Table of Contents

1 Introduction

This guideline is for the treatment of small vessel vasculitis with renal impairment based on the 2024 KDIGO guidelines and 2024 EULAR recommendations for the management of ANCA-associated vasculitis, covering:

- Granulomatosis with polyangiitis (GPA)
- Microscopic polyangiitis (MPA)
- Pauci-immune necrotising GN without extrarenal disease

Note: A negative ANCA does not exclude vasculitis
One third of GPA cases may be ANCA negative

2 Scope

This guideline is for use by the nephrology MDT team when managing patients with small vessel ANCA associated vasculitis (AAV) involving the kidneys. AAV are rare and potentially life-threatening and organ-threatening diseases and thus require multidisciplinary management.

3 Recommendations, Standards and Procedural Statements

3.1 Definition of disease states

Remission	**On Drug remission:** Prednisolone dose ≤ 10 mg and BVAS ≤ 1 for ≥ 6 months **Drug free remission:** off all drugs for vasculitis for ≥ 6 months
Relapsing disease	**Minor:** minor item of BVAS (Appendix 1) **Major:** major BVAS item or 2 systems involved (physicians' discretion)
Refractory disease	Persistent disease that is not fully responsive to current therapy

3.2 Assessing disease severity

Organ/Life threatening disease:	Glomerulonephritis, Pulmonary haemorrhage, CNS involvement, mononeuritis multiplex, mesenteric involvement, cardiac involvement, retro-orbital disease, deafness
Non organ/life threatening disease:	Nasal/Paranasal disease without bony erosion/cartilage collapse or olfactory dysfunction, skin involvement, myositis, non cavitating pulmonary nodules, episcleritis

Assessment of severity in the individual patient may differ (e.g. scleritis can become organ threatening under certain circumstances). However, these terms can be used to describe patient presentation for ease of risk stratification in MDT decision making.

3.3 Preparation for treatment

Informed consent

This can be given using the UHL Concentric app or via paper consent form stating the following key aspects:

1. Substantial benefits include:
    a. Improved survival
    b. Disease control
    c. Prevention of permanent organ damage

2. Serious complications and concerns related to treatment with **cyclophosphamide**
    a. Serious infections or sepsis
    b. Infertility, early menopause (circa 50%)
        i. Dependent on cumulative dose and age
    c. Teratogenicity – contraceptive advice as appropriate
    d. Malignancy
        i. Related to cumulative dose of cyclophosphamide > 30g
        ii. Lymphoma 4-11 fold increase
        iii. Skin cancer 4-10 fold increase
        iv. Bladder cancer 4-33 fold increase, 3% at 10 years
    e. Hair loss
    f. GI upset

3. Serious complications and concerns related to treatment with **rituximab**
    a. Infusion reactions
    b. Reduced response to vaccinations
    c. Serious infections or sepsis
    d. Anaemia or low platelet count leading to bruising or bleeding
    e. Progressive multifocal leukoencephalopathy (<1:10,000 patients)

4. Side effects of **glucocorticoids**
    a. Mood disturbance
    b. Change in appearance
    c. Weight gain
    d. Diabetes mellitus
    e. Bone disease
    f. Infections
    g. Peptic ulcer disease
    h. Secondary hypoadrenalism

Provide information

1. Information on how and when to seek advice
    a. Signpost to Vasculitis UK website: www.vasculitis.org.uk
    b. Immunosuppression medication booklets
    c. Steroid card
    d. Patients Know Best access
    e. Daily oral inspection for candidiasis

2. Vaccination / screening advice
    a. Follow the national vaccination schedule and refer to the Green Book for most current advice
    b. Live vaccinations should be avoided until ≥ 3 months after stopping immunosuppression
    c. Vaccinations should be completed before treatment if feasible (aim 4 weeks before). Otherwise, they should be postponed until after induction therapy completed.
    d. Annual influenza vaccination
    e. COVID-19 Vaccination.
    f. Pneumococcal vaccination every 5 years.
    g. Shingles Vaccination (Shingrix is recommended as it is a recombinant subunit vaccine).
    h. HPV vaccination where appropriate.
    i. Cervical screening following cyclophosphamide where appropriate.
        i. Annual for 3 years
        ii. Every 3 years thereafter

