasculitis



***For patients that have received intravenous pulses of Methylprednisolone or higher doses of oral GC prior to referral, the 2-week oral GC regimen should consist of Prednisolone 20mg once a day for 1 week followed by 10mg once a day for 1 week*

Monitoring

Page/ Section of Key Document	Key control:	Checks to be carried out to confirm compliance with the Policy:	How often the check will be carried out:	Responsible for carrying out the check:	Results of check reported to: *(Responsible for also ensuring actions are developed to address any areas of non-compliance)*	Frequency of reporting:
	WHAT?	**HOW?**	**WHEN?**	**WHO?**	**WHERE?**	**WHEN?**
	These are the 'key' parts of the process that we are relying on to manage risk. We may not be able to monitor every part of the process, but we MUST monitor the key elements, otherwise we won't know whether we are keeping patients, visitors and/or staff safe.	What are we going to do to make sure the key parts of the process we have identified are being followed? (Some techniques to consider are; audits, spot-checks, analysis of incident trends, monitoring of attendance at training.)	Be realistic. Set achievable frequencies. Use terms such as '10 times a year' instead of 'monthly'.	Who is responsible for the check? Is it listed in the 'duties' section of the Policy? Is it in the job description?	Who will receive the monitoring results? Where this is a committee the committee's specific responsibility for monitoring the process must be described within its terms of reference.	Use terms such as '10 times a year' instead of 'monthly'.
3-4	Blueteq	Checks will be made by pharmacy team to ensure Blueteq completed and patient fulfils treatment criteria before supply of medication	Prior to initiation of treatment for every patient	Part of clinical pharmacy team role. Will also be discussed and documented in medical notes by the Nephrology and/ or rheumatology team	For Rheumatology team, will be reported to Rheumatology Pharmacist or Rheumatology CNS team. For Nephrology team, will be to lead clinician and renal specialist pharmacist	For every patient – ad hoc as not commonly treated condition
3-4	Blood tests	Regular blood tests as per guideline	Minimum monthly for	Named consultant for	For Rheumatology team, will be reported to	As per guideline –

			each patient prior to supply of each month of medication (upto 1 year)	each patient and supporting team. Patient will see named consultant regularly in clinic for duration of treatment (and likely beyond)	Rheumatology Pharmacist or Rheumatology CNS team. For Nephrology team, will be to lead clinician and renal specialist pharmacist	minimum monthly for each patient upto 1 year

References

1. Induction of remission of ANCA associated vasculitis. University Hospitals Birmingham guideline (July 2023) .
2. Jayne DRW, Merkel PA, Schall TJ et al. Avacopan for the treatment of ANCA associated vasculitis. New England Journal of Medicine 2021 : 384: 599-609.
3. Avacopan for treating severe active granulomatosis with polyangiitis or microscopic polyangiitis. NICE Technology appraisal guidance. published 21st September 2022

Contribution List

Contribution List

This key document has been circulated to the following individuals for consultation;

Designation
Dr Bernard Dyke, Consultant Rheumatologist
Prof Ashok Rai, Consultant Rheumatologist
Dr Martin Ferring, Consultant Nephrologist and Physician
Dr Thelma Mushambi, Consultant Nephrologist and Physician
Dr Sarah Abbas, Consultant Nephrologist and Physician
Monica Gauntlett, Rheumatology Pharmacist
Lindsay Stewart, Clinical Team Lead, Specialty Medicine
Lucy Stratton, Renal Specialist Pharmacist

This key document has been circulated to the chair(s) of the following committee's / groups for comments;

Committee
Dr Bernard Dyke, Clinical Governance, Rheumatology
Alison Smith, Medicines Safety Committee

Supporting Document 1 - Equality Impact Assessment Tool

. To be completed by the key document author and included as an appendix to key document when submitted to the appropriate committee for consideration and approval.

Please complete assessment form on next page;

Herefordshire & Worcestershire STP - Equality Impact Assessment (EIA) Form
Please read EIA guidelines when completing this form

Section 1 - Name of Organisation (please tick)

Herefordshire & Worcestershire STP		Herefordshire Council		Herefordshire CCG	
Worcestershire Acute Hospitals NHS Trust	x	Worcestershire County Council		Worcestershire CCGs	
Worcestershire Health and Care NHS Trust		Wye Valley NHS Trust		Other (please state)	

Name of Lead for Activity	**Dr Caroline Cardy**

Details of individuals completing this assessment	**Name**	**Job title**	**e-mail contact**
	Monica Gauntlett	**Pharmacist, Rheumatology**	**monicagauntlett@nhs.net**
Date assessment completed	**19/10/2023**		

Section 2

Activity being assessed (e.g. policy/procedure, document, service redesign, policy, strategy etc.)	**Title:** Guideline for Avacopan treatment in patients with severe active granulomatosis with polyangiitis or microscopic polyangiitis			
What is the aim, purpose and/or intended outcomes of this Activity?	Guideline for treatment with Avacopan treatment in patients with severe active granulomatosis with polyangiitis or microscopic polyangiitis			
Who will be affected by the development & implementation of this activity?	❑	Service User	■	Staff
	■	Patient	❑	Communities
	❑	Carers	❑	Other _____
	❑	Visitors	❑	
Is this:	❑ Review of an existing activity ■ New activity			

