NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Health Technology Appraisal

Avacopan for treating anti-neutrophil cytoplasmic autoantibody-associated vasculitis [ID1581]

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of avacopan within its marketing authorisation for treating anti-neutrophil cytoplasmic autoantibody-associated vasculitis.

Background

Systemic vasculitis is an autoimmune condition characterised by damage to and inflammation of blood vessels. Anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis is an umbrella term for several related conditions, including granulomatosis with polyangiitis (GPA; Wegener's granulomatosis), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA). ANCA-associated vasculitis mostly affects small and medium sized blood vessels, particularly those in the respiratory and renal systems. One of the primary mediators of ANCA-associated vasculitis pathology is thought to be B-lymphocytes, but the precise mechanism is unknown.

The annual UK incidence of GPA is estimated to be around 11 per million population, and the prevalence is between 135 and 146 per million.[1,6] The annual incidence and prevalence of MPA is around 6 and 63 per million respectively.[1] This implies that fewer than 970 people are diagnosed with GPA and MPA each year in England, and there are about 12,200 people currently living with these conditions.[2] The incidence of ANCA-associated vasculitis increases with age and the peak age of onset is between 60 and 70 years.[3]

The aim of treatment is initially to induce remission (to reduce the risk of organ damage), then to maintain remission and treat relapse as needed while avoiding drug toxicity. Without treatment, the condition is fatal.

Clinical practice guidelines (BSR and BHPR 2014[4] and EULAR/EUVAS 2015[5]) recommend clinical management strategies based on disease progression. Methotrexate or mycophenolate mofetil with corticosteroids are recommended for non-organ-threatening disease, and cyclophosphamide or rituximab with corticosteroids are recommended for organ or life-threatening disease. After induction of remission, maintenance therapy with low dose corticosteroids and either azathioprine, rituximab, methotrexate or mycophenolate mofetil is recommended for at least 2 years.

NICE TA308 recommends rituximab, in combination with glucocorticoids, as an option for inducing remission in adults with ANCA-associated vasculitis (severely active GPA and MPA) if there is disease progression with cyclophosphamide, or if cyclophosphamide is not appropriate or not tolerated.

Rituximab is currently commissioned by NHS England as a treatment option for maintenance therapy in a specific subgroup of adults with ANCA-associated vasculitis.

The technology

Avacopan (tavneos, VFMCRP) is a small molecule, complement C5a receptor inhibitor that may reduce the inflammation-induced damage in certain autoimmune disorders, including ANCA-associated vasculitis. It is administered orally.

Avacopan does not currently have a marketing authorisation in the UK. Avacopan has been studied in clinical trials as an add-on treatment to standard care (this may include immunosuppressive treatment such as rituximab, cyclophosphamide plus azathioprine, with or without corticosteroids such as prednisone) to induce and maintain remission in people with ANCA-associated vasculitis compared with standard care alone.

Intervention	Avacopan
Population	People with newly diagnosed or relapsed anti-neutrophil cytoplasmic autoantibody-associated vasculitis
Comparators	To induce remission: • Established clinical management without avacopan including corticosteroids and rituximab, cyclophosphamide, methotrexate or mycophenolate mofetil Maintenance treatment: • Established clinical management without avacopan including low dose corticosteroids and rituximab (in line with the NHS England commissioning policy), azathioprine, methotrexate or mycophenolate mofetil
Outcomes	The outcome measures to be considered include: • mortality • morbidity including damage to organs • remission rate and duration of remission • change in renal function • use of immunosuppressants and corticosteroids (including corticosteroid toxicity) • adverse effects of treatment (including infection rates) • health-related quality of life.

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	The availability and cost of biosimilar and generic products should be taken into account. Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals**: 'Rituximab in combination with glucocorticoids for treating anti-neutrophil cytoplasmic antibody-associated vasculitis' (2014) NICE Technology Appraisal 308. Static list. **Appraisals in development (including suspended appraisals)** 'Rituximab for maintenance treatment of anti-neutrophil cytoplasmic antibody-associated vasculitis' Proposed NICE technology appraisal [ID1320]. To be confirmed. 'Mepolizumab for treating eosinophilic granulomatosis with polyangiitis' Proposed NICE technology appraisal [ID1186]. Suspended. **Related NICE Pathways**: Systemic connective tissue conditions (2016) NICE pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) chapter 5: Adult highly specialist rheumatology services. Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 to 3. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

	Clinical Commissioning Policy: Rituximab for the treatment of ANCA-associated vasculitis in adults NHS England (2015) https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2015/01/a13-ritux-anca-vascul.pdf

References

1 Watts, R. A., Mooney, J., Skinner, J., et al. (2012). The contrasting epidemiology of granulomatosis with polyangiitis (Wegener's) and microscopic polyangiitis. Rheumatology, 51(5), 926-931.

2 Office for National Statistics (2020) Mid-year population estimates for England in 2019. Accessed August 2020.

3 NHS England (2015). Clinical commissioning policy: rituximab for the treatment of ANCA-associated vasculitis in adults. Accessed August 2020.

4 Ntatsaki, E., Carruthers, D., Chakravarty, K., et al. (2014). BSR and BHPR guideline for the management of adults with ANCA-associated vasculitis. Rheumatology 53 (12):2306-2309. Accessed August 2020.

5 Yates M, Watts RA, Bajema IM et al. (2016) EULAR/ERA-EDTA recommendations for the management of ANCA-associated vasculitis. Annals of rheumatic Disease 75(9):1583-1594. Accessed August 2020.

6 Pearce, F. A., Grainge, M. J., Lanyon, P. C., Watts, R. A., & Hubbard, R. B. (2017). The incidence, prevalence and mortality of granulomatosis with polyangiitis in the UK Clinical Practice Research Datalink. Rheumatology, 56(4), 589-596.