Baseline investigations

- FBC, U+E, LFT, CRP, Immunoglobulin levels, TPMT level (if considering future use of azathioprine), urine dipstick, urine PCR

- Glucose, lipids

- HIV, Hepatitis B and C serology (including Hepatitis B core Ab (HBcAb))
    - Refer to infectious diseases team if positive
    - Rituximab is associated with a high risk of Hepatitis B reactivation, if HBsAg +ve, or HBsAg -ve and HBcAb+ve
    - Refer to UK systemic anti-cancer board guidelines for prevention of Hepatitis B reactivation:
        - https://www.uksactboard.org/position-statements
        - First line anti-viral prophylaxis is entecavir 500mg daily (or adjust for kidney function)

- CXR, QuantiFERON
    - Refer to TB team in cases of suspected TB or latent TB infection

4 Induction therapy

For induction of remission in patients, treatment with a combination of glucocorticoids and either rituximab, cyclophosphamide or a combination of rituximab and cyclophosphamide is recommended.

Rituximab is usually preferred in:

- PR3-ANCA +ve disease
- Relapsing disease
- Frail or older adults
- Where fertility preservation is of concern (both men and women)

Cyclophosphamide is usually preferred in severe glomerulonephritis (e.g. Creatinine >350 µmol/L or requiring dialysis at presentation).

Avacopan in combination with rituximab or cyclophosphamide may be considered for remission induction as part of a strategy to substantially reduce exposure to glucocorticoids. Patients with an increased risk of glucocorticoid toxicity are likely to receive the most benefit from avacopan. Patients with lower eGFR may benefit from greater eGFR recovery (See section 4.4).

Plasma exchange may also be considered in specific circumstances (see section 4.4).

4.1 Steroids

IV Methylprednisolone (usually 500mg daily over 3 days, maximum 3g over 3 days) should be given just prior to or with the first pulse of IV Cyclophosphamide or Rituximab, at the treating physician's discretion, followed by oral prednisolone. The following regimen for oral prednisolone is recommended, based on doses used in the PEXIVAS trial (reduced steroid arm) in the table below. Prophylactic co-trimoxazole 480mg od PO should be given with prednisolone ≥ 20mg daily.

Week	<50kg	50-75 kg	>75 kg
1	50	60	75
2	25	30	40
3-4	20	25	30
5-6	15	20	25
7-8	12.5	15	20
9-10	10	12.5	15
11-12	7.5	10	12.5
13-14	6	7.5	10
15-16	5	5	7.5
17-18	5	5	7.5
19-20	5	5	5
21-22	5	5	5
23-52	5	5	5
>52	See maintenance section below		

Table 1: Suggested regimen for oral prednisolone based on weight in kg. Doses are in mg.

If Avacopan is used, then give prednisolone 20mg once daily on starting avacopan, and taper by 5mg every week, to stop in 4 weeks.

4.2 Cyclophosphamide

Cyclophosphamide can be given as a daily oral dose or pulsed IV. The IV route is preferred – this delivers the lowest cumulative dose and a lower risk of leucopenia, but is associated with a higher risk of relapse.

Counsel the patient about risks and side effects, and obtain written consent (as section 3.3).

Cyclophosphamide should be avoided if:

- The person has not completed their family and treatment with cyclophosphamide may materially affect their fertility. Pre-menopausal women > 30 years of age are at particularly high risk of permanent infertility with cyclophosphamide therapy.
- The person has had uroepithelial malignancy.

The risk of malignancy increases with cumulative dose of cyclophosphamide, especially > 30g.

IV cyclophosphamide

Give a dose every 14 days for the first 3 doses then every 21 days until remission (minimum total time on cyclophosphamide 3 months and maximum 6 months). Dose adjust as per table below. Maximum dose is 1200 mg. Allow at least 24 hours after a dose of IV cyclophosphamide before performing plasma exchange.