	❑ Planning to withdraw or reduce a service, activity or presence?
What information and evidence have you reviewed to help inform this assessment? (Please name sources, eg demographic information for patients / services / staff groups affected, complaints etc.	This guideline has been developed to support the use of Avacopan for adults with severe active granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA). It is based on NICE TA825 (Sept 2022) and the Midlands region NHSE approved usage from 9th June 2023. This guideline will be used alongside WAHT-REN-014 Guideline for Cyclophosphamide treatment in patients with vasculitis and other organ/life threatening autoimmune disorders. It outlines the procedures and pathways for prescribing and supplying Avacopan for this patient group
Summary of engagement or consultation undertaken (e.g. who and how have you engaged with, or why do you believe this is not required)	See above. Renal, rheumatology and pharmacy colleagues in WAHT with input from Midlands Regional specialist centres for Rheumatology and Renal consulted
Summary of relevant findings	

Section 3

Please consider the potential impact of this activity (during development & implementation) on each of the equality groups outlined below. **Please tick one or more impact box below for each Equality Group and explain your rationale**. Please note it is possible for the potential impact to be both positive and negative within the same equality group and this should be recorded. Remember to consider the impact on e.g. staff, public, patients, carers etc. in these equality groups.

Equality Group	Potential positive impact	Potential neutral impact	Potential negative impact	Please explain your reasons for any potential positive, neutral or negative impact identified
Age	X		X	Guidelines, as per NICE and medication license, are for adult patients only. However, for adults, there is now treatment
Disability		X		Guidance based on clinical criteria only, does not differentiate treatment for patients based on this equality group
Gender Reassignment		X		Guidance based on clinical criteria only, does not differentiate treatment for patients based on this equality group
Marriage & Civil Partnerships		X		Guidance based on clinical criteria only, does not differentiate treatment for patients based on this equality group
Pregnancy & Maternity			X	Guidelines, as per NICE and medication license, has no safety data for pregnant patients
Race including Traveling Communities		X		Guidance based on clinical criteria only, does not differentiate treatment for patients based on this equality group

Equality Group	Potential positive impact	Potential neutral impact	Potential negative impact	Please explain your reasons for any potential positive, neutral or negative impact identified
Religion & Belief		X		Guidance based on clinical criteria only, does not differentiate treatment for patients based on this equality group
Sex		X		Guidance based on clinical criteria only, does not differentiate treatment for patients based on this equality group
Sexual Orientation		X		Guidance based on clinical criteria only, does not differentiate treatment for patients based on this equality group
Other Vulnerable and Disadvantaged Groups (e.g. carers; care leavers; homeless; Social/Economic deprivation, travelling communities etc.)		X		Guidance based on clinical criteria only, does not differentiate treatment for patients based on this equality group. However, if patient is unable to access regular blood tests or attend for treatment and clinic appointments then would be unable to continue treatment – likely need more support
Health Inequalities (any preventable, unfair & unjust differences in health status between groups, populations or individuals that arise from the unequal distribution of social, environmental & economic conditions within societies)		X		Guidance based on clinical criteria only, does not differentiate treatment for patients based on this equality group. However, if patient is unable to access regular blood tests or attend for treatment and clinic appointments, then would be unable to continue treatment – likely need more support

Section 4

What actions will you take to mitigate any potential negative impacts?	Risk identified	Actions required to reduce / eliminate negative impact	Who will lead on the action?	Timeframe
		.		
How will you monitor these actions?				
When will you review this EIA? (e.g in a service redesign, this EIA should be revisited regularly throughout the design & implementation)				

Section 5 - Please read and agree to the following Equality Statement

1. Equality Statement

1.1. All public bodies have a statutory duty under the Equality Act 2010 to set out arrangements to assess and consult on how their policies and functions impact on the 9 protected characteristics: Age; Disability; Gender Reassignment; Marriage & Civil Partnership; Pregnancy & Maternity; Race; Religion & Belief; Sex; Sexual Orientation

1.2. Our Organisations will challenge discrimination, promote equality, respect human rights, and aims to design and implement services, policies and measures that meet the diverse needs of our service, and population, ensuring that none are placed at a disadvantage over others.

1.3. All staff are expected to deliver services and provide services and care in a manner which respects the individuality of service users, patients, carer's etc, and as such treat them and members of the workforce respectfully, paying due regard to the 9 protected characteristics.

Signature of person completing EIA	
Date signed	
Comments:	
Signature of person the Leader Person for this activity	
Date signed	
Comments:	

Supporting Document 2 – Financial Impact Assessment

To be completed by the key document author and attached to key document when submitted to the appropriate committee for consideration and approval.

	Title of document:	Yes/No
1.	Does the implementation of this document require any additional Capital resources	No
2.	Does the implementation of this document require additional revenue	No
3.	Does the implementation of this document require additional manpower	No
4.	Does the implementation of this document release any manpower costs through a change in practice	No
5.	Are there additional staff training costs associated with implementing this document which cannot be delivered through current training programmes or allocated training times for staff	No
	Other comments:	High cost medication funded by NHSE (NICE TA approved)

If the response to any of the above is yes, please complete a business case and which is signed by your Finance Manager and Directorate Manager for consideration by the Accountable Director before progressing to the relevant committee for approval.