NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Avacopan for treating anti-neutrophil cytoplasmic antibody-associated vasculitis

Draft scope (pre-referral)

Draft remit/appraisal objective

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

Background

Systemic vasculitis is an autoimmune condition characterised by damage to and inflammation of blood vessels. Anti-neutrophil cytoplasmic antibody (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 and MPA has been estimated to be 11 and 6 per million population respectively, and the total prevalence of both conditions was estimated at approximately 209 per million.[1] This implies that fewer than 950 people are diagnosed with GPA and MPA each year in England, and there are about 11,400 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, then to maintain remission and treat relapse when necessary. 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.

The technology

Avacopan (brand name unknown, 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 combined with standard care (rituximab or cyclophosphamide) has been studied in clinical trials in people with ANCA-associated vasculitis (GPA or MPA) compared with placebo and standard care.

Intervention(s)	Avacopan in combination with standard care
Population(s)	People with anti-neutrophil cytoplasmic antibody-associated vasculitis (granulomatosis with polyangiitis or microscopic polyangiitis)
Comparators	Established clinical management without avacopan including: • rituximab • cyclophosphamide, azathioprine, methotrexate, mycophenolate mofetil and corticosteroids (do not currently have a marketing authorisation in the UK for this indication)
Outcomes	The outcome measures to be considered include: • mortality • morbidity including damage to organs • remission rate and duration of remission • number and severity of relapses • change in renal function • cumulative dose of immunosuppressants • cumulative dose of steroids and steroid toxicity • adverse effects of treatment • 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. 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	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. Review proposal in progress. **Appraisals in development (including suspended appraisals)** 'Mepolizumab for treating eosinophilic granulomatosis with polyangiitis' Proposed NICE technology appraisal [ID1186]. Publication date to be confirmed. **Related NICE Pathways**: Systemic connective tissue conditions (2016) NICE pathway
Related National Policy	Adult highly specialist rheumatology services. https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 2 and 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

Questions for consultation

How is avacopan expected to be used in clinical practice?

- In what patient groups will avacopan be used (for example for all ANCA vasculitis or severe disease only)?
- At what point in the treatment pathway will avacopan be used (induction, remission and/or relapse)?
- What drug combination is expected to be used with avacopan?

Have all relevant comparators for avacopan been included in the scope? Which treatments are considered to be established clinical practice in the NHS for anti-neutrophil cytoplasmic antibody associated vasculitis?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom avacopan is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider avacopan will fit into the existing NICE pathway, systemic connective tissue conditions?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which avacopan will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider avacopan to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of avacopan can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made. We welcome comments on the appropriateness and suitability of the cost comparison methodology to this topic.

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology that has not been considered? Are there any important ongoing trials reporting in the next year?

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 (2016) Mid-year population estimates for England in 2015. Accessed May 2017.

3 NHS England (2015). Clinical commissioning policy: rituximab for the treatment of ANCA-associated vasculitis in adults. Accessed April 2017.

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 May 2017.

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.