Age (years)	**eGFR (mL/min/1.73m^2)**	
	>30	**<30**
<60	15 mg/kg	12.5 mg/kg
60-70	12.5 mg/kg	10 mg/kg
>70	10 mg/kg	7.5 mg/kg
(MAXIMUM DOSE is 1200 mg)		

Table 2: Cyclophosphamide IV dose adjusted for age and eGFR

IV Cyclophosphamide checklist

- Written consent (section 3.3)
- Negative pregnancy test in women of childbearing potential.
- Hydration dependant on volume status and renal function. Aim for 2-3 litres oral intake on day prior to infusion or give 1000 ml 0.9% sodium chloride before infusion. 2-3 litres oral hydration should be encouraged for 3 days post IV cyclophosphamide (volume status permitting). If patient is dialysis dependent, volume overloaded or at risk of volume overload, modify fluid regimen accordingly.
- Prescribe on the paper proforma (for outpatients) or Nervecentre (for inpatients) which includes the supporting medication oral ondansetron 4 mg to be given two hours before commencement of IV cyclophosphamide.
- Three doses of 400 mg oral Mesna (2-Mercaptoethanesulfonate sodium) should be given - at two hours before, two hours after and six hours after IV cyclophosphamide. Mesna binds to acrolein, a toxic metabolite of cyclophosphamide, rendering it non-toxic.
- PJP prophylaxis: Co-trimoxazole (Septrin) 480 mg od PO for the duration of time on cyclophosphamide and a week after discontinuing or with high dose prednisolone (>20mg daily). For patients who are intolerant or allergic to co-trimoxazole, alternatives include dapsone 100mg od (2nd line), atovaquone 750mg bd (3rd line), or discuss with microbiologist.
- Ovarian protection should be considered during IV cyclophosphamide therapy for women who may wish to consider pregnancy in the future:
    - For Induction
        - 0 hours: Leuprorelin 3.75mg SC or IM injection.
        - 6 hours: Ganirelix 0.25mg SC injection (Day 1) and to continue 0.25mg ganirelix. SC injection daily (until day 5-7).
    - Cyclophosphamide can be given after 4th dose of ganirelix.
    - For Maintenance:
        - Repeat Leuprorelin 3.75mg SC or IM every 4 weeks until Cyclophosphamide is completed.
- Fungal infection prophylaxis: Nystatin 1ml qds
- Review FBC and ensure free of sepsis (see below)

Between IV Cyclophosphamide doses:

Measure FBC on day 7 and 10 and the day of the dose (or previous day).

If total WBC nadir is < $3x10^9$/L **or** neutrophil count is < $1.5x10^9$/L (even if the WBC is > $4x10^9$/L and neutrophil is > $2x10^9$/L on the day of the pulse) then reduce the cyclophosphamide IV dose by

- WBC nadir < 1-2 $x10^9$/L or neutrophil nadir 0.5-1 $x10^9$/L: reduce dose by 40%
- WBC nadir 2-3 $x10^9$/L or neutrophil nadir 1-1.5 $x10^9$/L: reduce dose by 20%

If WBC < 4 $x10^9$/L or neutrophil < 2 $x10^9$/L on the day of the pulse, postpone dose until counts recover to WBC > 4 $x10^9$/L or neutrophil > 2 $x10^9$/L, and reduce dose by 25%. With any further episodes of leucopenia or neutropenia, make a further 25% reduction in dose from the planned dose.

If the platelet count is less than 50 $x10^9$/L then cyclophosphamide should not be given. Between 50-100 $x10^9$/L, then give 50% of the previous dose. If above 100 $x10^9$/L then give the planned dose (source SPC datasheet).

Notes for prescribers:

For inpatients, IV cyclophosphamide and Mesna should be prescribed on Nervecentre as well as on the paper proforma.

For Renal Planned Care Hub patients, the paper proforma is adequate.

Contact renal pharmacists – contactable by bleep from Monday to Friday, bleeps 3135, 3616 and 3306. At weekends, the main pharmacy should be contacted. 24 hours' notice is required to prepare IV cyclophosphamide. If required more urgently and during on-call hours (weekend, bank holidays), discuss with the on-call or renal pharmacist.

Only nurses specifically trained in administering cyclophosphamide or chemotherapy can administer it on the renal wards.

Oral cyclophosphamide

- Dose is 2 mg/kg/day
  - If age >60 years: reduce to 1.5 mg/kg/day
  - If age >70 years: reduce to 1.0 mg/kg/day
  - If eGFR <30 mL/min/1.73m^2, reduce by 0.5 mg/kg/day.
- Maximum dose is 200 mg/day.
- Continue between 3 to 6 months until remission is induced. If remission is induced before 3 months, reduce dose to 1.5 mg/kg/day then convert to maintenance treatment at 3 months.
- Keep WCC > 3.5 x 10^9/L (reduce dose of oral cyclophosphamide as required).
- Mesna 400mg PO daily should be considered for the duration of oral cyclophosphamide therapy. PJP prophylaxis and fungal prophylaxis should be given as per IV cyclophosphamide.
- If the patient is also receiving Plasma Exchange (PLEX), give oral cyclophosphamide dose after the PLEX treatment.

4.3 Rituximab

Rituximab is a chimeric monoclonal antibody that depletes B cells, by binding to the CD20 antigen on the cell surface. B cell lysis occurs leading to a sustained reduction in B cells for approximately 6-12 months.

The evidence base for using Rituximab is from the randomised controlled trials RAVE, RITUXIVAS and Low-Dose Glucocorticoid Vasculitis Induction Study (LoVAS) for remission induction and MAINRITSAN and RITAZAREM for maintenance of remission.

4.3.1 Rituximab dosing

Either of the regimens below can be used depending on physician preference. Local preference is regimen A or the regimen that delivers the lowest cumulative dose.

A. Rituximab 1g on day 1 and day 14, administered as an IV infusion
B. Rituximab 375 mg/m^2 body surface area (rounded to the nearest 100mg), administered as an IV infusion, once weekly for four weeks

Regimen B is the licensed dose, but BSR guidelines (5), NHSE 2015 policy, and KDIGO 2024 guidelines suggest both regimens are effective and regimen A is more cost effective.

Rituximab must be prescribed on the paper proforma as well as Nervecentre if being administered to an inpatient. The paper proforma alone is adequate for outpatients.

4.3.2 Other requirements for use of Rituximab in AAV

The NHSE policy requires people receiving Rituximab for AAV to be recruited to UKIVAS. Please send patient details to the Renal research team to register with UKIVAS. Specified outcomes including BVAS and VDI scoring should ideally be measured and documented at baseline, 6 and 12 months after induction regimens and 6 and 12 monthly after each maintenance dose and annually thereafter.

4.3.3 Pre-treatment screening and consent

Standard Rituximab drug charts for the 2 different dosing regimens are available for use on the renal planned care hub and on renal wards.

Before initiating Rituximab, a pre-treatment assessment should be conducted and should include:

- Detailed history including chronic or recent co-morbidity such as cardiovascular and pulmonary disease, recurrent infections, allergies
- Physical examination
- Routine blood tests (FBC, renal profile, LFTs, CRP)
- Hepatitis B and C screen including Hepatitis B core antibodies (HBcAb) and Hepatitis B surface Ag (HBsAg). HBcAb should be added specifically on the request form. If HBcAb or HBsAg positive, refer to Infectious Diseases before initiating Rituximab. See ‘Baseline Investigations’, Page 4.
- Immunoglobulin levels.
- CD19 (B cell marker): There may be some value in baseline CD19 levels, but measuring CD19 post-treatment is not necessary to determine when to repeat treatment.
- MSU and CXR if indicated to exclude infection or pulmonary involvement
- Give Rituximab information leaflet
- Reinforce contraception and vaccination advice.
    - Rituximab crosses the placenta from around 16 weeks. Women should avoid pregnancy.
    - Based on limited evidence, rituximab should be stopped from conception.
    - Based on limited evidence, very low amounts of rituximab pass into the breast milk and breastfeeding is safe.
    - It is considered safe for men to be treated with rituximab while trying to father

a baby.

- Vaccination advice is the same as for Cyclophosphamide (see section 3.3)
- Inactivated vaccinations e.g. Flu, Shingles (Shingrix) etc. The course should ideally be completed 1 month prior to commencing rituximab, or given at least 4 weeks after treatment. Avoid live vaccinations.
- Consent for side effects including for Progressive Multifocal Leucoencephalopathy (rare side effect). This can be given using the UHL Concentric app (search Intravenous Rituximab) or via paper Consent form.

4.3.4 Additional information for Rituximab use

Rituximab is rapidly removed by plasma exchange; ensure there is a minimum gap of ≥48hrs between giving rituximab and plasma exchange.

Repeat rituximab doses may be indicated when:

- Absolute B cell count: >10 cells/μl
- Change from ANCA negative to positive status
- 25% rise in ANCA titre from nadir

Cautions:

- Hypogammaglobulinaemia (total IgG <5g/L; immunoglobulin levels should be monitored 3-6 monthly in patients receiving maintenance rituximab). Consider postponing rituximab if IgG <4g/L.
- Rituximab-associated late-onset neutropenia
- Pending scheduled vaccinations

Patients should receive PJP prophylaxis for a minimum of 6 months after each rituximab dose, unless contra-indicated. First line is cotrimoxazole 480 mg od PO. Alternative is dapsone 100mg od (2nd line), atovaquone 750mg bd (3rd line), or discuss with microbiologist.

Contraindications:

- Previous severe hypersensitivity to rituximab. For milder reactions, rituximab can be given with IV methylprednisolone (dose 100mg-1000mg depending on severity of reaction) pre-treatment an hour before start of rituximab infusion, and rituximab to be infused at slower rate.
- Active, severe infections (including Hepatitis B). Risk vs benefit of treatment of AAV in the context of infection should be considered on an individual patient basis.
- Patients in a severely immunocompromised state.
- Severe heart failure (NYHA Class IV) or severe, uncontrolled cardiac disease

Premedication regimen:

- One hour prior to infusion: Paracetamol 1g oral /IV STAT
  Chlorpheniramine 4mg oral
- Immediately prior to infusion: Hydrocortisone 100 - 200mg IV

(If methylprednisolone is being given immediately before rituximab, the hydrocortisone pre-medication can be omitted)

4.4 Avacopan

The ADVOCATE trial was a phase 3 randomised controlled trial which showed that avacopan was non-inferior to glucocorticoids at week 26, and superior to standard dose prednisolone at week 52. This has led to its use to facilitate steroid sparing regimes in the management of ANCA associated vasculitis. All patients also received cyclophosphamide or rituximab as induction therapy.

There was also an observed reduction of serious adverse events and fewer infections in the avacopan group.

Avacopan is dosed at 30mg BD orally.

- No dose adjustment is required in the elderly.
- No dose adjustment is required for impaired eGFR given its hepatic clearance.
- The ADVOCATE trial did not include patients with AAV with an eGFR <15 mL/min/1.73 m², or those on dialysis or plasma exchange.

For patients receiving avacopan, prednisolone can be tapered in the first 4 weeks. Start or reduce prednisolone to 20mg once daily on starting avacopan, and reduce by 5mg each week.

Safety & monitoring on avacopan

- Monitor liver function and white cell counts as per usual practice. Avacopan should not be initiated if:
  - Total WBC < 3.5 / Total neutrophil count <1.5 x103/mL
  - ALT or AST >3x ULN
  - Severe hepatic impairment (Child-Pugh Class C)
- Use with caution in the presence of active untreated infection, including TB, HBV, HCV, HIV
- Avacopan does not decrease the formation of the terminal complement membrane attack complex. No cases of Neisseria meningitidis have been identified in the avacopan clinical development programme, and vaccination against encapsulated bacteria is not routinely required prior to initiation of treatment.
- Avacopan is not recommended during pregnancy or in women of childbearing potential who are not using effective contraception.

Management of abnormal liver function tests and leucopenia whilst on treatment:

- Treatment must be re-assessed clinically and temporarily stopped if:
  - ALT or AST >3x ULN
- Treatment must be temporarily stopped if:
  - ALT or AST > 5x ULN
  - WBC < 2 x 10^9/L, or neutrophils <1 x 10^9/L, or lymphocytes <0.2 x 10^9/L
- Treatment may be resumed:
  - Upon normalisation of values and based on an individual benefit/risk assessment. If treatment is resumed, hepatic transaminases and total bilirubin must be monitored closely.
- Permanent discontinuation of treatment must be considered if:
  - ALT or AST > 8x ULN,
  - ALT or AST > 5x ULN for more than 2 weeks,
  - ALT or AST > 3x ULN and total bilirubin >2x ULN or INR >1.5
  - ALT or AST > 3x ULN with the appearance of fatigue, nausea, vomiting, right upper quadrant pain or tenderness, fever, rash, and/or eosinophilia (> 5%), and an association between avacopan and hepatic dysfunction has been established.

Notable drug interactions:

- Strong CYP3A4 enzyme inducers (e.g., carbamazepine, enzalutamide, phenytoin, rifampicin, St. John's Wort) may reduce the reduce the efficacy of avacopan.

- 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; patients on these should be monitored regularly for the development of leucopenia and/or transaminitis

4.5 Plasma exchange for induction of remission

The PEXIVAS study described no clear benefit for plasma exchange across a spectrum of disease severities and presentations. A subsequent meta-analysis demonstrated a reduction in risk of kidney failure at 12 months with plasma exchange, but with a concomitant increased risk of serious infections. Plasma exchange remains a treatment option and should be considered on an individual patient basis, e.g. in the following circumstances:

- Severe renal involvement e.g. serum Creatinine > 300 μmol/L.
- Refractory disease (i.e. RPGN not settling despite initial induction treatment)
- Severe pulmonary haemorrhage with hypoxaemia (e.g. oxygen saturations <85% on air or ventilated)
- Non-severe pulmonary haemorrhage, if there is respiratory deterioration despite initial treatment

Plasma exchange should be started for patients who have overlap syndrome of ANCA-associated vasculitis and anti-glomerular basement membrane disease (double positive disease).

Plasma exchange should always be discussed with the Nephrology Consultant leading the patient's care.

Refer to the guidelines on plasma exchange for information on prescribing.

4 Other medications during induction

- Proton pump inhibitor (e.g. Lansoprazole 30mg od)
- Co-trimoxazole 480 mg od for the duration of time on cyclophosphamide or high dose prednisolone (≥ 20mg od), and for a minimum of 6 months after induction with Rituximab. For patients intolerant or allergic to co-trimoxazole, alternatives include dapsone 100mg od (2nd line), atovaquone 750mg bd (3rd line), or discuss with microbiologist.
- Nystatin 1ml qds for patients receiving induction therapy with cyclophosphamide
- Adcal D3 (or Adcal if poor renal function)
- Ovarian protection when giving Cyclophosphamide (see section 4.2)

5 Maintenance therapy

Following successful disease remission with induction therapy, maintenance therapy should commence and continue for at least 24 months after which it can either be continued for "on drug" remission or stopped for "off drug remission".

Maintenance therapy with either rituximab, or azathioprine and low-dose glucocorticoids is recommended after induction of remission.

Patients with GPA who remain PR3-ANCA positive may require prolonged maintenance therapy (e.g. approximately 5 years).

For those commencing azathioprine, TPMT activity should be checked to stratify risk of using azathioprine and to guide dosing. Azathioprine is dosed at 1.5-2 mg/kg. If azathioprine is not tolerated, alternatives include methotrexate if renal function is preserved or mycophenolate mofetil. Note that azathioprine interacts with allopurinol and in combination can cause life-threatening bone marrow suppression – their co-prescription should be avoided.

Rituximab can be used as maintenance therapy, particularly for patients who received rituximab for induction of remission.

Prednisolone if used as per the regimen suggested previously should continue for at least 6 months - 1 year from first presentation. The 2016 ERA recommendations suggested continuation of maintenance low dose prednisolone for around 24 months. For patients at high risk of relapse, steroids may be continued for longer periods. Ideally, steroids should be withdrawn first and other immunosuppression tapered after at least 6 months from discontinuing steroid treatment.

For patients receiving avacopan, taper prednisolone rapidly as mentioned previously.

6 Withdrawal of immunosuppression

Patients who have received maintenance therapy for the duration suggested above and have been in continual remission should be considered for immunosuppression withdrawal.

Withdrawal of prednisolone can be considered after approximately 6-12 months for those who received rituximab. The optimal duration of maintenance therapy is between 18 months and 4 years after induction of remission. Following steroid withdrawal, other immunosuppression can be withdrawn at clinician's discretion. When considering withdrawal of maintenance therapy, the risk of relapse should be considered, and patients should be informed of the need for prompt attention if symptoms recur.

7 Relapsing disease

Identify drivers for relapse

- Infection
- Malignancy
- Changes in therapy

Minor relapse:

- Increase prednisolone and optimize immunosuppression

Major relapse:

- Consider repeat induction with rituximab or cyclophosphamide (or both).
- Increase the dose of prednisolone and consider pulsed IV Methylprednisolone and/or plasma exchange if indicated

8 Refractory disease

Patients with refractory disease should be managed with the guidance of the Vasculitis MDT. If the patient has not received rituximab, then this should be considered as first choice.

Other considerations include combined IV cyclophosphamide and rituximab, and this should be discussed in the Vasculitis MDT.

9 Assessment and monitoring of disease status

Validated disease activity scores such as BVAS, VDI and SF36 should ideally be performed by trained staff at least annually and more frequently in patients with active disease.

ANCA levels should be checked at diagnosis, relapse, change of therapy, and at a minimum of every 6 months while on treatment and annually while off treatment.

Follow up visits should continue indefinitely at reducing frequency. During visits:

- Monitor FBC, renal and liver function
- Monitor CRP
- Monitor ANCA levels as suggested above
- Urinalysis and referral for cystoscopy if suspicion of uroepithelial toxicity.
    - Patients who received cyclophosphamide should have lifelong regular urinalysis checks.
- Immunoglobulin monitoring if received rituximab or having recurrent infections
- Review prophylaxis against opportunistic infections.
- Offer vaccination advice (as section 3.3) and cardiovascular and thromboembolic risk assessment.

10 Monitoring and Audit Criteria

Key Performance Indicator	Method of Assessment	Frequency	Lead
Safe use of cyclophosphamide	Audit	Annual	S. Pepereke/MDT
Safe use of rituximab	Audit	Annual	S. Pepereke/MDT
Preventative treatments (osteoporosis, infection)	Audit	Annual	S. Pepereke/MDT

11 Legal Liability Guideline Statement

See section 6.4 of the UHL Policy for Policies for details of the Trust Legal Liability statement for Guidance documents

12 Supporting Documents and Key References

1. *Rheumatology* (2014) doi:10.1093/rheumatology/ket445 [first published online April 11, 2014] BSR BHPR guideline for the management of adults with ANCA-associated vasculitis.
2. Kidney Disease: Improving Global Outcomes (KDIGO) ANCA Vasculitis Work Group. KDIGO 2024 Clinical Practice Guideline for the Management of Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis *Kidney Int*. 2024;105(3S):S71-S116. doi:10.1016/j.kint.2023.10.008
3. NHSE Clinical Commissioning Policy: Rituximab for the treatment of ANCA-associated vasculitis in adults 2015
4. EULAR Recommendations for the management of ANCA-associated vasculitis: 2022 update
5. Russell MD, Dey M, Flint J, et al. British Society for Rheumatology guideline on prescribing drugs in pregnancy and breastfeeding: immunomodulatory anti-rheumatic drugs and corticosteroids [published correction appears in Rheumatology (Oxford). 2023 May 2;62(5):2021. doi: 10.1093/rheumatology/keac686]. *Rheumatology (Oxford)*. 2023;62(4):e48-e88. doi:10.1093/rheumatology/keac551

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13 Appendices

Appendix 1 : BVAS

BVAS assessment should be performed by trained clinicians. E-learning is available from bvasvdi@ndorms.ox.ac.uk

BVAS form link https://www.rarediseasesnetwork.org/vcrc/documents/BVAS_WG.pdf